Chapter 7

Theories on the Pathophysiology of Tinnitus

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Introduction

The literature has not yet reached a consensus on the pathophysiology of tinnitus. However, it is generally believed that the pathophysiology of tinnitus is related to functional changes in the peripheral or central auditory system. The auditory system is a complex structure involving many nuclei with afferent and efferent pathways. Due to this complex structure, there are many theories related to the pathophysiology of tinnitus. While some of these theories are related to inner ear damage in individuals, others are related to the influence of other sensory neuron networks on the auditory system. On the other hand, there are theories that bring all these theories together under a single roof and relate them to higher centers in the brain. The aim of this review article is to summarize the theories on the pathophysiology of tinnitus, a symptom that is frequently seen in clinics, and to contribute to the theoretical background of clinicians regarding the cause and effect relationship, which plays an important role in the treatment of tinnitus.

Discordance Theory

In case of hearing loss in individuals, depending on the severity of hearing loss, only the outer hair cells or both inner and outer hair cells can be damaged together. According to studies, after approximately 50 dB HL, losses in the inner hair cells are observed much more, while outer hair cells are damaged much more than inner hair cells up to 50 dB HL (Dallos et al., 1978; Salvi et al., 2018). If the configuration of hearing loss in the audiogram shown in Figure 1 is considered, in the frequency range where hearing loss begins (2000 Hz), the outer hair cells are mostly damaged while the inner hair cells are damaged much less than the outer hair cells. According to Jastreboff, in this case, at 2000 Hz, discordant activity is generated between afferent

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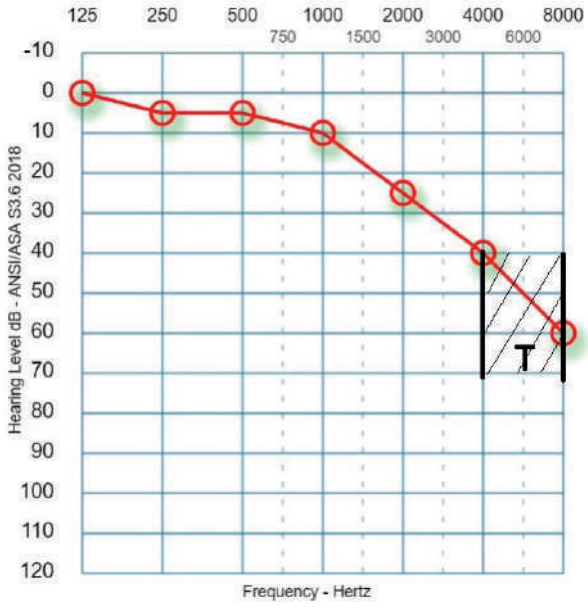
https://doi.org/10.58830/ozgur.pub125.c651

Type 1 nerve fibrils synapsing with inner hair cells and efferent Type 2 nerve fibrils synapsing with outer hair cells. However, the frequency range in which this discordant activity is maximal is not 2000 Hz. As can be seen in the audiogram shown in Figure 1, hearing loss continues to increase towards higher frequencies. When approximately 50 dB HL hearing loss is reached, the efferent activity in the system is minimized by the loss of Type 2 nerve fibrils as a result of damage to almost all of the outer hair cells, while the afferent activity will continue at a level close to normal with the continued existence of Type 1 nerve fibrils as a result of the intactness of almost all of the inner hair cells. Therefore, the mismatch between nerve fibrils will be maximized at a hearing loss level of approximately 50 dB HL, and the level of spontaneous activity in the frequency range where this hearing loss level is reached will be higher than in other frequency ranges. Finally, tinnitus perception will occur in the frequency range where the hearing loss reaches this level (Jastreboff, 2004). Therefore, considering the audiogram in Figure 1, if it is thought that the hearing loss level of approximately 50 dB is reached in the 6 kHz region, tinnitus would be expected to occur at this frequency or in a frequency range close to this frequency according to the mismatch theory (Jastreboff, 1990, 1995). The hatched area in Figure 1 shows the frequency range in which tinnitus perception is likely to occur according to the discordance theory (frequency ranges with hearing loss at approximately 50 dB HL).

Figure 1. The example of the audiogram.



Change in Spontaneous Activity

There is a continuous activity in the auditory nerve without any auditory stimulus. This activity is defined as spontaneous activity in many experimental studies. In studies trying to explain the pathophysiological theorem of tinnitus, it has been observed that spontaneous activity increases in the auditory system, especially in areas such as the dorsal cochlear nucleus, ventral cochlear nucleus and inferior colliculus when hearing loss is artificially induced (such as noise exposure, salicylate use). (Roberts et al., 2010). Homeostasis has been proposed as the primary cause of the mechanism of increased spontaneous activity in the central auditory system after hearing loss (Roberts et al., 2010). This mechanism aims to maintain balance within the system. The decrease in peripheral input in the first steps of the central auditory system due to hearing loss resulting from damage to the cochlea has to be compensated according to this mechanism. As a result of this compensation mechanism, there is an increase in activity in anatomical regions after the cochlea in the auditory system (Norena, 2011). It is thought that tinnitus occurs with this increase in spontaneous activity. In fact, studies have shown that the increase in spontaneous activity is not only limited to the auditory system but also causes an increase in neural activity in the limbic system, which provides mood control of individuals (Wallhäusser-Franke & Langner, 1999). Thus, it has been suggested that tinnitus occurs with the increase in spontaneous activity in the auditory system, and with the increase in neural activity in the limbic system, the person may develop negative thoughts against tinnitus by having difficulty in controlling his/her emotional state.

Maladaptive Synchronization

Another theory argued that spontaneous activity increase alone is insufficient to create tinnitus perception, and that this increased activity must create synchronization in the auditory system for tinnitus perception to occur (Roberts et al., 2010). Eggermont et al. suggested that in order for spontaneous activity to become synchronized, the spontaneous activity in question must both increase unusually and systematically maladaptive reorganization must begin with hearing loss. In the absence of one of these two factors, tinnitus perception cannot occur (Eggermont, 2006).

Somatic Modulation

It has been observed that some individuals with tinnitus perceive their tinnitus differently when performing somatic tasks, such as clenching their jaws or stimulating their skin (Cacace, 1999; Lockwood et al., 1998).

Levine investigated this phenomenon by requesting a series of head and neck movements from tinnitus patients presenting to his clinic. At the conclusion of his study, he found that 68% of these patients experienced a change in tinnitus intensity or frequency perception as a result of head or neck movement. This was also found to be more prevalent in patients with unilateral tinnitus. Some patients were also asked to perform limb movements, but these movements did not affect tinnitus in the same way that head and neck movements did. These results suggest that somatic inputs may influence the activity of the ipsilateral dorsal cochlear nucleus by activating the medullary somatosensory nucleus. It is believed that this relationship between the medullary somatosensory nucleus and the dorsal cochlear nucleus is crucial for altering sound localization in cats with ear movements (Nelken & Young, 1996). Despite the fact that studies on this relationship in humans have focused more on the trigeminal nerve, there is not yet as much evidence as there is in cats. The fact that somatic inputs can modulate tinnitus increases the likelihood that this will be used in the future to treat tinnitus.

Ephaptic interaction

Ephaptic interaction occurs when an excitable cell membrane comes into contact with and stimulates an unexcited cell membrane. Under normal circumstances, impulses are transmitted along the fibers of the auditory nerve without stimulating neighboring fibers. However, in some cases, this isolation is broken and impulses spread beyond the nerve fibers involved and begin to affect neighboring nerve fibers. This phenomenon has been linked specifically to hemifacial spasms and trigeminal neuralgia. It has been proposed that facial and trigeminal nerve compression by blood vessels is the cause of these pathologies (Møsller, 1984). It has been shown that by separating these nerve-compressing vessels from the nerves, the symptoms can be managed. It was hypothesized that this would also apply to the eighth cranial nerve, and that pressure from blood vessels or tumors like vestibular schwannomas would increase neural activity, resulting in tinnitus (Møsller, 1984). Eggermont also proposed that a space-occupying lesion, such as a vestibular schwannoma, could disrupt the auditory nerve's myelin layer, affecting neuronal activity and resulting in tinnitus (Eggermont, 1990). This hypothesis, however, is believed to be valid only for certain pathologies and can't be generalized to all tinnitus patients.

Neurophysiological Theory

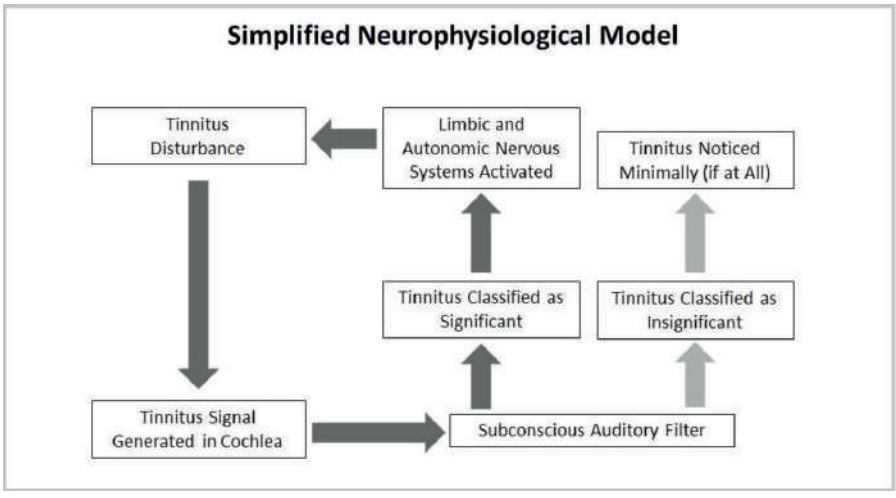
According to this theory, tinnitus may be caused by non-auditory pathways in the brain, such as the limbic system, autonomic nervous system

(Jastreboff et al., 1996). The tinnitus etiology can be related to many things such as hearing loss, cervical problems, cardiovascular problems. But the effect of these problems is mostly observed at the brainstem level (Rauschecker et al., 2010). Tinnitus is observed in many people as a result of these factors; however, in some people, tinnitus is very disturbing, whereas in others, tinnitus is not perceived as a bothersome symptom. It has been proposed that this difference cannot be explained solely by changes in brainstem activity, but that cortical areas may also be involved (Rauschecker et al., 2010).

Even in the absence of any external auditory stimulus, there is a continuous activity in the auditory nerve. The auditory system turns this activity into perception, which is especially noticeable in quiet environments. Individuals frequently refer to this activity's perceptual dimension as the sound of silence. This sound is normally filtered by the limbic system (particularly the amygdala and medial geniculate body), and many people do not notice it unless they pay attention to it (Jastreboff et al., 1996).

Considering that tinnitus is a sensory perception caused by changes in activity, particularly in the brainstem, the factor that causes this perception to be classified as disturbing by some people and as insignificant by others is the limbic system's filtering mechanism, according to neurophysiological theory. According to this theory, the most important reason why tinnitus perception reaches disturbing dimensions and individuals seek treatment for tinnitus is that the limbic system's filtering mechanism does not function normally (Jastreboff et al., 1996). The basis of the neurophysiological model is shown in Figure 2.

Figure 2 ***The simplified of the neurophysiological model (Benton, 2015)***



Conclusion

In this paper, we reviewed both previous and recent pathophysiological theories associated with tinnitus. However, it is essential to keep in mind that the research on tinnitus has uncovered a wide variety of potential causes of the etiology. Considering that each etiology has a unique mechanism to generate tinnitus, there are numerous unresolved issues regarding the pathophysiology of tinnitus. The theories are still being questioned and new pathophysiological mechanisms are being looked for out through research.

Benton, S. L. (2015). Steven L. Benton, Au.D.

Cacace, A. (1999). Delineating tinnitus-related activity in the nervous system: Application of functional imaging at the fin de siècle. Sixth International Tinnitus Seminar,

Dallos, P., Harris, D., Özdamar, Ö., & Ryan, A. (1978). Behavioral, compound action potential, and single unit thresholds: relationship in normal and abnormal ears. *The Journal of the Acoustical Society of America*, *64*(1), 151-157.

Eggermont, J. (2006). Cortical tonotopic map reorganization and its implications for treatment of tinnitus. *Acta Oto-Laryngologica*, *126*(sup556), 9-12.

Eggermont, J. J. (1990). On the pathophysiology of tinnitus; a review and a peripheral model. *Hearing research*, *48*(1-2), 111-123.

Jastreboff, P. J. (1990). Phantom auditory perception (tinnitus): mechanisms of generation and perception. *Neuroscience research*, *8*(4), 221-254.

JASTREBOFF, P. J. (1995). Tinnitus as a phantom perception theories and clinical implications. *Mechanisms of tinnitus*.

Jastreboff, P. J. (2004). The neurophysiological model of tinnitus. *Tinnitus: Theory and management*, 96-107.

Jastreboff, P. J., Gray, W. C., & Gold, S. L. (1996). Neurophysiological approach to tinnitus patients. *American Journal of Otology*, *17*(2), 236-240.

Lockwood, A. H., Salvi, R., Coad, M., Towsley, M., Wack, D., & Murphy, B. (1998). The functional neuroanatomy of tinnitus: evidence for limbic system links and neural plasticity. *Neurology*, *50*(1), 114-120.

Møsller, A. R. (1984). Pathophysiology of tinnitus. *Annals of Otology, Rhinology & Laryngology*, *93*(1), 39-44.

Nelken, I., & Young, E. D. (1996). Why do cats need a dorsal cochlear nucleus? *Journal of basic and clinical physiology and pharmacology*, *7*(3), 199-220.

Norena, A. J. (2011). An integrative model of tinnitus based on a central gain controlling neural sensitivity. *Neuroscience & Biobehavioral Reviews*, *35*(5), 1089-1109.

Rauschecker, J. P., Leaver, A. M., & Mühlau, M. (2010). Tuning out the noise: limbic-auditory interactions in tinnitus. *Neuron*, *66*(6), 819-826.

Roberts, L. E., Eggermont, J. J., Caspary, D. M., Shore, S. E., Melcher, J. R., & Kaltenbach, J. A. (2010). Ringing ears: the neuroscience of tinnitus. *Journal of Neuroscience*, *30*(45), 14972-14979.

Salvi, R., Ding, D., Jiang, H., Chen, G.-D., Greco, A., Manohar, S., Sun, W., & Ralli, M. (2018). Hidden age-related hearing loss and hearing disorders: current knowledge and future directions. *Hearing, balance and communication*, *16*(2), 74-82.

Wallhäusser-Franke, E., & Langner, G. (1999). Central activation patterns after experimental tinnitus induction in an animal model. Proceedings of the sixth international tinnitus seminar. London: The Tinnitus and Hyperacusis Centre,