

The state of the art of sound therapy for subjective tinnitus in adults

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Abstract

Background: Sound therapy is a clinically common method of tinnitus management. Various forms of sound therapy have been developed, but there are controversies regarding the selection criteria and the efficacy of different forms of sound therapy in the clinic. Our goal was to review the types and forms of sound therapy and our understanding of how the different characteristics of tinnitus patients influence their curative effects so as to provide a reference for personalized choice of tinnitus sound therapy.

Method: Using an established methodological framework, a search of six databases including PubMed identified 43 records that met our inclusion criteria. The search strategy used the following key words: tinnitus AND (acoustic OR sound OR music) AND (treatment OR therapy OR management OR intervention OR measure).

Results: There are various forms of sound therapy, and most of them show positive therapeutic effects. The effect of customized sound therapy is generally better than that of non-customized sound therapy, and patients with more severe initial tinnitus respond better to sound therapy.

Conclusion: Sound therapy can effectively suppress tinnitus, at least in some patients. However, there is a lack of randomized controlled trials to identify effective management strategies. Further studies are needed to identify the most effective form of sound therapy for individualized therapy, and large, multicenter, long-term follow-up studies are still needed in order to develop more effective and targeted sound-therapy protocols. In addition, it is necessary to analyze the characteristics of individual tinnitus patients and to unify the assessment criteria of tinnitus.

Keywords: tinnitus, acoustic stimulation, sound therapy, principle effect

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Introduction

Tinnitus is the perception of sound in the absence of exogenous sound stimulation, and widely accepted consensus guidelines divide tinnitus into objective tinnitus and subjective tinnitus. Objective tinnitus is defined as tinnitus associated with an identifiable organic cause other than sensorineural hearing loss. In contrast, subjective tinnitus is an idiopathic symptom that may or may not be associated with sensorineural hearing loss. Tinnitus has high incidence according to epidemiological data, and 10–15% of adults have long-term tinnitus, and in about 6–25% of patients the tinnitus interferes with their daily life.¹ Negative impacts of tinnitus

include sleep disturbance, poor concentration, distress, depression, and anxiety.² Consequently, restrictions caused by tinnitus might result in difficulties at work, at home, and in social relationships, thus reducing a person's quality of life.

Many attempts have been made to treat or even cure tinnitus, but no treatment or intervention yet offers a completely satisfactory solution. Current methods for the clinical management of tinnitus involve (a) education and counseling, (b) relaxation techniques, and (c) the use of sound therapy. The effectiveness of sound therapy in changing the tinnitus perception has been recognized for

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centuries, and in recent decades, the use of sound or sound enrichment to mask or suppress tinnitus or to disrupt the neural activity that causes tinnitus has become a central part of the clinical management. Currently, most tinnitus treatment strategies aim at reducing the tinnitus-associated distress, and there is a lack of treatment approaches for eliminating the tinnitus directly. Sound therapy is a widely used tinnitus management method that uses sound stimulation to promote the reorganization of the cortex with or without masking tinnitus, and such therapy is expected to completely eliminate tinnitus. In addition, sound therapy is non-invasive, simple, and readily accepted by patients. The purpose of this scoping review is to sort out the existing types of sound therapy, to determine the best treatment form of sound therapy, to summarize the limitations of current sound-therapy research, and to provide a reference for the direction and focus of future sound-therapy research.

Method

This review is reported according to the methodological framework developed by Arksey and O'Malley³ using the six-stage process. The process was as follows: (a) defining the purpose and research questions; (b) identifying the relevant studies; (c) selecting studies through title, abstract, and full-text screening; (d) extracting and charting the data; (e) collating, summarizing, and reporting the results; and (f) reviewing the findings.

The search strategy was divided into two steps. In the first step, we identified relevant studies in PubMed, Google Scholar, Web of Science, Embase, Scopus, and Cochrane for the 10-year period 2009–2019. The search strategy used the following key words: “tinnitus” AND (“acoustic” OR “sound” OR “music”) AND (“treatment” OR “therapy” OR “management” OR “intervention” OR “measure”). In the second step, we manually searched the list of references for articles on tinnitus therapy in order to identify more eligible literature.

Articles identified through the electronic and manual searches were exported with citations, title, and abstract into Endnote where duplicates were removed. The search records were screened by title and abstract and then by full text, and

articles that did not meet the inclusion criteria were excluded.

For inclusion, studies had to include adults (≥ 18 -years old) who reported chronic tinnitus (tinnitus duration ≥ 3 months) and who were treated with sound stimulation. In the included studies, the subjects did not receive any simultaneous treatments that might have interfered with the sound therapy. Studies were included where management strategies (i.e. interventions) were tested to address tinnitus. Eligible studies included randomized controlled trials (RCTs), clinical trials, and comparative studies. Review articles (including systematic reviews) and any sources reporting personal or expert opinions were excluded. No articles were excluded based on controls used, outcomes reached, timing, setting, or study design. A data extraction form was developed and included data on the type of intervention, sample size, research duration, assessment methods, and main findings (Table 1).

Results

Sound therapy can be divided into non-customized and customized sound therapy. Non-customized sound therapy includes masking therapy, tinnitus retraining therapy (TRT), and hearing aids. This strategy uses unmodified noise, music, or environmental sounds as stimulating sounds and seeks to improve the adverse physiological and emotional reactions associated with tinnitus by masking the tinnitus or helping patients become accustomed to the tinnitus. Customized sound therapy includes (a) Heidelberg neuromusic therapy (HNMT); (b) tailor-made notched music training (TMNMT); (c) tinnitus pitch-matched therapy; (d) acoustic coordinated reset neuromodulation therapy (CR); (e) neuromonics tinnitus therapy (NTT); (f) modulated wave therapy; and (g) auditory discrimination training (ADT). Customized sound therapy uses a tinnitus management strategy based on the individual's tinnitus symptoms, and it aims to promote cortical reorganization or to change the pathological synchronization of neurons in order to fully eliminate the tinnitus.

Masking therapy

Masking therapy was first proposed by Vernon in 1976.⁴⁷ This approach employs external noise to

Table 1. Type of intervention, sample size, research duration, assessment methods, and main findings of articles reviewed.

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time		
Masking	Hesser <i>et al.</i> ⁴	35	RCT	90 s × 4	90 s × 4	Self-reported tinnitus interference and the Digit-Symbol subtest	Individuals receiving the instructions to control the background sounds (group 1) exhibited a significantly steeper increase of tinnitus interference over the trials than those receiving the no-control instructions (group 2); moreover, group 2 improved at a significantly faster rate on the measure of cognitive functioning over trials in comparison with group 1; finally, none of presence of tinnitus and ratings of satisfaction with the performance, background sound interfering with performance, and background sound had impact on outcome
Masking	Li <i>et al.</i> ⁵	28	RCT	Treated for 30 min, three times a day, for a 3-month period	Pre-intervention (baseline), and 2, 4, 8 and 12 weeks post-intervention	THI, VAS	The mixed pure-tones group showed lower scores in THI, VAS loudness and annoyance than those at baseline after 3 months; the VAS loudness and annoyance scores of the mixed pure-tones group were lower than the BBN group at 8 and 12 weeks but there was no significant difference at 2 and 4 weeks
Masking	Henry <i>et al.</i> ⁶	148	RCT	6 months	18 months (0, 3, 6, 12, 18 months)	THI	The participants received TM, TRT, and TED had significantly decreased in THI relative to WLC group; the scores of THI in the three treatment groups got significantly decreased in the first 6 months, and relatively similar effectiveness by 6 months and beyond
TRT	Forti <i>et al.</i> ⁷	45	Clinical Trial	18 months (≥8 h per day)	36 months (18, 36 months)	THI, VAS	There were significant improvements during therapy and the mean THI was lowered by more than 20 points; these improvements persisted 18 months after treatment completion; furthermore, the percentage of patients reporting the disappearance of self-perceived disability induced by tinnitus increased continuously after treatment completion; there was only one patient whose condition worsened in the follow up
TRT	Korres <i>et al.</i> ⁸	63	Controlled Clinical Trial	12 months (≥8 h a day)	12 months (3, 6, and 12 months)	THI, VAS	On final evaluation the THI score was statistically significantly improved in the TRT group compared with control group (treated with vasoactive agents); additionally, mean VAS scores were statistically improved in the study group, in all measures (work, sleep, relaxation, concentration); none of these measures were significantly improved in the control group
TRT	Tyler <i>et al.</i> ⁹	48	RCT	12 months	12 months	THQ	After 12 months, no significant differences in improvement rate were observed among groups
TRT	Bauer and Brozowski ¹⁰	32	Controlled clinical trial	18 months	18 months (6, 12, and 18 months)	THI, TEQ, TIQ, subjective tinnitus loudness rating, and tinnitus LM	Both TRT and counseling are effective in reducing the annoyance and impact of tinnitus; compared with counseling, TRT participants rated their tinnitus less loud at 12 and 18 months (evaluated with TEQ); furthermore, the TRT group showed a very significant decrease of TIQ over time, whereas the control group did not; there were no significant decreases in tinnitus loudness sensation levels within each group across the four assessment periods

(Continued)

Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time:		
TRT	Barozzi <i>et al.</i> ¹¹	20	Controlled clinical trial	6 months (≥8h per day)	6 months (3 and 6 months)	THI, NRS	Significant improvements were obtained in both groups after fitting; no significant difference was found between the two groups using one or the other type of sound; two thirds of participants preferred to choose white noise as the treatment sound, while the rest indicated red noise as the preferred sound and no one chose pink noise
TRT	Reddy <i>et al.</i> ¹²	57	Clinical trial	3 months	3 months (1 and 3 months)	THI	After completion of therapy, tinnitus completely disappeared in 34 (59.65%) patients; improvement in tinnitus perception was observed in 49 (85.96%) patients; there was no improvement in tinnitus perception in 8 (14.03%) patients
HNMT	Argstatter <i>et al.</i> ¹³	290	Comparative study	5 days Treated for 50 min, twice a day, for a 5-day period	5 days	TQ	Both treatment groups achieved a statistically relevant reduction in TQ scores, though 66% of patients in the music therapy group attained a clinically meaningful improvement compared with 33% in the counseling group; it is found that initial tinnitus score and type of therapy with an OR for the music therapy compared with the counseling had an influence on therapy outcome
HNMT	Krick <i>et al.</i> ¹⁴	61	Clinical trial	1 week Treated for 50 min, twice a day, for a 5-day period	1 week	fMRI, TQ	Treatment of the TG with HNMT resulted in an augmented DMN activity in the PCC by 2.5% whereas no change was found in AC and PTC groups; this enhancement of PCC activity correlated with a reduction in tinnitus distress (measured by TQ)
HNMT	Krick and Argstatter ¹⁵	63	Clinical trial	1 week	3 weeks	TQ, MRI	The therapy significantly reduced the TQ score in the treatment group compared with the PTC group; in both treatment group and AC group, the 1-week therapy yielded GM increase in the precuneus
TMNMT	Okamoto <i>et al.</i> ¹⁶	23	RCT	12 months	12 months	TQ, VAS, MEG (ASSR and N1m)	The TMNMT group showed significantly reduced subjective tinnitus loudness and concomitantly exhibited reduced evoked activity in auditory cortex areas corresponding to the tinnitus frequency compared with patients who had received an analogous placebo notched music treatment or monitoring; moreover, all reduction effects observed in the target group were statistically significant already after 6 months of treatment; after 12 months of treatment the results of ASSR showed a highly significant correlation between tinnitus loudness change and auditory-evoked response ratio change
TMNMT	Stein <i>et al.</i> ¹⁷	100	RCT	Treated for 2h a day for 3 consecutive months	4 months (0, 3, and 4 months)	THQ, VAS, TQ, THQ, the subscales of the VAS	There were no significant effects for both primary outcome measures (pre versus post and treatment versus placebo); furthermore, a significant main effect for the factor Session (pre versus post) was found for the VAS subscale awareness revealing an overall reduction of VAS ratings for both groups; at follow up, there was a small but reliable reduction in VAS symptoms (tinnitus loudness) in the treatment group compared with the control group; besides, 29.4 % of the participants reported some form of harm

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Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures		Main findings
				Intervention time	Follow-up time	Intervention time	Follow-up time	
TMNMT	Teismann <i>et al.</i> ¹⁸	20	RCT	6 h/day, 5 subsequent days	31 days (3, 17, and 31 days)	TQ, MEG (ASSR and N1m)	A significant improvement in subjective tinnitus loudness, tinnitus-related distress, and tinnitus-related auditory-cortex-evoked activity (ASSR and N1m) were observed in patients with tinnitus frequencies ≤ 8 kHz; however, there was no improvement in patients with tinnitus frequencies > 8 kHz; though tinnitus loudness and N1m were significantly reduced after TMNMT completion, the effects becoming less with time	
TMNMT	Schad <i>et al.</i> ¹⁹	30	RCT	Treated for 6 h a day for 2 weeks	4 weeks (0, 2, and 4 weeks)	VNS, LM, TFI	All groups showed a pronounced decrease in mean TFI; however, only the improvement seen for the notched group is considered a clinically meaningful reduction based on criteria set for the TFI; the VNS and LM results showed the most improvement for the notched group immediately following treatment	
TMNMT	Stein <i>et al.</i> ²⁰	9	Clinical trial	3 h on 3 consecutive days	3 days	VAS-L, MEG	TMNMT exposure reduced subjective tinnitus loudness and neural activity evoked by the tinnitus tone in the temporal, parietal, and frontal regions within the N1m time interval; the reduction of auditory cortex activity was related to the decrease of tinnitus loudness; in addition, the reduction of tinnitus-related neural activity persisted and accumulated over 3 days	
PM	Theodoroff <i>et al.</i> ²¹	60	RCT	3 months	3 months (Follow-up evaluation was performed four times)	TFI, NRS, and tinnitus LM	Treatment with PM or NS had a greater reduction in mean TFI compared with treatment with BSG, and treatment with PM results in greater reduction in mean NRS of tinnitus loudness compared with the other groups; the effects on the LM at 1 kHz are virtually indistinguishable between PM and NS group	
PM	Vanneste <i>et al.</i> ²²	26	RCT	Treated for 3 h a day for 1 month	1 month	HADS, VAS-L and VAS-A, EEG	Compared with baseline, the sham and compensation treatment groups revealed no significant outcomes for VAS-L, VAS-A, depression and anxiety as measured with the HADS or EEG; however, the overcompensation treatment group scored worse in VAS-L, VAS-A, and depression, and demonstrated for an increase of $\alpha 2$ activity within the left dorsal anterior cingulate cortex, as well as for $\beta 1$ and $\beta 2$ band in the left pregenual anterior cingulate cortex	
PM	Mahboubi <i>et al.</i> ²³	18	RCT	Treated for 2 h a day for 3 months	3 months	VAS-L, THI, BAI, MML, and RI	With customized sound therapy, all of mean loudness, the scores of THI and BAI, and MML decreased; the residual inhibition type and duration did not change significantly; however, the number of subjects with complete RI increased from 1 to 4; after 3 months of BBN therapy, only significant improvements in BAI and MML were seen; the changes in tinnitus loudness and THI with the customized sound therapy were statistically greater than those of BBN therapy	
CR	Hauptmann <i>et al.</i> ²⁴	189	Clinical trial	12 months (Treated for 4–6 h a day)	12 months	TBF-12, CGI-I7 and NRS	The scores of TBF-12 and CGI-I7 had a significant decrease after 12 months of treatment; NRS loudness and annoyance improved; after 12 months of treatment, about half of patients reported that tinnitus has no negative influence on their life anymore	

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Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time:		
CR	Tass ⁵	63	RCT	12 weeks	10 months	VAS, TQ and EEG	TQ scores and VAS-L/VAS-A were significantly reduced compared with baseline in G1 to G4 with the strongest improvements in G1 and G3 (CR group); while in G2 (noisy CR group), the VAS-L/VAS-A only showed significant reductions in on-stimulation and the difference between on- and off-stimulation effect was strongest; G4 (reduced stimulation time of 1 h/day) showed a similar effect to G1 and G3 but was less effective; in contrast, G5 (the placebo group) showed no change in on- and off-stimulation; furthermore, the effects gained in 12 weeks of treatment showed sustained long-term effects in LTE; concomitantly, EEG revealed a significant decrease of δ and γ activity in primary and secondary auditory cortex as well as in frontal brain areas with enhanced α activity in auditory and prefrontal areas; additionally, tinnitus-related reduction of activity was reversed, and enhanced activity reoccurred in auditory and prefrontal areas
CR	Adamchic <i>et al.</i> ⁶	18	Clinical trial	16 min	16 min Assessed in the stimulation-on condition; 15 min after turning on stimulation; assessed in the stimulation-off condition; after having turned off stimulation for at least 2.5h	VAS-L, VAS-A, and EEG	Under stimulation-on conditions, both the CR group and noisy CR-like group had a reduction of VAS-L and VAS-A scores, together with a decrease of auditory δ power and an increase of auditory α and γ power; in contrast, the LFR group had less effects under stimulation-on conditions; the CR group had the longest significant reduction of δ and γ , and an increase of α power in the auditory cortex region; the noisy CR-like group had weaker electrophysiological after-effects, and the LFR group had hardly any electrophysiological after effects
NTT	Vieira <i>et al.</i> ²⁷	70	Clinical trial	6 months	Transition: 2-month review appointment; follow up: 4-month review appointment; final: 6-month review appointment; long-term review: 6-36 months after termination of the treatment	TRQ, tinnitus awareness and disturbance	There was a significant decrease in TRQ scores and tinnitus awareness and disturbance at the end of the treatment and at the long-term appointment, relative to the scores before treatment started; and the treatment outcome was stable beyond the conclusion of the NTT treatment program, since there was no significant change in any of the scores between the end of the treatment and long-term appointments, and patients meeting applicable standards had better outcomes
NTT	Li <i>et al.</i> ²⁸	34	RCT	12 months	12 months (3, 6, and 12 months)	THI and TFI	The treatment group reported significantly lower scores of THI (include tinnitus distress, severity, and functional impairment) than the control group (received unaltered music) throughout the treatment and follow-up period; among the treatment group, the total scores of THI and TFI were significantly lower at follow-up period than at baseline; despite sustained tinnitus severity, improvement for the treatment group, the anxiety symptoms relapsed at the 12-month follow up

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Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time		
NTT	Newman and Sandridge ²⁹	56	Comparative study	6 months	6 months	THI	THI scores indicated a significant improvement in tinnitus reduction for both treatment types, yet inter-group differences were not statistically significant; those patients with more severe THI scores at the beginning of therapy received greater benefit from treatment
NTT	Jang <i>et al.</i> ³⁰	11	Clinical trial	6 months (Treated for at least 2 h a day for 6 months)	6 months	TRQ, awareness score, disturbance score, GBI	The participants achieved universal improvement in the scores of TRQ, GBI, and the awareness of tinnitus; 40% participants reported a reduction of the time they were disturbed by their tinnitus
NTT	Wazen <i>et al.</i> ³¹	38	RCT	Treated for 2–4 h per day for 6 months	24 months (Assessed at 6, 12, and 24 months)	TRQ, THI	The TRQ score was significantly reduced in 74% of patients at 12 months and in 84% of patients at 24 months; THI scores were significantly reduced in 77% of patients at 12 months and in 50% of patients at 24 months
NTT	McMahon <i>et al.</i> ³²	12	Clinical trial	30 weeks	30 weeks (5, 10, 20, and 30 weeks)	MEG, TRQ	MEG recordings showed that the tinnitus participants had significantly larger and more anteriorly located source strengths when compared with the non-tinnitus participants; during the 30-week tinnitus treatment, the participants' 500 Hz and 1000 Hz source strengths remained higher than the non-tinnitus participants; however, the source locations shifted toward the direction recorded from the non-tinnitus control group; further, the perceptual changes in tinnitus perception preceded neurophysiological changes by 5 weeks; in addition, the mild-severe subgroup had 500 Hz and 1000 Hz source locations located that were more anteriorly located compared with the mild-moderate group, which suggests that those with greater magnitudes of hearing loss showed greater cortical disruptions with tinnitus
Modulated sounds	Reavis <i>et al.</i> ³³	20	Clinical trial	3 min	3 min	Tinnitus Severity Index, THI, loudness growth experiment, tinnitus LM	After adjusting for stimulus frequency, all stimuli except for pure tones produced significantly greater amounts of suppression than white noise, with the amplitude-modulated tones producing the most (1.9 times more than white noise), after adjusting for stimulus type, only the highest-frequency stimuli (6–9 kHz) produced 1.5 times more suppression than white noise; besides, compared with good responders, poor responders matched their tinnitus to significantly lower sensation levels but had higher loudness rankings
Modulated sounds	Tyler <i>et al.</i> ³⁴	56	RCT	6 min	8 min (Tinnitus loudness was scored every 30 s)	THQ, Tinnitus Pitch Match	In about one third (21/56) of subjects, there was no significant effect from any masker; in other subjects, 54.3% (19/35) showed a greater reduction for the S-tones, 20% (7/35) showed a greater reduction with the noise, and 25.7% (9/35) showed similar performance between the two stimuli; the S-tones showed a statistically significant benefit versus noise at reducing the patient's tinnitus perception

(Continued)

Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time:		
Modulated sounds	Durai <i>et al.</i> ³⁵ <i>et al.</i> ³⁶	23	Clinical trial	2 weeks (Treated for 30 min in each condition)	2 weeks	VAS-L, VAS-A, loudness level match	After short-term administration of 30 min, the scores of VAS-L and VAS-A were significantly lower for unpredictable sounds in comparison with baseline; and tinnitus was significantly less annoying, but to a lesser extent, after predictable sound administration than baseline; the loudness level matches are similar between conditions (baseline, predictable, unpredictable, and silent); the participants who had benefited from sound therapy reported a preference of unpredictable over predictable sounds
Modulated sounds	Schoisswohl <i>et al.</i> ³⁶	29	Clinical trial	3 min × 7	Assessed after each stimuli	VAS-L, RI	The results indicated a general efficacy of noise stimuli for the temporary suppression of tinnitus, but no significant differences between AM and unmodulated individualized bandpass-filtered stimuli; compared with the group with tonal tinnitus, the group with noise-like tinnitus revealed significantly better effects (showing a shorter duration of tinnitus and a lower VAS-L), especially directly after stimulation offset; further, no differences were found in scores of TQ and THI between the two subgroups
Modulated sounds	Neff <i>et al.</i> ³⁷	29	Comparative study	3 min	Assessed every 30 s after the stimulation	RI, VAS-L	This study confirmed similar or slightly stronger tinnitus suppression or RI effects of AM compared with PTs and slightly better tolerability of the AM stimulus class by tinnitus sufferers
ADT	Herraiz <i>et al.</i> ³⁸	67	RCT	Treated for 20 min a day for 1 month	1 month	RESP, THI, VAS	ADT patients improved significantly compared with WLG in RESP and THI scores; the NONSAME group (training frequencies one octave below the tinnitus pitch) had significantly decreased THI scores compared with the SAME group (patients trained frequencies similar to tinnitus pitch); RESP and VAS scores decreased more in the NONSAME group though differences were not significant; the result had not shown any differences when comparing the group training the deepest hearing-impaired frequency and the group who trained other frequencies
ADT	Hoare <i>et al.</i> ³⁹	70	RCT	1 month	1 month	THQ	An overall reduction in self-reported tinnitus handicap after training was maintained at a 1-month follow-up assessment, but there were no significant differences between groups (trained with different frequencies of stimulus/trained with different duration)
HA	Rocha and Mondell ⁴⁰	30	RCT	6 months	6 months (0, 3, and 6 months)	THI, VAS	The scores of the THI showed a reduction >20 points for 100% of the patients; additionally, in the results obtained by the VAS, both of the groups indicated an initial high improvement, with a lasting effect until the final assessment
HA	Henry <i>et al.</i> ⁴¹	55	RCT	5 months	5 months (2 and 5 months)	TFI, hearing-specific questionnaires and QuickSIN	All the groups had improvements in TFI, the hearing-specific questionnaires, and QuickSIN, but these improvements did not differ across device groups; but that the HA and HA+SG devices provided twice as much benefit as the EWHA device for listening to speech in noise; similarly, participants who wore the HA and HA+SG devices reported better overall objective and subjective auditory outcome than those who wore EWHA devices

(Continued)

Table 1. (Continued)

Intervention	Reference	Sample size	Study design	Research duration		Outcome measures	Main findings
				Intervention time	Follow-up time:		
HA	Henry <i>et al.</i> ⁴²	30	RCT	3 months	3 months	TFI	87% of the participants with HA showed a significantly improvement in their TFI scores
HA	Santos <i>et al.</i> ⁴³	49	RCT	3 months (Treated for at least 8 h per day)	3 months	THI, numeric scale of tinnitus loudness	The results showed not statistically significant difference between the group of 'HA+SG' and 'HA'; both of the groups showed a significant reduction in THI and MML; the results also show a positive correlation between the MML and the discomfort from tinnitus and the tinnitus loudness
HA	Sweetow and Sabes ⁴⁴	14	Clinical trial	6 months	6 months	THI, TRQ	The participants were tested wearing HAs that contained several programs including amplification only, fractal tones only, and a combination of amplification, noise, and/or fractal tones; the majority reported improvements for at least one of the amplified conditions (with or without fractal tones or noise), relative to the unaided condition, and indicated that it was easier to relax while listening to fractal signals
CI	Buechner <i>et al.</i> ⁴⁵	5	Clinical trial	12 months	12 months (Assessed at 1, 3, 6, and 12 months)	characterization of tinnitus, questionnaires regarding sound quality and tinnitus, VAS	Participants 2 and 3 reported nearly complete suppression of the tinnitus while the implant was activated; however, the tinnitus returned after a couple of minutes to hours after switching off the device; although participants 2 and 5 reported a continuous improvement, for participants 3 and 4, the stress caused by the tinnitus increased again after the initial months; participant 1 did not notice any long-term effect of the CI on his tinnitus
CI	Zeng <i>et al.</i> ⁴⁶	1	Case report	360 s	720 s (Assessed every 30 s during stimulation and then for another 60–360 s after the stimulus was turned off)	VAS-L, EEG	A low-rate (20–100 Hz) and a low-level (softer than the tinnitus) electric stimulus delivered by CI totally abolished tinnitus; compared with the results obtained in the tinnitus-present state, the low-rate stimulus reduced cortical N100 potentials while increasing the spontaneous α power in the auditory cortex

AC, active healthy control; ADT, auditory discrimination training; AM, amplitude modulated sound therapy; ASSR, auditory steady state response; BAI, Beck Anxiety Inventory; BBN, broadband noise; BSG, bedside sound generator; CGI-I7, Clinical Global Impression-Improvement Scale; CI, cochlear implant; CR, acoustic coordinated reset neuromodulation therapy; DMN, brain's default-mode network; EEG, electroencephalogram; EWAH, extended-wear hearing aid; fMRI, functional magnetic resonance imaging; GBI, Glasgow Benefit Inventory; GM, gray matter; HA, hearing aid; HA+SG, hearing aid with a sound generator; HADS, Hospital Anxiety and Depression Scale; HNMT, Heidelberg neuro-music therapy; LFR, low-frequency-range stimulation; LM, tinnitus loudness matching; LTE, long-term extension period; MEG, magnetoencephalography; MML, minimum masking levels; NRS, Numeric Rating Scale; NS, noise stimulus; NTT, neuromonics tinnitus therapy; PCC, posterior cingulate cortex; PM, tinnitus pitch matching; PTC, pure tones; QuickSIN, Quick Speech in Noise test; PTC, passive tinnitus control; RCT, randomized controlled trial; RESP, patient's answer to the question 'Is your tinnitus better, the same, or worse since we started the treatment?'; RI, residual inhibition; SG, sound generator; TBF-12, Tinnitus-Beeinträchtigungs-Fragebogen; TED, tinnitus educational counseling; TEQ, Tinnitus Experience Questionnaire; TFI, Tinnitus Functional Index; TG, treatment group; THI, Tinnitus Handicap Inventory; THQ, Tinnitus Handicap Questionnaire; TIQ, Tinnitus Lifestyle Inventory Questionnaire; TM, tinnitus masking; TMNMT, tailor-made notched music training; TQ, Tinnitus Questionnaire total scores; TRT, tinnitus retraining therapy; TRQ, Tinnitus Reaction Questionnaire; VAS, Visual Analog Scale; VAS-A, Visual Analog Scale of tinnitus annoyance; VAS-L, Visual Analog Scale of tinnitus loudness; VNS, Visual Numeric Scale; WLC, wait-list control group; WLG, waiting list group.

mask tinnitus, thereby distracting patients and reducing the contrast between the tinnitus signal and the background activity of the auditory system.⁴⁸ According to whether the tinnitus can be heard or not, there are two types of masking therapy: total masking and partial masking. Early reports by Vernon described the purpose of masking as making the tinnitus inaudible, that is, to achieve 'total masking'.⁴⁷ He later noted that partial masking can also be effective and further reported that the masking noise sometimes produced 'only a partial reduction in the tinnitus: it is still perceivable but in a suppressed form'.^{49,50} There are also different types of sounds used to mask tinnitus, and those currently in use include white noise, broadband noise (BBN), narrow-band noise, ambient sounds, music, and customized sounds.

Three of the studies included in this review have explored the influencing factors of masking therapy. It is widely agreed that customized sound stimulation has a better tinnitus-suppression effect than non-customized sound. In one RCT, the group receiving mixed pure-tone stimulation [which stimulated the patient with carrier frequencies consisting of mixed pure tones of nine different frequencies (n_i represents the i -th stimulus frequency, $i = 1, 2, 3, 4, 5, 6, 7, 8,$ and 9 ; the frequency step was one third of an octave, $n_i/n_{i-1} = 1.26$; and n_5 kHz was the tinnitus pitch, which was determined by subjective tinnitus pitch matching)] showed lower scores on the Tinnitus Handicap Scale (THI) and the visual analog scale for loudness (VAS-L) and annoyance (VAS-A) compared with baseline after 12 weeks of treatment. The mixed pure-tone group also had lower scores for VAS-L and VAS-A compared with the BBN group at 8 and 12 weeks, although the difference was not significant in the first 4 weeks.⁵ This implies a link between efficacy and duration of treatment, and a longer duration of treatment might produce a better outcome. Henry *et al.* reported significantly decreased THI scores in all groups (masking therapy, TRT, and tinnitus counseling), with a similar effectiveness during long-term follow up. In addition, the authors found that patients with better outcomes tended to have higher initial THI scores.⁶ Hesser *et al.* reported that individuals who were allowed to control the background sounds exhibited a significantly steeper increase in tinnitus interference over the trials and a poorer improvement rate on

the measure of cognitive function in comparison with those who were not given control over the background sounds.⁴ From a theoretical perspective, having control over background sounds gives the individual more behavioral control and also confidence, which might be associated with a positive effect on tinnitus interference, at first. However, being in control of the sounds in order to mask the perception of tinnitus might lead to increased focus on the sensation resulting in a later rebound phase with increased tinnitus interference.

Tinnitus retraining therapy

TRT represents an amalgamation of sound-therapy protocols, originally described by Hazell and Sheldrake,⁵¹ with an expanded directive counseling protocol. TRT is a combined therapy consisting of counseling the patient to help them experience tinnitus as a neutral stimulus and sound therapy to decrease the strength of the tinnitus signal.⁵² This model emphasizes the importance of both conscious and subconscious connections. Grewal *et al.* proposed that the incorporated psychotherapeutic elements (which are closely related to tinnitus annoyance) and auditory stimulation procedures are the most promising tinnitus treatment options.⁵³ The counseling aims to teach patients to understand tinnitus correctly and to adjust their psychological state so as to relieve the negative emotions associated with tinnitus. Simultaneously, long-term retraining can reduce the sensitivity to tinnitus and improve central inhibition or central filtering function.

Six studies explored the effectiveness of TRT, two of which were devoted to exploring the efficacy of different treatment modalities on tinnitus with one reporting that the effective rate of TRT in treating tinnitus was 85.96%.¹² The argument surrounding the sound stimulation was that the mixing point was the optimal noise level to mask the tinnitus because habituation to tinnitus might not occur if the tinnitus is inaudible as is the case in total masking. However, a clinical trial by Tyler *et al.* reported that individuals treated with total masking or partial masking had no difference in the improvement rate on the Tinnitus Handicap Questionnaire (THQ).⁹ Barozzi *et al.* found that using different types of sound led to similar significant improvements and that white noise was

the most popular therapeutic sound,¹¹ and Bauer *et al.* found that the TRT group showed a significant decrease in tinnitus loudness whereas the group receiving counseling alone did not. This was the exact opposite of the results reported by Tyler *et al.*⁹ In addition, Bauer *et al.* found no significant change in tinnitus loudness sensation level within any group during treatment. The authors concluded that TRT promoted the habituation of tinnitus but did not change the tinnitus loudness level, and they proposed that a more severe initial THI score might indicate a better outcome.¹⁰ The improvement was shown to appear 3 months after TRT and it increased with time,⁵⁴ and normally TRT is recommended to continue for 18 months in order to obtain stable results.⁵⁵ Both Forti and Korres investigated the effect of providing TRT for longer than 1 year, and they reported a significant decrease in THI score and significant relief from the disability induced by tinnitus. After 18 months of TRT treatment, Forti *et al.* observed a sustained tinnitus-suppression effect.^{7,8}

Heidelberg neuro-music therapy

HNMT was first offered in 2004,⁵⁶ and the theoretical basis of HNMT for tinnitus lies in the neurophysiological plasticity of the cortex and the psychological factors related to tinnitus. HNMT combines the psychological management strategy of tinnitus and special vocal training to develop a relatively fixed and standardized tinnitus management strategy. This short-term treatment mode consists of nine 50-minute sessions of individualized therapy, comprising directive counseling, resonance training, intonation training, and tinnitus reconditioning (including relaxation training, habit training, and pressure management). The treatment is performed twice a day for 50 min each time and lasts for 5 days.

Tinnitus counseling and guidance can help patients correctly understand tinnitus, enhance patients' subjective initiative in subsequent treatment, and strengthen self-management awareness of tinnitus. Both resonance training and intonation training are forms of positive music therapy. Resonance training intends to stimulate the cranio-cervical resonating cavities and treats tinnitus through the interaction of auditory perception and somatosensory input in the early stages of neuron processing. During resonance

training, both the therapist and the patient themselves can check whether there is a resonance movement of the skull by touching the trigger point of the root of the nose, the temporomandibular joint of the cheek, and the muscle of the neck. Intonation training mainly focuses on the abnormal expression areas in the auditory cortex within the frequency range of transposition tinnitus. The patient imitates the tone sequence provided by the therapist and conducts systematic and targeted training on inaccurately intonated musical sounds so that the patient learns to actively filter the sound information and to concentrate on only part of the auditory stimulation. In addition to increased auditory attention control, this training aims at a neuronal reorganization of the auditory cortex. Tinnitus reconditioning is a passive music therapy mode, and it offers coping mechanisms related to stress control, along with a sound-based habituation procedure (including relaxation training, habituation training, and stress management).

Results from several clinical trials suggest that short-duration HNMT is effective in treating tinnitus and that it has long-lasting effects.^{13,57} Three studies on HNMT were included in this review. Two of the studies used objective methods to observe changes in gray matter reorganization in default-model network (DMN) regions and in primary auditory areas. Intrinsic DMN activation and gray matter activity are shown to be reduced in patients experiencing tinnitus-related distress.⁵⁸⁻⁶¹ Krick used task-negative activity to observe the brain's DMN in the context of the HNMT tinnitus-therapy control task, and the results indicated greater DMN activity and a decreased Tinnitus Questionnaire (TQ) score after HNMT treatment.¹⁴ The author postulated that the enhancement of posterior cingulate cortex activity correlated with a reduction in tinnitus distress. Similarly, Krick *et al.* reported a decrease in TQ score and an accompanying increase in gray matter activity in the precuneus in the participants treated by HNMT.¹⁵ Additionally, Krick and Argstatter found that healthy participants who received HNMT also showed an increase in gray matter activity.¹⁵ These results confirmed that some kind of neural rehabilitation of the DMN occurs as a result of HNMT. Compared with education counseling, the patients receiving HNMT attained a clinically meaningful improvement in TQ score, and patients with high initial

tinnitus scores were more likely to have more positive outcomes.⁶²

Compared with other sound treatments, HNMT has the following advantages: (a) patients are confronted actively with their tinnitus, rather than passively inhibited or covering up their tinnitus. This treatment process is relatively interesting and will help patients change their attitude toward tinnitus instead of blindly trying to avoid the tinnitus. (b) The main parts of the therapy consist of active music therapy modules, and thus there is no need to change the frequency spectrum of the music used and the processing of sound is relatively simple for the therapist. (c) The duration of the music therapy does not exceed 5 consecutive training days, and this greatly increases the acceptability of the treatment. In addition, despite the short intervention interval, the therapy shows long-term effects in tinnitus patients.⁵⁷ However, due to the combined use of counseling and sound therapy, it is unclear whether HNMT's effect relies on the explicit perception of frequency relations or on emotional relaxation.

Tailor-made notched music training

Pantev *et al.* proposed that tinnitus could be inhibited by presenting band-eliminated sounds to the auditory system.⁶³ TMNMT as a treatment for tonal tinnitus relies on the fact that the removal of a frequency band from an auditory stimulus will cause the brain to reorganize around tonotopic regions coding the frequencies within the band.¹⁶

TMNMT does not provide any afferent input to the auditory cortex neurons that are activated in response to the tinnitus frequency, but neighboring neurons are activated to inhibit the frequencies within the notch region *via* lateral inhibition. In order to enhance the lateral inhibition effect within the notch area corresponding to the tinnitus frequency, the music energy spectrum is processed in three steps. First, the amplitude of the music frequency spectrum in all frequency ranges is equalized by the redistribution of energy from low to high frequency ranges. This guarantees an equal energy spectrum below and above the frequency area suppressed by the notch filter. Second, a frequency band of half an octave's width centered at the tinnitus frequency is removed. Third, a width of three eighths of an octave on both sides of the notch frequency is

increased by 20 dB to amplify the energy difference between the notch region and the edge frequency.^{17,20}

TMNMT has been shown to reduce auditory-evoked cortex activity measured by means of magnetoencephalography (MEG) specifically for the tinnitus frequency, and concomitantly it leads to significantly reduced subjective tinnitus loudness.^{16,18,64} Although the overall effect of TMNMT in tinnitus patients is significant, the outcomes in individuals show inconsistencies. Teismann reported that training was more effective in the case of tinnitus frequencies ≤ 8 kHz compared with tinnitus frequencies > 8 kHz,¹⁸ and this difference in curative effect might be partially explained by the lower musical energy content in the frequency region above 8 kHz. In addition to the frequency of tinnitus, the duration of treatment might also affect the efficacy of TMNMT. Okamoto and Stein explored the potential treatment benefits for tinnitus patients receiving different durations of treatment. TMNMT was not superior to placebo treatment directly after 3 months (evaluated by THQ and VAS),⁶⁵ while TMNMT affected tinnitus loudness after 6 months and was shown to be superior to placebo after 12 months.¹⁶ However, the research by Stein *et al.* suggested that short-term changes in neurophysiological brain activity elicited through TMNMT already begin to occur after 3 days.^{17,64} This indicates that brain plasticity is often first observed on a neural level and then manifests behaviorally at a later time.⁶⁴ Currently, the optimal duration of TMNMT for tinnitus is unclear, but it is generally agreed that a longer treatment time is necessary to demonstrate the positive effect of TMNMT. In addition to using notched music as the stimulating acoustic signal, notched BBN is also used in tinnitus treatment and is shown to be beneficial for relieving the effects of tinnitus based on the Tinnitus Functional Index (TFI), Visual Numeric Scale (loudness rating), and loudness matching. In contrast, the group receiving tinnitus pitch-matched frequency or low frequency noise did not show a significant effect like was seen in the TMNMT group.¹⁹

Tinnitus pitch-matched therapy

Tinnitus pitch-matched therapy uses the opposite technical approach to TMNMT, which selectively amplifies the hearing-loss frequency region of the pitch area of tinnitus.⁶⁶ Animal research

has shown that keeping animals in an acoustic environment enriched by high frequencies after noise trauma prevents tonotopic map reorganization in the auditory cortex and reduces the changes in the pattern of spontaneous firing after noise exposure.⁶⁷ This suggests that the compensation for hearing loss or hearing stimulation in the pitch area of tinnitus at the early stage of noise exposure (or early tinnitus onset) might reduce the restructuring of the auditory cortex and thus suppress tinnitus. However, few patients begin tinnitus treatment immediately after tinnitus onset, and there is no research on the changes in the auditory cortex of people or animals undergoing sound therapy after having already experienced tinnitus or noise exposure for some time. This requires more research in the future to understand the effects of treatment timing.

Despite contrasting forms of treatment by TMNMT and tinnitus pitch-matched therapy, both of the methods reportedly lead to significant tinnitus reduction after long term (6–12 months) and regular (2–4 h daily) listening to the modified sounds. However, the research of Schad *et al.* demonstrated that compared with tinnitus-matched therapy and BBN stimulation, the patients who received TMNMT showed the most improvement immediately following treatment.¹⁹ There is currently no standardized tinnitus evaluation method, but it can be seen from different evaluation methods (numeric rating scales of tinnitus loudness, THI, and the number of subjects with complete residual inhibition) that the effect of tinnitus pitch-matched therapy is better than non-customized noise stimulation.^{21,23} In an RCT using 1 month of pitch-matched stimulus on tinnitus patients, the compensation for the frequency of hearing loss was not beneficial in suppressing tinnitus, whereas excessive compensation worsened tinnitus both clinically and electrophysiologically.²² It remains unclear why the efficacy of tinnitus pitch-matched therapy is inconsistent in different studies, and factors such as the etiology of the tinnitus, the intensity of the stimulating sound, adaptation to the stimulating sound, understanding of tinnitus, and treatment duration might all have an effect on the efficacy of tinnitus pitch-matched therapy.

Acoustic coordinated reset neuromodulation

CR neuromodulation was initially developed for electrical deep-brain stimulation in treating Parkinson's disease,²⁵ and in recent years CR has

been proposed to specifically counteract the electrophysiological correlation of tinnitus (pathological neural synchrony). CR uses computer-based auditory stimuli presented as short tones in a random varying sequence above and below the tinnitus frequency⁶⁸ and aims at counteracting pathological neural synchrony by sustainably reducing the strength of the synaptic connectivity between neurons within an affected cell population.^{68,69}

Three studies were included in this review, and all of them reported that CR was an effective way to treat tinnitus.^{24,26,68} In a clinical trial, individuals receiving CR stimulation 4–6 h/day showed better efficacy than those being stimulated for 1 h/day as measured by both subjective questionnaires and electrophysiology.⁶⁸ Moreover, CR was also shown to have sustained long-term effects on tinnitus suppression. In addition to the treatment time, different stimulation sounds also had an effect on the outcome. Patients using CR showed a stable effect in on- and off-stimulation, while patients receiving noisy CR-like stimulation (the noisy CR-like stimulation shares the basic rhythmic CR pattern with CR, but the stimulation tones are randomly selected from a larger frequency range that are not related to the tinnitus pitch) only showed efficacy in on-stimulation.^{26,68} Tass argued that ideally, the CR stimulation should be limited to the area of enhanced synchronized activity. The distance of the stimulation sites (frequencies) needs to be controlled, and the distance should be sufficient to achieve optimal desynchronizing CR effects. In fact, for sufficiently dense spacing of the stimulation sites, the effect of CR stimulation approaches the synchronizing effect of a spatially homogenous stimulation that is periodic in time.⁷⁰

Neuromonics tinnitus treatment

Davis developed NTT as an acoustic desensitization protocol that follows a surplus scheme by adding individually customized broadband frequency sounds to relaxation music.⁷¹ It was designed to provide stimulation to auditory pathways deprived by hearing loss, to engage positively with the limbic system, and to allow intermittent momentary tinnitus perception within a pleasant and relaxing stimulus, thereby facilitating desensitization to the tinnitus signal. The NTT requires patients to undergo treatment for at least 2 h a day for 6 months. During the first

2 months of NTT, the customized broadband noise is embedded in pleasant music, which stimulates the deprived auditory pathways and aims to achieve high interaction with the tinnitus perception. For the next 4 months, the noise component is removed from the customized acoustic stimulus, thus allowing only intermittent interaction with the tinnitus. The patient is able to cover up their tinnitus during the peaks of intensity and to still perceive it during the intensity troughs, thereby facilitating habituation to the tinnitus, leading to a gradual reduction in awareness and disturbance from the tinnitus.^{71,72}

NTT is shown to be effective in reducing the severity of tinnitus and to have a stable and lasting effect.^{27–31} In an RCT by Li *et al.*, it was found that despite the sustained improvement in tinnitus severity after NTT, the anxiety symptoms tended to relapse at the 12-month follow up.²⁸ The same regions of the brain are involved in the pathogenesis of both anxiety and tinnitus, suggesting the close inter-relationship between the disorders.⁷³ MEG recordings have shown that the N1m source strengths and location change in tinnitus patients compared with non-tinnitus participants. Also, during the NTT treatment, the source locations of tinnitus patients shift toward the direction recorded from the non-tinnitus participants. At the same time, tinnitus perception is improved.³² This might be objective evidence that NTT works. It remains uncertain whether the severity of tinnitus will recur due to anxiety, and there are no follow-up studies that have been performed for more than 12 months to investigate the longer-term efficacy of NTT. Wazen *et al.* investigated the continued efficacy of NTT after 24 months and showed a positive result.³¹ However, due to the low sample follow-up rate, their conclusion needs to be verified. Although the long-term efficacy of NTT is not clear, McMahon *et al.* proposed that the perceptual changes in tinnitus perception precede neurophysiological changes by 5 weeks,³² and this indicates that patients still need to continue treatment after the self-perception of tinnitus has diminished.

Vieira *et al.* classified patients into suitability levels as follows. Tier 1 represents the most suitable patients to receive NTT. Tier 2 represents patients who present with at least one of the following complicating factors: high level of psychological disturbance, low level of distress [Tinnitus Reaction Questionnaire (TRQ) scores below 17],

and severe hearing loss, that is, an average threshold increase of greater than 50 dB in the worse ear for four frequencies (0.5, 1, 2, and 4 kHz). Tier 3 represents the least suitable patients for NTT and includes patients with reactive tinnitus, ongoing noise exposure without adequate protection, multi-tone tinnitus, severe hearing loss [i.e. hearing thresholds greater than 50 dB for four frequencies (0.5, 1, 2, and 4 kHz) in the better hearing ear], Ménière's disease, or poor ability to follow the treatment protocol. Vieira *et al.* found that the most suitable patients (Tier 1) presented better clinical outcomes than Tier 2 and Tier 3.^{27,74} In addition, patients with high initial THI scores showed better treatment effects.²⁹

Modulated wave therapy

Reavis *et al.*⁶⁴ suggested that a novel approach focusing on the tinnitus pitch-matched frequency might have an effect on tinnitus interference. Liang *et al.* showed that pure-tones pitch matched to a patient's tinnitus and then sinusoidally amplitude modulated with a rate constant produced highly synchronized cortical firing in animal models.⁷⁵ Modulated wave therapy includes frequency modulation and amplitude modulation. Tyler *et al.* applied the modulated wave therapy by exposing patients to different types of sound that were presented at one point below the subject's perceived tinnitus loudness (on a 0–10 scale), and the subjects were asked to rank the loudness of their tinnitus at 30 s intervals.³⁴ Compared with pure tones and noises that mostly induce or counteract auditory cortical activity to mask the tinnitus, the modulated stimuli produce robust and sustained acoustically driven activity that might rearrange the cortical firing patterns in such a way as to prevent the generation of tinnitus. At present, research on modulating sound for tinnitus is mainly focused on the short-term effects of tinnitus suppression, and the residual suppression test is often used to predict the long-term effect that stimulating sounds have on tinnitus. The effectiveness of modulated sound in the temporary suppression of tinnitus has been confirmed,^{64,34,37} but the long-term effect of the therapy remains to be studied.

Like other types of sound therapy, modulated wave sound therapy is effective for tinnitus treatment, but not for all patients. The research by Tyler *et al.* showed a positive effect of amplitude

modulation treatment in 54.3% of patients. The patients with poor responses matched their tinnitus to significantly lower sensation levels but higher loudness rankings, and patients with normal loudness experienced a greater tinnitus-suppression effect. This suggests that patients with either severe loudness recruitment or hyperacusis or both would see less benefit from modulated wave therapy.^{76,77} Further, Schoisswohl *et al.* proposed that the type of tinnitus has an impact on the efficacy of the treatment. Compared with patients with tonal tinnitus, patients with noise-like tinnitus saw significantly better treatment effects, especially directly after stimulation termination.³⁶ In addition to the influence of individual factors, the type of modulated sound also has an effect on the efficacy of the therapy. The clinical trial by Reavis *et al.* provided evidence that low-rate amplitude-modulated tones with a high carrier frequency in the tinnitus pitch range were the most effective at reducing tinnitus loudness. Durai *et al.* found that unpredictable stimulating sounds might result in a better outcome than predictable stimulating sounds, and patients who responded well to modulated wave therapy preferred using unpredictable stimulating sounds for their treatment.³⁵

Auditory discrimination training

The development of tinnitus has been associated with cortical reorganization. Based on MEG, Muhlneckel *et al.* demonstrated that activation of cortical areas stimulated by a sound with the same frequency as the tinnitus pitch led to activation of adjacent zones.³⁸ In addition, Weisz *et al.* proposed that acoustic stimulation with the same frequency as the tinnitus pitch led to maladaptive compensatory responses to deafferentation (tinnitus).⁷⁸ In the study by Recanzone *et al.*,⁷⁹ monkeys were trained to discriminate among close-frequency tones and then learned to exhibit different behaviors in response to the trained frequencies. This showed that reorganization could be induced by external sound stimulation. Based on this finding, Recanzone *et al.*⁷⁹ first proposed the treatment method of discrimination training. ADT provides specific acoustic stimulation of damaged cochlear frequencies to enhance the activity in the auditory cortex corresponding to these frequencies and to reduce the over-represented adjacent zones, thereby effectively suppressing tinnitus. It has been electrophysiologically demonstrated that these remodeling processes

can take place regardless of whether the sound targets are explicitly trained or are presented as a background signal. Therefore, ADT training does not require participants to concentrate, and they only need to be repeatedly and extensively exposed to appropriate sound signals.⁸⁰

ADT treatment has been shown to have an effect on the suppression of tinnitus, but it is not clear which treatment mode has the greatest efficacy. Herraiz *et al.* provided the first indication that training at tones that differed from the dominant tinnitus pitch had a greater benefit than training at tones that had a frequency similar to or the same as the tinnitus pitch.⁸⁰ This might be due to the effect of lateral inhibition, and stimulating specific frequency regions close to but not within the tinnitus frequency region will likely promote or strengthen lateral inhibitory activity and thereby disrupt the pathological synchronous activity of the tinnitus-generating region. Although the frequency of tinnitus is usually consistent with the frequency of hearing loss, studies have shown that whether or not the frequency of the stimulus sound is consistent with the frequency of hearing loss has no significant influence on the efficacy of the treatment.^{39,80} Hoare *et al.* found that the training period (duration and intensity) had no effect on the outcome,³⁹ and this demonstrated that training that provided enrichment stimulation at hearing-loss frequencies was not specifically associated with the outcome of the treatment. In addition, patients with low initial THQ scores had better ADT training efficacy.

Hearing aids for tinnitus

Since 1976, externally generated sound has been used as a clinical technique to provide tinnitus masking.⁴ This approach employs wearable devices in the ears to provide masking sounds to patients, including noise generators ('tinnitus maskers'), hearing aids, combination instruments (amplifiers and noise generators combined), and cochlear implants. Hearing aids are an important component of treatments with tinnitus masking,⁷ and the beneficial effects of hearing aids on tinnitus might be due to the amelioration of communication difficulties caused by hearing loss but attributed to tinnitus,⁸¹ reduced stress related to hearing impairment,^{82,83} the provision of an enriched acoustic environment that can mask tinnitus or make it less noticeable,⁷ or the sound stimulation in

hearing-loss areas possibly reversing the cortical reorganization associated with tinnitus.⁸⁴ In subjects who are deaf in the ear experiencing tinnitus, tinnitus treatment based on acoustic input is impossible. In this case, electric stimulation *via* cochlear implants can be used to suppress tinnitus. The synchronized neural activity generated by these devices reduces tinnitus-related neural hyperactivity and thus provides temporary suppression of tinnitus.⁴⁶

Clinical studies on tinnitus patients with hearing loss demonstrate that the use of hearing aids or cochlear implants can effectively relieve tinnitus.^{40–42,44,85} A survey of 230 hearing-care professionals suggested that 60% of the patients experience minor to major relief of tinnitus when wearing hearing aids, less than 2% of patients experience a worsening of their tinnitus when wearing hearing aids, and 39% receive no benefit.⁸⁶ The benefits of using hearing aids alone or as combination instruments have been studied, and both hearing aids and hearing aids combined with signal generators show significant improvement in the primary tinnitus outcome measure, but no statistically significant difference between devices.^{41,43} Hearing aids reduce the perception of tinnitus by amplifying environmental sounds. Based on this principle, some researchers have suggested that the wearing time of hearing aids may be positively related to the efficacy of the treatment. However, the research of Henry *et al.* showed that hearing aids and hearing aids combined with signal generators indicated greater behavioral and subjective benefits than extended-wear hearing aids (EWAHA, hearing aids that are worn for as long as possible; theoretically, for 24 h a day every day). In addition, patients treated with EWHAAs perceive lower satisfaction and less benefit to their quality of life from the devices than the patients using hearing aids or hearing aids combined with signal generators.⁴² The use of electrical stimulation shows improvements in both tinnitus status and speech perception,^{45,87} and low-rate stimulation to suppress tinnitus has also shown both psychophysical and neurophysiological improvements.⁴⁶ However, the efficacy of cochlear implants shows large individual differences, and further work needs to be performed to help define the appropriate indications for such implant recipients. While hearing aids are sometimes prescribed as part of tinnitus management, there is currently no evidence to support or refute their use as a routine intervention for tinnitus.⁸³

Discussion

Dauman and Tyler⁸⁸ proposed the importance of distinguish the physiological mechanisms of tinnitus from the reactions to tinnitus. It is widely accepted to categorize the mechanisms of tinnitus into three broad categories: (a) deafferentation and maladaptive compensatory responses to deafferentation; (b) increases in spontaneous activity of central auditory neurons; and (c) increases in cross-fiber connections.⁸⁹ Animal studies of tinnitus have shown reorganization of the tonotopic map (with cortical neurons in the hearing-loss region being tuned to the edge of the normal hearing region⁹⁰) and overall hyperactivity in the central auditory pathway from the cochlear nuclei to the auditory cortices,^{91–93} and this suggests that cortical reorganization plays a significant role in tinnitus generation. In addition, in almost all cases of chronic tinnitus, non-auditory brain structures are involved in the generation and maintenance of tinnitus.⁹⁴

Patients with severe subjective tinnitus are often accompanied by significant emotional disorders. The tinnitus signal is transmitted from the cochlea to the subcortical center, and this signal is sensed and evaluated by the cortex, which further stimulates the corresponding response of the limbic system and the autonomic nervous system. In tinnitus patients, the tinnitus signal is perceived by the cortex as a negative stimulus, thereby activating the limbic system to produce negative emotions such as fear and anxiety and further stimulating the autonomic nervous system to produce a 'stress response' (such as sleep disorders). This series of stress reactions causes patients to become more nervous and anxious (because the limbic system is more active), thus forming a vicious circle between hearing, the limbic system, and the autonomic nervous system.

The combination of sound therapy and counseling guides patients to properly acquaint themselves with the tinnitus and to perceive tinnitus as part of a pleasant listening experience, which promotes the patient's sense of relief and control. This is done with the intention of tempering the limbic system-mediated secondary reaction that is believed to be a major contributor to the emotional disorders associated with tinnitus. In addition, sound therapy reduces the contrast between the tinnitus signal and the background activity of the auditory system. Thus, even if the subcortical

center detects the tinnitus signal, the signal does not reach the level of perception thus achieving perceptual adaptation to the tinnitus signal.⁹⁵ Habituation to a tinnitus signal does not change the signal level, but rather the interpretation of, or response to, the signal. Further, precise, and specific sound therapy targeting defined auditory neural populations through individual customized sounds can lead to changes in tinnitus-related neuronal activity and thus can completely eliminate tinnitus.

In addition to subjective data (individual perception of tinnitus distress and severity), audiometric measurements of tinnitus masking levels of objective data from brain imaging might substantiate the proposed working mechanisms of tinnitus treatments.⁸⁰ Questionnaires (THI, TFI, THQ, TQ, VAS, etc.) are widely used to evaluate the efficacy of tinnitus treatment. In the clinic, the detection and evaluation of tinnitus are mostly through subjective questionnaires and lack objective evaluation methods. Although MEG has shown encouraging results in reflecting the changes in the auditory cortex in patients with tinnitus, the utility of MEG as an objective indicator of tinnitus is still debated. Usually, an increase of band power in MEG, electroencephalogram, and local field potential signals is typically interpreted as an increase in neuronal synchronization in terms of coincident firing within a neuronal population. A study on MEG showed that in tinnitus patients, the α -band power was significantly reduced, whereas the δ -band power was significantly increased, particularly in the temporal regions.⁹⁶ Furthermore, studies have shown that tinnitus-related distress is correlated with this abnormal pattern of spontaneous activity. Epidural recordings from the secondary auditory cortex in tinnitus patients showed that abnormal θ -band activity was highly correlated with tinnitus loudness.⁹⁷ Adamchic proposed that the temporal pattern of neurons plays a key role in shaping synaptic connections,⁹⁸ and this suggests that MEG might objectively reflect tinnitus by recording abnormal cortex activities.

There are still numerous limitations regarding sound therapy that should be addressed in future studies. (a) Although many studies report that sound therapy is effective, most of them are based on individual case studies and there is a lack of RCTs to identify effective management strategies.

(b) At present, tinnitus management often uses a combination of sound stimulation and educational consultation, and the therapeutic effect of individual acoustic stimulation has not been clearly defined. (c) The severity of tinnitus is mainly evaluated through various questionnaire scales. There is a lack of objective and quantifiable tinnitus evaluation methods and the evaluation methods used in clinical research are not uniform, thus making it difficult to conduct meta-analyses or systematic reviews. (d) The mechanism through which sound therapy suppresses tinnitus is not clear. For example, two opposing treatment methods have both been shown to improve tinnitus-related quality of life. Thus, it is currently not possible to determine which treatment method is the most effective in suppressing tinnitus. (e) Different individuals respond differently to the same sound therapy, thus the analysis of tinnitus patient characteristics prior to treatment should be improved in order to provide the most suitable form of sound treatment for patients. (f) The treatment duration should be optimized to ensure the best treatment effects, and evaluations need to be made regarding the potential for long-term suppression of tinnitus.

Conclusion

Sound therapy is a non-invasive treatment⁹⁹ with broad applicability. After intervention is ruled out for a medically manageable disease or other contributing medical problems, almost all patients qualify for treatment.¹⁰⁰ Sound therapy can effectively suppress tinnitus, at least in some patients,¹⁰¹ but there is still a lack of research on the efficacy of sound therapy. It is necessary to analyze the characteristics of individual tinnitus patients and to unify the assessment criteria of tinnitus. Further studies are needed to determine the most effective forms of sound therapy for individual patients, and large multicenter samples and long-term follow up are still needed to develop more accurate and targeted sound-therapy schemes.

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