

Current Therapies for Chronic Subjective Tinnitus

Subjects: **Otorhinolaryngology**

Contributor: Ki Wan Park , Peter Kullar , Charvi Malhotra , Konstantina M. Stankovic

Chronic subjective tinnitus, the perception of sound without an external source for longer than six months, may be a greatly debilitating condition for some people, and is associated with psychiatric comorbidities and high healthcare costs.

tinnitus

emerging therapeutics

electrical stimulation

1. Introduction

Broadly, treatment mechanisms for bothersome chronic tinnitus can be subdivided into two categories: tinnitus perception and response to tinnitus. Treatments modulating tinnitus perception, such as electrical and magnetic stimulation, aim to reduce or eliminate symptoms. On the other hand, tinnitus-response treatments aim to reduce the patient's negative affect or response to tinnitus and include cognitive behavioral therapy (CBT) and sound therapy.

The clinical guidelines for tinnitus from the AAO-HNF recommend hearing aid evaluation and CBT as options for chronic bothersome tinnitus and present sound therapy as another potential option [1]. The guidelines discourage the use of any medical drug therapy, dietary supplements, or repetitive transcranial magnetic stimulation (rTMS), given the lack of effective data at the time of the guidelines' publication in 2014. More recent guidelines from Europe (2019) and Japan (2020) continue to strongly recommend CBT, but provide poor to no recommendations against dietary supplements, sound therapy, medications, rTMS, and supplements [2][3]. New advances in both medical and surgical modalities for tinnitus have been developed which may hold promise for treating this chronic condition.

2. CBT

CBT, a type of psychotherapy, is used as an intervention for a wide variety of psychiatric conditions, including anxiety, depression, and the distress associated with tinnitus [4]. It aims to modulate negative thoughts associated with maladaptive behavior through reframing, using techniques like the development of positive coping skills, distraction, and relaxation. Duration of therapy for tinnitus can range from 8 to 24 weekly sessions with a trained professional [5].

To date, CBT is the only intervention for tinnitus to receive strong recommendations in clinical practice guidelines, but the benefits are primarily limited to managing tinnitus-related distress [1][2][3]. For example, several systemic reviews and meta-analyses have demonstrated that CBT is effective in improving patients' negative interpretations of tinnitus, but that its impact on anxiety or health-related quality of life may be less than that of audiological care, and that evidence of long-term outcomes are lacking [6][7][8]. A recent (2020) Cochrane review found that, compared to waiting or receiving no treatment for tinnitus, CBT meaningfully improved perception of tinnitus severity (THI score) and, to a lesser extent, measures of quality of life, anxiety, and depression [9]. Similarly, CBT provided a greater improvement on quality of life compared to usual audiological care and tinnitus retraining therapy, but there was no difference seen in depression and anxiety given the lack of long-term follow-up [6]. A randomized controlled trial (RCT) of internet-based versus in-person CBT for patients with distressing tinnitus found that both modalities were equally effective in reducing tinnitus-related distress measured with the TFI [9], although a meta-analysis of RCTs indicated that in-person CBT was more effective for tinnitus-related quality of life [7]. However, internet-based therapies may offer access to therapy for a larger subpopulation of tinnitus patients, especially in the era of the COVID pandemic. Other forms of psychotherapy have also demonstrated beneficial effects for tinnitus. For example, an RCT comparing the efficacy of mindfulness-based cognitive therapy (MBCT) and intensive relaxation therapy for chronic, distressing tinnitus found significantly greater reductions in self-reported tinnitus severity with MBCT, and persistent effects at 6 months of follow-up [10]. Improvement was observed in both tinnitus loudness and severity, along with improvements in psychological distress.

3. Hearing Aids

As the primary risk factor for tinnitus development is hearing loss, hearing aids are also recommended for chronic tinnitus [11]. This relationship however is not linear and many people with tinnitus have audiometrically normal hearing while many with severe hearing loss do not report tinnitus [19]. While hearing aids are recommended for patients with hearing loss and concurrent tinnitus in all guidelines [1][2][3], hearing aids for tinnitus alone is given a weak recommendation due to the lack of high-quality, robust data in the literature [3]. Several systemic reviews investigating the efficacy of hearing aids for tinnitus have found a lack of high-quality RCTs in the literature and noted equivocal results with a need for further studies [12][13].

4. Sound Therapy

Sound therapy aims to reduce the intensity of tinnitus by using an external sound to distract the listener [14]. This method is hypothesized to promote the habituation of tinnitus and stimulate the hypoactive neural auditory pathways impacted by hearing loss [15]. Therapy can be offered in the form of a device providing broadband low-level white noise or noise at the tinnitus frequency, or through a hearing aid to amplify external noise.

Numerous studies have investigated the efficacy of sound masking for managing tinnitus, although the results have been heterogenous. A Cochrane review investigating efficacy of the masking determined that there was weak evidence to show efficacy of sound therapy for tinnitus due to limited data and bias in the studies [16]. An RCT

assessing the impact of masking, retraining therapy, educational counseling with hearing aids, or waiting (no intervention) on the perception of tinnitus severity reported similar improvement in all three intervention groups at 6 and 18 months, but no improvement in patients who waited [17].

5. Eye-Movement Desensitization Reprocessing

EMDR is a form of conditioning psychotherapy traditionally used for post-traumatic stress disorder and more recently applied to tinnitus, with the most recent study published in 2018 [18]. EMDR is hypothesized to reduce tinnitus distress via desensitization and reprocessing of memories and images associated with negative perceptions of tinnitus [19]. As a newer form of therapy, few studies have investigated the efficacy of EMDR for the reduction of tinnitus-related distress, although initial reports have been positive [19][20][21]. Prospective trials on EMDR for chronic tinnitus have found clinically significant benefits on quality-of-life tinnitus surveys [19][20]. Further, an RCT comparing bimodal therapy with tinnitus retraining therapy plus EMDR or tinnitus retraining therapy plus CBT found that both treatment modalities resulted in equivalent reductions in tinnitus severity [21].

6. Cochlear Implantation

Cochlear implants are surgically implanted hearing prosthetics which electrically stimulate the auditory nerve and are therapeutic options for patients with moderate to severe hearing loss, with or without tinnitus, which has not improved with hearing aids. An estimated 68–86% of adult cochlear implant candidates also experience tinnitus [22][23]. Notably, numerous studies have reported secondary improvement or even resolution of tinnitus symptoms following cochlear implantation, ranging from 34 to 92% of implantees [24][25][26][27]. Systematic reviews and meta-analyses have similarly described the beneficial effects of cochlear implantation on both quality of life and tinnitus symptoms, with Levy et al. concluding that approximately 75% of implantees across 17 studies experienced improvement in tinnitus symptoms while 15% achieved complete resolution [28][29]. The exact therapeutic mechanism is unclear, but it has been hypothesized that increased afferent input to the auditory nerve from the implant may attenuate maladaptive neural activity and initiate neuroplastic reorganization of the central auditory pathways and associated brain areas [30]. This is supported by studies reporting gradual improvement in tinnitus symptoms over the course of several months post-implantation [22].

Interestingly, however, several studies have reported worsening of tinnitus severity in a subset of patients (<5%) following cochlear implantation [29][31]. Some cochlear implantation surgeries involve the creation of a cochleostomy for electrode insertion, and this trauma may damage remaining hair cells, potentially decreasing residual hearing and worsening tinnitus. However, modification of the surgical technique to a less traumatic round window approach to insert the electrode may reduce this trauma and associated risk [32]. For example, a prospective study by Kloostera et al. assessing the post-cochlear implantation outcomes of 44 patients (66% with preoperative tinnitus) who received either a cochleostomy or round window approach found that 75% who achieved tinnitus cessation received the round window approach versus cochleostomy [33]. Thus, it is possible that a round window approach

instead of a separate cochleostomy for electrode insertion may offer advantages for patients with preoperative tinnitus, although further prospective studies are needed.

Additionally, there is some evidence that the duration and chronicity of tinnitus prior to implantation impacts the likelihood of tinnitus cessation, perhaps due to entrenchment of maladaptive changes [33][34][35]. The abovementioned study by Kloostera et al. noted that the mean time from tinnitus onset was 32.2 years for patients who did not have cessation of tinnitus symptoms versus just 5.2 years for patients who achieved cessation [33]. Similarly, Miyamoto et al. observed that preoperative tinnitus duration of <20 years was significantly correlated with post-implantation improvement in tinnitus symptoms among 78 adult implantees [36]. While cochlear implantation remains a viable option for the treatment of tinnitus with accompanying hearing loss, there is a risk of worsening tinnitus, and thus should be used for patients who specifically want to improve their hearing ability.

7. Bimodal Neuromodulation

Bimodal neuromodulation, which pairs sound and electrical stimulation of peripheral nerves, is an emerging therapy for tinnitus. Bimodal neuromodulation is thought to drive plasticity and changes in the auditory pathway (midbrain, cortex, or brainstem) involved with tinnitus in several animal studies. Congruent with animal studies, clinical trials have also appeared promising for chronic tinnitus, with the Food and Drug Administration (FDA) granting de novo approval for the biomodulation wearable Lenire® in March of 2023. Lenire® is a Class IIa device delivering electrical stimulation to the tongue with an oral device and sound stimulation. In a randomized, blinded trial of 326 patients with chronic subjective tinnitus, the efficacy of Lenire® was tested in three separate groups with different stimulation settings. Over a 12-week period, all intervention groups had a statistically significant reduction in tinnitus symptom severity, with sustained therapeutic improvement seen at a 12-month follow-up. However, there were diminishing returns on the second 6 weeks of treatment, likely due to treatment habituation. In a follow-up clinical trial, there were enhanced therapeutic benefits in tinnitus symptom severity achieved by changing stimulation parameters during the second 6-week treatment period, overcoming treatment habituation. Bimodal stimulation appears promising for the treatment of chronic tinnitus, with the advantage of an FDA-approved at-home device for treatment. Further investigations will be needed to follow up long-term therapeutic benefit past 12 months, to delineate specific stimulation patterns among tinnitus populations, and to evaluate the effect of bimodal stimulation over a placebo in a real-world setting.

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