Chapter 36
Cochlear and Non-cochlear Age-Related Hearing Loss and Tinnitus

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Keypoints

1. Age-related changes are some of the most common causes of disorders of sensory systems.
2. The most common age-related change in hearing is elevation of the hearing threshold beginning at the highest audible frequencies, progressing toward lower frequencies while deepening.
3. Age-related changes in hearing are often, but not always, accompanied by tinnitus.
4. Age-related changes in hearing function may be caused by:

    (a) Degeneration of sensory receptor cells, in the cochlea
    (b) Change in the conduction velocity of sensory nerve fibers
    (c) Change in the access to neural transmitters, such as gamma amino butyric acid (GABA), and subsequent increases in GABA receptor sites

5. Change in processing of information may also occur, causing deterioration of speech comprehension.
6. Animal studies have shown that the progression of age-related changes in hearing might be affected (slowed down) by exposure to sound ("enhanced sound environment") indicating expression of neural plasticity plays a role in some age-related changes of sensory functions.
7. The large individual variability in age-related changes in hearing has many causes, such as exposure to loud sounds, environmental factors, genetics, different expression of genes (epigenetics), and unknown factors.

Keywords Presbycusis • Age-related hearing loss • Tinnitus • Neural plasticity

Abbreviations

ARHI   Age-related hearing impairment
EPSP   Excitatory postsynaptic potentials
GABA   Gamma amino butyric acid

Introduction

Age-related impairment of hearing (presbycusis[1]) is the most common disorder of the auditory system. The most obvious changes in hearing that occur with increasing age are an elevated hearing threshold for high frequencies. Presbycusis normally refers to the elevation of hearing threshold. In addition, the elevation of hearing threshold and impaired processing of sound, known as phonemic regression[2] may occur. Many individuals acquire tinnitus in old age, and it often accompanies presbycusis. However, it may also occur together with minimal hearing loss. Most elderly people have tinnitus when placed in a silent room, such as a room used for audiologic tests.

[1]Presbycusis: Loss of hearing associated with aging; manifest as reduced ability to perceive or discriminate sounds; the pattern and age of onset vary (Stedman's Electronic Medical Dictionary).

[2]Phonemic regression: a decrease in intelligibility of speech out of proportion to the pure tone hearing loss associated with aging (Stedman's Electronic Medical Dictionary).

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Epidemiology of Presbycusis

Normally, hearing loss increases gradually with age, as shown in many studies. Spoor et al. [1] have reviewed the literature and presented average audiograms for different age groups from eight different population studies based on a total of 7,617 ears – including both men and women (Fig. 36.1). This classical study of age-related hearing loss included the effect of environmental factors, such as noise exposure, and did not show the individual variations.

There is a distinct difference between hearing loss in men and women (Fig. 36.1), but that may be at least partly a result of different degrees of noise-induced hearing loss. It has been preferentially men who were working in industries with heavy noise exposure. This effect of noise exposure is particularly prominent with participants in the older studies, such as those summarized by Spoor with the hearing loss depicted in Fig. 36.1. Some of the individual variations in presbycusis may thus be attributed to environmental factors, mainly the varying degree of exposure to sounds.

Large individual variations were mentioned in several studies. One study [2] quantified these variations (Fig. 36.2). This study showed the individual variations in hearing loss and in speech discrimination. Also, this study included individuals who have had exposure to noise that caused hearing loss, affecting mostly men.

It seems likely that genetic factors also play a role. In fact, a gene that affects age-related hearing loss has been identified in a mice strain [3]. There are many genetic disorders that affect hearing in general [4], but not specifically regarding the deterioration of hearing with age. A study that specifically addressed genetic predisposition for age-related hearing loss [5] found that approximately half of the variance of Age-Related Hearing Impairment (ARHI) is attributable to environmental risk factors. The other half is linked to genetic factors.

Gates and co-authors [6] described the results of a large population study (Farmingham). Hearing sensitivity and word recognition tests in 1662 men and women between the age of 60 and 90 showed that the pure-tone thresholds increased with age at a rate that did not differ by gender. However, men had poorer hearing threshold in general. This means the result of noise exposure had its full effect on hearing thresholds before a person reaches the age of 60 , which is the age at which this population study began. Maximum word recognition ability declined with age more rapidly in men than in women and was also poorer in men than women at younger ages.

One more recent study [7] found that the hearing threshold increased approximately 1 dB per year in individuals of 60 years and above. Females of 70 years and above had a faster rate of change in hearing threshold at 0.25 to 3, 10, and 11 kHz than females in the age group of 60–69 years.

Other authors [8] found a true gender difference in hearing threshold, including a difference in older individuals where women have less age-related hearing loss. Jerger et al. also referred to the hypothesis about
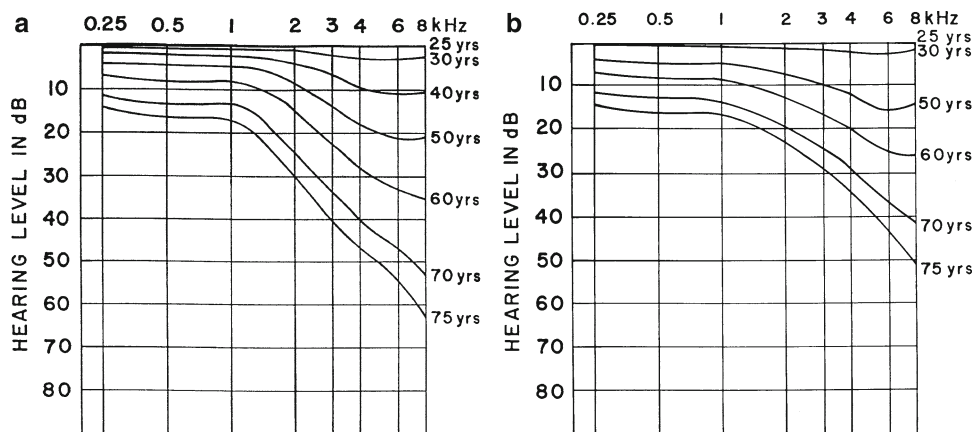

Fig. 36.1 (**a**) Average hearing loss in different age groups of men. Combined results from eight different published studies based on a total of 7,617 ears. (**b**) Average hearing loss in different age groups of women. Results from eight different published studies based on 5,990 ears. Reprinted from Møller AR (2006) Neural plasticity and disorders of the nervous system [1] with permission
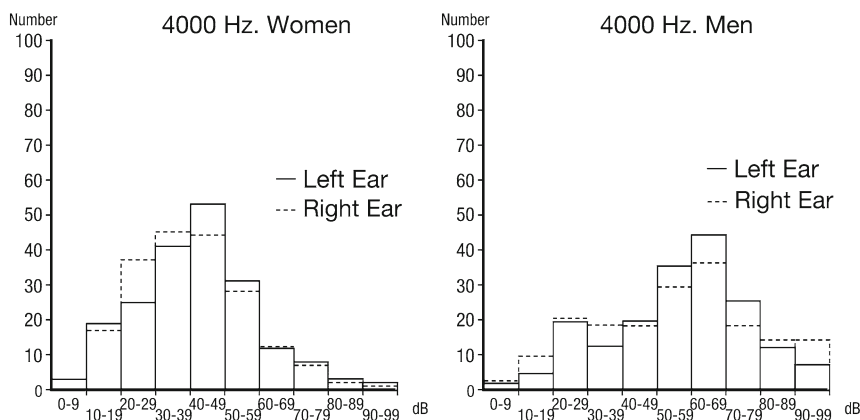
Fig. 36.2 Distribution of hearing loss at different frequencies from a cross-sectional population study of hearing in people of age 70; for women (*left* column) and men (*right* column). Solid lines represent left ear and dashed lines represent right ear. Data from Møller [2]

cardiovascular diseases promoting hearing loss [8], or perhaps, the same genetic factors that promote development of cardiovascular disorders also promote hearing loss. For example, animals studies of rats with predisposition for hypertension also acquire more age related hearing loss and more hearing loss from noise exposure [9, 10]. Other animal experiments have shown the progression of the age-related elevation of the hearing threshold can be arrested by appropriate sound stimulation [11].

Epidemiology of Age-Related Tinnitus

Tinnitus almost always occurs together with hearing loss (see Chaps. 35 and 37). Tinnitus is one of the three symptoms that define Ménière's disease (see Chaps. 38 and 60). Tinnitus is also often associated with presbycusis, but different studies of the prevalence of tinnitus have arrived at different results. The reported concomitant presence of tinnitus varies between 8 and 72% [12–14]. The risk for the development of tinnitus rises with increasing age and with increasing noise exposure [15]. In the age group of 55–65 years, one study found that tinnitus occurred in 19.3% or 11.8%, depending on the questions asked in such studies [16]. Other studies have found very varying incidences of tinnitus together with age-related hearing loss [13, 14], but it is generally agreed that the incidence of tinnitus increases with age [15].

Tinnitus is related not only to the size of the hearing loss but also to the shape of the audiogram, being more common in individuals with a high-frequency, steeply sloping audiogram than in individuals with a flat audiogram [16].

Tinnitus cannot be measured in a similar way as in the case of hearing loss. The evaluation depends on the individual's own assessments of the severity of his or her tinnitus. This adds uncertainties to epidemiologic studies of the prevalence of tinnitus and is the main cause of the differences reported by different authors.

Most people above the age of 60 have experienced some form of tinnitus, but these epidemiologic studies have only included individuals with tinnitus of a certain severity. Some of the causes of variations between the studies of individual investigators are diverse definitions of the different degrees of tinnitus, such as "bothersome tinnitus." Most epidemiologic studies are performed using written questionnaires. The outcome of such epidemiological studies is affected not only by the definitions used for the level of severity, but also in the way the questions are phrased about the participant's perception of his or her tinnitus.

The use of common medications that are associated with tinnitus such as certain diuretics increases with age [17] and this may count for some of the observed age-related increase in the incidence of tinnitus.

As is the case for presbycusis, environmental factors such as noise exposure, exposure to chemicals, and other environmental factors, thus similar reasons for causing more hearing loss in men than women, influence the occurrence of tinnitus. This was confirmed by the findings that tinnitus is more common in males than in females [16].

Pathology of Presbycusis

Many studies have shown that hair cells, especially outer hair cells, are injured in individuals with presbycusis [18] and that these injuries correspond to the hearing loss, as it is reflected in a person's audiogram.

The hearing loss, as it is described by the pure tone audiogram, has been attributed to impairment or loss of cochlear hair cells – mostly affecting outer hair cells. Outer hair cells function to amplify the basilar membrane vibration (act as motors), but the outer hair cells probably do not participate in the signal transduction; that is done by inner hair cells [19] (see Chap. 8). The fact that the morphological changes in the cochlea are so apparent has made investigators and clinicians focus on this aspect of aging in hearing. More recent studies have shown evidence that hair cell damage is not the only cause of presbycusis.

Although morphologic changes in the cochlea of individuals with presbycusis are convincing, it is not the only reason for presbycusis. Other changes in the auditory system that occur normally with age also contribute to the loss of hearing. The abundant efferent innervation of especially outer hair cells makes it possible for the function of outer hair cells to be modulated by signals from the central nervous system (see Chap. 8). Plastic changes that affect the auditory nervous system may thereby affect the transduction process in the cochlea by changing the amplification in the cochlear amplifier. This means that the pathology causing hearing to deteriorate with age is located not only in the cochlea but also in the CNS.

The nervous system is involved in noise-induced hearing loss, as confirmed by the finding that noise-induced hearing loss can be reduced by pre-exposure to moderately strong sounds [20, 21].

It is difficult to distinguish between the deterioration of the hearing from noise exposure from that caused by age-related factors, although the shape of the audiogram of age-related hearing is different from the common noise-induced hearing loss (Chap. 37). The age-related hearing loss is greatest at high frequencies, whereas noise-induced hearing loss is, as a rule, greatest around 4 kHz [19].

The complexity of presbycusis is supported by the results of animal studies where different kinds of rats' hearing loss during their lifetime were studied while the rats were housed under different conditions; with and without noise exposure.

In this study, three groups of rats were exposed to 85 dB, 105 dB, and no noise for 8 h every day during their lifetime [9]. Each group of rats consisted of normotensive and spontaneous hypertensive[3] rats. The hearing loss from noise exposure in the 85 dB group was minimal when compared with those that, were not exposed to noise. The animals in the group that were exposed to 105 dB noise acquired considerable hearing loss. However, it was different for normotensive rats compared with spontaneous hypertensive rats, acquiring an average hearing loss of 30 dB and 60 dB, respectively [22]. The larger hearing loss from exposure to noise in the spontaneous hypertensive rats did not seem to be caused by the elevated blood pressure as such because hypertension induced by ligation of a kidney artery in normotensive rats did not cause larger noise-induced hearing loss [23]. Ligation of one kidney artery caused similar elevation of blood pressure as observed with age in the spontaneous hypertensive rats.

The results of these studies points to a genetic cause of the larger age-related hearing loss in spontaneous hypertensive rats when compared with that of normotensive rates. The genetic cause of hypertension also resulted in greater noise-induced hearing loss in spontaneously hypertensive rats rather than the effect of the high blood pressure as such. These animal studies have thus supported the hypothesis that genetic predisposition for hypertension also promotes hearing loss. The genetic abnormality of spontaneous hypertensive rats also predisposed the rats for acquiring larger than normal elevation of hearing threshold with age. That one genetic abnormality or risk factor can predispose, for more than one pathologic sign is not uncommon.

It has been hypothesized that female reproductive hormones may be involved in causing hearing loss [24]. Estrogen affects auditory neural function, as evidenced from its effect on auditory brainstem responses (ABR) [25]. It is known that female reproductive hormones can modulate the function of GABA receptors [26]. That may be the basis for the effect of female reproductive hormones on hearing loss.

The increased release of the afferent transmitter glutamate can exert a direct as well as an indirect neurotoxic effect at higher concentrations [27]. The age-related reduction in dopamine receptors may also be involved in the effect of age on the incidence of tinnitus [28].

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[3] Spontaneous hypertensive rats: Rats with genetic predisposition for greater increase in blood pressure with age than normal.

Loss of the inhibitory neural transmitter, GABA, that occurs with age may promote presbycusis [29] and perhaps, in particular, tinnitus. The change in female reproductive hormones with age may therefore affect the development of presbycusis, and this effect may cause some of the differences between the development of presbycusis in men and women. The pathology of presbycusis is far more complex than just damaged hair cells.

It was mentioned above that the central nervous system could influence the function of the hair cells in the cochlea. Injuries to cochlear hair cells can also influence the function of the auditory nervous system. The auditory nervous system can influence how normal hair cells (especially outer hair cells) are damaged or get an abnormal injured function.

While injuries to cochlear hair cells can themselves cause symptoms, pathologies of hair cells can also promote expressions of neural plasticity, which can cause symptoms of hyperactivity, redirection of information, etc. (see Chap. 12). This may explain why injuries to cochlear hair cells are not the sole reason for the symptoms of age-related changes. Hearing loss that occurs when hair cells are injured is therefore not only caused by these injuries as such, but the function of the central auditory nervous system pathways may also be altered. This contributes to hearing loss caused by cochlear pathologies.

In a similar way, the fact that tinnitus is often associated with injuries to hair cells does not mean that it is the hair cells that generate the abnormal neural activity that causes tinnitus. The anatomical location of the abnormal function that causes these symptoms is thus not only the cochlear hair cells, but changes in the function of specific structures of the auditory nervous system may also contribute to some forms of tinnitus.

Presbycusis and age-related tinnitus are caused by a complex combination of deficits in the cochlea and changes in the central auditory nervous system [30, 31]. Advances in our knowledge about the disorders of the auditory system have now blurred the distinction between cochlear and nervous system disorders.

Problems to understand speech, even after that the loss in hearing sensitivity has been compensated for by amplification is common in elderly individuals. Age-related changes in the auditory nerve, where the variation in diameter of auditory nerve fibers increases with age [32] (Fig. 36.3), might contribute to hearing problems. Greater variation in the diameter of auditory nerve fibers in turn causes the conduction velocity to
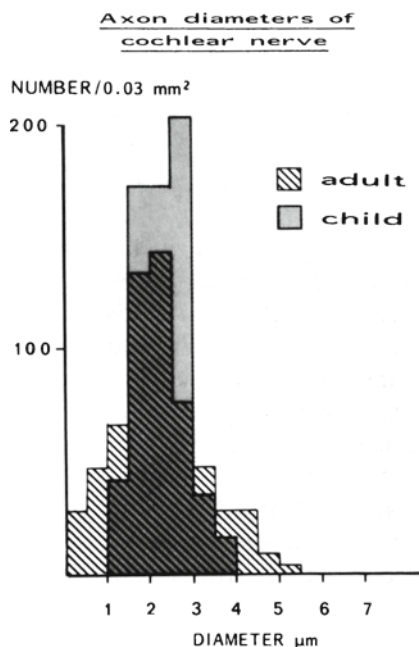
Fig. 36.3 Distribution of diameters of myelinated auditory nerve fibers in humans. Results obtained in an adult are compared with that found in a child. Reprinted from Spoendlin H and A Schrott (1989) Analysis of the human auditory nerve. Hear. Res. 43: 25–38. [32] Reproduced with permission of Elsevier

vary. Subsequently, the arrival time of neural activity at the cochlear nucleus will vary with the degree and kind of injury. This result in a temporal dispersion can have different effects on activation of cochlear nucleus cells [33] (Fig. 36.4). It is evident from Fig. 36.4 that increased temporal dispersion can cause both decreased excitation of target neurons or increased excitation. The latter may be a cause of some forms of tinnitus. Processing in the other nuclei and the cerebral cortex of the auditory system may also change as a result of age-related changes, contributing to difficulties in understanding speech.

Epidemiology of Age-Related Tinnitus

As has been pointed out in other parts of this book, data on epidemiology of tinnitus in general are sparse, and epidemiologic data on age-related are few. A study of the prevalence of tinnitus in children and the elderly [34] found the incidence of tinnitus in presbycusis to be 11%. A study in Sweden of 153 individuals from age 70 to 79
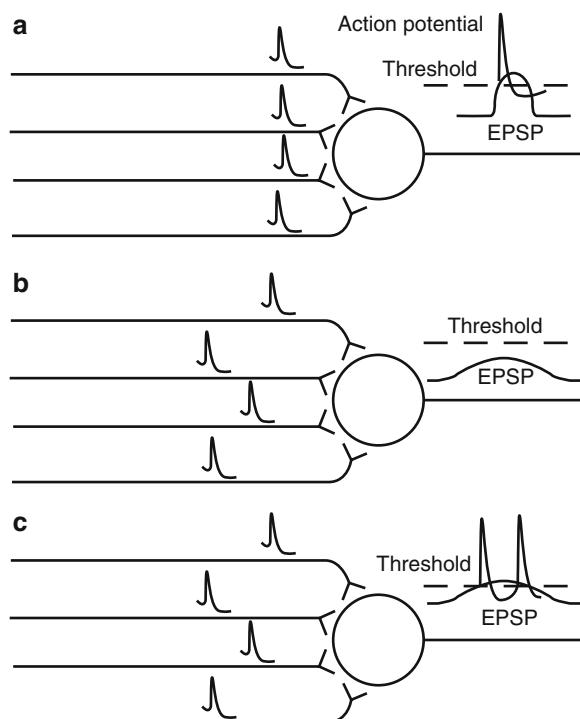
Fig. 36.4 Hypothetical illustration of the effect of spatial integration by a cell on which many axons converge. (**a**) Little spatial dispersion (**b**) Increased spatial dispersion, but the high threshold of the neuron prevents it from firing. (**c**) Large degree of spatial dispersion and low threshold of the neuron. The prolonged EPSP makes the neuron fire twice. From Møller AR (2006) Neural plasticity and disorders of the nervous system. 2006, Cambridge: Cambridge University Press [33]. Reproduced with permission of Cambridge University Press

Fig. 36.5 Graph showing the odds of having tinnitus as a function of hearing loss at 4 kHz. Data from a study in the United Kingdom, National Study of Hearing [37]

showed that the incidence of tinnitus increased from 31% at age 70, to 44% at age 79. A few participants (11) in this study had less tinnitus at age 79 compared with what they had at age 70, thus some form of remission [35, 36].

Relationship Between Hearing Loss and Tinnitus

While there are individuals with tinnitus who have normal or near normal hearing, most forms of tinnitus are associated with hearing loss. A study has shown a clear relationship between hearing loss at 4 kHz and the odds of having tinnitus [37] (Fig. 36.5).

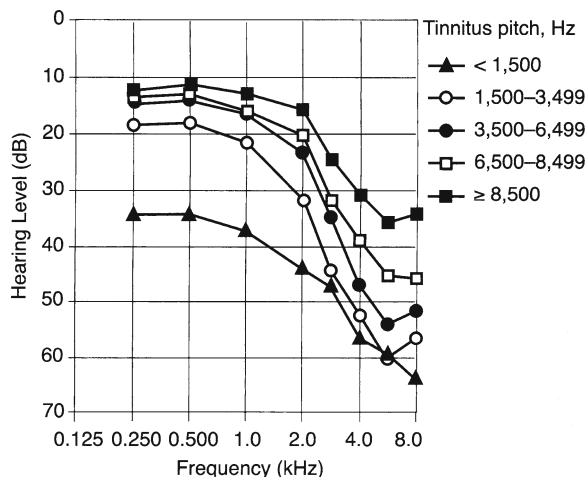It should be noted that 4 kHz is the frequency of greatest hearing loss from noise exposure, and it can be assumed that a noticeable portion of the hearing loss of many of the participants in this study comes from noise exposure (see Chap. 37).

There are also individuals with considerable hearing loss who do not have tinnitus. Hearing loss may therefore not be regarded to always cause tinnitus, although hearing loss – including conductive hearing loss – may be associated with tinnitus, because deprivation of sound activates neural plasticity (see Chaps. 11 and 12).

Individuals with low-frequency tinnitus tend to have more severe hearing loss than people with high-frequency tinnitus [38] (see Fig. 36.6). Tinnitus in connection with age-related hearing loss can have several causes. It can be caused by activation of neural plasticity because of reduced input to the nervous system from the ear (deprivation of sensory input is a strong promoter of plastic changes) (see Chap. 12). It can be caused by aging factors other than those that cause hearing loss. The reduced GABA activity that occurs with age [39] reduces inhibition in general in the nervous system and that may promote hyperactivity, which can cause tinnitus.

It has become evident that risk factors for age-related deterioration of CNS functions causing disorders, such as different forms of dementia, overlap with risk factors for cardiovascular diseases [40]. Little is known about the relation between dementia and hearing loss or about the risk factors for presbycusis and various forms of dementia. However, it has been found that many of the changes that occur with age can be slowed down or prevented by appropriate exposure to sound [11].

Fig. 36.6 Audiograms of individuals with tinnitus in different frequency ranges. Reproduced from Henry JA, M Meikle and A Gilbert, (1999) Audiometric correlates of tinnitus pitch, in *Proceedings of the Sixth International Tinnitus Semminar*, J Hazell, Editor. The Tinnitus and Hyperacusis Centre: London. 51–7. [38]
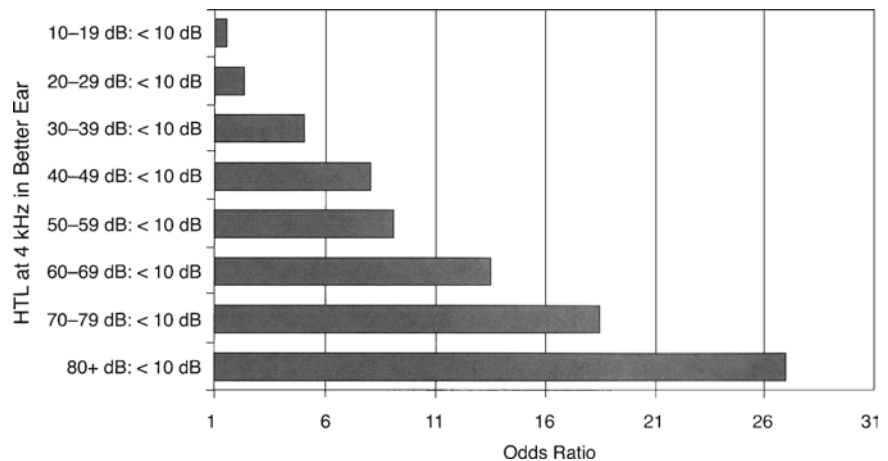
Conclusion

The cause of tinnitus is complex, as discussed in several chapters in this book. Although the likelihood of having tinnitus increases with age, as does hearing loss, the casual relationship between hearing loss and tinnitus is complex and many other factors than hearing loss are involved in causing age-related tinnitus.

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