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Review Article

A Review of Hyperacusis and Future Directions: Part II. Measurement, Mechanisms, and Treatment

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Purpose: Hyperacusis can be extremely debilitating, and at present, there is no cure. In this detailed review of the field, we consolidate present knowledge in the hope of facilitating future research.
Method: We review and reference the literature on hyperacusis and related areas. This is the 2nd of a 2-part review.
Results: Hyperacusis encompasses a wide range of reactions to sounds, which can be grouped into the categories of excessive loudness, annoyance, fear, and pain. Reasonable approaches to assessing the different forms of hyperacusis are emerging, including brain-imaging studies. Researchers are only beginning to understand the many mechanisms at play, and valid animal models are still evolving. There are many counseling and sound-therapy approaches that some patients find helpful, but well-controlled studies are needed to measure their long-term efficacy and to test new approaches.
Conclusions: Hyperacusis can make life difficult in this increasingly noisy world, forcing sufferers to dramatically alter their work and social habits. We believe this is an opportune time to explore approaches to better understand and treat hyperacusis.

There are at least two approaches to quantifying loudness hyperacusis. The first involves measuring only the uncomfortable loudness level (ULL), whereas the second involves a more complete assessment of the loudness growth function.

Measuring Hyperacusis

Loudness Hyperacusis

ULLs. By definition, people with loudness hyperacusis have lower ULLs than normal (see Figure 1 of Part I). This may occur over a part or all of the audible frequency range, in one or both ears (Baguley & Andersson, 2007). Therefore, measuring ULLs for both ears and over a range of frequencies is an important diagnostic first step. The specific instructions for obtaining ULLs are critical: Table 1 shows the results of two studies on listeners with normal hearing (with no complaints of hyperacusis) using different instructions (Dawson, 1981; Hawkins, 1980). We suggest that "definitely uncomfortable" is an appropriate instruction, but the best definition is probably the one that leads to the smallest inter- or intrasubject variability (an important consideration for future research). Sherlock and Formby (2005) noted that ULLs for listeners with normal hearing varied greatly, with some being as low as 80 dB HL. Anari and colleagues (Axelsson & Anari, 1995; Anari, Axelsson, Eliasson, & Magnusson, 1999) suggested that ULLs of 70 dB HL or less be used as a criterion for diagnosing loudness hyperacusis.

Kamm, Dirks, and Mickey (1978) estimated ULLs as a function of hearing level at 500 and 2000 Hz for subjects with both normal hearing and hearing impairment, although it is unclear whether subjects with hyperacusis were included. Subjects with normal hearing at the test frequencies had ULLs of about 106 dB SPL (95 dB HL) at 500 Hz and about 104 dB SPL (95 dB HL) at 2000 Hz. For subjects with hearing losses greater than about 50 dB, the ULLs were higher. Most hearing losses of less than 50 dB are

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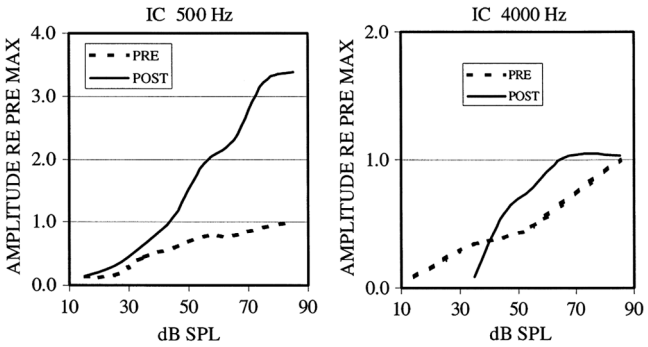
Figure 1. Illustrations of typical chinchilla inferior colliculus (IC) response-amplitude versus sound-level functions at 500 Hz (left) and 4000 Hz (right), before and 30 days after a 5-day exposure to a 2-kHz tone at 105 dB SPL. Note the threshold shift and loudness recruitment but no hyperactivity at 4000 Hz, which is the frequency of greatest exposure-induced hearing loss. In contrast, marked hyperactivity is seen at 500 Hz, which is below the frequency range of the hearing loss. RE PRE MAX = relative to maximum amplitude prior to noise exposure. Reproduced with permission from "Auditory Plasticity and Hyperactivity Following Cochlear Damage," by R. J. Salvi, J. Wang, and D. Ding, 2000, *Hearing Research, 147*, p. 264. Copyright 2000 by Elsevier.



probably caused largely by outer hair cell (OHC) damage, in which case loudness at high sound levels, including the ULL, is not much affected (i.e., there is complete loudness recruitment; see Part I and Moore & Glasberg, 2004). On the other hand, for purely inner hair cell (IHC)–based or neural losses, as in auditory neuropathy, perceived loudness may be lower than normal over a wide range of sound levels, so that for a loss of say 30 dB, the ULL could potentially increase by 30 dB. This explains why hyperacusis is not common in cases of auditory neuropathy; but, see Hickox and Liberman (2014), described further below, for the special case of noise-induced neuropathy.

We propose that the diagnosis of loudness hyperacusis should be based on comparisons with listeners with comparable audiometric thresholds. For example, for a person with normal hearing, a ULL of 80 dB HL might be abnormally low. For someone with a hearing loss of 70 dB, a ULL of 100 dB HL might be abnormally low. More work is needed to develop norms for the range of ULLs associated with specific degrees and types of hearing loss.

Loudness growth functions. A loudness growth function describes the relationship between the level of a sound and its perceived loudness (see Figure 1 of Part I). There are several interval and category scales used to measure loudness (e.g., Al-Salim et al., 2010; Formby, Sherlock, & Gold, 2003; Hébert, Fournier, & Noreña, 2013; for a review, see Florentine, Fay, & Popper, 2011) and an International Organization for Standardization standard for category scales (International Organization for Standardization, 2006). Tyler, Noble, Coelho, Haskell, and Bardia (2009) suggested a clinical procedure for measuring loudness hyperacusis. Patients were asked to assign a number from 0 to 100 to represent the loudness of tones, with 100 described as representing the loudest tone that they could imagine. Lower level sounds were presented first (so as not to frighten the patient), and the highest sound level used was that which produced a loudness rating of 80. Such loudness growth functions provide additional confidence in the diagnosis of loudness hyperacusis or may be used in place of the potentially more unpleasant determination of ULLs.

Table 1. Uncomfortable loudness levels obtained from listeners with normal hearing using different instructions.

Author	No. of listeners	Reference level	Frequency (Hz) 250	500	1000	2000	4000
		Definitely uncomfortable					
Hawkins (1980)	19	dB SPL	118	111	107	108	106
		dB HL	93	100	100	99	97
		Slightly uncomfortable					
Dawson (1981)	3	dB SPL	93	84	84	85	82
		dB HL	68	73	77	76	73

Annoyance and Fear Hyperacusis

R. Dauman and Bouscau-Faure (2005) developed a scale for annoyance hyperacusis (see Part I for definitions), which is referred to as the Multiple-Activity Scale for Hyperacusis. They interviewed 249 tinnitus patients (79% of whom had hyperacusis), asking them to rate the annoyance produced by sounds in each of 15 different settings (e.g., shopping center, concert, work, room with children, church). An average annoyance score was calculated only for those situations that were relevant (annoying) for each individual. The situations that most commonly created annoyance were doing housework, driving a car, and watching TV or attending a cinema, whereas sounds producing the highest annoyance ratings were those of motorcycles, traffic noise, and concerts.

There is an interest and a need to develop new, standard questionnaires focusing on (annoyance) hyperacusis. As an example, Tyler and colleagues (Tyler, Bergan, Preece, & Nagase, 2003; Tyler et al., 2009) have proposed a preliminary questionnaire called The Loudness and Annoyance of Everyday Sounds—which is intended to determine the types and categories of annoying sounds in hyperacusis—as well as The Relative Handicap of Hearing Loss, Tinnitus, and Hyperacusis—which is intended to assess the relative importance of common listening situations for those affected by these hearing disorders. Results on the use of these questionnaires have not yet been published, but they provide a basis for further research and development in this area.

Medical Evaluation

The medical investigation of a patient with hyperacusis is intended to differentially diagnose possible associated or underlying diseases (see Table 2; also see Part I and Katzenell & Segal, 2001), some of which can be treated. Treatment might alleviate the hyperacusis and associated symptoms and might possibly cure a life-threatening disease.

Table 2. Clinical conditions associated with hyperacusis.

Condition	Examples
Otologic	Bell's palsy, Ramsay Hunt syndrome, Ménière's disease, perilymph fistula, superior semicircular canal dehiscence, acoustic trauma, barotrauma, noise-induced hearing loss, stapedectomy, tympanoplasty
Neurologic	Autism, carotid aneurysm, middle cerebral aneurysm, migrainous cerebral infarction, head injury, Chiari's malformation, sympathetic reflex dystrophy, multiple sclerosis, migraine, epilepsy, myasthenia gravis, cerebrospinal hypertonia, primary thalamo deficiency, attention-deficit disorder, anxiety and depression disorders, posttraumatic stress disorder, complication of spinal anesthesia
Endocrine	Addison's disease, pan-hypopituitarism, hyperthyroidism
Infection	Neurosyphilis, Lyme disease, typhoid fever
Medication	Benzodiazepine and antidepressant withdrawal, acute phenytoin intoxication
Deficiency	Magnesium and pyridoxine
Genetic or congenital	Williams syndrome, idiopathic hypercalcemy (Fanconi and Williams–Beuren syndrome), Cri du Chat syndrome, Tay–Sachs disease, Cogan syndrome, GM1 gangliosidosis, spina bifida
Other	Temporomandibular disorders, fibromyalgia

Clinical History

The clinical history can provide important clues about etiology (e.g., noise exposure) and is used to select laboratory and radiological examinations as well as treatments. Anxiety, depression, and concentration and sleep problems are frequent comorbidities.

Physical Examination

A complete neurotologic physical examination is required, including otoscopy, pneumatoscopy (to determine the mobility of the tympanic membrane), and assessment of whether vertigo is experienced. The presence of a clicking or popping sound during chewing, jaw locking, and changes in the biting pattern and dental occlusion are likely to indicate the presence of temporomandibular dysfunction, which has been linked with hyperacusis (Burris, Evans, & Carlson, 2010; Hilgenberg, Saldanha, Cunha, Rubo, & Conti, 2012).

Laboratory Evaluation

Blood tests can include a whole blood count and measures of sodium, potassium, thyroid stimulating hormone, and free thyroxine, useful in screening for infections and endocrinological diseases. Deficiencies in magnesium and Vitamin B6 levels can cause syndromes linked to neural hyperactivity. Serological tests, which measure the levels of specific antibodies in the blood, are used to diagnose diseases linked with hyperacusis, such as syphilis, herpes zoster, and Lyme disease.

Imaging Tests

Imaging tests are used to diagnose otologic and neurologic problems. For example, if the suspicion is a semicircular canal dehiscence (Minor et al., 2001) or facial paralysis (Byl & Adour, 1977), high-resolution computed tomography of the temporal bone (Belden, Weg, Minor, & Zinreich, 2003) is recommended. If a dural vascular malformation is suspected, an angiography is indicated. Carotid aneurysm can be explored with neck magnetic resonance imaging, computed tomography, as well as angiography or magnetic resonance angiography (Weissman & Hirsch, 2000).

Animal Models

Laboratory animals with compromised hearing can show neural responses and behavior that have been interpreted as evidence of hyperacusis.

Physiological Models

Liberman and Kiang (1978) showed that auditory nerve fibers in cats with noise-damaged cochleas exhibited a loss of sensitivity around the tips of their tuning curves (i.e., for frequencies close to their characteristic frequencies) but exhibited increased sensitivity for frequencies well below the characteristic frequency (i.e., the tuning curves showed hypersensitive tails). Thus, cochlear output was enhanced in the frequency range below that of the greatest hearing loss, and this could plausibly contribute to hyperacusis. It is thought that hypersensitive auditory nerve tuning curve tails result from a decreased stiffness of the organ of Corti following a widespread destruction of OHCs (see, e.g., Versnel, Prijs, & Schoonhoven, 1997).

Hyperacusis-like phenomena have been reported at the level of the dorsal cochlear nucleus (DCN) in the auditory brain stem. Chinchillas with minimally elevated hearing thresholds caused by a moderate acoustic overexposure several months prior showed elevated spontaneous and stimulus-driven activity of second-order DCN neurons (fusiform cells) relative to unexposed animals tested under identical conditions (Brozoski, Bauer, & Caspary, 2002). The elevated spontaneous activity was interpreted as evidence of tinnitus, whereas the elevated stimulus-driven activity, which encompassed both higher asymptotic spike rates and steeper spike rate versus sound level functions, was interpreted as evidence of hyperacusis and loudness recruitment, respectively. This noise-induced hyperactivity of DCN neurons presumably influences the activity of higher central auditory centers, including the inferior colliculus and auditory cortex, as described below.

Salvi, Saunders, Gratton, Arehole, and Powers (1990) measured local field potentials (LFPs) in the inferior

colliculus of chinchillas several weeks after a 5-day exposure to a 2-kHz tone at 105 dB SPL. At the frequencies of greatest hearing loss (20–30 dB between 2 and 8 kHz), LFP thresholds were elevated, and maximum LFP amplitudes were typically reduced or normal (recruitment). However, at 0.5 kHz, for which there was no loss of sensitivity, LFP amplitudes were in most cases substantially larger than normal, again suggestive of hyperacusis (see Figure 1). These results were confirmed by the same group a decade later (Salvi, Wang, & Ding, 2000).

Noreña, Moffat, Blanc, Pezard, and Cazals (2010) found elevated sound-evoked activity in the auditory cortex of awake guinea pigs immediately and up to 14 days after exposure to intense sound (120 dB SPL at 8 kHz for 2 hr). The thresholds of cortically recorded LFPs were elevated, indicative of hearing loss, but at suprathreshold sound levels, LFP amplitudes were significantly greater than before exposure. Similarly elevated cortical LFPs at suprathreshold sound levels were obtained for up to 1 day following a large (350-mg/kg) systemic dose of sodium salicylate (aspirin). It was concluded that both acoustic trauma and high-dose salicylate can induce hyperactivity in the auditory thalmocortical pathways (Noreña et al., 2010).

A similar finding was reported by Sun et al. (2009) in rats systemically administered sodium salicylate (250 mg/kg). LFPs recorded from awake animals within 4 hr of salicylate treatment were elevated across a broad frequency range in auditory cortex but not in the inferior colliculus and not in the cochlea (assessed via compound action potentials recorded from the round window). Furthermore, salicylate applied directly to the cochlea failed to produce central hyperactivity (Sun et al., 2009). Zhang, Yang, Cao, Qin, and Sato (2011) replicated these findings in awake cats following a 200-mg/kg systemic dose of sodium salicylate. Sun, Deng, Jayaram, and Gibson (2012) followed up by reporting sound-evoked cortical hyperactivity in the rat following an acute noise trauma, confirming the earlier work of Noreña et al. (2010).

Caution is needed when interpreting experiments that use salicylate to induce hyperacusis-like phenomena. Salicylate produces a wide range of peripheral and central effects. It reduces the action of the inhibitory neurotransmitters gamma-aminobutyric acid (J. Lu et al., 2011) and glycine (Y.-G. Lu et al., 2009), which would be expected to increase neural activity. In vitro studies have shown that salicylate inhibits outward potassium currents in cochlear IHCs, which is expected to maintain hair cell depolarization and to increase spike firing in the auditory nerve (Kimitsuki et al., 2011). However, salicylate also inhibits prestin (the molecular motor of the OHCs; see, e.g., Chen et al., 2010), inhibits the cellular cyclooxygenase pathway, lowers intracellular pH, and negatively affects intracellular calcium balance, with broad physiological consequences. It remains unclear whether salicylate-induced hyperactivity is relevant to the forms of hyperacusis that are commonly encountered in the clinic. A recent review addresses the relevance of the salicylate model of tinnitus (Stolzberg, Salvi, & Allman, 2012).

Behavioral Models

Behavioral evidence of hyperacusis in animals has commonly been inferred on the basis of acoustic startle reflex testing. When exposed to a brief but intense burst of sound (e.g., 120 dB SPL for a few milliseconds), animals, including humans, will reflexively flinch. In small animals, such as rats and mice, this whole-body, postural-muscle reflex can be measured using a test chamber equipped with a sensitive accelerometer. It can also be measured using evoked potentials. Mice with congenital age-related, high-frequency hearing loss (e.g., C57BL/6J mice) have been shown to have a greatly exaggerated startle reflex to tonotopically overrepresented low-frequency pips (Ison & Allen, 2003; Ison, Allen, & O'Neill, 2007). This increased startle response has been interpreted as behavioral evidence for (low-frequency) hyperacusis.

The startle reflex can be reduced if a moderately intense sound precedes the very intense, startle-evoking sound, a phenomenon called *prepulse inhibition*. Turner and Parish (2008) reported that systemic sodium salicylate (150–300 mg/kg) increased the effect of prepulse inhibition. The interpretation is that as the salience of the (startle-warning) prepulse increased, because of salicylate-induced central hyperactivity (i.e., hyperacusis), the startle reflex became more inhibited. Similarly, Sun et al. (2009) reported that in rats, systemic sodium salicylate produced a significant, transient increase of approximately 70% in the acoustic startle reflex. The above-mentioned caution about interpreting salicylate-induced auditory effects applies here as well.

In a recent study, Chen et al. (2013) recorded startle responses in hamsters over several months following an acute overexposure (10 kHz, 115 dB SPL, 4 hr). Compared with controls, exposed animals exhibited about a twofold increase in startle amplitudes. Addition of background noise had little effect on startle amplitudes in controls, but it significantly decreased startle in the exposed animals (in proportion to the level of the background noise), suggesting that they were perceiving the noise as louder than normal and that this noise sensitization inhibited the startle response. Finally, exposed animals also showed reduced prepulse inhibition of startle compared with controls when the prepulse was a silent gap embedded in a noise background; this has been interpreted as evidence of tinnitus (Chen et al., 2013; Turner et al., 2006), suggesting that both tinnitus and hyperacusis may have been induced following the acute overexposure.

Most recently, Hickox and Liberman (2014) studied the startle response in mice following an exposure regimen (8–16 kHz noise for 2 hr at 94–100 dB SPL) that produced extensive inner hair cell synapse loss and (in the longer term) auditory nerve fiber degeneration but, importantly, no loss of the hair cells themselves and no permanent threshold shifts. Both startle amplitudes and their prepulse inhibition suggested hyperacusis-like behavior (as described above) in noise-exposed animals with neuronal loss, compared with both controls and with exposed animals that did not develop neuronal loss. The results of the gap-startle

test for tinnitus were less conclusive. Such noise-induced neuropathy could explain the emergence of hyperacusis (and perhaps also tinnitus) in patients with normal audiometric thresholds.

Mechanisms of Hyperacusis

We limit ourselves to a discussion of the mechanisms of loudness hyperacusis, as the mechanisms of annoyance, fear, and pain hyperacusis are less well understood (see Wagenaar, Wieringa, & Verschuure, 2010). It is likely that these latter forms of hyperacusis include mechanisms common to all reactions of annoyance, fear, and pain.

Neural Codes for Loudness

Much progress has been made in understanding how the auditory system encodes the intensity of sound, although researchers' understanding remains incomplete (see reviews, and the references therein, by Lopez-Poveda, 2005; Moore, 2012; Robles & Ruggero, 2001; Ruggero, 1992). Briefly, as sound intensity increases above the threshold of a (Type I) auditory nerve fiber, its spike rate rises monotonically from some spontaneous value and saturates at some maximal value, which is maintained at higher intensities. The 10 or so auditory nerve fibers normally innervating a single IHC have graded thresholds, so the number of activated nerve fibers grows with increasing sound intensity. Because the less sensitive (high-threshold) fibers tend to saturate at higher intensities than the more sensitive (low-threshold) fibers, changes in sound intensity produce changes in firing rate in some fibers across the full hearing intensity range (normally >100 dB) despite the more limited dynamic ranges (typically <40 dB) of the individual fibers.

Furthermore, as sound intensity increases, the initially sharply tuned basilar membrane vibration profile evoked by narrowband sounds broadens toward the cochlear base, which also increases the number of auditory nerve fibers activated at higher intensities. Finally, for sounds with frequencies up to a few kHz (a limit imposed by the capacitance of the IHC membrane), spikes are phase-locked to individual cycles of the waveform on the basilar membrane. Improvements in phase-locking with sound level may also provide a "neural code" for loudness.

As mentioned above, both the firing rate and the precision of phase-locking in individual auditory nerve fibers increase with increasing sound level. This results in an increased synchrony of firing across auditory nerve fibers. In the cochlear nucleus, some of the bushy and stellate cells are sensitive to coincident inputs from different auditory nerve fibers (Oertel, Wu, & Hirsch, 1988). In general, synchronous firing more strongly activates higher level neurons, especially in the auditory cortex, where many individually weak afferent inputs converge on a single cell (Eggermont, 2000). However, it is not clear whether neural synchrony plays a role in loudness perception independent of its role in signaling the presence of steady-state sounds (deCharms & Merzenich, 1996; Eggermont, 1997). Studies of the frog auditory midbrain (Eggermont, 1989) and cat auditory cortex (Eggermont, 2000) showed that although neural synchrony did increase during sound stimulation compared with during spontaneous firing, the increase did not depend on sound intensity.

A major complication for neural models of sound intensity representation is that the primary goal of the auditory system is to recognize a meaningful sound regardless of its intensity or signal-to-noise ratio. Thus, by the level of auditory cortex, complex sounds may be represented in a largely intensity-independent, "object-oriented" fashion (Billimoria, Kraus, Narayan, Maddox, & Sen, 2008; Pienkowski & Eggermont, 2011c; for a review, see Barbour, 2011), particularly during attentive listening (Ding & Simon, 2012; Mesgarani & Chang, 2012), although the basis for such representations may begin to emerge in the cochlear nucleus (Blackburn & Sachs, 1990; for a review, see Young, 1998). The level-tolerant cortical representation of complex sounds contrasts with the more predictable (auditory nerve-like) cortical representation of simple tones: Several functional magnetic resonance imaging studies have demonstrated a positive correlation between stimulus tone levels and the magnitude and extent of the blood oxygen level dependent responses in human and monkey auditory cortex (Bilecen, Seifritz, Scheffler, Henning, & Schulte, 2002; Hall et al., 2001; Hart, Hall, & Palmer, 2003; Tanji et al., 2010). Nevertheless, even for simple sounds, the mechanisms by which neural activity is integrated and ultimately decoded as loudness, including the spatiotemporal scales on which this integration occurs, remain largely unknown (Florentine et al., 2011).

Possible Mechanisms Underlying Loudness Hyperacusis

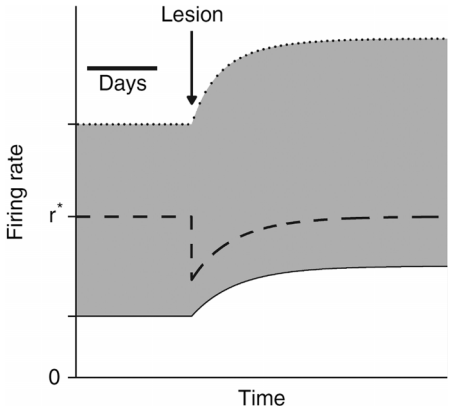
Elevated sound-evoked firing rates as a consequence of homeostatic plasticity and related gain adaptation phenomena. Homeostatic plasticity is the process by which the central nervous system attempts to stabilize neural firing rates within a prescribed long-term range (when averaged over hours or days) by adjusting the intrinsic excitability of neurons (Desai, Rutherford, & Turrigiano, 1999) and/or the number and strength of their excitatory (Turrigiano, Leslie, Desai, Rutherford, & Nelson, 1998) and inhibitory (Kilman, van Rossum, & Turrigiano, 2002) synaptic inputs (Burrone & Murthy, 2003; Maffei & Fontanini, 2009; Turrigiano, 1999, 2008; Turrigiano & Nelson, 2004). Such plasticity can be triggered by changes in the prevailing patterns of sensory stimuli. In the auditory system, reduced sound input (e.g., following hearing loss) can lead to an increase in central auditory excitability (Argence et al., 2006; Kotak et al., 2005; McAlpine, Martin, Mossop, & Moore, 1997; Vale & Sanes, 2002; Walmsley, Berntson, Leao, & Fyffe, 2006), whereas increased sound input (e.g., following persistent exposure to moderate-level noise) can lead to a decrease in central auditory excitability (Noreña et al., 2010; Pienkowski & Eggermont, 2009, 2011b; Zhou & Merzenich, 2012). A similar, homeostatic-type gain adaptation mechanism can tune neural responses to much more

rapid (on the order of seconds) fluctuations in sensory stimulus statistics (Brenner, Bialek, & de Ruyter van Steveninck, 2000; Dean, Harper, & McAlpine, 2005; Dean, Robinson, Harper, & McAlpine, 2008; Dragoi, Sharma, & Sur, 2000; Dunn & Rieke, 2006; Robinson & McAlpine, 2009; Schwartz & Simoncelli, 2001; Simoncelli & Olshausen, 2001). Both slow homeostatic plasticity and the faster gain adaptation phenomena may function to optimize precision in neural encoding by matching afferent activity levels to the operating ranges of central neurons; this is akin to adjusting the amplifier gain in a digital signal processing application to utilize the full input range of the analog-to-digital converter.

In compensating for reduced auditory nerve fiber activity following hearing loss, homeostatic phenomena can lead to increased spontaneous and sound-evoked firing rates in the central auditory system (Chrostowski, Yang, Wilson, Bruce, & Becker, 2011; Parra & Pearlmutter, 2007; Schaette & Kempter, 2006, 2008, 2012; Zeng, 2013) and even induce epileptic seizures (Fröhlich, Bazhenov, Iragui-Madoz, & Sejnowski, 2008; Trasande & Ramirez, 2007). The increase in central auditory spontaneous rates is a potential substrate of tinnitus, whereas the increase in sound-evoked rates may be a substrate of hyperacusis. To illustrate this idea, consider a hearing loss due almost entirely to OHC dysfunction (e.g., caused by gentamycin ototoxicity). This will reduce average evoked activity rates in auditory nerve fibers (Heinz & Young, 2004; Liberman & Dodds, 1984) but not their spontaneous rates—which are determined solely by the integrity of the IHCs (Dallos & Harris, 1978)—and not their responses to very intense sounds—which are determined solely by passive basilar membrane mechanics, independent of the OHCs (Robles & Ruggero, 2001). A homeostatic mechanism based on a multiplicative scaling of synaptic gains, aimed at restoring activity in central auditory neurons to the same average activity levels as before the OHC loss, would increase spontaneous firing rates, potentially leading to tinnitus, and would increase firing rates in response to moderately intense sounds, potentially leading to hyperacusis (see Figure 2).

According to this model, it is crucial for the generation of tinnitus or hyperacusis that the hearing loss (or some other factor) decreases the normal ratio of the mean to the spontaneous firing rate (for tinnitus) or the mean to the maximum firing rate (for hyperacusis). If these ratios are not reduced, as for example in a hearing loss due almost entirely to IHC dysfunction (which will affect spontaneous, mean, and maximal rates in the auditory nerve roughly equally), multiplicative synaptic scaling to restore the mean rates of central neurons would also restore—but not elevate—their former spontaneous and maximum rates. Thus, the homeostatic model can potentially explain why not all types and degrees of hearing loss lead to tinnitus or hyperacusis. This is supported by the finding that the magnitude of the hyperactivity induced in the DCN of hamsters following cisplatin administration was strongly correlated with the extent of OHC damage but not with the extent of IHC damage (Kaltenbach et al., 2002). The same model can explain the emergence of tinnitus or hyperacusis in cases of conductive hearing loss (Schaette & Kempter, 2012) or noise-induced damage specific to the high-threshold, low-spontaneous rate auditory nerve fibers (Schaette & McAlpine, 2011).

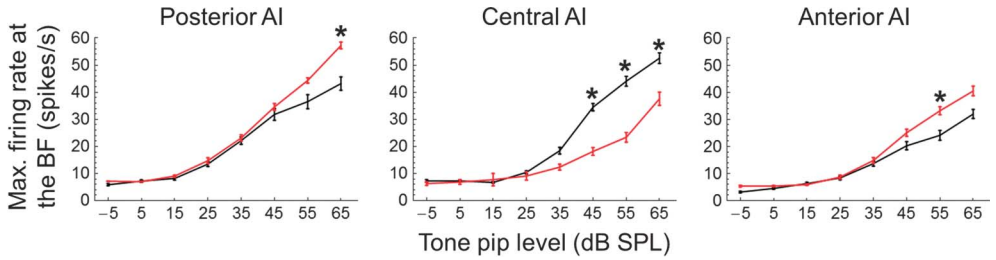
Figure 2. Hypothetical range of neural firing rates (gray) in a population of central auditory neurons before and after a sudden lesion restricted to the outer hair cells (OHCs). The mean firing rate over time is indicated by the dashed curve and has a prelesion value of r^*; spontaneous and maximal sound-evoked rates bound the range and are shown with solid and dotted curves, respectively. Because OHC loss affects only the mean but not the spontaneous or maximal rates (see text), a homeostatic restoration of the mean rate back to r^* could lead to increased spontaneous and maximal rates, potentially resulting in tinnitus and hyperacusis, respectively. Reproduced with permission from "Development of Tinnitus-Related Neuronal Hyperactivity Through Homeostatic Plasticity After Hearing Loss: A Computational Model," by R. Schaette and R. Kempter, 2006, *European Journal of Neuroscience, 23*, p. 3127. Copyright 2006 by John Wiley and Sons.



A common objection raised against this model is that tinnitus or hyperacusis may be present in subjects with otherwise apparently normal hearing, which the model cannot explain. However, normal hearing thresholds (the only metric reported by most studies) do not necessarily indicate the absence of more subtle cochlear damage (Job, Raynal, & Kossowski, 2007; Kujawa & Liberman, 2009; Schaette & McAlpine, 2011; Weisz, Hartmann, Dohrmann, Schlee, & Noreña, 2006), which, as the model predicts, could lead to the generation of central auditory hyperactivity (tinnitus and/or hyperacusis) in the absence of audiometric threshold shifts (Hickox & Liberman, 2014).

Consistent with the homeostatic plasticity model, recent animal studies have shown that several weeks to months of passive exposure to moderate-level (65–80 dB SPL) noise can profoundly alter the long-term representation of sound intensity in the auditory cortex of mature cats and rats, in the apparent absence of damage to the cochlea (Noreña et al., 2010; Pienkowski & Eggermont, 2009, 2011b; Zhou & Merzenich, 2012). In particular, exposure to bandlimited sounds can lead to a decrease of auditory cortical activity in response to sound frequencies in the region of the exposure band and to an increase of activity in response to sound frequencies well away from the exposure band (see Figure 3). This exposure-induced

Figure 3. Auditory cortical population firing rate versus sound-level functions (i.e., rate-level functions) obtained by averaging the peak responses to characteristic frequency (CF) tones of large samples of neurons recorded extracellularly in the primary auditory cortex (AI) of cats. Black curves show results from unexposed adult control cats, and red curves show results from adult cats exposed continuously for 6 weeks to a 4–20-kHz band of noise at ~70 dB SPL. Data from individual neurons were pooled and averaged according to recording electrode location in AI: "Posterior AI" contained neurons with CFs <4 kHz (below the frequency range of the noise exposure band); "Central AI" contained neurons with CFs in the range of 4–20 kHz (within the exposure band); and "Anterior AI" contained neurons with CFs >20 kHz (above the exposure band). Error bars show ±1 standard error, and asterisks indicate pairwise differences significant at $p < .05$ (analysis of variance with post hoc Bonferroni tests). It can be seen that noise exposure induced neural hyperactivity in the posterior and anterior regions of AI and that it induced hypoactivity in central AI. BF = best frequency. Adapted from "Can Persistent Exposure to Moderately Loud Sound Lead to Hyperacusis and/or Tinnitus?" by M. Pienkowski and J. J. Eggermont, 2011, *Proceedings of the Fifth Meeting of the Tinnitus Research Initiative*, p. 40.



cortical plasticity could cause a frequency-specific rescaling of loudness growth functions. The suppression of cortical responses to sounds within the exposure frequency range could lead to hypoacusis (reduced sensitivity to sound) over that range, whereas the enhancement of cortical responses to sounds outside of the exposure frequency range could lead to a hyperacusis over that range. Additional animal studies linking changes in auditory cortical activity to changes in loudness perception are needed to test such hypotheses.

In spite of the paucity of studies combining neural and behavioral approaches to the problem of loudness perception, there is substantial psychophysical evidence of loudness rescaling in human subjects following long-term changes to their listening environments, which indirectly supports the homeostatic plasticity model for the emergence of hyperacusis and tinnitus. Formby et al. (2003) demonstrated reversible hyperacusis in a group of subjects with normal hearing who wore ear plugs for 2 weeks, and a reversible hypoacusis in another group after 2 weeks of exposure to moderate-level (50 dB SPL) noise (see also Munro & Blount, 2009). Noreña and Chery-Croze (2007) found that existing hyperacusis was ameliorated in patients after 2–15 weeks of listening for 1–3 hr daily to a moderate-level ensemble of tones whose component levels (maximum 75 dB SPL) were matched to the hearing loss so as to be just audible.

Other studies (Gatehouse, 1992; Hamilton & Munro, 2010; Olsen, Rasmussen, Nielsen, & Borgkvist, 1999; Philibert, Collet, Vesson, & Veuillet, 2005) have shown that hearing aid use leads to higher ULLs (reduces hyperacusis) for binaurally aided subjects compared with hearing-loss-matched, nonaided controls as well as for monaurally aided subjects (with similar binaural losses) in the aided relative to the nonaided ear. It has also long been known that spending even a short time in a very quiet environment (e.g., a good sound-attenuating booth) leads the majority of subjects with normal hearing to experience a transient tinnitus (Del Bo et al., 2008; Heller & Bergman, 1953; Tucker et al., 2005). As this sensation takes at least a few minutes to develop, it is unlikely to be because of unmasking of an already-present tinnitus by the elimination of background noise but probably reflects the operation of a fast-acting gain adaptation mechanism (Noreña, 2011). Finally, in a related recent study, Schaette and Kempter (2012) noted that reversible tinnitus developed in a majority of their subjects after 1 week of ear plug wearing.

Elevated neural synchrony. Animal studies have shown that increases in spontaneous firing rates following an acute exposure to loud noise develop only after delays of a few hours in the primary auditory cortex (A1; Noreña & Eggermont, 2003) and a few days in the DCN (Kaltenbach et al., 2002) and inferior colliculus (Mulders & Robertson, 2009), although shorter onsets in the colliculus of between 4 and 12 hr were recently reported (Mulders & Robertson, 2013). However, humans commonly experience tinnitus immediately after a loud noise exposure (Atherly, Hempstock, & Noble, 1968), and increases in spontaneous firing rate cannot explain this immediate and usually transient occurrence of tinnitus. In contrast to the delay in the emergence of spontaneous hyperactivity, localized increases in the synchrony of spontaneous firing were observed in cat primary auditory cortex immediately following noise trauma (Noreña & Eggermont, 2003; Seki & Eggermont, 2003). This increase in spontaneous synchrony has been hypothesized to contribute to tinnitus (Eggermont & Roberts, 2004). It may also contribute to hyperacusis. The increased synchrony probably arises from the increase in common inputs between cortical cells because of the unmasking of intracortical connections as a result of the noise-induced partial loss of (thalamocortical) afferent activity (Noreña & Farley, 2013). Studies of human subjects with tinnitus have shown higher than normal synchrony in the theta and gamma bands of electroencephalography and magnetoencephalography

recordings (Llinas, Urbano, Leznik, Ramirez, & van Marle, 2005; Weisz et al., 2007), although it remains unclear whether increased neural synchrony in the absence of sound actually causes tinnitus or is merely a correlate of tinnitus.

We previously raised the possibility that the perception of loudness depends partly on the degree of neural synchrony in the auditory brain, independent of the firing rate. Just as tinnitus could result from abnormally synchronized spontaneous activity, perhaps even in the absence of changes in average spontaneous rates, hyperacusis could result from an abnormally high synchrony of sound-evoked activity. As far as we know, this issue has not yet been investigated.

Central tonotopic map reorganization. Damage to parts of the receptor epithelium can lead to a reorganization of primary somatosensory (Merzenich et al., 1984), auditory (Rajan, Irvine, Wise, & Heil, 1993; Robertson & Irvine, 1989), and visual (Kaas et al., 1990) cortex. Topographically ordered cortical neurons deprived of their normal afferent inputs gradually became tuned to stimuli activating nearby undamaged areas of epithelium. For example, following a (sufficiently severe) high-frequency hearing loss, the normally transduced "lesion-edge" frequencies become overrepresented and activate a larger than normal region of A1. Such a reorganization of A1 has been found in both developing and mature animals of a large number of species (Irvine, Rajan, & McDermott, 2000). However, it has proven more difficult to demonstrate such effects in humans using noninvasive imaging techniques (Dietrich, Nieschalk, Stoll, Rajan, & Pantev, 2001; Lütkenhöner, Krumbholz, & Seither-Preisler, 2003; Wienbruch, Paul, Weisz, Elbert, & Roberts, 2006).

What are the perceptual consequences of the cortical overrepresentation of lesion-edge frequencies following a high-frequency hearing loss? Willott, Carlson, and Chen (1994) studied the prepulse inhibition of the acoustic startle reflex in the C57BL/6J mouse. As mentioned earlier, this mouse suffers from a progressive high-frequency loss shortly into its adult life. They found that the startle reflex was suppressed most effectively when the prepulse was delivered at the overrepresented midfrequencies, suggesting that these were perceived as louder (indicating hyperacusis) than when the prepulse was delivered at low frequencies for which sensitivity was normal.

In human subjects with putative cortical reorganization due to steeply sloping, moderate-to-severe, high-frequency hearing loss, small but significant improvements in frequency discrimination have been noted at the lesion-edge frequencies, relative to lower frequencies with similar or better absolute thresholds (McDermott, Lech, Kornblum, & Irvine, 1998; Moore & Vinay, 2009; Thai-Van et al., 2007). In addition, subjects with hearing impairment showed better intelligibility of low-pass filtered speech than controls with normal hearing, and they also showed better intelligibility for their worse compared with their better ears, although the differences were not large (Moore & Vinay, 2009; Vestergaard, 2003). These illustrations of improved discrimination performance of overrepresented sounds are in line with findings of enhanced auditory cortical representations in musicians (Pantev & Herholz, 2011) and of enhanced function of the remaining senses in cases of total blindness or deafness (Merabet & Pascual-Leone, 2010). However, more direct evidence is needed to test the hypothesis that an increase in the cortical representation of a given sound frequency range can lead to hyperacusis for that frequency range. Furthermore, although it has been reported that there is a strong correlation between cortical reorganization following arm amputation and phantom-limb pain in human amputees (Flor et al., 1995), evidence for a causal link between cortical tonotopic map reorganization and tinnitus (Engineer et al., 2011) remains contentious (Langers, de Kleine, & van Dijk, 2012) as does the legitimacy of the analogy between phantom-limb pain and tinnitus.

Treatments

Counseling

Like tinnitus, hyperacusis can have an impact on a patient's emotional well-being, hearing and communication, as well as sleep and concentration (Tyler et al., 2009). Secondary adverse effects can include poorer socialization, physical health, work performance, education, and finances. Basic aspects of good counseling for tinnitus patients include the ability to listen, have patience, be encouraging to the patient, and talk candidly about emotional psychological issues (Tyler, Haskell, Preece, & Bergan, 2001; Tyler et al., 2009), and these apply also to patients with hyperacusis. Patients with hyperacusis often suffer from a lack of understanding from others, mainly because their condition is subjective and invisible. A first step is to learn, and to help the patient learn, about his or her individual motivations and behaviors associated with hyperacusis (N. Dauman & Erlandsson, 2012). This should include identifying the precise situations that hinder daily activities (R. Dauman & Bouscau-Faure, 2005).

A collaborative approach to counseling will do the following:

1. Encourage the patient to express his or her reluctance or fear of being exposed to sound by describing specific situations in which problems occur (Bläsing & Kröner-Herwig, 2012).
2. Identify behaviors and emotions attributed to others who are making the noise (e.g., lack of consideration) that might contribute to the patient's annoyance.
3. Discuss repressed behaviors that might be associated with the annoyance or fear produced by sounds (Levy-Leboyer & Naturel, 1991).
4. Identify noisy circumstances over which the patient has some control—this has the potential to assure him or her that he or she is able to tolerate some sounds (R. Dauman & Bouscau-Faure, 2005).

Methods of counseling hyperacusis patients could benefit from further research into the influence of social environments from the individual patient's perspective.

Hyperacusis Activities Treatment

With the high coexistence of tinnitus and hyperacusis, many therapies for hyperacusis follow paradigms established to treat tinnitus. One example is the Hyperacusis Activities Treatment (Tyler et al., 2009), modeled after the Tinnitus Activities Treatment (Tyler et al., 2006). The counseling components focus on (a) thoughts and emotions, (b) hearing and communication, (c) sleep, and (d) concentration. It is important to help the patient recognize the relationship between the loudness of a sound and his or her reaction to it. The sound-therapy components (further details provided below) include (a) continuous low-level broadband noise, (b) successive approximations to high levels of noise, (c) successive approximations to troublesome sounds, (d) partial masking with a variety of sounds (including music), and (e) the gradual increase of the maximum output of hearing aids.

Social Support

As discussed in Part I of this article, the annoyance of sound is influenced by the listener's perceived degree of control over the sound, by the interpretation of the motives of those involved in producing the sound, and by the social relationship between the listener and sound-producer. Counselors of people with hyperacusis should bear this in mind, and they should also remember that the sufferer may not be aware of the many factors that influence the extent of the annoyance or distress that he or she feels.

Social support can be used in a progressive habituation approach to annoyance hyperacusis, in which the patient is encouraged to face a problematic situation in the company of a trusted counselor (Hallberg, Hallberg, Johansson, Jansson, & Wiberg, 2005). Social support might be an important nonacoustic moderator of annoyance, helping to decrease the apprehension of loudness in social situations. Also helpful in the treatment of hyperacusis is the use of techniques derived from motivational interviewing (Miller & Rollnick, 2002), as persons with hyperacusis may feel reluctant to confront their fears if being pushed too hard. Future studies should address this support and the relationship of the hyperacusis patient with people and other sources of annoying sound.

Cognitive Behavioral Therapy (CBT)

CBT for hyperacusis (Andersson & Lyttkens, 1999; Baguley & Andersson, 2007; Miller & Rollnick, 2002) has evolved from CBT for tinnitus and anxiety disorders. Briefly, the treatment includes education, applied relaxation, graded exposure to sounds, and cognitive therapy for distressing thoughts and beliefs regarding sounds. CBT was recently studied in a randomized, controlled trial with 60 hyperacusis patients, and it showed promising results with large effects (Jüris, Andersson, Larsen, & Ekselius, 2014). In this study, patients with hyperacusis undergoing CBT were compared with waiting-list controls on the basis of loudness discomfort levels (LDLs), the Hyperacusis Questionnaire (Khalfa et al., 2002), the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), the Quality of Life Inventory (Frisch, Cornell, Villanueva, & Retzlaff, 1992), and an adapted version of the Tampa Scale of Kinesiophobia (Miller, Kori, & Todd, 1991). The treatment included six therapy sessions, the first lasting 90 min and the others 45 min each. There were significant between-groups effects in favor of the CBT group on all measures except for the Hospital Anxiety and Depression Scales. The effect sizes were moderate to high, with Cohen's $d = 0.68$ for the primary LDL measure, and ranging from $d = 0.32$ to $d = 1.36$ for the secondary measures. The differences between groups disappeared when the waiting-list group was treated later with CBT, and the effects of treatment were largely maintained after 12 months.

Sound Therapies

Listening to low-level sounds for several months can be effective in alleviating both tinnitus (Schaette, König, Hornig, Gross, & Kempter, 2010) and hyperacusis (Noreña & Chery-Croze, 2007). Patients with hyperacusis and tinnitus may be more responsive to sound therapy than patients with tinnitus alone (Hiller & Haerkötter, 2005). Over time, gradual increases of the level and/or duration of the sound treatment should be implemented along with positive reinforcement by the clinician. The association of positive experiences with the sound treatment can result in the complete elimination of hyperacusis symptoms. In cases of fear hyperacusis, behavioral modification is necessary to reduce aversion to phobic stimuli before loudness desensitization can occur. We review four general sound-therapy strategies for hyperacusis.

Continuous low-level broadband noise. Hazell, Sheldrake, and Graham (2002) suggested presenting the patient with a continuous low-level broadband noise. Formby and Gold (2002) and Formby et al. (2013) have reported success with this strategy for some people with loudness hyperacusis: There were substantial increases in LDLs. Several other studies have noted that such sound therapy can be effective for treating loudness hyperacusis for some but not all patients (Formby et al., 2003; Gold, Formby, Frederick, & Suter, 2002; Hazell et al., 2002; Jastreboff, Gray, & Gold, 1996; Jastreboff & Jastreboff, 2003; McKinney, Hazell, & Graham, 1999; Vernon, 1987; Wolk & Seefeld, 1999).

R. Dauman and Bouscau-Faure (2005) also reported improvements in hyperacusis following low-level sound therapy for some patients, but they noted that "noise generators do not provide a rapid solution to the problem" (p. 506) and that annoyance hyperacusis "does not improve as rapidly as usually reported" (p. 509). Gold and Formby (2000) observed that in their clinical practice, the use of low-level sound to help tinnitus patients took from 6 months to 2 years before benefit was typically observed.

Successive approximations to high-level broadband noise. Another approach is to choose a time of day for specific sound exposure and to gradually increase the level and/or duration over several days, weeks, and perhaps months (Vernon & Press, 1998). Vernon and Press (1998)

recommended the use of pink noise for this (no outcome study was reported, however).

Successive approximations to troublesome sounds. Another strategy involves recording specific sounds or noises that are troublesome for patients (Tyler et al., 2009). The patient then listens to the sounds at a time when he or she can relax (perhaps in a quiet room in the evening). The level and duration of these sounds are gradually (over weeks) increased until the patient is comfortable listening to the sounds at his or her typically encountered levels. Eventually, when they feel ready, the patients can expose themselves to the actual sounds. It is sometimes helpful if this is first done with some support (perhaps with family members) and sometimes with control over the duration and level of the real sounds. In treating children, Prizant and Meyer (1993) recommended simultaneous support provided by caregivers to show that the sounds and environment are safe for the child. Koegel, Openden, and Koegel (2004) successfully treated children with autism with a similar "successive approximation" approach, exposing children first to sounds in the distance and gradually bringing them closer.

Gradual increase of maximum output of hearing aid. The amplification provided by hearing aids might be the last thing someone with hyperacusis wants, particularly for moderate to high input levels. Decreasing the gain for moderate to high levels, and lowering the maximum output level, should help. However, this is likely to negatively influence speech perception, and therefore a gradual return to appropriate gain settings is desirable (Searchfield, 2006). Sammeth, Preves, and Brandy (2000) fitted 14 hyperacusis patients with custom-designed hearing aids that provided standard amplification for low-level sounds but that markedly reduced amplification for moderate to high-level sounds. All patients perceived some benefit, but the devices were not effective in all environments (see also Katzenell & Segal, 2001).

The Use of Hearing Protection

For some patients with hyperacusis, sound therapy might seem counterproductive, as it could potentially cause stress. Furthermore, adverse reactions to sound can prompt the use of hearing protection to reduce the problem. Unfortunately, the use of hearing protection might cause further increases in central gain, exacerbating the symptoms of hyperacusis when hearing protection is not in place (Hazell, 1987; Coles & Sood, 1988; Tyler & Baker, 1983). Formby et al. (2003) described evidence for the adaptive plasticity of loudness under the influence of ambient noise levels. When compared with baseline measures, subjects with normal hearing who wore earplugs demonstrated increased judged loudness for sounds (hyperacusis), whereas subjects who listened to a low-level wideband noise showed decreased judged loudness (hypoacusis). Thus, rather than treating the problem, wearing hearing protection only strengthens dependence on a treatment that isolates hyperacusis sufferers from the world around them.

Many people with hyperacusis wear earplugs or earmuffs at all times or in situations in which they believe their hyperacusis will be a problem (Gabriels, 1996). It might be that people with hyperacusis are more susceptible to (further) noise-induced hearing damage than the average person without hearing loss (Wang & Ren, 2012). Hearing protection is desirable for everyone when they are exposed to very intense sounds, which can of course cause hearing loss and tinnitus and can worsen hyperacusis. However, when they are used by hyperacusis patients for everyday sounds with moderate levels, the results can be counterproductive. Patients should be informed that the use of hearing protection can reinforce the association between the sounds and distress and, hence, maintain the underlying fears and concerns (Aazh, Moore, & Prasher, 2011). Active hearing protection devices can attenuate higher level sounds while not attenuating low-to-conversational level sounds; these could potentially be utilized in people with hyperacusis.

Medications

The use of medication to treat hyperacusis has not been investigated in clinical trials, but interest is high. The published work is limited to clinical case reports. Johnson, Brummett, and Schleuning (1993) described the use of Alprazolam (a short-acting anxiolytic) in five patients presenting with tinnitus and hyperacusis. A complete remission of hyperacusis was observed after 8 weeks of treatment. Nields, Fallon, and Jastreboff (1999) described the use of Carbamazepine (an anticonvulsant and mood-stabilizing drug) for the relief of hyperacusis in two patients diagnosed with Lyme disease. Gopal, Daly, Daniloff, and Pennartz (2000) described the use of selective serotonin receptor inhibitors (Fuvloxamine and Fluoxetine) for one patient with complete remission of hyperacusis and increase of ULLs. Some anecdotal success has also been reported for Citalopran (another selective serotonin receptor inhibitor). Controlled studies are needed.

Implications for Future Research

Subgroups

There are likely many causes and mechanisms of hyperacusis, and an understanding of these is required to find the many cures needed. Studies are needed to identify different subgroups of hyperacusis, as for tinnitus (e.g., Shailer, Tyler, & Coles, 1981; Tyler et al., 2008). Critical measurements are likely to include psychoacoustic measures of loudness hyperacusis, hyperacusis questionnaires, auditory evoked potentials, and brain imaging. It is also important to study the relationship between hyperacusis and other symptoms that often coexist, such as fullness, distortion (including fluttering), pain, and throbbing. Some patients can even report a clear time sequence of these related symptoms during troublesome periods of their hyperacusis.

Qualitative Descriptive Research

Exploration of the reactions and experiences of individuals with hyperacusis may help to understand their perspectives (Knudsen et al., 2012; Malterud, 2001). Structured

analyses of patients' discourse have already been used for patients with Ménière's disease (Erlandsson, Eriksson-Mangold, & Wiberg, 1996), hyperacusis after brain injury (Hallberg et al., 2005), childhood (Fitzpatrick, Angus, Durieux-Smith, Graham, & Coyle, 2008) and adult (Laplante-Lévesque et al., 2012) hearing loss, and tinnitus (Tyler & Baker, 1983). Similar analyses have been used to study perception of the risk posed by loud music (Bohlin & Erlandsson, 2007) and hearing aid use in older people (Lockey, Jennings, & Shaw, 2010). A similar approach should be useful for patients with hyperacusis.

Mechanisms

Uncovering the mechanisms of hyperacusis is an important step toward finding treatments and cures. Reliable animal behavioral models of hyperacusis are needed. The animals should also have hearing loss and tinnitus, as is the usual case for humans, but behavioral testing—whether based on the acoustic startle reflex or on operant conditioning—should be specific for hyperacusis and not be confounded by hearing loss and tinnitus (similarly, behavioral tests for tinnitus should not be confounded by hearing loss and hyperacusis). Hyperacusis can be induced by noise and/or drugs, and responses should be studied by combined physiological (e.g., spike activity, LFPs, evoked potentials, functional magnetic resonance imaging, and magnetoencephalography) and behavioral measures.

Additionally, more imaging studies of humans with hyperacusis are needed, for example, along the lines of Gu, Halpin, Nam, Levine, and Melcher (2010), as discussed above, but with an emphasis on patients with various types, severities, and etiologies of hyperacusis. It is expected that annoyance and fear hyperacusis will involve the limbic system—the emotion and memory center of the brain.

Drug Trials

There is a paucity of drug trials for hyperacusis. As for tinnitus, most people with hyperacusis would prefer a pill to cure them (Tyler, 2012). Physiological and behavioral animal models will help define the mechanisms and therefore provide some direction for chemical interventions. However, there are many forms of hyperacusis involving complex behaviors, and it will be difficult and require much time to develop valid animal models for all forms. Perhaps it is comforting to note that there are effective drug therapies for many maladies, such as mental illness, in which the underlying mechanisms are not completely understood. Additionally, drug trials should focus on individuals, not groups (Tyler, Oleson, Noble, Coelho, & Ji, 2007). Coelho et al. (2013) provided a recent example of an approach using a placebo-controlled crossover design in treating tinnitus with zinc (unfortunately, zinc was unsuccessful as a treatment).

Sound Therapy

Many sufferers from hyperacusis purchase sound-therapy devices and report benefit. Well-controlled studies with large numbers of subjects are required to test the benefit of sound therapies for hyperacusis. Current studies on the effectiveness of sound therapy for tinnitus have not always demonstrated significant benefit (e.g., Bauer & Brozoski, 2011). Newer approaches, such as tailoring sound to hearing loss using either noise (Noreña & Chery-Croze, 2007; Schaette et al., 2010) or music (Davis, Paki, & Hanley, 2007; Okamoto, Stracke, Stoll, & Pantev, 2010), have been reported. The benefits of sound therapy have typically only been evaluated immediately after months of therapy. Noreña and Chery-Croze (2007) examined benefits 1 month following the completion of treatment, and they found that the benefits were substantially smaller than immediately following treatment. Thus, it is not clear whether sound therapy can ameliorate tinnitus and hyperacusis in the long term.

Electrical Stimulation

It has been shown that electrical stimulation of the cochlea can reduce or eliminate tinnitus (for a review, see Tyler et al., 2008), and given the coexistence of tinnitus and hyperacusis, it is possible that electrical stimulation will also be an effective treatment for hyperacusis. A potentially promising approach is to pair sound therapy with stimulation of the vagus nerve (Engineer et al., 2011), which may potentiate cortical plasticity and lead to longer term benefits.

Conclusions

Hyperacusis can significantly impair the quality of life of many sufferers. Important strides have been made in identifying different characteristics of those bothered by hyperacusis. Critical to research and clinical trials, measurement procedures are now available. Good counseling and sound therapies are available, but clinical trials are needed to assess their effectiveness so that they can become part of standard reimbursed health care. Work has begun on understanding different mechanisms, and perhaps this will lead to new understanding and treatments.

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