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Tinnitus and Decreased Sound Tolerance

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Tinnitus is commonly described as a perception of sound that is not related to an external acoustic source or electrical stimulation.[1] The National Center for Health Statistics categorizes tinnitus as chronic if it lasts at least three months.[2] Tinnitus is an extremely common condition, but only a fraction of those who experience it are significantly disturbed by it.[3] Moreover, it has been shown that the perception of tinnitus can be evoked in 94% of young, healthy subjects by putting them in a setting with a sufficiently low level of sound.[4] A recent experiment has confirmed this effect.[5] Although there is a lack of objective measures of tinnitus and no clear agreement on an efficient way to help those who suffer from tinnitus, as well as many unanswered questions, significant progress has been made over the past quarter century in the tinnitus field. Still, most patients are given the unfortunate advice: "Learn to live with it."

Tinnitus is not a disease. It is a symptom that, similar to pain, headache, or fever, can vary in severity and can affect patients' lives to varying degrees. Sounds described by patients can have different spectra and loudness, can change in loudness and type of sound, and can persist or be transient.[1] Tinnitus can be annoying to those who experience it and lead to a vicious circle where it becomes the center of attention in patients' lives. Tinnitus affects people of all ages.[2]

Tinnitus can exist independently or as part of a complex medical condition.[6] The cause is unclear, and no specific site or molecular or cellular mechanism has been proven to be responsible for the initiation and continuation of tinnitus.

Tinnitus is frequently accompanied by decreased sound tolerance (DST) and hearing loss.[2,7,8] Decreased sound tolerance includes hyperacusis and/or misophonia.[9,10] There is no consensus regarding testing of DST. Only limited normative data are available for Loudness Discomfort Levels (LDLs), which are typically used to assess the presence of hyperacusis[11] and one questionnaire has been proposed to evaluate the severity of hyperacusis,[12] the validity of which still needs to be evaluated.[13] The prevalence and epidemiology of hyperacusis are not well-documented, and its etiology and mechanisms are poorly understood. Hyperacusis can occur alone or as an adjunct to complex medical conditions. Gradual desensitization can lead to the successful treatment of the problem.[6]

It is crucial to distinguish between the mere presence of tinnitus perception (predicted primarily by hearing loss) and the presence of clinically significant, bothersome tinnitus, from which people suffer and experience a number of negative reactions to it. Unfortunately, this distinction is frequently not taken into account in research and in proposed mechanisms of tinnitus.

In recent years, tinnitus has become better recognized in the United States (US) due to its high prevalence in individuals who serve in the military and with the growing costs for providing treatment for it. Forty-nine percent of American soldiers involved in explosions develop tinnitus, while only 25% have hearing loss.[14] The Veterans Administration spent 1.1 billion dollars for compensation for tinnitus in 2010 alone,[15,16] and it is expected this amount will rise to 2.26 billion by 2014.[17] The societal cost of tinnitus is significant as well. A recent study estimates the average cost to society in the Netherlands is over $7,000 per patient per year.[18] Taking the differences in medical systems between the Netherlands and the US into account, and using 5% to denote the prevalence of bothersome tinnitus in the US, the estimated conservative cost to American society is over $30 billion per year.

TINNITUS

Definitions

Writings about tinnitus can be found in ancient documentation of Babylonian, Egyptian, Greek, Indian, and Assyrian medicine. Throughout the world, a variety of terms have been used to describe a ringing, tinkling (Latin, tinnire), buzzing, and whistling in the ears or the head, leaving us with the two most commonly used terms, tinnitus (in English) and acufenos (in Spanish). Historical reviews of tinnitus may be found in a number of publications; of particular note are those by Stephens.[19]

There is no precise, short, and distinctive definition of tinnitus. Commonly used definitions focus on its psychoacoustical characteristics (eg, definitions based on patients' experiences describe tinnitus as ringing, buzzing, the sound of escaping steam, hissing, humming, crickets, or noise in the ears).[1,3] A physiological definition of tinnitus as "a phantom auditory perception" points to the lack of a physical acoustic stimulus related to tinnitus.[20] The definition proposed by the Committee on Hearing, Bioacoustics and Biomechanics of the US National Research Council describes tinnitus as "a conscious experience of sound that originates in the head" of its owner.[1]

Evaluation of Tinnitus

There is no objective method to detect and measure tinnitus. Interview and psychoacoustic characterization are the typical approaches used in clinical practice, sometimes augmented with physiologic testing. New advances in research offer the possibility to detect tinnitus objectively by using imaging techniques[21,22] or magnetoencephalography.[23] These techniques are promising but cannot yet be used in clinical practice as none has been shown to work. Table 31-1 lists the methods used to evaluate tinnitus (adapted from[24–27]).

Problems Evoked by Tinnitus

As tinnitus can present as a part of a complex medical condition, a thoughtful medical evaluation is necessary to exclude all medically treatable problems that can be linked to tinnitus. Although tinnitus is classified as a symptom and not a disease, it does require treatment as it can cause significant emotional and somatic distress and can significantly influence a patient's quality of life. This need for treatment particularly exists if tinnitus is allowed to become a chronic problem. The list of reported associated complaints is long and includes: 1) emotional problems, such as irritation, annoyance, anxiety, stress and depression; 2) hearing problems such as difficulty with speech comprehension; and 3) somatic problems such as headache, neck pain, and jaw pain.[1,28] Tinnitus can be intrusive and may cause difficulty with sleep and concentration and a decreased ability to participate in everyday activities, work, and social events. Tinnitus may also create problems in relationships. A detailed interview aimed at

Table 31-1 Methods Used for Evaluation of Tinnitus

Interview/questionnaires
Psychoacoustical
- Perceptual location
- Pitch match
- Loudness match
- Maskability (minimal masking levels)
- Postmasking effects (residual inhibition)

Physiological
- Otoacoustic emissions
- Auditory brainstem responses
- Late cortical potentials
- Positron emission tomography/single photon emission tomography
- Functional magnetic resonance imaging
- Magnetoencephalography
- Efferent-mediated suppression of otoacoustic emissions
- Spontaneous auditory nerve activity

characterizing the specifics and degree of tinnitus impact on the patient's life, coupled with an otorhinolaryngological evaluation, provide the most thorough assessment and allow the practitioner to address the issues that need to be considered, including the potential intervention of a psychologist or psychiatrist to accompany treatment.

Etiology, Prevalence and Epidemiology

Studies conducted around the world have shown a significant variability in the estimation of tinnitus prevalence in the general population.[2] One explanation for the variability is that every survey used different questions when asking about tinnitus. Recent epidemiological data confirmed the main aspects of the previous findings, pointing to an even higher prevalence of bothersome tinnitus in the US (about 8%) compared with the 4% previously reported.[2] From 6 to 17% of the general population experience tinnitus that lasts for at least five minutes. From 3 to 7% of the general population seek help for their tinnitus, and 0.5 to 2.5% report tinnitus has a severe effect on their lives.[1,3] The prevalence of tinnitus in adults with hearing problems is high (59 to 86%), and it is estimated that tinnitus is present in 50% of patients with sudden hearing loss, 70% with presbyacusis, and in 50 to 90% with noise-induced hearing loss.[2]

People of all ages experience tinnitus and its prevalence is typically reported as increasing significantly with aging.[2,3,29] Notably, tinnitus prevalence increases with hearing loss.[2] However, when hearing loss is taken into account in the analysis and controlled, the prevalence of tinnitus actually decreases with age.[2] While it is frequently not reported, children are also affected by tinnitus; and the estimated prevalence is similar to the estimated prevalence of tinnitus reported in adults. The prevalence of tinnitus has been reported in the range of 15 to 34% in healthy children and approximately 50% in children with otologic problems or hearing loss.[30–32] A significant proportion of children report having problems with tinnitus including: sleep disturbance (42%), problems with concentration (47%), and sensitivity to sound (33%). A study of 1, 100 children performed in Italy showed that 34% had tinnitus and 6.5% complained about it.[33] A recent study of 118,005 seven-year-old and 23,339 12-year-old children in Poland revealed that 29.3% and 34.5% of children reported tinnitus in the seven and 12-year-old groups, respectively.[32]

Extensive studies have been performed in an attempt to link various factors with tinnitus prevalence.[1,2] Hearing loss, and specifically the extent of high frequency impairment in the worse ear, is one of the main predicting factors for tinnitus. Conductive hearing loss seems to be a separate factor,[34] and noise exposure has also been correlated with tinnitus.[2] Tinnitus is also experienced by those with normal hearing; 18% of tinnitus patients were reported to have normal hearing.[34] Pregnancy has been shown to significantly increase the probability of tinnitus.[35]

Other factors do not appear to be correlated with tinnitus. Neither coffee nor alcohol has been shown to increase tinnitus prevalence directly.[6,36] Tinnitus severity is associated with severity of anxiety and depression[37] and seems to affect patients' cognitive abilities.[38,39] The main risk factors associated with the presence of tinnitus are age, male sex, lower level of education, lower annual income, being a military service veteran, poor general health status, obesity, significant hearing loss, exposure to loud sound at work for more than 15 hours per week, exposure to impulse noise, and smoking cigarettes on a daily basis.[2] Interestingly, being in a managerial, administrative or technical sales occupational group as well as moderate alcohol consumption were associated with *reduced* risk for tinnitus.[2] Notably, all the above risk factors linked to the increased prevalence of tinnitus are the risk factors for hearing loss as well, which has been shown to be associated with tinnitus. Therefore, these risk factors may not be associated directly with tinnitus, but indirectly via hearing loss. Unless hearing loss factor is not controlled for, these risk factors cannot be accepted as valid, as has been shown in the case of age, which turned out not to be directly related to tinnitus, but only via hearing loss.[2]

Mechanisms and Models

Our knowledge of the mechanisms of tinnitus is still limited and based more on theoretical speculations than on strong research data or stringent clinical studies. Past models focused on peripheral mechanisms in the auditory system,[40–43] whereas recent models involve or focus on information processing within the central auditory pathways and central nervous system.[20,44] Although the molecular and genetic basis for tinnitus is unknown, brain-derived neurotrophic factors (BDNF) and the activity-dependent cytoskeletal protein (Arg3.1/arc) have been found to be potentially related with acoustic trauma induced tinnitus at both the peripheral and central levels.[45]

The neurophysiological model of tinnitus postulates the involvement of many systems in the brain (in addition to the auditory system) in clinically significant tinnitus, both at the peripheral and central levels. Furthermore, the model differentiates between the perception of tinnitus versus tinnitus-induced negative reactions, for which activation of non-auditory structures in the brain is responsible.[6,8,20,40] Furthermore, the discordant damage/dysfunction theory of the generation of the tinnitus signal postulates the signal is generated at the level of the dorsal cochlear nucleus due to imbalanced activation coming from the outer and inner hair cells.[6,20] Specifically, when the outer hair cells are dysfunctional in a certain region of the basilar membrane and the inner hair cells in the same region still work properly, disinhibition in the dorsal cochlear nucleus occurs and may result in the generation of the tinnitus signal.[40] This theory explains many tinnitus conundrums[20,40] and is gathering support from experimental data.[46–48] Table 31-2 summarizes various approaches to the mechanisms of tinnitus.[40,41,49–63]

Tinnitus as a Symptom of Medically Treatable Diseases

Tinnitus may also be part of more complex medical conditions. Some of these are identified in Table 31-3, (adapted from[40,64,65]).

DECREASED SOUND TOLERANCE

Tinnitus is frequently accompanied by DST, that is, oversensitivity to sound,[6,66–69] which is often a combination of hyperacusis and misophonia.[6,9,10]

Definitions

While there is no generally-accepted definition of DST, various terms have been proposed, and the term hyperacusis has been used most frequently. According to Stedman's Medical Dictionary,[70] hyperacusis is defined as an "Abnormal acuteness of hearing due to increased irritability of the sensory neural mechanism. Syn: auditory hyperesthesia," while hyperesthesia is defined as an "Abnormal acuteness of sensitivity to touch, pain, or other sensory stimuli" or, according to the American Heritage Dictionary, as "An abnormal or pathological increase in sensitivity to sensory stimuli, as of the skin to touch or the ear to sound."[71] It has been recognized that DST might reflect physical discomfort or be related to a fear of sound.[6]

We proposed an approach to DST based on neurophysiology and recognized the main systems that can be involved, namely, the peripheral

Table 31-2 Main Concepts Related to Proposed Mechanisms of Tinnitus

Structures involved

- Auditory system
  - Periphery (cochlea, auditory nerve)
  - Central auditory pathways
- Auditory and central nervous system

Manifestation of tinnitus-related neuronal activity

Increase in spontaneous activity
Modification in temporal patterns of discharges, including bursting activity
Synchronization of the activity between neurons

Proposed mechanisms responsible for the emergence of tinnitus-related neuronal activity

- Local decrease of spontaneous activity in the auditory system enhanced by lateral inhibition
- Discordant damage/dysfunction of outer and inner hair cells
- Unbalanced activation of Type I and II auditory nerve fibers
- Neuronal plasticity and cortical reorganization
- Cortical reorganization of tonotopic maps and hypersynchrony
- Somatosensory-auditory interaction
- Abnormal neurotransmitter release from inner hair cells
- Decreased activity of the efferent system
- Abnormal coupling between neurons
- Mechanical displacement within the organ of Corti
- Abnormalities in transduction processes
- Various aspects of calcium function
- Physical/biochemical stress on the auditory nerve
- Auditory fibers deafferentation
- Enhanced sensitivity of the auditory pathways after decreased auditory input
- Hypoxia and ischemia in the cochlea

Level of interest

- Molecular-ion channels, synapses, cellular membranes
- Single neuron-processing information within one cell
- Neuronal assemblies-interaction within group of cells
- System-interaction between various systems in the brain

Somatosounds

- Included as "objective tinnitus"
- Separated, with name "tinnitus" reserved to auditory phantom perception

and central parts of the auditory system, as well as the limbic, and the autonomic nervous systems. Consequently we propose the following definitions.

Decreased sound tolerance is present when a subject exhibits negative reactions when exposed to sound that would not evoke the same response in an average listener.[9,10] Various negative emotional responses such as a discomfort, dislike, distress, annoyance, anxiety, and fear are reported, sometimes together with negative sensations such as pain and fullness in the ears. The level of sound that evokes these negative reactions can be low, moderate, or high and is not used as a criterion to determine the presence of DST or its components.

Hyperacusis is defined as present when negative reactions to a sound depend only on its physical characteristics (ie, its spectrum and intensity). The sound's meaning and the context in which it occurs are irrelevant. The presumed mechanism of hyperacusis is an abnormally strong activation evoked by sound occurring within the auditory pathways, with other systems such as the limbic and autonomic nervous systems activated as a consequence of a high-level of auditory-system activation.[6,9,10]

Misophonia is defined as an abnormally strong reaction to a sound with a specific pattern and *meaning* to a given subject. The physical characteristics of a sound are secondary. Indeed, the strength of a patient's reaction to the sound is only partially determined by the physical characterization of the sound and depends to a large extent on non-auditory factors like the subject's previous evaluation of the sound (for example, the belief that the sound is harmful or may be a potential threat), her/his psychological profile and past history, and the context in which the sound is presented. Postulated mechanisms of misophonia involve enhanced functional connections between the auditory system and other systems in the brain (mainly the limbic and autonomic nervous systems) to subject-specific patterns of sound, while the auditory system functions normally.[6,9,10]

A specific type of misophonia occurs when fear is the dominant emotion and patients are afraid of sound (phonophobia; phobia – fear).[6,9,10]

Most frequently, DST results from a combination of hyperacusis and misophonia. Notably, patients with hyperacusis or misophonia report the same negative emotional and physiological reactions. This combination leads us to conclude that all cases of bothersome DST involve the limbic system and other systems in the brain, in addition to the auditory system, as well as connections between the auditory and other systems.[6,10,72]

It is important to assess the presence and the extent of *both* conditions in a patient as each need to be treated using different approaches. As the literature does not differentiate between these problems, and DST is typically described as hyperacusis, we will use the term hyperacusis in our discussion of the literature.

Neither hyperacusis nor misophonia have any relation to the threshold of hearing, which can be normal or can reflect hearing loss. Therefore, recruitment is not related to DST. Recruitment refers to an unusually rapid growth of loudness as the volume of a tone is increased. It occurs in association with hearing loss and is a purely cochlear phenomenon. It may coexist with DST, but there is no functional link between these two phenomena.

Methods of Evaluation of Decreased Sound Tolerance

Whereas there is no one clearly accepted method to evaluate DST, hyperacusis, and misophonia, there is general agreement that LDLs provide clinicians with a means to estimate the problem. There are several variants of the protocols of LDL evaluation. For example: continuous sound, pulsed sound or beeps of sound, as well as pure tone versus narrow-band noise have been used.[73–75] The approach we use modifies the standard procedure[11] and is aimed at diagnosing the presence and extent of hyperacusis by keeping the effects of the misophonic component of DST to a minimum. To achieve this, an environment is created during testing where patients feel in full control over the maximal sound level to which they will be exposed. As normative data are not uniform, and there is substantial individual variability (even when using one method) in measuring LDLs,[76]

Table 31-3 Medical Conditions That May Be Associated with Tinnitus

Sensorineural hearing losses

- Noise-induced hearing loss
- Menière disease
- Presbyacusis
- Vestibular schwannoma
- Sudden hearing loss
- Cochlear otosclerosis

Conductive hearing losses

- Otitis media
- Cerumen impaction
- Ossicular stiffness/discontinuity
- Otosclerosis

Hormonal changes

- Pregnancy or menopause
- Thyroid dysfunction

Some medications or withdrawal from them

Somatosounds

- Produced by structures adjacent to the ear
  - Pulsatile Neoplasm
  - Arterial
  - Venous
  - Beginning of intracranial hypertension
  - Great vessel bruits
- "Third windows" of the otic capsule allowing internal sounds to be heard unusually well
  - Superior canal dehiscence
  - Perilymphatic fistula (otic capsule defects not visualized by CT)
- Nonpulsatile
  - Tensor tympani myoclonus
  - Tensor veli palatini myoclonus
  - Patent eustachian tube
- Produced by structures in the ear
  - Spontaneous otoacoustic emissions
- Produced by joint abnormalities
  - Temporomandibular joint disorders

it is advisable to pay attention to the potential presence of hyperacusis when the average LDL values across the tested frequencies are lower than 95 to 100 dB hearing level (HL). When hyperacusis is present, LDLs are typically in the 60 to 85 dB HL range; however, low values alone are not enough to diagnose hyperacusis. The situation is complicated because a wide range of LDL values (eg, an average of 30 dB HL to an average of 120 dB, HL) are found in patients with misophonia. Therefore LDLs alone are insufficient to diagnose hyperacusis as low values may be due to misophonia. Therefore, in addition to a properly administered LDL test, a detailed interview is crucially important to help the clinician determine the relative contribution of hyperacusis and misophonia to DST. In the interview, it is important to identify sounds which evoke negative reactions as well as sounds which are well-tolerated by the patient to detect any discrepancies between reactions and the intensity of the sound. Normal LDLs exclude the possibility of hyperacusis, but DST can still be present. A questionnaire has been proposed to assess the extent of hyperacusis,[12] but its specificity and selectivity need to be evaluated.

Hyperacusis and Misophonia as a Problem

Decreased sound tolerance can have an extremely strong effect on patients' lives and can be even more debilitating than tinnitus. Whereas tinnitus may affect attention, sleep, work, and enjoyment of life, and can make social contact less rewarding, hyperacusis can prevent people from exposing themselves to louder environments and therefore prevent them from working and interacting socially. In extreme severity, patients do not leave their homes, and both their own lives and the lives of their families are controlled by the avoidance of sound. Misophonia can have the same effect as hyperacusis. Because misophonia is present in all patients with significant hyperacusis, misophonia further enhances the effects of hyperacusis.

Prevalence and Epidemiology of Decreased Sound Tolerance

Limited data are available on the prevalence of hyperacusis. Various questionnaires are used to provide an assessment of hyperacusis prevalence in the general population. Data gathered from 10,349 randomly selected subjects showed that 15.3% reported hyperacusis.[77] Patients evaluated for other otologic problems frequently undergo audiologic evaluation, which involves an assessment of speech discomfort level and pure tone LDLs. Several studies indicated that in the normal population, LDLs are in the range of 90 to 110 dB sound pressure level (SPL), with varied results depending on the specific methods used (for example, stimuli: pure tone, warble tone; noise; presentation: free field, insert earphones, headphones) and instructions given to patients.[11,73,76] Moreover, these measurements are not part of a routine audiologic evaluation. The results tend to cluster within 95 to 110 dB SPL for frequencies from 500 to 8,000 Hz, which correspond to approximately 90 to 100 dB hearing level (HL).[11] A specific study aimed at this issue showed that the average LDL value for subjects without sound tolerance problems was 100 dB HL.[11]

Hyperacusis and tinnitus frequently coexist, and it has been postulated that in some patients, hyperacusis might actually be a pre-tinnitus state.[67] Approximately 60% of patients with tinnitus exhibit DST with about 30% requiring specific treatment for hyperacusis.[9,10] Conversely, a study of 100 patients with hypersensitivity to sound showed that 86% suffered from tinnitus.[78] Considering the clinical observation that approximately 30% of tinnitus patients required treatment for hyperacusis and 86% of hyperacusis patients reported tinnitus, and acknowledging that about 4% of the general population have clinically significant tinnitus, it is possible to estimate that significant hyperacusis exists in approximately 1.75% of the general population. Considering data which indicate about half of patients with DST have hyperacusis, the estimate of the prevalence of DST in the general population is 3.5%.

Mechanisms of Decreased Sound Tolerance

In the majority of patients, the cause of hyperacusis is unknown. Hyperacusis has been linked to loud sound exposure (particularly short, impulse noise), head injury, stress, medication, and some medical conditions. The lack of strong epidemiological data and of an animal model of hyperacusis prevents us from proving the validity of any potential mechanism responsible for hyperacusis.

At the peripheral level, it is possible to speculate that the abnormal enhancement of vibratory signals within the cochlea by the outer hair cells might result in overstimulation of the inner hair cells and subsequently yield hyperacusis.[6,20] Indeed, in some patients, it is possible to observe high amplitude distortion product otoacoustic emissions and distortion products evoked by low level primaries.[6] The presence of asymmetric hyperacusis might indicate a peripheral mechanism since central mechanisms would more likely act similarly on both sides; however, in nearly all patients DST is symmetrical – which suggests the dominant role of the central mechanisms.

Laboratory research has shown that damage to the cochlea or a decrease in the auditory input result in a decrease of the threshold of response in a significant portion of neurons in the ventral cochlear nucleus and inferior colliculus.[79] Studies with evoked potentials have indicated an abnormal increase of gain in the auditory pathways after such manipulations.[80] This increase in gain has been discussed and promoted in a recently proposed approach concerning the mechanisms of tinnitus and hyperacusis.[57] Some medical conditions listed in Table 31-4 can be linked to the central processing of signals and modification of the level of neuromodulators as possible factors that induce or enhance hyperacusis. Moreover, serotonin has been implicated in hyperacusis,[81] and a case report has indicated that serotonin reuptake inhibitors might be helpful for hyperacusis.[82]

Table 31-4 Medical Conditions Linked to Decreased Sound Tolerance

Tinnitus
Williams syndrome
Bell palsy
Lyme disease
Ramsay Hunt syndrome
Post-stapedectomy
Perilymphatic fistula
Head injury
Migraine
Depression
Withdrawal from benzodiazepines
Cerebrospinal fluid high pressure
Addison disease
Translabyrinthine excision of a vestibular schwannoma

Mechanisms of misophonia could involve an enhancement of the functional links between the auditory and limbic systems at both the cognitive and subconscious levels.[6,20] Alternatively, a tonic high level of activation of the limbic and autonomic nervous systems may result in strong behavioral reactions to moderate sounds.[6]

Decreased Sound Tolerance as a Symptom of Medical Conditions

Hyperacusis has been linked to a number of medical conditions (Table 31-4), adapted from.[6,82–88]

REVIEW OF TREATMENTS FOR TINNITUS

The list of approaches and techniques attempted to help tinnitus patients is long. Table 31-5 lists the most commonlyused treatments, adapted from.[64,89–99]

Anti-reassurance

Notably, some clinicians provide positive suggestions to their patients (eg, you do not have a dangerous condition, you are not going deaf, tinnitus is common, there are things you can do that can help). However, it seems the most common advice given to tinnitus patients has been: "Nothing can be done—go home and learn to live with it.[8,67] This advice is a powerful form of negative counseling, sufficient on many occasions to convert a person who just experiences tinnitus into a patient who suffers from it.[6,20,66,100]

Pharmacotherapy

Many pharmacologic agents have been considered for tinnitus treatment[6,89] (Table 31-6,

Table 31-5 Review of Treatments for Tinnitus

Antireassurance
Pharmacology
Surgery
Electrical stimulation
Sound therapies
Psychological approaches
Tinnitus retraining therapy
Other approaches
Biofeedback
Temporomandibular joint treatment
Acupuncture
Hyperbaric oxygen therapy
Homeopathy
Magnets

Table 31-6 Drugs Frequently Prescribed for Treatment for Tinnitus

Local anesthetics (lidocaine, procaine, tocainide, flecainide)
Sedatives (diazepam, flurazepam, oxazepam, alprazolam)
Antidepressants (nortriptyline, trimipramine)
Anticonvulsants (carbamazepine, clonazepam, aminooxyacetic acid, lamotrigine, baclofen)
Vasodilators (niacin)
Calcium channel blockers (nimodipine, nifedipine)
Others (misoprostol, zinc, betahistine, cinnarizine, caroverine, melatonin, furosemide, ginkgo biloba)

adapted from.[6,89] but no single, effective, specific, secure, and reliable drug has yet to be identified.[91,92,94,101,102] In this respect, strong consideration must be given to the side effects of pharmacologic treatments, such as tolerance, dependence, and withdrawal effects. Recent reviews of randomized clinical trials of drugs for tinnitus have shown that all the drugs that were studied have failed to prove their efficacy when compared with a placebo.[89] Future double-blind randomized studies, with proper outcome measurements and adequate sample size, might identify some promising pharmacologic agents.

Surgery

Surgery can offer help to some patients with somatosound or conductive hearing loss.[6] In the case of Menière disease, successful treatment provides control of vertigo; however, tinnitus and hearing loss remain the same or become worse.[103] The surgical removal of vestibular schwannoma may provide improvement in tinnitus in some patients, while in others it may evoke tinnitus or make it worse.[104] No specific surgical procedure has been shown to be consistently effective for tinnitus that does not have a clear surgically treatable cause. Although promoted in the past,[43] neither transection nor microvascular decompression of the auditory nerve has proven to be effective,[64,105,106]

Sound Therapies

A wide variety of sound therapies is used to treat tinnitus, such as music therapies, auditory discrimination therapy, pink noise therapy, desensitization, the dynamic tinnitus mitigation system, phase shift tinnitus reduction, auditory integration training, masking relief therapy, Neuromonics,[107,108] acoustic coordinated reset neuromodulation,[109] SoundCure (S-Tones)[110] and the use of hearing aids.[6,111–114] These approaches are based on various presumed mechanisms of sound upon tinnitus. Sound modification may involve varying intensity within a short time, applying different intensities for specific stages of treatment, or using phase modification or complex processing of the sound. It is not clear which type of sound processing and sound protocol are optimal. For most of these approaches, results have not been published in peer-reviewed journals and there are not sufficiently strong data from systematic studies to determine which methods might be effective in alleviating tinnitus. A counseling component in these therapies is either limited or minimal.

It has been postulated that improving frequency discrimination via proper training should be beneficial for tinnitus and some clinical trials have indicated positive effects.[115,116] However, the results of randomized controlled trials have not shown the expected benefits.[117]

There are some recent variants of sound therapy. Coordinated reset (CR) neuromodulation presents pure tones below and above the tinnitus pitch match according to a specific algorithm.[109] This method is currently being tested in a randomized controlled trial (RTC, ClinicalTrials.gov, NCT01541969).[118]

Another approach, commercially promoted as SoundCure® or S-Tones ®, uses sound centered at the tinnitus pitch with a modulated amplitude.[110] Preliminary results of the study performed on a small number of subjects looks promising but require confirmation on a large scale from independent investigators.

An interesting variant of sound therapy involves pairing sound with vagus nerve stimulation.[119,120]

All these methods are promoted with encouraging preliminary results, but there is a lack of confirmation from independent groups of investigators and from randomized clinical trails.

Specific version of sound therapy is used as an integral part of tinnitus retraining therapy (TRT) to achieve consistent and prolonged weakening of the tinnitus signal and desensitization of the auditory system. The type and protocol of the sound used are based on the neurophysiological model of tinnitus.[6] According to the model, any sound is better than silence, provided it does not annoy, create discomfort, or damage hearing. Counseling in combination with a given implementation of sound therapy is crucial. TRT is described in detail later in this chapter.

Electrical Suppression

Electrical suppression of tinnitus was first reported in 1855.[121] Over the years, many different approaches have been attempted, and methods based on electrical stimulation are still of interest (Table 31-7), adapted from.[121–124] Three new variants of electrical stimulation for tinnitus have been introduced in the last several years. One variant involves deep brain stimulation, which is sometimes performed for movement disorder and chronic pain.[125] Recently it has been shown that stimulation of locus of caudate neurons (area LC) can trigger, enhance or suppress tinnitus.[126–128] A second approach involves high frequency electrical stimulation of the cochlea performed by placing an electrode on the promontory or via a cochlear implant.[129] A third approach involves direct electrical stimulation of the auditory cortex via electrodes placed on or within the auditory cortex.[130]

All these approaches are at an early stage of investigation. Only intra-cochlear or promontory stimulation has shown consistent and positive results in approximately 50% of patients.[131,132] Other approaches were less effective.[121] Although positive direct/pulsed current can provide tinnitus suppression,[121] it has no clinical application as it would damage the cochlea if used for a prolonged time.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) uses short pulses of a powerful magnetic field to stimulate the brain cortex. The method, primarily used for psychiatric disorders, has been extensively investigated for tinnitus.[133] The magnetic field easily crosses the skull and induces a strong electrical field, perpendicular to the magnetic field, which in turn activates neurons in the cortex and

Table 31-7 Conditions Used in Electrical Stimulation for Suppression of Tinnitus

Sites of stimulation
• Behind the ear lobe/around the ear
• Mastoid
• Near cheeks
• External auditory canal
• Promontory
• Tympanic membrane
• Round window
• Intracochlear
• Auditory cortex
• Deep brain stimulation
Type of stimulus
• Direct current/positive pulses
• Alternating current
• Amplitude-modulated high-frequency carrier
Electrodes
• Acute/chronic

results in the electrical stimulation of the cortex. The relative position of the axons and dendrites of neurons to the evoked electrical field is crucial; depending on this relationship, one group of neurons can be activated while another group in the same area will not be activated. Consequently, changing the angle of the magnetic coil will modify which neurons will be stimulated within the active area, which is about one inch in diameter. Moreover, as the cortex is highly convoluted, only some parts will be activated. All these factors, combined with the fact that the auditory cortex is in a deeper part of a sulcus, create a challenge to achieve repetitive, stable results when this method is used to treat tinnitus.

In addition to immediate effects, the longer lasting consequences are of clinical interest. There are two types of TMS differentiated by the frequency of stimulation. When a higher frequency is used, TMS has an inhibitory effect on cortical activity reflected in an immediate attenuation of tinnitus perception, which lasts only for a limited time.[134] When low frequency (1 Hz) stimulation is used over several days, plastic changes are presumably evoked in the cortical areas and their connections with subcortical centers. The initial effect of TMS might be an absence of tinnitus or the tinnitus might even increase. But over time, the tinnitus can be attenuated and the effects of TMS may last for some time. A recent critical review of TMS reported positive (a success rate from 51 to 64%) and negative treatment outcomes. The report concluded that a number of fundamental questions remain unsolved that prevent a clear conclusion regarding the effectiveness of TMS in the treatment of chronic tinnitus.[97,135,136]

A strong positive aspect of TMS is that it does not require opening the skull and can easily be performed on conscious subjects, thus encouraging its use and the number of studies of its effect on tinnitus.[137] The results showed a statistically significant attenuation of tinnitus and a decrease in the negative impact of tinnitus. Nevertheless, it is still not clear to what extent this improvement has practical clinical value and how long it can be sustained.[138] There is also concern regarding permanent changes induced in the brain by TMS and, therefore, the safety of the method.

Masking

The use of an external sound to cover tinnitus and bring immediate relief to patients, known as masking, was first used in 1825 by Itard.[19] At the end of the 1970s, Vernon and Schleuning revisited this idea and introduced the first commercial masker.[139] Initial reports proclaimed high success,[139,140] but the approach did not withstand the test of time.[89,95] One problem involved the criterion used to evaluate the effectiveness of masking. For example, if the masker was still in use after six months it was counted as a success.[139,140] Presently, this method is rarely used.

Recently, the term "masking" has been redefined, as Henry and colleagues have proposed to refer to "masking" to describe the use of any sound that brings immediate relief regardless of whether the patient's perception of tinnitus is covered or not.[113] This approach involves no specific counseling, other than instruction for sound setting. "Masking", which should more appropriately be labeled as "relief therapy" uses sound levels close to those used in a variety of sound-based therapies, including TRT. While not as effective as TRT, masking can be helpful for some patients, particularly those with a low level of tinnitus severity.[113]

Psychological Management

The psychological management of chronic tinnitus can be helpful for some patients.[141] As tinnitus affects patients' well-being, the application of cognitive therapy may have a positive impact on the quality of life by improving their ability to cope with tinnitus. Cognitive therapies, behavioral modifications, coping strategies, cognitive distraction, and minimizing distress are examples of psychological approaches.[142–144] Cognitive Behavioral Therapy (CBT) is of particular interest.[145] A recent meta-analysis of all controlled, randomized clinical trials listed in the Cochrane ENT Group Trials Register, the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE, identified six trials involving 285 patients that showed while there was no effect of CBT on the subjective loudness of tinnitus or on depression, CBT significantly improved quality of life.[146] A prospective study of 434 patients treated with an integrative behavioral medicine approach showed significant improvement as well.[143] A recently published randomized study claimed the effectiveness of CBT;[147] close examination of the procedures described in this paper revealed that the authors used a modified version of TRT for five months, followed by CBT only for patients who did not experience sufficient improvement in the TRT stage of treatment.[147] This combined approach was considerably less effective than TRT alone as shown in a clinical study by Henry et al.[113,148]

Combined Approaches

One approach that combines counseling with sound therapy is called Tinnitus Activities Treatment.[149] The approach takes four areas into account: thoughts and emotions, hearing and communication, sleep, and concentration. For sound therapy, the lowest sound level which provides immediate relief is recommended. Patients are given homework and encouraged to be involved in some activities to facilitate progress. This approach has been claimed to be in use since 1980, but to date there are no published, peer-reviewed clinical studies that show its effectiveness.

A large proportion of veterans experience tinnitus[17] with various level of severity. Considering the economical aspects of providing help, a progressive intervention approach called Progressive Audiologic Tinnitus Management (PATM) has been introduced.[150] Five hierarchical levels of intervention are implemented from Triage (an interview and basic relevant information) to Individualized Management (which involves multiple treatment modalities).

Counseling is a key component of PATM. It is used to help patients learn how to adjust to the bothersome auditory symptom by employing tools from the therapeutic use of sound and techniques from cognitive behavioral psychology.[151] Counseling is closely related to the counseling performed in TRT.[152] Sound therapy consists of three types of sound: soothing sound, background sound, and interesting sound.[153] Preliminary positive results of the use of the counseling part of PATM have been presented.[152] The results of full PATM – counseling combined with sound therapy – have not been published.

NEUROPHYSIOLOGICAL MODEL OF TINNITUS AND TINNITUS RETRAINING THERAPY

The neurophysiological model of tinnitus and the treatment approach based on the model, known as TRT, were introduced in 1990.[8,154–157] Several observations led to the neurophysiological model of tinnitus and DST. It is known that tinnitus induces distress in only about 20% of those who perceive it.[2] There is no correlation between the psychoacoustic characterization of tinnitus, tinnitus-induced distress, and the treatment outcome.[158] The experiment performed by Heller and Bergman showed that the perception of tinnitus cannot be pathologic since the vast majority of people experience tinnitus when they are put in a sufficiently quiet environment, as shown by the emergence of tinnitus in 94% of people without prior tinnitus when isolated for several minutes in an anechoic chamber.[4] This phenomenon has been recently confirmed.[5] These observations strongly argue that the auditory system plays a secondary role, and other systems in the brain are dominant in clinically relevant tinnitus, that is, tinnitus that creates discomfort and annoyance and requires intervention.

An analysis of the problems reported by tinnitus patients, who exhibit strong emotional reactions to its presence, a high level of anxiety, and other psychosomatic problems, indicated that the involvement of the limbic and autonomic nervous systems is crucial in individuals with clinically relevant tinnitus. It was postulated that the sustained activation of the limbic and autonomic nervous systems is essential in creating distress and, therefore, clinically relevant tinnitus.[20] Other systems in the brain seem to be involved as well (eg, prefrontal cortex, attention networks systems involved in memory and cerebellum)[44,159–161] and the default mode network,[57,162,163] but the

limbic and autonomic nervous systems seem to have a crucial role in tinnitus-related distress and DST.[6] Since the model has been proposed, a number of imaging studies have shown a high activation of non-auditory areas in tinnitus (eg, the limbic system and various non-auditory cortical areas),[21,163–168] an essential postulate of the neurophysiological model.

It is possible to distinguish several feedback loops, with two major categories: a loop involving the conscious processing of the tinnitus signal including its perception and a loop acting at a subconscious level (Figure 31-1), with the subconscious loop dominant in most patients.[8] It is further suggested that the activation of the limbic and autonomic nervous systems by tinnitus-related neuronal activity follows the principles of conditioned reflexes.[100,156,157]

The processing of tinnitus-related neuronal activity occurs in a dynamic balance scenario, with continuous modification of the weight of synaptic connections. Learning and memory have a physiological basis in the modification of the strength of synaptic connections.[169] A continuous presence of tinnitus, combined with the attention given to it, result in plastic modifications of synaptic connections, yielding the modification of receptive fields which correspond to the tinnitus signal and its subsequent enhancement.[40,170] This postulate has been proven using magnetoencephalography.[23]

Whereas the initial signal provided by the auditory system is needed to start the cascade of events, *its strength is irrelevant*, as the extent of activation of the limbic and autonomic nervous systems depends on the strength of negative associations linked to tinnitus and the susceptibility of the feed-back loops to modification.[171] It appears that tinnitus-related neuronal activity may result from compensatory processes that occur within the cochlea and the auditory pathways to minor dysfunction at the periphery.[20,40]

Notably, once plasticity-related modifications of neuronal connections occur, the peripheral signal itself may become of little importance, as is similarly observed in chronic pain.[172] Indeed, there are clear similarities between tinnitus and chronic pain, including the phenomenon of prolonged exacerbation of tinnitus as a result of exposure to sound, which is observed in some patients.[100]

The neurophysiologic model includes several systems of the brain involved in clinically relevant tinnitus. All levels of the auditory pathways, starting from the cochlea through the subcortical centers and ending at the auditory cortex, are essential in creating the perception of tinnitus.[20] When subjects are not bothered or annoyed by tinnitus, the auditory pathways are the only pathways involved, and tinnitus-related neuronal activity is constrained within the auditory system. Therefore, although these subjects perceive tinnitus, they are not disturbed by it.[156,157,171]

In approximately 20% of individuals with tinnitus, strong negative emotions are evoked, which, in turn, activate a variety of physiological defense mechanisms of the brain. In this process the limbic and autonomic nervous systems play a crucial role, and improper activation of these systems by tinnitus-related neuronal activity results at the behavioral level in the problems described by these patients. The connections between the auditory, limbic, and autonomic systems with various cortical areas, as proposed in the neurophysiological model of tinnitus,[8,20,40] are outlined in Figure 31-1.

The model emphasizes that the sustained activation of the limbic and autonomic nervous systems is responsible for the distress induced by clinically relevant tinnitus. Activation of both systems can be achieved through two routes branching at the level of the thalamus (medial geniculate body). The first includes stimulation of the limbic and autonomic nervous systems from higher level cortical areas which are involved in our awareness, verbalization, and beliefs. This loop is called high, conscious, or cortical, in the neurophysiologic model of tinnitus.[8] The signal is passed from the medial geniculate body to the auditory cortices and then down to the amygdala. The second loop, which arises from the subconscious level, is called low, subconscious, or subcortical in the model. It provides stimulation from the lower level auditory centers, directly linking the medial geniculate body with the amygdala, and involves the extralemniscal auditory pathways.[53] These two paths are labeled the "high road" and the "low road" in relation to the general functioning of the emotional system."[173]

In the early stages of tinnitus, the high loop is dominant, and the activation of the limbic and autonomic nervous systems is due to cognitive processing of the information and thinking about tinnitus. Later this loop and corticothalamic and corticolimbic interaction might still play a role in the activation of the limbic and autonomic nervous systems. This postulate is supported by an analysis of spontaneous magnetoencephalography activity in tinnitus and control subjects which revealed enhancement of gamma band activity in tinnitus subjects and allows prediction of the laterality of tinnitus perception.[54] Other studies that provide support assess the function of the limbic system in patients with tinnitus[174,175] and the results obtained when using an animal model.[176]

However, once negative associations with tinnitus are initiated, the low loop is automatically created and becomes dominant. The low loop does not involve cognition and is controlled by principles governing conditioned reflexes. Consequently, it is fast, and the limbic and autonomic nervous systems are activated before the higher loop may potentially modify reactions. Notably, conditioned reflexes cannot be modified by conscious thinking. Therefore, although the patient may be convinced tinnitus is benign, negative reactions to the tinnitus signal can still occur.

The development of tinnitus as a clinical problem can be traced to activation through these two routes, which, with changes of the strength of the synaptic connections enhance the stimulation of the limbic and autonomic nervous systems by the tinnitus-related neuronal activity that comes from the auditory system. The question of how the neutral signal of tinnitus may evoke persistent, strong distress can be explained by the principles of conditioned reflexes.[177] To create a conditional reflex, the temporal coincidence of sensory stimuli with negative (or positive) reinforcement is sufficient[171,177,178] (Figure 31-2). This initial association can be coincidental, without any real

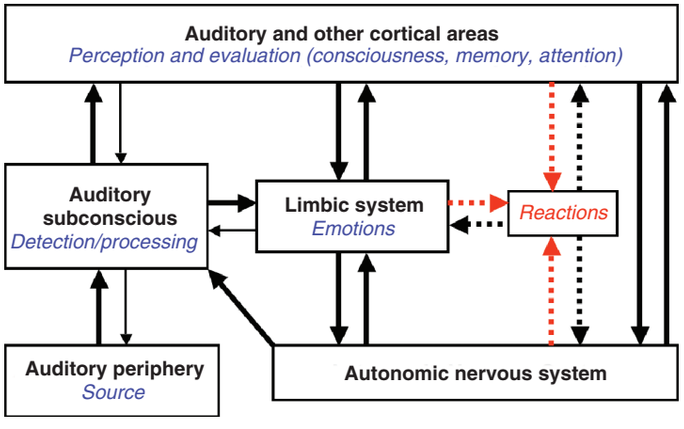

Figure 31-1 The neurophysiological model of tinnitus.

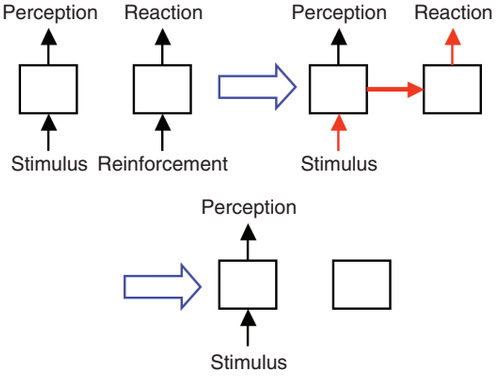

Figure 31-2 Principles of establishing conditioned reflexes and their passive extinction.

dependence. These types of associations of sensory stimuli are constantly created in normal life.

As long as the sensory stimulus is limited in time and there is no functional link between stimulus and reinforcement, the conditioned reflex will gradually disappear (ie, habituate) owing to the passive extinction of the reflex, ie, the sensory stimulus is present but it is not accompanied by reinforcement (see Figure 31-2). Since the 1930s, habituation has been defined as "The extinction of a conditioned reflex by repetition of the conditioned stimulus… the method by which the nervous system reduces or inhibits responsiveness during repeated stimulation."[177] Habituation of perception of this stimulus will follow in the same manner as for all unimportant stimuli.[6]

Notably, there are two types of habituation. The first type, called habituation of reaction, is defined as the "disappearance of a reaction to a neutral stimulus due to its repetitive appearance without reinforcement."[179] The second type, known as habituation of perception, occurs when awareness of this particular stimulus disappears[8] (Figure 31-3). Habituation of reaction and habituation of perception are natural processes. Habituation is a fundamental characteristic of brain function necessitated by the brain's inability to perform two tasks that require complete simultaneous attention.

When the brain is forced to carry out two tasks concurrently that require full consciousness, it uses task switching and is conscious of only one task at a time. The brain areas involved in task switching have been indicated by a functional magnetic resonance imaging study.[180] If forced to monitor all incoming sensory stimuli, our brain would not be able to perform any tasks, except that of switching perception from one sensory stimulus to another, and ultimately paralyzing us in our actions.

To solve this problem, the central nervous system screens and categorizes all stimuli at the subconscious level. If the stimulus is new and unknown, it is passed to a higher cortical level where it is perceived and evaluated. In the case of a stimulus to which we have previously been exposed, the stimulus is compared with patterns stored in memory. If the stimulus is classified as unimportant and does not require action, it is blocked at the subconscious level of the auditory pathways and neither produces any reactions nor reaches the level of awareness. As a result, the reaction to this stimulus and its perception are habituated. In everyday life, habituation occurs to the majority of sensory stimuli surrounding us.

However, if a specific stimulus has been previously classified as important and, on the basis of comparison with the patterns stored in memory, it was linked to something unpleasant or dangerous, this stimulus is perceived and attracts attention. Furthermore, the sympathetic part of the autonomic nervous system is activated, inducing a reaction to this stimulus (frequently of the "fight or flight" variety), which further reinforces memory patterns associated with this stimulus. Consequently, if the previous assessment of the importance of a stimulus has been confirmed, the stimulus becomes even more important; its next appearance will result in faster identification, even in the presence of other competing stimuli, preventing the habituation of this stimulus. In the case of auditory stimuli, our auditory system becomes tuned to recognizing specific patterns of sound that have negative links. In such conditions, the natural habituation of the tinnitus signal becomes impossible. In everyday life, this causes people to have problems with their work, concentration, and sleep.

A simplistic description of the above processes can be outlined to a patient. Increased concern for tinnitus results in an increase in its significance which, in turn, increases the amount of time the patient pays attention to it. This reaction is a classic feedback loop or "vicious circle" scenario, which dramatically increases a patient's level of distress up to the limit of mental and physical endurance. At this stage, the patient will shift from acute tinnitus, which can be easily relieved by proper counseling, to a chronic stage, which is much more difficult to treat.

In the case of tinnitus, it is impossible to remove or substantially change the reactions induced by the excitation of the sympathetic part of the autonomic nervous system. To achieve passive extinction of the conditioned reflex, where stimulus (tinnitus) and negative reinforcement are continuously present, is to decrease the magnitude of negative reinforcement and at the same time the strength of conditioned stimulus (tinnitus) over time. This situation will result in a partial weakening of the reflex, but must be applied consistently to yield positive effects. Moreover, it is fundamental that patients understand these principles so that enhancement of the reflex due to verbal thinking and incorrect beliefs can be minimalized.

Once the activation of the autonomic nervous system is lowered, this in turn decreases negative reinforcement to a signal that is continuously present and consequently gradually decreases the strength of the conditioned reflex. In turn, this further decreases the reaction. Once tinnitus is regarded as neutral, its habituation is inevitable in the same way that the brain continuously habituates to other types of stimuli providing that they are of no significance.

Consequently, retraining counseling (the first component of TRT) is oriented toward reclassifying tinnitus into a category of neutral stimuli and removing the patient's negative associations with tinnitus. This reorientation is accomplished by teaching the patient that tinnitus results from a normal compensatory mechanism which occurs in the auditory system in response to typically minor changes in the cochlea. During counseling, it is important to demystify the mechanisms through which tinnitus may affect a patient's life.

Tinnitus retraining therapy counseling is a teaching session aimed at providing the patient with a new frame of reference by explaining the potential mechanisms of tinnitus generation and the neurophysiological mechanisms through which tinnitus influences various aspects of the patient's life. The patient is taught that by activating a naturally occurring mechanism of brain function (habituation and the plasticity which underlies it), it is possible to achieve habituation of the tinnitus-induced reaction of the brain and body and habituation of the tinnitus perception.

The second component of TRT is sound therapy aimed at deceasing the strength of the tinnitus signal in a systematic manner over the course of treatment.[6,40,157] Sound therapy is based on an important feature of brain function. Our senses work according to the principle of differences of a given stimuli from the background. Moreover, the perceived strength of a signal is not linked directly to the physical strength of a stimulus. Presently, we cannot easily suppress tinnitus-related neuronal activity, but by increasing background neuronal activity we can effectively decrease the strength of the tinnitus signal, which activates the limbic and autonomic nervous systems and which is processed in all the centers involved. By decreasing the strength of the tinnitus signal, we can achieve a decrease of reactions induced by tinnitus and, as a result, facilitate the extinction of the conditioned reflex.

The principles of sound therapy have been supported by results published by independent groups of investigators. For example, the postulate that enriched sound environment yields a regulation of compensatory processes operating within the central auditory pathways, including compensation triggered by decreased auditory input,[20,100,181,182] received support from

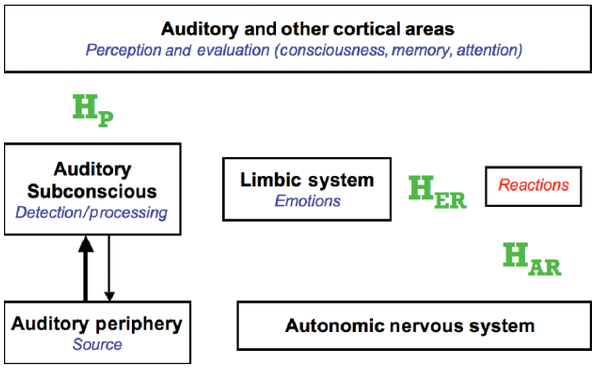

Figure 31-3 Habituation of autonomic (H_{AR}) and emotional reactions (H_{ER}), and habituation of perception (H_P).

basic science[58,183–186] as well as from clinical evidence.[187–189] A trial specifically aimed at evaluating adaptive chronic gain revealed highly statistically and clinically significant improvement as a result of TRT treatment.[190,191]

It is important to analyze the theoretical relationships that exist between the physical intensity of sound and its effectiveness on tinnitus habituation (Figure 31-4). Five principles influence this relationship[6,154] as follows: 1) The negative activation of the limbic and autonomic nervous systems by sounds which could induce annoyance or other problems; 2) stochastic resonance (enhancement of the signal by adding low level noise); 3) dependence of the signal's strength on its contrast with the background; 4) total suppression of the signal, preventing any retraining and habituation; and 5) partial suppression ("partial masking"), which does not prevent retraining but makes it more difficult as training is performed on a different stimulus than the original.

The first principle is dominant over all other principles and relates to the necessity to avoid sounds which would activate the limbic system in a negative manner. Sound used as a part of sound therapy should never evoke annoyance or other problems (eg, worsening speech discrimination) as this would hinder or prevent habituation.

The second principle is that when the sound level is below, but close to, the threshold of detection, stochastic resonance may come into play where the addition of low-level noise can decrease the threshold of detection of the stimulus and enhance it when the stimulus is weak and close to the threshold of detection.[192] The presence of stochastic resonance has been shown at the level of hair cells, the auditory nerve, and all around the brain, and preliminary data indicate its effect on the loudness of tinnitus.[6,193,194] The effective sound level that induces stochastic resonance covers a range of about 15 dB, beginning at about –9 dB below the threshold of detection of the additional noise. Thus, owing to stochastic resonance, enhancement of the tinnitus signal may be caused by adding low-level external noise (eg, by using sound generators set at the threshold of hearing). In turn, this setting will make habituation more difficult. The results of a study in which a comparison was performed among groups with counseling only (including advice on using environmental sounds), counseling combined with sound generators set at the threshold of hearing, and counseling combined with sound generators set close to the "mixing" point fully support the notion of the importance of stochastic resonance. The patients who performed the worst had the sound level set close to the threshold of hearing, whereas the patients who performed best had the sound level set at the "mixing point," with the counseling-only group in the middle.[195]

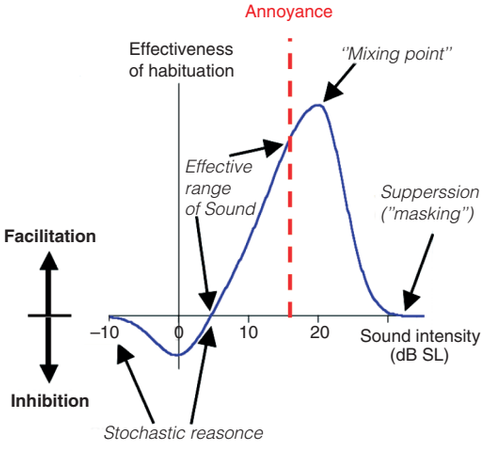

Figure 31-4 Functional dependence of habituation effectiveness on physical intensity of a sound. Notice the need to avoid sound levels close to the threshold of hearing, those inducing partial or total suppression and those evoking annoyance.

The third principle is that when the sound level is further increased, the mechanism involving the decreased difference between the tinnitus signal and background neuronal activity becomes the dominant factor. As with all perception, the difference between signal and background plays a central role. Decreasing the difference between the tinnitus-related neuronal activity and background neuronal activity, yields a decrease of the strength of the tinnitus signal. In turn, the weaker signal is passed to the higher-level cortical areas and, most importantly, to the limbic and autonomic nervous systems. This passing of the signal helps initiate and sustain the process of the passive extinction of conditioned reflexes that link tinnitus to negative reactions.[6,157] As the background activity is the sum of spontaneous and evoked activities, a decrease in the difference between the tinnitus signal and the background neuronal activity can be achieved by exposing patients to additional external sound.

Taken by itself, this principle implies we should use a sound that is as intense as possible. However, it is important to consider two other principles. The fourth principle has two components: 1) once the tinnitus signal is suppressed, by definition habituation will not occur owing to the lack of a signal to habituate; and 2) when the sound level surpasses the threshold of partial tinnitus suppression ("partial masking"), it will modify not only the intensity but also the quality (spectrum) of the tinnitus signal.

The fifth principle is that retraining of neuronal networks will then occur to the modified tinnitus signal and not to the original one. Owing to the generalization principle (ie, reaction can be induced to stimuli similar to the original, with the strength depending on the difference between the original and the modified signal), some habituation may still occur. The higher the external sound is, above the threshold of partial masking, the smaller its contribution to habituation will be. Finally, once the level of total suppression is reached, the effectiveness of habituation is decreased to zero as by definition, any retraining (including habituation) is prevented because the brain cannot change reactions to a stimulus it cannot detect.

In the past we have recommended a different (ie, lower) setting of the sound level emitted by the sound generators when hyperacusis is the dominant or the only problem. However, measurements performed with the use of the Real Ear Measurement system revealed there was no difference in the initial setting of the sound generators in patients with tinnitus only versus patients with tinnitus and hyperacusis.[6] Thus, the first principle is dominant with regard to setting the sound level for all patients.

The beneficial effects of the use of sound have been recently supported by the results of experiments in which animals were exposed to a damaging sound level, which caused hearing loss and presumably tinnitus. Three groups of animals were studied: control, which were exposed to a standard, low level laboratory sound background, and two groups, which were subsequently exposed for several weeks to continuous broadband, low, or high frequency sound. Control animals and animals exposed to low frequency continuous sound exhibited modification of the spontaneous activity recorded from the auditory cortex linked to tinnitus.[55] However, the neuronal activity recorded from animals exposed to continuous high frequency sound was similar to the activity recorded from animals which were not exposed to damaging sound and who did not have tinnitus.[51,55] These data support the view that continuous broadband sound may reverse tinnitus-related changes in the neuronal activity of the auditory cortex.

The need to preserve stimulation in the low frequency range makes it advisable for people with relatively normal, low frequency hearing to be provided devices or hearing aids with fittings that are as open as possible. It is not sufficiently appreciated that in the normal acoustic environment there is a high proportion of low frequency sounds below 200 Hz which provide constant stimulation of the auditory pathways. Since the majority of patients have relatively normal hearing in this frequency range, they benefit from this stimulation. Consequently, blocking the ear canal with closed ear molds decreases the auditory input, and many patients experience the enhancement of tinnitus when their ears are blocked.

Note that even the best hearing aids act as earplugs in low frequencies whether they are the in-the-canal type or are fitted with a closed mold as they are unable to reproduce frequencies below 200 to 250 Hz owing to restriction based on the physics of sound generation by a loudspeaker. Hearing aids for patients with tinnitus are used primarily as a part of sound therapy to provide extra amplification of background sounds and only secondarily for communication. There are other distinct specifics in selection, programming, and the use of hearing aids labeled "tinnitus fitting."[114] Other tools may also be used to enrich the auditory background, such as nature sounds, neutral music, or tabletop sound generators.

Both counseling and sound use are dependent on patient categorization, and issues related to sound are summarized in Table 31-8, adapted from.[196] Details of TRT implementation are presented elsewhere.[6,156,157,160] Categorization provides general guidance for treatment with TRT.[154,197] During treatment, patients may move from one category to another. For example, hyperacusis can be totally eliminated and consequently the patient may move from category 3 to category 1, wherein recommendations regarding sound use should be modified. This change is one reason why follow-up contacts are so important, – first, to continue counseling; second, to check patient status; and third, to modify protocol, if necessary.

Typically, the first effects of TRT can be seen in about one to three months, with clear improvement in about six months. Many patients achieve a high level of control of their tinnitus by about 12 months.[100,113,157] Patients are advised to follow the TRT protocol for at least nine months to prevent a relapse. Improvement in hyperacusis is typically faster than it is for tinnitus; however, the time required for improvement in misophonia is similar to that observed for tinnitus and reflects the similarity of mechanisms and centers involved for both phenomena.[6] The results from other centers and our own when using TRT show satisfactory results in over 80% of patients.[69,96,113,148,195,198–211] Currently, an NIH sponsored randomized clinical trial is being conducted to evaluate the effectiveness of TRT (grants U01DC007411, PI C. Formby, and U01DC007422, PI R. Scherer, ClinicalTrials.gov identifier: NCT01177137). Formby's grant has been described in detail.[205]

TREATMENTS FOR HYPERACUSIS

Treatments for hyperacusis move in two contrary directions. The most common approach is to advise patients to avoid sound and use ear protection. This advice is based on reasoning including since patients became sensitive to sound, they are supposedly more susceptible to sound exposure and consequently need extra protection. Patients easily embrace this philosophy and begin to protect their ears, even to the extent of using earplugs in quiet environments. Unfortunately, this approach makes the auditory system even more sensitive and further exacerbates hyperacusis.[68,69,184,212,213]

Another approach to treating hyperacusis involves desensitization in which patients are exposed to a variety of sounds. The desensitization approach has been promoted for some time with a number of protocols and types of sounds used, such as using sound with certain frequencies removed, short exposure to moderately loud sound or prolonged exposure to low level sounds.[100,212] According to the principles of the neurophysiological model of tinnitus, the latter approach is recommended and is used as part of TRT. Independent results dramatically support the highly statistically and clinically significant effect of TRT treatment for hyperacusis.[69,190] Importantly, the misophonic component cannot be removed by desensitization, and therefore a separate approach must be implemented.[9,10,72,214]

Tinnitus Retraining Therapy for Decreased Sound Tolerance

Tinnitus retraining therapy can help patients with both tinnitus and hyperacusis. The presence of hyperacusis is one of the key factors in the categorization of patients (Table 31-8) and in determining the optimal protocol for treatment. It is recommended that if hyperacusis is present, it must be treated first. Although TRT offers a treatment for tinnitus rather than a cure, for some patients with DST, it can completely remove hyperacusis and misophonia, and thus provide a cure for these conditions.[10,154]

In some patients, tinnitus and hyperacusis are two manifestations of the same internal mechanisms of increased gain within the auditory pathways, and the improvement in hyperacusis results in the improvement in tinnitus as well. Moreover, the removal of hyperacusis yields a decrease in general anxiety and stress which, in combination with proper counseling, significantly facilitates tinnitus habituation.

A few parameters of the TRT protocol are of specific importance when treating patients with hyperacusis: avoiding silence and continually being exposed to sound are even more important for these patients than for patients who only have tinnitus. The sound level should be better controlled during treatment, which necessitates the use of wearable sound generators. The sound used should never induce discomfort or annoyance.

Patients with DST and particularly misophonia tend to set the sound level of their devices close to or at the threshold of hearing, which might

Table 31-8 Categories of Patients with Tinnitus and Hyperacusis

Category	Impact on life	Tinnitus	Significant hearing loss	Hyperacusis	Prolonged sound induced exacerbation	Counseling	Instrumentation
0	**Low**	Present	–	–	–	Abbreviated, with special care to avoid presentation that tinnitus can be worse that in specific case	No wearable devices necessary, but still can be used
1	High	**Present**	–	–	–	Extensive, focused at mechanisms involved in tinnitus generation and in inducing reactions.	SG set, if possible, at a mixing point
2	High	Present	**Present**	–	–	Extensive, focused at mechanisms linking tinnitus and hearing loss.	Combi or HA with stress on enrichment of the auditory background
3	High	Present or absent	Present or absent	**Present**	–	Extensive, focused at mechanisms of decreased sound tolerance. When hearing loss is present as well, the mechanisms linking it with decreased sound tolerance and tinnitus are discussed.	SG only in cases of normal hearing. Combi (or HA) when significant hearing loss present.
4	High	Present or absent	Present or absent	Present	**Present**	Extensive, highly individualized with discussion of potential medical problems. Crucial to exclude existence of misophonia.	SG set at low level; slow increase of sound level

Abbreviations: Impact on life — the extent tinnitus and/or hyperacusis influence patient's life; Prolonged sound-induced exacerbation of tinnitus/hyperacusis — when the effects persists to the following day or longer; Significant hearing loss — having a significant impact on patient's life; SG - sound generators; Combi - combination instruments. HA - hearing aids. Common treatment for each category involves counseling and the use of enriched auditory background. Sound used in sound therapy is always set below annoyance level. Note that the presence of misophonia, which is treated concurrently, is not affecting categorization. The dominant features for each category are shown in bold.

induce stochastic resonance and enhance tinnitus for some patients. Furthermore, a low sound level is less efficient for tinnitus and hyperacusis. The use of real-ear measurements, as a guide in setting and checking the sound level for all patients with instrumentation during the initial and follow-up visits, is helpful for patients with DST.

Desensitization works on the auditory system; consequently, this approach will not affect misophonia, which should be addressed via the active extinction of conditioned reflexes between the auditory and limbic systems. In addition to counseling, desensitization is achieved by instructing patients to engage systematically in activities that the patient enjoys in which sound plays an indispensable role and is pleasant, such as actively listening to one's favorite music or audiobooks following a specific protocol.[9] Other activities could be shopping in a mall, going to parties, dining in restaurants, attending movies, etc. The main concept is to create an association of sound with a pleasant situation (implementing the active extinction of conditioned reflexes). There are four classes of protocols for misophonia. Each protocol is geared toward creating a positive association with a sound, but they differ with respect to the extent of control a patient has over the sound environment and (in the case of protocol 4) the use of sounds with positive association together with bothersome sounds which evoke negative reactions.

Protocol level 1 provides the patient with full control over the selection of sound, its level, and duration. As such, it can be used even for patients with coexisting significant hyperacusis and can be implemented from the start of treatment.

Protocol level 2 affords the patient full control over the type of sound, but only partial, indirect control over the sound level, by yielding this control to someone close to the patient, who is instructed to set the sound volume to a level he or she thinks the patient will accept. After a listening session, the patient should provide feedback as to whether the sound level was too high, too low or just fine.

Protocol level 3 enables the patient to select the type of sound, but the sound level is out of the patient's control. This protocol can be used only when significant hyperacusis is absent or has already been eliminated by treatment. Therefore, the introduction of this protocol is frequently delayed.

Protocol level 4 uses the concept of complex conditioned stimuli and combines exposure to sounds which evoke negative reactions with the simultaneous exposure to sound the patient regards as highly positive and enjoyable. The ratio of sound levels of positive-to-negative sound is gradually decreased. Furthermore, in this protocol, the environment where it is implemented is taken into account, as many patients react differently depending on *where* they are exposed to bothersome sound (ie, home, school, a public place, a restaurant, a friend's home). The multisensory aspect of stimuli is also taken into account as some patients react even to seeing someone producing an offensive sound (eg, eating). The specific protocol employed is tailored to the individual patient. Frequently more than one protocol for misophonia is implemented.

CONCLUSIONS

Tinnitus and hyperacusis remain challenging topics to study, and patients with these symptoms are challenging to treat. Many questions are unanswered. The mechanisms of tinnitus and hyperacusis are speculative and not yet proven. At this time, we do not have objective methods to detect and evaluate tinnitus. We believe the neurophysiological model of tinnitus and TRT provide a promising approach that may ultimately result in a better understanding of tinnitus and provide greater help to patients with tinnitus and hyperacusis.

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