Review Research

TINNITUS: A COMPREHENSIVE REVIEW OF TREATMENT MODALITIES

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ABSTRACT

Tinnitus is caused by auditory dysfunction, and it affects about 10 -15% of the adult population. fortunately, in most cases, it is not dangerous however, in 20% of cases it can be life-disturbing especially with aging. Several types of therapies have been found to have a rule in the management of tinnitus including voice therapy, vagus nerve stimulation, hyperbaric oxygen therapy as well as a pharmacological intervention using several medications such as anesthetic, anticonvulsant, antidepressant anxiolytic, and antihistamine. The focus of treatment for tinnitus should include the annoyance associated with the tinnitus. Therefore, tinnitus retraining therapy (TRT) principle which includes meticulous diagnosis, educational counselling, and sound base therapy should be followed in all patients. The optimal results in the management of tinnitus can be achieved by proper counselling and patient education, in addition to providing an acoustic environment and the use of drugs that control some of the symptoms associated with tinnitus.

Keywords: tinnitus, tinnitus retraining therapy (TRT), anesthetic, acoustic environment

Introduction

Tinnitus refers to a sound that is not caused by an external sound source, this means that only a person with tinnitus can hear a sound in the ear that can be whistling or humming (Ziai et al., 2017). It is estimated that 10-15% of the population has tinnitus, but most do not treat it, this is due to a lack of knowledge and the fact that most people do not know who to turn to (McCormack et al., 2016). Some cases are mild, but some require more specific treatment to address potential long-term effects. These may include sleep and concentration disorders, stress, or social isolation (Ziai et al., 2017). Tinnitus is often described as ringing in the ears, but it can also occur as a buzzing, rattling, or whistling sound, or just general noise in the ears. The sound can always be the same or vary and can only affect one or both ears (Schlee et al., 2018). Millions of people find tinnitus distressing, but few are aware of the various methods that can help them manage tinnitus to reduce irritation (Phillips & McFerran, 2010; Hoekstra et al., 2011; Meng et al., 2011; Baldo et al., 2012; Bennett et al., 2012; Hobson et al., 2012; Hilton et al., 2013; Espinosa-Sánchez et al., 2014; Hoare et al., 2014; Person et al., 2016). Although there is no cure for tinnitus, there are several effective counseling and management techniques available.

The goal of sound therapy is to reduce awareness of tinnitus by providing the ears with sounds that actively mask and divert attention away from it (Roberts et al., 2013). Over time, the brain is trained to ignore tinnitus because a lack of attention allows the brain to classify it as irrelevant and confuse it with the background (Weisz et al., 2005). If a person has both tinnitus and hearing loss, using a hearing aid makes it easier to listen in general and helps reduce awareness of ringing in the ears (Cuny et al., 2004). According to Møller (2016), Phonak^{R} hearing aids also provide additional support for tinnitus by providing sounds that can be used in sound therapy. Stress and anxiety can make tinnitus worse, so they should be brought under control to prevent tinnitus from growing worse. Adequate night sleep, smoking cessation, and exercise are good for health, so they are helpful in the fight against tinnitus (Dawes, et al., 2020).

Impact of tinnitus

Certain types of tinnitus are associated with hearing loss caused by aging. With aging, the number of nerve fibers in the ears decreases, this can often cause hearing problems associated with tinnitus (Møller, 2016). Loud noise is one of the most common causes of tinnitus. If people have been exposed to loud music, the sounds of shots or explosions, or loud construction or garden machinery, they may have symptoms of tinnitus (Bennett et al., 2012; Hoare et al., 2014; McCormack et al., 2016). Sometimes blockages caused by ear wax can cause tinnitus (El-Shunnar et al., 2011). Certain medications can cause tinnitus (Scherer et al., 2019). In this case, tinnitus is a side effect rather than a disease. In addition, upper respiratory tract infections and jaw joint (TMJ) can induce tinnitus-like symptoms.

People are sometimes faced with situations where a patient says they have had tinnitus after starting a medication and would like to know that that medication may be the cause of the tinnitus (Seligmann et al., 1996). It is difficult to give such a clear and reasoned answer to this question. There can be numerous reasons why tinnitus has started. It usually results from a combination of several factors over a longer period (McFerran et al., 2019). Recent events, such as starting taking medication could be the initiation of the tinnitus, but on the other hand, it may have nothing to do with the onset of tinnitus (Seligmann et al., 1996). Nevertheless, some particular change in life, such as starting medication, is easily linked in thought to tinnitus that started at the same time (Salvi et al., 2021). However, tinnitus is quite a common ailment and also nowadays medications are used in great amounts. These together naturally increase their likelihood of occurring at the same time. Nevertheless, tinnitus is very rare compared to many other drug-induced side effects. However, they have been repeatedly reported, suggesting that tinnitus may be linked to the side effects of certain medications (Henry et al., 2014).

The Ototoxicity of certain drugs is the cause of tinnitus. Ototoxicity refers to damage to the inner ear due to ingestion of or exposure to certain drugs or chemicals (Henry et al., 2014; Salvi et al., 2021). It can lead to the destruction of sensory hair cells in the inner ear and thus cause hearing loss and tinnitus (Claussen, 1996). The damage and consequent hearing loss and tinnitus may be permanent or temporary, depending on the drug, its dose, and the length of the course. Such drugs include e.g. Aspirin, Quinine, non-steroidal anti-inflammatory drugs, certain antibiotics, cytostats, and diuretics (Claussen, 1996).

However, there are far more drugs that have not been shown to have an ototoxic effect in studies (Claussen, 1996; Henry et al., 2014; Salvi et al., 2021). Nevertheless, their association has been reported and has also been mentioned as a side effect of many such drugs. Such drugs include e.g. statins, antihypertensive, and antidepressants (Claussen, 1996). However, the causal link between these is unclear, but their effect cannot be completely ruled out either. It can be a complex and long-term combination of very many factors where the effect of the drug is either minor or significant (Langguth et al., 2019). The onset of tinnitus with medication can also be a mere coincidence. One significant factor may be that the disease itself is a major stressor that initiates and intensifies the body's stress response. The stress response is known to play a significant role in tinnitus and there are strong indications of its possible effect on the onset of tinnitus (Mazurek et al., 2015).

No medication prescribed by the doctor should be stopped or changed on people's own. The doctor should be informed if people suspect that the medicine has caused tinnitus. Under no circumstances should tinnitus be underestimated as a side effect, as tinnitus can have serious consequences (Kleinjung & Langguth, 2020). Primarily, it would be a good idea to find out if there is a connection between medication and tinnitus. This can be seen, for example, by taking a break from medication to find out its effect on tinnitus. The effect of changing the dose size should also be investigated. Medication can be critical to the illness, so taking a break is out of the question (Hall et al., 2019). People should try other similar medicines. However, it is especially important to weigh tinnitus as a side effect of the consequences of untreated disease (Kim et al., 2015).

Drug Therapy for Tinnitus

There are many causes of tinnitus ringing in the ear or humming. Up to half of the population has to experience transient tinnitus and up to half a million patients live chronically with the problem (Heller, 2003). Tinnitus can occur as a result of ear disease or noise injury, for example. It can start after dental treatment or as a side effect of some medications (Crummer & Hassan, 2004). There are numerous causes of tinnitus, so there are different treatments. Tinnitus can come from dizziness problems, for example. When a person tries to keep himself upright, the necks also stiffen and are in a bad position (Crummer & Hassan, 2004). The first and most cost-effective treatment is to try thus called post-dizziness treatment, which can also help with tinnitus. According to Crummer and Hassan (2004), tinnitus can also come as a result of ear disease. The cause may be, for example, inflammation. A common cause of tinnitus is also noise injury. Those exposed to loud noise, for example in an explosion accident, can be treated with hyperbaric oxygen therapy immediately after the accident. On the other hand, treating teeth, biting, and biting problems can also make tinnitus go away (Crummer & Hassan, 2004; Widen & Erlandsson, 2004).

Voice therapy

Voice therapy is one of the basic pillars of tinnitus treatment for all levels of tinnitus: in mild tinnitus, it is usually sufficient to avoid silence by enriching the sound environment and the knowledge that voice therapy can be controlled by covering up, i.e. masking, tinnitus whenever it feels disturbing (Arts et al., 2016). The goal of voice therapy in acute tinnitus is to help prevent subconsciously easily sensitized nerves and in chronic tinnitus to make the patient tolerate the tinnitus so that it no longer harms patients and thus causes no anxiety or fear and thus reduces the stress response it causes (Kochilas et al., 2020). Voice therapy for tinnitus consists of three parts. Enriching, masking, i.e. masking, and customized sound therapy for the sound environment. Enriching the sound environment means adding a muffled background noise if it is not naturally sufficient, such as indoors and especially in the evenings (Hobson et al., 2012; Hoare et al., 2014). The purpose is not to consciously listen to the sounds of the environment, but to allow them to unknowingly suppress tinnitus to the unheard status. This helps focus on other chores and makes it easier to fall asleep (Hobson et al., 2012). Suitable sound sources for enriching the sound environment include radio (music or noise), alarm clock, fan, refrigerator, humidifier, and other electrical devices that maintain a steady sound (Møller, 2016).

Masking means covering the tinnitus with an external sound source and is recommended whenever the tinnitus is disturbing. This avoids the intensification of tinnitus in the acute phase and the exacerbation of the resulting stress reaction and other symptoms. In chronic tinnitus, masking enrichment of the sound environment can make tinnitus unnoticeable, and thus habituation or habitation can take place more easily (Hobson et al., 2012). Chronic tinnitus does not aim to completely cover the tinnitus, but only partially and thus reduce the contrast. Natural water sounds such as a shower, a crackling rain, the roar of waves, a waterfall, and a fountain are best for covering (Ziai et al., 2017). People can also use music. Tailor-made sound therapy is sound material made individually based on the hearing and tinnitus profile, which is to be listened to according to the treatment schedule for 2-3 hours a day.

Because it is a learning process, it requires repetition and commitment to a long-term and daily treatment program to succeed. The sound material is best suited for music, but it can also be natural sounds such as rain sounds and other water noises, wind sounds, sea sounds, and the singing of birds. By the principles of music therapy, the sound should be pleasant, not overbearing, music, and even preferably pleasing music (Kronenberg et al., 1992; McCormack et al., 2016).

Vagus nerve stimulation (tVNS)

Vagal nerve stimulation is intended to affect the stress response caused by tinnitus. Through the electrode attached to the ear bundle, i.e. the tragus, the vagus stimulator device provides a slight electrical current that stimulates the small ear branch of the vagus nerve. It plays a key role in the function of the parasympathetic part of the autonomic nervous system. It regulates all the functions of the body. Stimulation of the vagus nerve thus stimulates the parasympathetic autonomic system and at the same time attenuates the sympathetic system and thereby the production of stress hormone secreted by the adrenal glands, and thus anxiety and fear do not dominate the mind (Schlee et al., 2018). Reducing stress relieves tinnitus because stress hormone-enhanced tinnitus decreases due to decreased bioelectrical activity. Vagus nerve stimulation also has a general sedative and relaxing effect, and side effects are very minor and not permanent.

Hyperbaric oxygen therapy (Hbot)

Hyperbaric oxygen therapy (Hbot) is often helpful in the acute phase of tinnitus if treatment is started less than six weeks after the onset of tinnitus. In acute tinnitus, we recommend hyperbaric oxygen therapy if the tinnitus does not show signs of attenuation within a week. Also in the case of long-lasting tinnitus, treatment comes into question if the tinnitus has worsened. In the treatment, the patient breathes 100% oxygen at an overpressure of 1.0 to 1.5 bar, which corresponds to a diving depth of 10 to 15 meters. The treatment increases the oxygen content of the inner ear fluids by about 500% and thereby provides the inner cells of the inner ear with optimal conditions for the spontaneous repair of damage (Bennett et al., 2012).

PHARMACOLOGICAL THERAPIES

Some drug therapies normally prescribed for tinnitus are not specific for tinnitus, drugs are used with the specific purpose of fighting the anxiety and depression resulting from the onset of tinnitus (Langguth et al., 2019; Kleinjung & Langguth, 2020). Among the drugs normally used:

1. **Vasoactive drugs** - These drugs work by increasing blood flow both systemically and locally (Acheson et al., 2009).
2. **Local anesthetics** – It causes motor paralysis and temporary sensory reversibly blocking the conduction of the nerve impulse. They can cause side effects on the central nervous system, such as convulsions, dizziness, nausea, drowsiness, tremors, and vision changes (Rosenberg et al., 1998).

3. **Melatonin**: Some controlled studies have evaluated the melatonin administration effects in patients with tinnitus. While no significant changes were found in the perception of tinnitus in treated subjects compared to placebo, it appears that melatonin can improve patients' sleep disturbance (McFerran & Phillips, 2007).

4. **Homeopathic medicines** - The homeopathic medicines used in patients with chronic tinnitus did not show greater efficacy of these medicines compared to placebo (Hoekstra et al., 2011).

5. **Anticonvulsants** – As tinnitus condition is often associated with the hyperactivity of the auditory system, anticonvulsants such as Carbamazepine, could be potentially used for tinnitus (Baldo et al., 2012). It is because anticonvulsants tend to enhance the activity of the GABA neurotransmitter to substantiate the inhibition of the central auditory system.

6. **Antidepressants –** Studies have demonstrated a high association between depression and tinnitus condition. Therefore, antidepressant drugs are used to relieve tinnitus-associated depression, anxiety, and stress. The use of nortriptyline, a TCA (tricyclic antidepressant), tends to reduce the tinnitus loudness, depression scores, and tinnitus disability scores among patients suffering from serious tinnitus conditions (Kim et al., 2021).

7. **Antihistamine –** Antihistamine drugs are used to treat significant factors contributing to the onset of tinnitus condition. As consistent physical pressure extending towards the cochlea often leads to tinnitus condition, antihistamine could reduce the tinnitus incidence by lowering the pressure in the tympanic cavity. Moreover, antihistamines tend to provide a drying effect to the auditory tubes, therefore, improving their function during tinnitus (Salvi et al., 2009; Jufas & Wood, 2015). Some common side effects of these drugs include anxiety, sedation, etc.

8. **Anxiolytics –** Anxiolytics such as Benzodiazepines (BDZs), tend to bind with the gamma-Aminobutyric acid (GABA) receptors while reinforcing its inhibition activity. Benzodiazepines tend to inhibit the tinnitus from extending toward the acoustic centers. Moreover, BDZs also promote sleeping while reducing the expression of anxiety associated with tinnitus (Salvi et al., 2009; Jufas & Wood, 2015). Some prominent side effects of BDZs include personality changes, sedation, memory failure, and drug dependence.

9. **Calcium channel blockers** – The development of tinnitus is often triggered due to the concentrations of calcium within or outside of the cochlear cells. However, some studies have also indicated the contradictory effects of some calcium channel blockers such as nimodipine, among patients suffering from tinnitus (Salvi et al., 2009; Jufas & Wood, 2015; Kim et al., 202).

SOUND ENRICHMENT THERAPY

On a physical and psychological level, music has a dual psychotherapeutic effect. Music evokes specific sensations and moods, it can trigger unconscious mechanisms, it can help to strengthen the ego, and it can act as a bridge between the conscious and unconscious, allowing the impulses and complexes that cause conflicts and neuro-psychic disorders to emerge at the conscious level, unblocking repressions and resistances through the cathartic tension-liberation process (36-40). The limbic cortex, which is connected to the orbitofrontal-mesial cortex, the septal nuclei, the amygdala, the hypothalamus, some nuclei of the mesoncephalus, and the pons, is the nerve pathway's fulcrum; the various sections of the limbic system are then connected (Hobson et al., 2012; Hoare et al., 2014; Arts et al., 2016; Kochilas et al., 2020).

As a result, listening to musical works with relaxing effects, limited variations, and very uniform tones is related to some relaxation activities. These tapes are recorded at a constant frequency that must match the frequency of the patient's tinnitus. The fundamental note or basic sound, which is comparable to tinnitus, blends with the melody to provide a welcome break from the monotony (Hobson et al., 2012; Hoare et al., 2014; Arts et al., 2016; Kochilas et al., 2020). In any event, great effort is taken to select tunes that are unrelated to memories or specific situations encountered in everyday life (works, famous songs, advertisements, soundtracks, etc.). Sound Therapy aids habituation by reducing the influence of tinnitus and neuronal activity in the auditory system, as well as the auditory system's connection to the limbic and autonomic systems. As a result, the intensity of the tinnitus and related activities decreases, making tinnitus habituation easier (Hobson et al., 2012; Hoare et al., 2014).

Conclusion

Medical examinations are appropriate if tinnitus develops rapidly, is associated with other symptoms such as dizziness or rapid hearing loss or is unilateral or fluctuates with the heart rate. Examination of a patient with tinnitus may also be appropriate to determine if the cause is a treatable disease, such as Meniere’s disease or otosclerosis. In addition to the tinnitus retraining therapy (TRT) treatment mentioned above, tinnitus can be treated with sound treatments that use noise or, for example, Natural Tones, to cover the tinnitus and refresh the auditory pathway. There is no reliable research evidence for drug treatments for tinnitus. For some, medication to improve blood circulation in the inner ear either by the direct effect of vasodilators that result from the relaxation of smooth muscle in the arteries e.g., nitrate, or through the blockage of some vasoconstriction pathways e.g., calcium and angiotensin. In Meniere's disease, a dehydration medication may still be helpful. In some cases, people with very disturbing tinnitus can be helped by treating side effects such as depression and insomnia.

Tinnitus is a phantom sensation that occurs when damage or dysfunction of a mussel causes hyperactivity of the auditory neural network, first in the auditory nuclei of the brainstem, then higher up in the auditory canal area. Almost everyone has tinnitus, most just don't notice it. If negative and frightening emotions are associated with tinnitus, the body's normal adaptation to tinnitus is prevented, the disruption of tinnitus is subconsciously intensified, and stress response may develop. Close connections of the auditory pathway to the limbic system can cause sleep disturbances, anxiety, and depression. All tinnitus patients should be treated according to TRT principles, and the target should be the patient, not the symptom. Treatment should focus on reducing the annoyance, not just eliminating the phenomenon. Therefore, proper teaching and counselling are a mainstay of tinnitus treatment, which should be combined with acoustic treatment, which is considered specific treatment, and possibly medical supportive treatment.

Conflicts of Interest

The author declares no conflicts of interest.

References

- Acheson, A., Rayment, S., Eames, T., Mundey, M., Nisar, P., Scholefield, J., & Wilson, V. G. (2009). Investigation of the role of adrenergic and non-nitrergic, non-adrenergic neurotransmission in the sheep isolated internal anal sphincter. Neurogastroenterology & Motility, 21(3), 335-345.
- Altissimi, G., Colizza, A., Cianfrone, G., de Vincentiis, M., Greco, A., Taurone, S., ... & Ralli, M. (2020). Drugs inducing hearing loss, tinnitus, dizziness, and vertigo: an updated guide. Eur Rev Med Pharmacol Sci, 24(15), 7946-7952.
- Arts, R. A., George, E. L., Griessner, A., Zierhofer, C., & Stokroos, R. J. (2016). Long-term effects of intracochlear electrical stimulation with looped patterns on tinnitus: A case study. Ear, Nose & Throat Journal, 95(4-5), E9-E29.
- Baldo, P., Doree, C., Molin, P., McFerran, D., & Cecco, S. (2012). Antidepressants for patients with tinnitus. Cochrane database of systematic reviews, (9). doi: 10.1002/14651858.CD003853.pub3
- Bennett, M. H., Kertesz, T., Perleth, M., Yeung, P., and Lehm, J. P. (2012). Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database Syst. Rev. 10:CD004739. doi: 10.1002/14651858.CD004739.pub4
- Cederroth, C. R., Dyhrfjeld-Johnsen, J., & Langguth, B. (2018). An update: emerging drugs for tinnitus. Expert opinion on emerging drugs, 23(4), 251-260.
- Claussen, C. F. (1996). Chemically induced or drug induced tinnitus. Int Tinn J, 2(1), 1-2.
- Crummer, R. W., & Hassan, G. (2004). Diagnostic approach to tinnitus. American family physician, 69(1), 120-126.
- Cuny, C., Norena, A., El Massioui, F., & Chéry-Croze, S. (2004). Reduced attention shift in response to auditory changes in subjects with tinnitus. Audiology and Neurotology, 9(5), 294-302.
- Dawes, P., Newall, J., Stockdale, D., & Baguley, D. M. (2020). Natural history of tinnitus in adults: a cross-sectional and longitudinal analysis. BMJ open, 10(12), e041290.
- El-Shunnar, S. K., Hoare, D. J., Smith, S., Gander, P. E., Kang, S., Fackrell, K., & Hall, D. A.

(2011). Primary care for tinnitus: practice and opinion among GPs in England. Journal of Evaluation in Clinical Practice, 17(4), 684-692.

- Espinosa-Sánchez, J. M., Heitzmann-Hernández, T., and López-Escámez, J. A. (2014). Pharmacotherapy for tinnitus: much ado about nothing. Rev. Neurol. 59, 164–174.
- Hall, D. A., Hibbert, A., Smith, H., Haider, H. F., Londero, A., Mazurek, B., ... & Core Outcome Measures in Tinnitus (COMiT) initiative. (2019). One size does not fit all: developing common standards for outcomes in early-phase clinical trials of sound-, psychology-, and pharmacology-based interventions for chronic subjective tinnitus in adults. Trends in Hearing, 23, 2331216518824827.
- Heller, A. J. (2003). Classification and epidemiology of tinnitus. Otolaryngologic Clinics of North America, 36(2), 239-248.
- Henry, J. A., Roberts, L. E., Caspary, D. M., Theodoroff, S. M., & Salvi, R. J. (2014). Underlying mechanisms of tinnitus: review and clinical implications. Journal of the American Academy of Audiology, 25(01), 005-022.
- Hilton, M. P., Zimmermann, E. F., and Hunt, W. T. (2013). Ginkgo biloba for tinnitus. Cochrane Database Syst. Rev. 28:CD003852. doi: 10.1002/14651858.CD003852.pub3
- Hoare, D. J., Edmondson-Jones, M., Sereda, M., Akeroyd, M. A., and Hall, D. (2014). Amplification with hearing aids for patients with tinnitus and co-existing hearing loss. Cochrane Database Syst. Rev. 31:CD010151. doi: 10.1002/14651858.CD010151.pub2
- Hoare, D. J., Searchfield, G. D., El Refaie, A., & Henry, J. A. (2014). Sound therapy for tinnitus management: practicable options. Journal of the American Academy of Audiology, 25(01), 062-075.
- Hobson, J., Chisholm, E., & El Refaie, A. (2012). Sound therapy (masking) in the management of tinnitus in adults. Cochrane Database of Systematic Reviews, (11). doi: 10.1002/14651858.CD006371.pub3
- Hoekstra, C. E., Rynja, S. P., van Zanten, G. A., & Rovers, M. M. (2011). Anticonvulsants for tinnitus. Cochrane Database of Systematic Reviews, (7). doi: 10.1002/14651858.CD007960.pub2
- Jufas, N. E., & Wood, R. (2015). The use of benzodiazepines for tinnitus: systematic review. The Journal of Laryngology & Otology, 129(S3), S14-S22. doi:10.1017/S0022215115000808
- Kim, H. J., Lee, H. J., An, S. Y., Sim, S., Park, B., Kim, S. W., ... & Choi, H. G. (2015). Analysis of the prevalence and associated risk factors of tinnitus in adults. PloS one, 10(5), e0127578.
- Kim, S. H., Kim, D., Lee, J. M., Lee, S. K., Kang, H. J., & Yeo, S. G. (2021). Review of pharmacotherapy for tinnitus. In Healthcare 9, (6), 779.
- Kleinjung, T., & Langguth, B. (2020). Avenue for future tinnitus treatments. Otolaryngologic Clinics of North America, 53(4), 667-683.
- Kochilas, H. L., Cacace, A. T., Arnold, A., Seidman, M. D., & Tarver, W. B. (2020). Vagus nerve stimulation paired with tones for tinnitus suppression: Effects on voice and hearing. Laryngoscope Investigative Otolaryngology, 5(2), 286-296.
- Kronenberg, J., Almagor, M., Bendet, E., & Kushnir, D. (1992). Vasoactive therapy versus placebo in the treatment of sudden hearing loss: A double-blind clinical study. The Laryngoscope, 102(1), 65-68.
- Langguth, B., Elgoyhen, A. B., & Cederroth, C. R. (2019). Therapeutic approaches to the treatment of tinnitus. Annual review of pharmacology and toxicology, 59, 291-313.
- Mazurek, B., Szczepek, A. J., & Hebert, S. (2015). Stress and tinnitus. Hno, 63(4), 258-265. doi: 10.1007/s00106-014-2973-7
- McCormack, A., Edmondson-Jones, M., Somerset, S., and Hall, D. (2016). A systematic review of the reporting of tinnitus prevalence and severity. Hear. Res. 337, 70–79. doi:

10.1016/j.heares.2016.05.009

- McFerran DJ, Phillips JS. (2007). Tinnitus. The Journal of Laryngology & Otology. 121(3):201-8.
- McFerran, D. J., Stockdale, D., Holme, R., Large, C. H., & Baguley, D. M. (2019). Why is there no cure for tinnitus? Frontiers in neuroscience, 13, 802.
- Meng, Z., Liu, S., Zheng, Y., and Phillips, J. S. (2011). Repetitive transcranial magnetic stimulation for tinnitus. Cochrane Database Syst. Rev. 5:CD007946. doi: 10.1002/14651858.CD007946.pub2
- Møller, A. R. (2016). Sensorineural tinnitus: its pathology and probable therapies. International journal of otolaryngology, 2016.
- Person, O. C., Puga, M. E., da Silva, E. M., and Torloni, M. R. (2016). Zinc supplementation for tinnitus. Cochrane Database Syst. Rev. 11:CD009832. doi: 10.1002/14651858.CD009832.pub2
- Phillips, J. S., and McFerran, D. (2010). Tinnitus retraining therapy (TRT) for tinnitus. Cochrane Database Syst. Rev. 17:CD007330. doi: 10.1002/14651858.CD007330.pub2
- Roberts, L. E., Husain, F. T., & Eggermont, J. J. (2013). Role of attention in the generation and modulation of tinnitus. Neuroscience & Biobehavioral Reviews, 37(8), 1754-1773.
- Rosenberg, S. I., Silverstein, H., Rowan, P. T., & Olds, M. J. (1998). Effect of melatonin on tinnitus. The Laryngoscope, 108(3), 305-310.
- Salvi, R., Lobarinas, E., & Sun, W. (2009). Pharmacological treatments for tinnitus: new and old. Drugs of the Future, 34(5), 381.
- Salvi, R., Radziwon, K., Manohar, S., Auerbach, B., Ding, D., Liu, X., ... & Chen, G. D. (2021). Neural mechanisms of tinnitus and hyperacusis in acute drug-induced ototoxicity. American journal of audiology, 30(3S), 901-915.
- Scherer, R. W., Formby, C., & Tinnitus Retraining Therapy Trial Research Group. (2019). Effect of tinnitus retraining therapy vs standard of care on tinnitus-related quality of life: a randomized clinical trial. JAMA Otolaryngology–Head & Neck Surgery, 145(7), 597-608.
- Schlee, W., Hall, D. A., Canlon, B., Cima, R. F., de Kleine, E., Hauck, F., ... & Cederroth, C. R. (2018). Innovations in doctoral training and research on tinnitus: The European School on Interdisciplinary Tinnitus Research (ESIT) Perspective. Frontiers in aging neuroscience, 9, 447.
- Seligmann, H., Podoshin, L., Ben-David, J., Fradis, M., & Goldsher, M. (1996). Drug-induced tinnitus and other hearing disorders. Drug Safety, 14(3), 198-212.
- Weisz, N., Moratti, S., Meinzer, M., Dohrmann, K., & Elbert, T. (2005). Tinnitus perception and distress is related to abnormal spontaneous brain activity as measured by magnetoencephalography. PLoS medicine, 2(6), e153.
- Widen, S. O., & Erlandsson, S. I. (2004). Self-reported tinnitus and noise sensitivity among adolescents in Sweden. Noise and health, 7(25), 29.
- Ziai, K., Moshtaghi, O., Mahboubi, H., & Djalilian, H. R. (2017). Tinnitus patients suffering from anxiety and depression: a review. The International Tinnitus Journal, 21(1), 68-73.