

Review Article

A Review of Hyperacusis and Future Directions: Part I. Definitions and Manifestations

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Purpose: Hyperacusis can be extremely debilitating, and at present, there is no cure. We provide an overview of the field, and possible related areas, in the hope of facilitating future research.

Method: We review and reference literature on hyperacusis and related areas. We have divided the review into 2 articles. In Part I, we discuss definitions, epidemiology, different etiologies and subgroups, and how hyperacusis affects people. In Part II, we review measurements, models, mechanisms, and treatments, and we finish with some suggestions for further research.

Results: Hyperacusis encompasses a wide range of reactions to sound, which can be grouped into the categories of excessive loudness, annoyance, fear, and pain. Many different causes have been proposed, and it will be important to appreciate and quantify different subgroups. Reasonable approaches to assessing the different forms of hyperacusis are emerging, including psychoacoustical measures, questionnaires, and brain imaging.

Conclusions: Hyperacusis can make life difficult for many, 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.

Hyperacusis can be devastating for those who suffer from it. This review is intended to clarify what is known at present about hyperacusis and its underlying mechanisms to focus research and to promote the development of new treatments. A group of researchers and clinicians with a variety of backgrounds was gathered by the senior author. Several topic areas relevant to hyperacusis were identified. We were not interested in focusing on clinical trials. Hyperacusis covers many disciplines, and because the terminology is not standardized, we wanted freedom to explore areas we thought were relevant and important. We used our diverse backgrounds to explore

refereed publications, books, and conference proceedings. We highlighted what we believe are key issues that are important to move forward, sometimes even drawing from areas not normally associated with hyperacusis. In Part I, we set the background by discussing terminology, prevalence, different etiologies and subgroups, related symptoms, and imaging studies. This sets the stage for Part II, in which we discuss mechanisms, models, and treatments. We provide a broad perspective on many areas related to hyperacusis. Our intent is to provide a comprehensive review that will motivate and assist those interested in developing future treatments.

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Definitions

Numerous descriptions of hyperacusis have been put forward, but there are no universally accepted definitions. “Hyper” implies excessive, perhaps abnormal, and “acusis” represents sound. We begin by reviewing the ways authors have described and defined this abnormal, excessive response to sound.

First, it is relevant to note that the perception of high-intensity sounds by listeners with normal hearing, without complaints of hyperacusis, has been described as a “tickle”

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(von Bekesy, 1936; Silverman, Harrison, & Lane, 1946), a “discomfort” (Silverman et al., 1946; Wegel, 1932), and a “pain” (Cox, 1981). In the following discussion, we focus on descriptions in which the authors believe the responses are abnormal.

Some have defined hyperacusis as a heightened awareness of sounds (Phillips & Carr, 1998). Others have referred to an abnormally strong response to moderate sound (Gold, Frederick, & Formby, 1999), a pathological auditory hypersensitivity (Khalifa et al., 2004), an increased auditory sensitivity (Hébert, Fournier, & Noreña, 2013), a noise sensitivity (Stansfeld, 1992; Taylor, 1984), an audio-sensitivity (Gordon, 1986), a soft sound sensitivity, or a select sound sensitivity (McKenzie, 2012; Neal & Cavanna, 2012).

Traditionally in psychoacoustics, the term *sensitivity* refers to hearing threshold. Thus, if one has hearing thresholds that are better than normal (below 0 dB HL), one is hypersensitive. Hyperacusis is not usually associated with such hypersensitivity. However, very little information has been published about this, in part perhaps because hearing thresholds below 0 dB HL are seldom measured, and many audiometers do not allow the measurement of thresholds below -10 dB HL. We discourage the use of the term *hypersensitivity* to refer to hyperacusis.

Hyperacusis has also been described as a disturbed loudness function (Phillips & Carr, 1998). Sounds that are perceived as moderately loud by people with normal hearing and without hyperacusis are perceived as very loud by someone with hyperacusis. Another emphasis has been on tolerating sounds. Hyperacusis has been referred to as an intolerance (Hébert, Paiement, & Lupien, 2004), as an unusual intolerance to ordinary environmental sounds (Khalifa et al., 2004; Vernon, 1987), or as a sound intolerance problem (Khalifa et al., 2004).

Another definition involves discomfort (Krassnig, 1924). Hyperacusis is a discomfort for sounds that would be acceptable to most normally hearing people (Khalifa et al., 2004). Hyperacusis is also a hyperresponsiveness to sound stimuli (Song et al., 2013) or a hyperresponsiveness to noise (Dauman & Bouscau-Faure, 2005). An abnormally low tolerance for sound levels (Johnson, 1999), a loudness tolerance problem (Stephens, 1970), and sound intolerance (Formby & Gold, 2002) have also been emphasized. Although this suggests that hyperacusis is not being able to tolerate sounds, most people have no choice but to tolerate loud sounds, even though they might be annoyed by them. We have also observed clinically that some hyperacusis patients mention that loud sounds can be distorted.

Several authors have argued that it is critical to highlight the emotional aspects of hyperacusis. The emotional responses to sounds are critical in hyperacusis (Phillips & Carr, 1998). The attentional, emotional, and behavioral consequences were emphasized by Khalifa et al. (2004). Phillips and Carr (1998) proposed the term *phonophobia* to describe the aversive emotional responses. Gold et al. (1999) described phonophobia as an emotional or learned response. Other emotional descriptions include irritability (coined

“hyperesthesia dolorosa”; Krassnig, 1924; cited by Perlman, 1938), misophonia (a dislike; Jastreboff & Jastreboff, 2003), annoyance (Dauman & Bouscau-Faure, 2005), and fear (Blomberg, Rosander, & Andersson, 2005). A specific question on fear was included in a questionnaire to quantify hyperacusis by Khalifa et al. (2004). Another definition of hyperacusis includes pain (Chemtob, Roitblat, Hamada, Carlson, & Twentyman, 1988).

To summarize, definitions and descriptions of hyperacusis have included heightened awareness, hypersensitivity, loudness, discomfort, hyperresponsiveness, intolerance, phonophobia, irritability, misophonia, annoyance, fear, and pain. So what is a reasonable way to approach and define hyperacusis? Phillips and Carr (1998) commented on this confusion of terminology. They noted that the same terms are often used to describe different sensations, probably with different underlying mechanisms. Conversely, different terms are sometimes used to describe similar sensations. Dauman and Bouscau-Faure (2005) also commented that the terminology describing the annoyance caused by everyday sounds is misleading. We agree with Phillips and Carr that the emotional aspects of hyperacusis should be treated distinctly from its loudness aspects. The definitions of hyperacusis should be clear, distinct, and easy to interpret and recognize by different professions and by the general public.

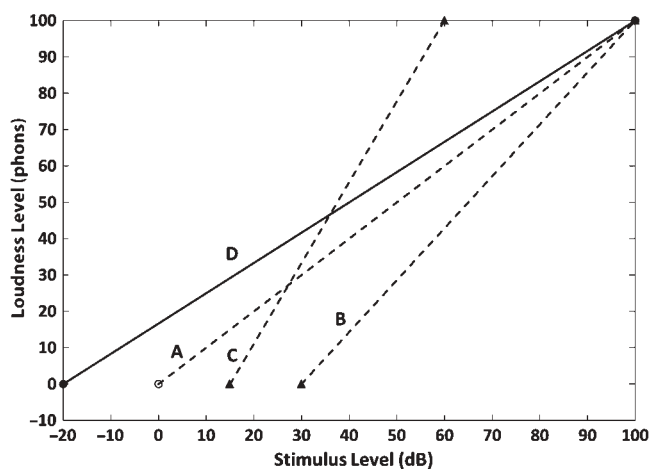
We suggest that the simplest and clearest distinction of the different forms of hyperacusis should focus on loudness, annoyance, fear, and pain. We believe that these four categories capture the general perceptions and associated reactions, and we distinguish between them in a meaningful fashion. People with hyperacusis can experience these different reactions singly or in combination. The loudness percept could be considered as a basic primary psychoacoustical response, and the annoyance and fear could be considered as self-report emotional reactions. Pain hyperacusis might be one or the other, or both. In this article, we use these specific terms when authors are precise about what they are referring to; otherwise, we use the general term *hyperacusis*.

Loudness Hyperacusis

Early discussions of the perception of loudness by hearing-impaired people included a category of over-recruitment, whereby the *loudness discomfort level* (LDL) or (interchangeably) the *uncomfortable loudness level* (ULL)—defined as the lowest sound level judged by the listener to be uncomfortably loud—was lower than for individuals with normal hearing (Fowler, 1965). We consider loudness hyperacusis to be present when moderately intense sounds are judged to be very loud compared with what a person with normal hearing would perceive.

Figure 1 shows hypothetical examples of the relationship between the physical level of a sound (e.g., a 1-kHz tone) and its loudness level in phons. The loudness level of a sound is the level of a 1-kHz tone that sounds equally loud to the sound in question for people with normal hearing.

Figure 1. The relationship between the level of a sound and its judged loudness level for individuals with (A) normal hearing, (B) loudness recruitment, (C) loudness hyperacusis, and (D) threshold hypersensitivity.



If the sound is a 1-kHz tone, then its loudness level in phons is equal to its physical level, and the ULL is typically reached at about 100 phons (the exact value depends on the instructions used and on the individual, as described in the second section of Part II).

In Figure 1, loudness level as a function of sound level for people with normal hearing is shown with Line A. A typical loudness growth function for an individual with a sensorineural hearing loss of 30 dB is shown by Line B. This hearing loss is accompanied by loudness recruitment (Line B is steeper than Line A), such that the person with hearing impairment perceives high-level sounds with a loudness approaching that for listeners with normal hearing. This is called “complete” recruitment, and no hyperacusis is present. An example of a loudness-growth function for a person with a 15-dB hearing loss and hyperacusis is shown by Line C. For low sound levels, the loudness is lower than normal, whereas for high sound levels, the loudness is greater than normal, with a lower than normal ULL. A hypothetical case of threshold hypersensitivity is shown by Line D. Here, the loudness is greater than normal at low levels, but it reaches normal values at high levels; in practice, such cases are rarely encountered.

Another issue needs to be considered. A “pure” loudness hyperacusis might require that ULLs be lower than normal for all sounds on the basis of their intensity and spectral characteristics (e.g., pure tones at all frequencies, fans, crying). This would be a purely psychoacoustical dimension. However, it is possible that only some sounds, some tonal frequencies, or even one ear might result in loudness hyperacusis. They might be considered very loud compared with normal. It might be that only some frequency regions are affected or that some waveforms affect the loudness perception differently than other waveforms. However, this is complicated because it would be critical to

distinguish loudness perceptions from annoyance or fear hyperacusis. This area deserves further study and will aid in the determination of subcategories.

Annoyance Hyperacusis

Annoyance hyperacusis is a negative emotional reaction to sounds. The sounds are often, but not always, reported as being loud. The reaction can be specific to particular sounds or groups of sounds. The reaction would be pervasive and persistent (as opposed to an occasional situational reaction, such as someone sitting nearby playing loud, unpleasant music). The annoyance can be manifested as irritation, anxiety, and tension (Urnau & Tochetto, 2011).

Fear Hyperacusis

Fear hyperacusis is an aversive response to sounds that results in an anticipatory response and avoidance behavior. It can include particular sounds or a class of sounds. Fear hyperacusis results in behaviors such that the individual sufferer often takes steps to avoid situations. This results in people shunning places where they fear these sounds might occur, such as restaurants or sporting events, and reduced participations in normal social, recreational, and vocational activities.

Pain Hyperacusis

Some with hyperacusis experience pain at much lower sound levels than listeners with normal hearing (typically around 120 dB SPL). This can be reported, for example, as a stabbing pain in the ear or the head. The pain may be severe. It is not clear whether the pain reflects a lowering of the normal pain threshold or a different process or mechanism altogether. Pain hyperacusis should be distinguished from cases in which people with ear disease experience pain unrelated to the presence of sound.

Advantages of Clear Definitions

The importance of these distinct definitions is that clinicians should be able to describe the prevalence, risk factors, prognosis, and management of patients who fall into different categories. Of course, there would be many cases with more than one element present. This should also assist researchers in distinguishing psychoacoustical and emotional mechanisms.

Some Additional Related Definitions

Autophony

Autophony occurs when one’s own voice is perceived as very loud, hollow, or reverberant. One reason is that the Eustachian tube is unusually open, and sounds in the mouth travel directly into the middle ear and cause the eardrum to vibrate (O’Connor & Shea, 1981). Sometimes when the sufferer leans forward, the Eustachian tube closes, and his or her voice is perceived at a normal loudness.

Superior Semicircular Dehiscence Syndrome

Superior semicircular dehiscence syndrome is thought to be caused by a thinning of the bony covering of the superior semicircular canal (Minor et al., 2001). Air-conduction audiometric thresholds are normal, but bone-conduction thresholds are usually lower than normal (Banerjee, Whyte, & Atlas, 2005). This greater sensitivity to bone-conducted sound is a direct result of the dehiscent superior semicircular bone acting as a third window into the inner ear (Minor et al., 2001). This has also been called *conductive hyperacusis* (Watson, Halmagyi, & Colebatch, 2000). Symptoms of superior semicircular dehiscence syndrome are autophonia, vertigo, ear fullness, and hyperacusis. Some sufferers can hear internal sounds, for example, those produced by eye movements when reading (Brantberg, Bergenius, & Tribukait, 1999).

Stapedius Reflex Dysfunction and Dysacusis

The stapedius muscle reflex is activated by intense sounds and reduces the transmission of low-frequency sounds into the cochlea, at least for sounds lasting longer than the reflex onset time of about 20 ms. The acoustic reflex arc includes transmission of sound through the cochlea to the auditory nerve, the cochlear nucleus, superior olivary complex, and to a muscle attached to the stapes via the facial nerve. If the stapedius reflex is impaired (e.g., because of neuro-muscular dysfunction or injury during stapedectomy), then intense low-frequency sounds may appear louder than normal. This could be considered a form of loudness hyperacusis. Bell's palsy and Ramsay-Hunt syndrome can impair the acoustic reflex (McCandless & Schumacher, 1979; Sweeney & Gilden, 2001). The term *dysacusis* was proposed by Phillips and Carr (1998) for cases in which the stapedius reflex is impaired by facial nerve injury.

An Environment-Centered Approach to Hyperacusis

Studies of hyperacusis should take into account normal reactions, such as annoyance, to everyday sounds (e.g., Andersson, Lindvall, Hursti, & Carlbring, 2002; Goebel & Floetzing, 2008; Wallen, Hasson, Theorell, & Canlon, 2012). There are many factors and circumstances that can affect the reaction of an individual to a specific sound or class of sounds.

Annoyance Can Be Unrelated to Loudness

Loudness does not necessarily predict annoyance (Anari, Axelsson, Eliasson, & Magnusson, 1999; Coelho, Sanchez, & Tyler, 2007; Goebel & Floetzing, 2008), and ULLs for pure tones do not always predict the loudness or annoyance of everyday sounds (Bläsing, Goebel, Floetzing, Berthold, & Kröner-Herwig, 2010; Meeus, Spaepen, De Ridder, & Van de Heyning, 2010; Wallen et al., 2012). Anari et al. (1999) reported that only 59 of 100 hyperacusis patients accepted exposure to specific sounds at moderate

levels (such as a baby crying, a dog barking, a bird singing, or speech-weighted noise). They noted that some of these also had low ULLs, but many others did not. Moreover, the ULLs for specific everyday sounds were generally lower than the ULLs for pure tones. Anari et al. suggested that there were two distinct groups related to this difference. Group 1 typically had near-normal ULLs for pure tones (above about 80 dB HL), and their ULLs for specific everyday sounds were 30 dB or more below their ULLs for pure tones. Group 2 had lower pure tone ULLs (below 70 dB HL on average), and their ULLs for specific everyday sounds were 20 dB or less below their ULLs for pure tones. The results of questionnaires showed a similar pattern. Almost half of the patients (48%) reported hyperacusis for certain sounds only, independently of their loudness. These patients fell into Group 1, and they had relatively high ULLs for pure tones. Fewer patients (14%) reported hyperacusis for all tested sounds; they tended to fall into Group 2, and their pure tone ULL was, on average, 10 dB lower than for the patients who only had hyperacusis for certain sounds. Anari et al. suggested that annoyance is related to loudness for Group 2, whereas for Group 1, the spectral content of the sounds might be more relevant. Anari et al. also concluded that the individuals' experience of their sound environment has an important influence on their assessment of loudness. Loudness might be increased by the apprehension of discomfort and annoyance (i.e., fear hyperacusis) on the basis of previous sounds. This is exemplified by patients who refused to listen to specific sounds that they had previously experienced as uncomfortable or annoying. Therefore, an understanding of hyperacusis must include emotional reactions to sounds, not only their loudness. We also suggest that concepts related to NOYS and perceived noise levels (Kryter, 1960) could be applied to hyperacusis in an attempt to understand hyperacusis responses to different types of sound.

Social Situation Influences Hyperacusis

Generally, studies that asked subjects to judge the annoyance of a list of sounds have not found patterns or relationships that identify which sounds are judged as most annoying. For adults, sounds as different as a drilling machine, rattling of dishes, hammering, or a child crying can all be associated with annoyance hyperacusis (Anari et al., 1999). Screams and whistles are among the more frequently annoying noises reported by children (Coelho et al., 2007). Clearly, the annoyance of environmental sounds differs vastly across individuals (Dauman & Bouscau-Faure, 2005). It might be that the annoying sounds are linked with the person or object that is producing the sounds. Hallberg, Hallberg, Johansson, Jansson, and Wiberg (2005) noted that environments reported as problematic by hyperacusis patients included social gatherings, business meetings, restaurants, and interactions with children.

Social studies on urban noise annoyance have also failed to find a clear relationship between noise level and people's reactions to noise. Reasonably, noise level is the

single best predictor of subjective responses to traffic noise (Jonah, Bradley, & Dawson, 1981). However, other studies have shown that loudness judgments cannot explain more than 25% of the variance of the annoyance ratings (Griffiths & Langdon, 1968; Weinstein, 1980). In studies on urban noise annoyance, situational factors have been identified as crucial (Moser, 2009), and these could be highly relevant for hyperacusis patients as well.

Perceived Control Influences Annoyance

Perceived control over the noisy situation has been suggested as another significant nonacoustic factor in hyperacusis. According to Dauman and Bouscau-Faure (2005), “several activities in the Multiple-Activity Scale for Hyperacusis are better tolerated when the person uses the noisy instrument themselves and thus has control over it” (p. 508). For example, sounds produced by one person in a social situation can be controlled only to a limited extent by another person in that situation, and this may exacerbate annoyance. A baby crying (Anari et al., 1999) is an excellent example of an annoying sound involving both a social relationship (parents–child) and a lack of control (over the baby’s behavior). Conversely, sounds that are under a person’s control can be better tolerated (e.g., sounds produced using a drill, chainsaw, lawnmower, or gun; Dauman & Bouscau-Faure, 2005). Children with hyperacusis complain infrequently about sounds from television, telephone, and toys, over which they have some control (Coelho et al., 2007). Even perceived control (as opposed to actual control) can be effective when actual control is lacking. According to Hallberg et al. (2005), the mere possession of earplugs gave some users a sense of security and control in social situations that they otherwise feared.

Reactions to environmental sounds depend on the physical characteristics of the sound (e.g., intensity, spectrum, temporal pattern, duration), the nature of the sound source, the circumstances surrounding the sound (e.g., intention attributed to the person making the sound), and the listener’s previous experience with similar sounds. Levy-Leboyer and Naturel (1991) studied neighborhood noise annoyance, asking subjects to describe noisy situations with details of the people who were involved, the way the people making the noise were perceived, their relationship with these people, and their reaction to the noise. High annoyance was reported for noises that were judged as not normal (i.e., unacceptable) by the sufferer. Such noises were described as too loud, or if they occurred during the night, as unnecessary. Subjects were more tolerant when the noises were related to normal everyday activities (such as sounds produced by a vacuum cleaner or washing machine), unless they lasted too long. Annoyance was higher when the noises were judged as incongruent with the individual’s conception of a normal living neighborhood, and when the individual considered that he or she would not behave like his or her neighbors.

Another factor influencing annoyance was the perceived lack of concern (as judged by the sufferer) of the

person making the noise. People seldom confronted their neighbors when they considered that the noises could not be prevented. When the person making the noise was perceived as being inconsiderate, the reaction was influenced by the relationship between the person making the noise and the listener. Negative reactions were more frequent when the person making the noise was known by the listener, but they were moderated by the fear of creating a conflict. Neighborhood noise annoyance is known to be a frequent cause of conflicts in urban life (Levy-Leboyer & Naturel, 1991).

In summary, the annoyance of a sound is influenced by the listener’s perceived degree of control over that sound, by the interpretation of the motives of humans involved in producing the sound, and by the social relationship of the listener to human sources of the sound.

Epidemiology

Hyperacusis in Adulthood

There are few studies on the prevalence of hyperacusis. Andersson et al. (2002) assessed prevalence in the general population of Sweden using questionnaires, with responses collected via the post and the Internet. Their definition was unusual intolerance to ordinary environmental sounds, and they found a prevalence of 8.6%. Fabijanska, Rogowski, Bartnik, and Skarzynski (1999), using a postal questionnaire, reported that 15.2% had hyperacusis among 10,349 respondents in Poland, but the specific wording of the question was not reported. Of course, without a clear accepted definition of hyperacusis, or definitions of hyperacusis subgroups, variability across studies will be large.

Hyperacusis in Childhood

Hyperacusis also occurs in children and is frequently associated with tinnitus and noise exposure (Coelho, 2006). Moderately intense sound from the television, games, and telephone can cause some children to cover their ears with their hands. The symptoms can be so severe that activities—such as car rides, vacuum cleaning, and lawn mowing—are avoided (Einfeld, Tonge, & Florio, 1997; Martin, Verman, & Miles, 1984). Coelho et al. (2007) assessed hyperacusis in a randomly selected group of 506 children from Brazil (5–12 years of age), and they reported a 3.2% prevalence by questionnaire (annoyance hyperacusis) and a 1.2% prevalence by lowered ULL (loudness hyperacusis).

Etiologies

Hyperacusis has many known causes and associations, although most cases have no known cause. There are a few diseases and syndromes that are associated with hyperacusis, as described below—for example, migraine, depression, posttraumatic stress disorder, head injury, Lyme disease, Williams syndrome, fibromyalgia, Addison’s disease, autism, myasthenia gravis, and middle cerebral aneurysm.

Peripheral Versus Central Initiation

Like hearing loss and tinnitus, hyperacusis probably can be associated with both peripheral and central factors. Hyperacusis is often accompanied by a cochlear hearing loss (although we discuss below how this might be over-emphasized), and this usually involves damage to cochlear hair cells and subsequent auditory nerve degeneration. However, annoyance, fear, and pain hyperacusis must involve central mechanisms. An often cited theory of hyperacusis is that the central auditory system turns up a “central gain” to compensate for peripheral hearing loss (Hazell, 1987). This and other potential mechanisms of hyperacusis associated with hearing loss are treated in depth in Part II.

Hyperacusis and Tinnitus

Hyperacusis and tinnitus are often related (Tyler & Conrad-Armes, 1983). Estimates of the prevalence of tinnitus in hyperacusis patients include 86% (Anari et al., 1999), 60% (Andersson, Vretblad, Larsen, & Lyttkens, 2001), and 40% (Jastreboff & Jastreboff, 2000). Other studies have reported estimates ranging from 40% to 79% (Bläsing et al., 2010; Coles, 1996; Dauman & Bouscau-Faure, 2005; Jastreboff, Gray, & Gold, 1996; Sood & Coles, 1998). However, Andersson et al. (2002) found that only 21% (Internet sample) and 9% (postal sample) of people reporting hyperacusis also reported tinnitus. The variation in the prevalence of tinnitus with hyperacusis across studies is influenced by different definitions and criteria for diagnosing hyperacusis and tinnitus. It should also be noted that much of the literature on tinnitus and hyperacusis comes from tinnitus clinics and might not be representative of the general population. Thus, the reports on hyperacusis are more likely to be populations with tinnitus (and with hearing loss). There might very well be a large population of people with hyperacusis but without tinnitus or without hearing loss. The prevalence of hyperacusis in those with tinnitus may be higher than in the population at large. It is also important to recognize that loud noise can make tinnitus worse in some tinnitus sufferers (Tyler & Baker, 1983). This might be confused with loudness hyperacusis.

Hyperacusis and Hearing Loss

The relationship between hyperacusis and hearing loss is unclear, and complex. It is likely that many with hyperacusis also have sensorineural hearing loss (Nelson & Chen, 2004; Sood & Coles, 1998). Hearing loss is very common, and sometimes the loss may be subtle. Although hearing thresholds of < 20 dB HL at frequencies from 125 to 8000 Hz are often considered to be within normal limits, the typical implication of this statement is that we do not expect speech hearing difficulties to exist. Actually, in some individuals, a threshold of 10 dB HL could represent a hearing threshold loss. Also, thresholds might be elevated for frequencies that are not usually assessed, for example, above 8000 Hz or at interoctave frequencies (such as 1500 Hz). Additionally, the

audiogram only represents pure tone thresholds; many people have hearing deficiencies (e.g., problems in understanding speech-in-noise) with “normal” audiograms (Hind et al., 2011).

Hannula, Bloigu, Majamaa, Sorri, and Mäki-Torkko (2011) examined the prevalence of hearing difficulties in 54- to 66-year-old people. The authors asked subjects whether they were particularly sensitive to loud sounds, and they grouped the responses on the basis of average audiometric thresholds. Of 850 subjects, 146 (17%) stated that they were sensitive to loud sounds, and of those 146 subjects, 96 had average hearing thresholds less than 20 dB HL in the better ear. In a multivariate analysis (in which they controlled for age, gender, and self-report of hearing loss and tinnitus), there was no significant relationship between hyperacusis and average hearing threshold loss. It is also noteworthy that Brandy and Lynn (1995) reported no difference in hearing thresholds between 25 subjects with hyperacusis and 13 subjects without hyperacusis. We must conclude that the relationship between hyperacusis and hearing loss is unclear. This is in contrast with the association between hearing loss and tinnitus (e.g., Shargorodsky, Curhan, & Farwell, 2010).

Noise Exposure

Occupational noise exposure is often associated with increased risk of hyperacusis, often together with tinnitus. Many patients with hyperacusis and tinnitus report that background noise makes their tinnitus worse. Although it is likely that noise exposure is the most common cause of hyperacusis, the data are limited. It has also been reported in several studies that hyperacusis is associated with recreational noise exposure, for example, to loud music (Anari et al., 1999; Kähärit, Zachau, Eklöf, & Möller, 2004; Kähärit, Zachau, Eklöf, Sandsjö, & Möller, 2003). It should also be noted that some with diagnosed noise-avoid breaking hearing loss might have an adult-onset, genetically based hearing loss. Susceptibility to noise-induced hearing loss, tinnitus, and/or hyperacusis could be influenced by genetic factors.

There is increasing concern that national standards for the protection of hearing (National Institute for Occupational Safety and Health, 1998; Occupational Safety and Health Administration, 2002) are inadequate to prevent hearing loss, tinnitus, and hyperacusis. Recent evidence suggests that the effects of noise extend beyond the duration of the noise exposure. Kujawa and Liberman (2009) showed in mice that a single noise exposure causing temporary (but not permanent) threshold shifts can destroy inner hair cell synapses, leading to a slow degeneration of the denervated auditory nerve fibers. This has recently been replicated in guinea pigs and has been extended to lower noise exposure levels (Lin, Furman, Kujawa, & Liberman, 2011; Maison, Usubuchi, & Liberman, 2013). Such degeneration could give rise to tinnitus (Schaette & McAlpine, 2011) and perhaps hyperacusis as well as to impaired speech perception in noise and eventual permanent threshold shifts.

Unexpected Intense Impulsive Noise

An unexpected intense sound, sometimes referred to as an *acoustic shock*, can result in hyperacusis. Mrena, Pääkkönen, Bäck, Pirvola, and Ylikoski (2004) reported that of 29 people affected by a shopping mall bomb explosion, 28% ($n = 8$) developed hyperacusis. Westcott et al. (2013) suggested that an unexpected intense impulse can trigger *tonic tensor tympani syndrome*, which they described as an involuntary, anxiety-based condition in which the reflex threshold for tensor tympani muscle activity is reduced, causing a frequent spasm. They suggested that this can trigger aural symptoms resulting from tympanic membrane tension, middle ear ventilation alterations, and trigeminal nerve irritability. However, the tensor tympani muscle is not traditionally linked to the acoustic reflex in humans, so the logic behind this is unclear. We also note the possible role of conditioning in producing fear hyperacusis: The fear of sounds may be induced by an unpleasant event associated with a sound or the device that produced the sound. This might be especially the case for hyperacusis in children.

Music Exposure

Several studies have reported hyperacusis among musicians (e.g., Kähärit et al., 2003; Laitinen & Poulsen, 2008; Toppila, Koskinen, & Pyykkö, 2011). Anari et al. (1999) reported that among 100 patients who reported “an abnormal discomfort to sounds that do not annoy healthy individuals” (p. 220), the sounds were most likely to be music (31%), occupational noise (13%), or leisure noise (7%). Both musicians and those exposed to loud music while attending concerts, clubs, or discotheques could be at higher risk for developing hyperacusis and tinnitus. In a field study on the use of portable music players, Kähärit, Äslund, and Olsson (2011) found that among 60 musicians, 12% reported being often or always sensitive to sounds.

The Medial Olivocochlear Efferent System

The medial olivocochlear efferent system consists of neurons projecting from the medial superior olivary nucleus to the cochlea. The efferent fibers terminate on the outer hair cells and regulate the gain of their active amplification of sound. This may serve to protect the cochlea from intense sounds (Maison, Luebke, Liberman, & Zuo, 2002; Maison et al., 2013) and to improve the detection of signals in noise (Giraud, Wable, Chays, Collet, & Chéry-Croze, 1997; Micheyl & Collet, 1996). The effectiveness of the medial olivocochlear efferent system could differ across individuals, and it might be defective in some people (Lustig, 2006). It might decline with age (Kim, Frisina, & Frisina, 2006) and it be adversely affected by head trauma (Attias, Zwecher-Lazar, Nageris, Keren, & Groswasser, 2005). Failure of the medial olivocochlear efferent system and the resulting loss of control over the gain of cochlear amplification could result in hyperacusis without any hearing loss, as suggested by studies of people with brain injury (Attias et al., 2005).

Otoacoustic emissions are often used as a noninvasive, objective tool to measure the effectiveness of the medial olivocochlear efferent system. In a preliminary study (article in Chinese; abstract available in English), Zheng, Jiang, and Gu (1996) reported on some patients with tinnitus and hyperacusis who showed a dysfunction of the medial olivocochlear system using otoacoustic emissions.

Autism

Autism can include the symptoms of exaggerated responses of the senses of vision, hearing, touch, smell, or taste (Caronna, Milunsky, & Tager-Flusberg, 2008). For example, people with autism might refuse to wear itchy clothes, and they may become distressed if they are forced to wear them (Stiegler & Davis, 2010). Autism can affect both social and communicative development, and it has been linked to hyperacusis in several studies (e.g., Coelho et al., 2007; Danesh & Kaf, 2012; Khalfa et al., 2004; Rosenhall, Nordin, Sandström, Ahlsen, & Gillberg, 1999).

The reported prevalence of hyperacusis in autism varies widely across studies. Rosenhall et al. (1999) tested a group of autistic children and compared them with an age-matched control group without autism. They used a behavioral response to an acoustic click to define hyperacusis. In the autism group ($n = 192$), 18% had hyperacusis, whereas none did in the control group ($n = 57$). Khalfa et al. (2004) noted that of 11 autistic children, six children had pure-tone LDLs below 80 dB HL.

Other studies found no particular relationship between autism and hyperacusis (Gravel, Dunn, Lee, & Ellis, 2006; Tharpe et al., 2006). Both of these studies noted that sound annoyance and fear in children with autism were unrelated to loudness. Furthermore, Jackson and King (1982) observed that when sounds were played out of context (e.g., a tape recording of a toilet flushing played in a clinic room), the annoyance hyperacusis response was absent.

Multiple Sclerosis

A link has been suggested between multiple sclerosis and annoyance and pain hyperacusis (Asha'ari, Mat Zain, & Razali, 2010; Olek, 2005; Weber, Pfadenhauer, Stohr, & Rosler, 2002). *Multiple sclerosis* is an inflammatory disease damaging nerve cell sheaths, and it affects neural transmission. The link between hyperacusis and multiple sclerosis is unclear, but Weber et al. (2002) speculated on demyelination in the pons and in the central auditory pathways.

Ménière's Syndrome

Ménière's syndrome involves severe dizziness, tinnitus, and hearing loss, primarily resulting from increased endolymph pressure in the cochlear and vestibular canals. Hyperacusis in patients with Ménière's syndrome has been reported in some studies (Brandy & Lynn, 1995; Gordon, 2000; Vattoh, Shah, & Curé, 2010). In a clinic sample of 102 individuals with Ménière's syndrome, Herraiz, Tapia, and Plaza (2006) reported that louder tinnitus was correlated

with more severe hyperacusis and hearing loss but not with vertigo.

Williams Syndrome and a Possible Genetic Link

Williams syndrome (also known as Williams–Beuren syndrome) is a multisystem neurodevelopmental genetic disorder characterized by several facial abnormalities (e.g., short upturned nose with long philtrum and wide mouth), developmental delay learning disabilities, cardiovascular abnormalities, hearing loss, and hyperacusis (Heller, Rauch, Luttgren, Schroder, & Winterpacht, 2003). Psychological features often include deficits in visual-spatial processing (e.g., of human faces), lack of fear of strangers, preserved language abilities, and interest and potential aptitude in music. The prevalence of hyperacusis in Williams syndrome is not clear, but some have reported that it might be as high as 95% (de Klaver et al., 2007; Klein, Armstrong, Greer, & Brown, 1990). In children with Williams syndrome, the prevalence might even be higher (Gothelf, Farber, Raveh, Apter, & Attias, 2006).

It is particularly noteworthy that a genetic disorder has hyperacusis as a symptom. The mechanism of the origin of hyperacusis in Williams syndrome is still unknown. Genetically, Williams syndrome is caused by an approximately 1.5 megabase chromosomal microdeletion at band 7q11.23, which contains about 26 genes (Heller et al., 2003), including the gene for elastin. Elastin is important in the movement of hair cell stereocilia (Selvakumar, Drescher, & Drescher, 2013), which triggers the mechano-electric transduction process. Thus, Williams syndrome patients often have a high-frequency hearing loss (Gothelf et al., 2006). Additionally, elastin deficiency can stiffen the stapedius tendon and thereby diminish or abolish the acoustic reflex, contributing to hyperacusis (Marler, Sitcovsky, Mervis, Kistler, & Wightman, 2010).

Another gene deleted in Williams syndrome is LIM kinase 1 (*LIMK 1*). It encodes a serine/threonine kinase, which regulates outer hair cell motility by its effect on actin (Stanyon & Bernard, 1999). Meng et al. (2002) showed that *LIMK 1* knock-out mice had increased startle responses to sound (interpreted as loudness hyperacusis) compared with wild type mice. The interpretation of the startle reflex in hyperacusis is not clear. Lower than normal startle reflexes could be related to lower ULLs. An increase in the strength of a measured startle response in an animal will require further validation. Matsumoto, Kitani, and Kalinec (2011) proposed that a deficiency of *LIMK 1* might cause an increase in outer hair cell motility, leading to increased amplification of sound and thus to hyperacusis (Matsumoto, Kitani, & Kalinec, 2011).

Middle Cerebral Aneurysm

Khalil, Ogunyemi, and Osbourne (2002) described a case of middle cerebral aneurysm presenting with brief, intermittent episodes of bilateral hyperacusis. Audiologic and otologic examinations were completely normal, and no

tinnitus was present. The middle cerebral artery supplies the lateral cerebrum, which includes the auditory cortex. The authors postulated that turbulent arterial blood-flow and pressure influence serotonin regulation of the auditory cortex. Serotonin, specifically 5-HT, is an inhibitory regulator of central sensory processing, and a pathological disruption to this system could result in central hyperacusis (Marriage & Barnes, 1995). Treatment of the aneurysm resulted in a reduction in hyperacusis symptoms.

Pain

Several authors have drawn an analogy between pain and tinnitus (e.g., Moller, 2007; Salvi, Lockwood, & Burkard, 2000). There may be a similar analogy between pain and hyperacusis. Indeed, as noted earlier, hyperacusis is sometimes manifested as pain.

Pain Receptors

The sensation of pain results from the stimulation of nociceptors (damage receptors). Pain is thought to act as a warning system for things that might harm the body. This is termed *acute pain* (Aguggia, 2003). Chronic pain remains after the stimulus is gone (Bolay & Moskowitz, 2002; Mannion & Woolf, 2000). The precise mechanisms by which pain is signaled are not clear. What lowers the threshold of pain? Could such factors be involved in hyperacusis?

The sensation of pain is transmitted to the spinal cord via two classes of afferent neurons: the myelinated A δ fibers and the unmyelinated C fibers. Both respond to mechanical stimuli, but C fibers also respond to thermal stimuli (Julius & Basbaum, 2001). Pain receptors are absent in the cochlea, so it is not clear why specific sounds are sometimes reported as painful.

Pain in the Brain

Pain information ascends to the brain through two main pathways and is interpreted by different brain structures. One path goes from the spinal cord to the thalamus and ends in the somatosensory cortex, and the other goes from the brain stem to the insular cortex through the amygdala (Basbaum, Bautista, Scherrer, & Julius, 2009). Glutamate, an excitatory amino acid, is the main neurotransmitter in the pain pathway (Julius & Basbaum, 2001; Pappagallo, 2005). Changes in pain intensity are processed in contralateral somatosensory and insular cortex (Rainville, 2002), but the anterior cingulate cortex is the main area thought to be responsible for the interpretation of the emotional significance of the noxious input (Rainville, Duncan, Price, Carrier, & Bushnell, 1997). The brain has a descending pathway that involves the peri-aqueductal gray and anterior cingulate. These pathways are thought to regulate the pain-related effects, such as analgesia and behavioral responses (Fields, 2000; Rainville, 2002).

Allodynia

Allodynia refers to a sensation of pain due to a stimulus that is not normally painful. Temperature and static or dynamic mechanical stimuli can evoke allodynia, and it often occurs after injury of peripheral nociceptors. Allodynia is different from hyperalgesia, which is an extreme, exaggerated reaction to a stimulus that is normally painful. A sensitization of the central nervous system following repetitive stimulation might contribute to the development of allodynia (Nagata, Duggan, Kumar, & García-Añoveros, 2005).

Both allodynia and hyperacusis might be related to sensitization. Allodynia, like hyperacusis, is often associated with migraine. About 40% of migraine sufferers reported allodynia and fear hyperacusis (Ashkenazi, Yang, Mushtaq, & Oshinsky, 2010).

Complex Regional Pain Syndrome

Complex regional pain syndrome is characterized by pain and other sensory alterations in extremities after a traumatic injury. It might be secondary to inflammatory processes with release of cytokines and tissue-released nerve growth factor (Marinus et al., 2011; Pappagallo, 2005), or it might result from sensitization of the central nervous system, such that a normal stimulus is interpreted as noxious (Marinus et al., 2011). Hyperacusis has been observed in patients who have complex regional pain syndrome with allodynia and dystonia (a state of abnormal muscle tone resulting in muscular spasm and abnormal posture) in three to four extremities. This motor dysfunction has been proposed to result from an alteration of inhibitory neurotransmitter mechanisms (de Klaver et al., 2007, Marinus et al., 2011). Although loudness hyperacusis is not always reported with complex regional pain syndrome, many of these patients do have significantly lower ULLs (de Klaver et al., 2007).

Fibromyalgia

Fibromyalgia is a disease characterized by pain over the whole body and tenderness in joints and muscles. Pain thresholds are lower in about 70% of cases, especially if the course of disease has been long (Gerster & Hadj-Djilani, 1984). Fibromyalgia patients sometimes have some otoneurological complaints despite the ear itself being normal; for example, tinnitus is reported in about 17% of cases (Bayazit, Gürsoy, Ozer, Karakurum, & Madenci, 2002; prevalence of hyperacusis not reported). An alteration in the processing of sounds in the central nervous system has been proposed as an explanation (Geisser et al., 2008). Specifically, there may be an alteration of the habituation mechanism involved in the attenuation of responses to repeated somatosensory stimuli (Montoya et al., 2006).

Geisser et al. (2008) observed lower LDLs and higher scores on an annoyance hyperacusis questionnaire in all the patients with fibromyalgia, and they found a correlation between these hyperacusis metrics and pain thresholds that were lower than normal. Abnormal auditory brain stem

responses have also been found in cases of fibromyalgia, and these might be the product of the central dysfunction (Bayazit et al., 2002; Rosenhall, Johansson, & Orndahl, 1996). In summary, hyperacusis in cases of fibromyalgia seems to be associated with a general hypersensitivity (see also Geisser et al., 2008).

Phantom-Limb Pain

Phantom-limb pain is pain perceived at the site of an extremity that has been amputated. Stimulation of nociceptors has two consequences: permanent stimulation from the residual limb and alteration of inhibitory control mechanisms of central neurons by alteration of the incoming information (Flor, 2002). The final result is reorganization of the sensorimotor cortex (Flor, 2002).

Several authors have drawn an analogy between phantom-limb pain and tinnitus (e.g., Møller, 2007; Salvi et al., 2000). For example, tinnitus can occur after the auditory nerve has been severed. As with phantom pain, patients with tinnitus might have a topographically reorganized auditory cortex (Mühlnickel, Elbert, Taub, & Flor, 1998), although such reorganization has not always been observed, at least for the case of tinnitus in the absence of substantial hearing loss (van Dijk & Langers, 2013).

Hyperacusis could also be analogous to phantom-limb pain. Central sensitization might play a role via the loss of inhibition in the pain pathway in the spinal cord (Flor, 2002). This resembles dystonia in complex regional pain syndrome.

Migraine

Fear hyperacusis is the most frequent hearing symptom associated with migraine: 81%–90% of sufferers experience hyperacusis during the migraine attack (Kayan & Hood, 1984; Vingen, Pareja, Støren, White, & Stovner, 1998). In addition, migraine sufferers are more likely to have hyperacusis between attacks than people without migraine (Main, Dowson, & Gross, 1997; Vingen et al., 1998). The sound levels that result in hyperacusis are reportedly lower during migraine attacks and occur without changes of hearing thresholds in most cases (Woodhouse & Drummond, 1993). Importantly, people with migraine combined with allodynia have lower LDLs than people with migraine alone (Ashkenazi et al., 2010).

Despite the coexistence of hyperacusis and migraine, the relationship between the two is unclear. Woodhouse and Drummond (1993) suggested that a discharge of noradrenaline in the thalamus and cerebral cortex during the migraine attack increases the likelihood of hyperacusis. Serotonin may play an important role in both hyperacusis and migraine (Marriage & Barnes, 1995). Hyperacusis has also been associated with headaches in which the central nervous system is primarily affected, for instance, cervicogenic headaches and tension-type headaches (Vingen et al., 1998).

Using inclusion criteria of episodic migraine with or without aura and a normal pure-tone audiogram, Ashkenazi

et al. (2010) studied individuals with migraine with and without allodynia elicited by brushing the skin with a gauze pad. Loudness hyperacusis was measured using bilaterally presented tonal stimuli that were increased in intensity until they were deemed unpleasant or painful. Lower sound aversion thresholds were negatively correlated with allodynia scores. In other words, migraineurs who exhibited greater brush allodynia during an acute attack were more averse to sound.

Many migraine patients experience hypersensitivity to multisensory stimuli during a migraine attack (Main et al., 1997; Woodhouse & Drummond, 1993; Zanchin et al., 2007). Andersson et al. (2002) showed an association between hyperacusis and hypersensitivity to light and color, but it is not clear whether these cases included patients who experienced migraine. Stimulation with light can cause a migraine attack in cases of migraine with aura (Drummond, 1986; Hay, Mortimer, Barker, Debney, & Good, 1994). The general hypersensitivity in migraine has been attributed to hyperexcitability of the sensory cortex (Aurora & Wilkinson, 2007; Welch, D'Andrea, Tepley, Barkley, & Ramadan, 1990). However, others have proposed involvement of the thalamo-cortical systems (Coppola, Pierelli, & Schoenen, 2007).

Hyperacusis and Nonauditory Excessive Responses

Sensory systems other than hearing can exhibit excessive responses, including vision, smell, and taste. According to a prevalence study, some people with hyperacusis also showed excessive responses to other sensory stimuli, such as light and odor (Andersson et al., 2002). We do not know whether this reflects different manifestations of the same underlying disorder. We review below types of sensory hypersensitivity other than hyperacusis because these might provide clues to understanding the mechanisms of hyperacusis.

Visual Hypersensitivity (*Photophobia*)

Photophobia refers to exaggerated response to light. Peripheral eye problems, such as uveitis and corneal disease, can cause photophobia, as can central problems, including meningitis, subarachnoid hemorrhage, and migraine (Lamonte, Silberstein, & Marcelis, 1995; Welty & Horner, 1990). Photophobia is a symptom of migraine, along with nausea and vomiting (Headache Classification Subcommittee of the International Headache Society, 2004; Woodhouse & Drummond, 1993). At present, no mechanism linking photophobia and hyperacusis is known.

Smell (*Osmophobia*)

Osmophobia refers to a fear, aversion, or excessive reaction to smells or odors, usually in association with migraine. Migraine sufferers can show lowered thresholds for odors between migraine attacks (Snyder & Drummond, 1997). Demarquay et al. (2006) evaluated olfactory

reactions between attacks in 74 patients with migraines and 30 controls. Thirty-five percent of patients with migraines had such an olfactory reaction. Olfactory excessive reactions can also occur in conditions associated with low blood concentration of cortisol, for example, Addison's disease (Henkin & Bartter, 1966).

Taste (*Hypergeusia*)

Hypergeusia is an excessive reaction involving taste. Other terms related to taste disorders include hypogeusia, dysgeusia, and phantogeusia (Deems et al., 1991). For example, Fark, Hummel, Hahner, Nin, and Hummel (2013) studied patients who had visited their clinic for taste and smell disorders. The most common taste disorder they observed was an increased threshold for detecting different tastes (hypogeusia). Some migraine patients have hypergeusia (Kelman & Tanis, 2006), but Kelman and Tanis (2006) could not find any link between those with hyperacusis and taste disorders. Similarly, Andersson et al. (2002) did not find an association between hyperacusis and taste sensitivity.

Imaging Studies in Hyperacusis

Various types of functional and structural neuroimaging data (functional magnetic resonance imaging [fMRI], diffusion tensor imaging [DTI], voxel-based morphometry [VBM], and standard magnetic resonance imaging [MRI]) might help to provide insight, either directly or indirectly, into relationships between anatomy, physiology, and symptoms in specific disorders and brain lesions associated with hyperacusis. It should be kept in mind that early studies describing hyperacusis in persons with brain lesions are clinical and often qualitative in nature; they rely on the clinician's acumen, experience, and intuition and usually do not have any confirmatory psychoacoustic measures to supplement the clinical observations. Obviously, contemporary studies need to improve on these deficiencies, but we argue that case studies nonetheless can be very revealing and should be encouraged as a means of advancing the field.

fMRI

The use of functional imaging could help establish brain networks relevant to hyperacusis. To date, however, only limited information is available in this domain. Below, we compare and contrast two studies to provide insight into this area.

Hwang, Chou, Wu, Chen, and Liu (2009) used binaural white-noise stimulation to compare brain activation patterns for three people with idiopathic loudness hyperacusis (two women and one man, ranging in age from 32 to 57 years) and three individuals with normal hearing and without hyperacusis. The hearing status (pure-tone average) was considered in the normal range in all subjects. The report suggested that for those with loudness hyperacusis, fMRI activations were greater in the temporal lobes and in various

frontal and occipital lobe structures—including the parahippocampus areas (in two of the three subjects). The activation patterns of those with loudness hyperacusis were quite different and more diverse from those observed in the controls. On the basis of the patterns of activation observed, the authors speculated that the neural network associated with loudness hyperacusis might be associated with ventral and dorsal emotion systems, as proposed by Phillips, Vigneault-MacLean, Boekne, and Hall (2003).

In another acoustic stimulation fMRI study using binaurally presented white noise stimuli at multiple levels (50, 70, and 80 dB SPL), Gu, Halpin, Nam, Levine, and Melcher (2010) studied individuals with normal hearing with and without tinnitus and evaluated the relationship of these groups to questionnaire data, LDLs, and perceived loudness on the basis of a 7-point numerical rating scale. The general fMRI activation patterns in regions of interest within midbrain (inferior colliculus) and thalamus (medial geniculate body) showed a dependence on loudness hyperacusis but not on tinnitus. In contrast, only primary auditory cortex and core regions (anterior lateral Heschl's gyrus and anterior lateral regions) but not surrounding belt regions (planum temporale or anterior medial areas) showed dependencies on both loudness hyperacusis and tinnitus. The authors noted that their results were limited to individuals with mild loudness hyperacusis "because hyperacusis was never the primary complaint among tinnitus patients recruited for this study and was self-recognized by only a few of the subjects who ultimately showed abnormal sound level tolerance under the controlled conditions of our testing" (Gu et al., 2010, p. 3368). Further studies in this area would be valuable.

fMRI has also been used to study individuals with Williams syndrome. As noted earlier, *Williams syndrome* is a multisystem neurodevelopmental genetic disorder characterized by several facial abnormalities, learning disabilities, cardiovascular abnormalities, hearing loss, and hyperacusis. For people with Williams syndrome with hyperacusis, fMRI activation was significantly reduced (relative to that for control subjects) in the temporal lobes and was increased in the right amygdala during auditory processing of music (Levitan et al., 2003). These subjects also showed a widely distributed network of activation in cortical and subcortical structures.

Structural MRI (VBM)

VBM is an automated and generally unbiased group comparison technique that allows differences in anatomy to be ascertained and hypotheses to be developed with respect to disease states or dysfunctions (i.e., evaluating atrophy or expansions in specific brain regions). In addition, regression analyses can be used to correlate anatomical changes with cognitive or behavioral deficits (see Whitwell, 2009, for a review). On the basis of a retrospective study of semantic dementia encompassing an 18-year time frame, Mahoney et al. (2011) used VBM to compare individuals with and without auditory symptoms (i.e., tinnitus and hyperacusis).

Hyperacusis was determined by questionnaire assessment, although the number of questionnaires actually completed was not reported. In the subgroup with auditory symptoms (combined tinnitus and hyperacusis), they found increased gray matter in the right posterior superior temporal gyrus and sulcus and reduced gray matter bilaterally in orbito-frontal cortices. The subgroup with tinnitus alone showed similar results. However, the subgroup with hyperacusis alone showed reduced gray matter in the left medial geniculate area. Audiometric thresholds were not obtained, so it not clear whether peripheral processes affected the pathogenesis of the auditory symptoms and/or the neuroanatomical effects observed.

DTI

DTI measures the displacement of water molecules (diffusion) along white matter tracts and serves as a biomarker of tissue integrity (e.g., Ling et al., 2012). DTI can provide insight into plastic/reactive changes in white matter microstructure and connectivity associated with tinnitus and hyperacusis that cannot be detected by MRI. For each voxel under consideration, DTI estimates diffusion in terms of the axes of an ellipsoid, characterized by one major and two orthogonal minor axes. The main metric used to quantify diffusion is fractional anisotropy (FA), a normalized scalar that represents the fraction of the tensor that can be assigned to anisotropic diffusion. FA has values between 0 and 1, where 0 represents unrestricted or "isotropic" diffusion, as is found in the cerebro-spinal fluid, and 1 represents "anisotropic" or restricted diffusion, as is found in organized white matter fibers. Increases in FA have been related to factors such as increased myelination, decreased axonal diameter, decreased axonal branching, and increased packing density of white matter fibers (Beaulieu, 2002).

Increased FA values in white matter tracts have been observed for people with Williams syndrome (e.g., Arlinghaus, Thornton-Wells, Dykens, & Anderson, 2011; Hoeft et al., 2007). Although the mechanisms for increased FA remain unknown, there is indirect linkage to increased packing density in other brain areas associated with Williams syndrome, such as the laminar-specific area of visual cortex (IVc β). There was also an increased expression of small diameter "parvocellular" neurons in this and other sublayers of the visual cortex, including IVA, IVc α , IVc β , V, and VI (e.g., Galaburda, Holinger, Bellugi, & Sherman, 2002). Individuals with Williams syndrome also have smaller brains than controls. When viewed together, these findings might help to explain the abnormalities in white matter microstructure and connectivity patterns noted above. Increased packing density and increased expression of small diameter neurons appear consistent with increased FA values observed in white matter microstructure (e.g., Jernigan & Bellugi, 1990; Reiss et al., 2000; Schmitt, Eliez, Warsofsky, Bellugi, & Reiss, 2001).

In addition to auditory anomalies such as hyperacusis (Attias, Raveh, Ben-Naftali, Zarchi, & Gothelf, 2008; Elsabbagh, Cohen, Cohen, Rosen, & Karmiloff-Smith,

2011; Levitan, Cole, Lincoln, & Bellugi, 2005; Matsumoto et al., 2011), other reported phenomena in Williams syndrome include auditory allodynia (Levitan & Bellugi, 1998; Levitan et al., 2005, 2003; Miani, Passon, Bracale, Barotti, & Panzoli, 2001). Cortical anatomical abnormalities have in part been attributed to reduced volume and altered sulcal morphology of the Sylvian fissure, atypical primary auditory cortex cytoarchitecture, and increased volume of the superior temporal gyrus.

These findings suggest that the FA metric is a local biomarker of aberrant neural connectivity. This aberrant connectivity may be either causally linked to various functional abnormalities or a secondary effect of synaptic alterations that vary with the specific disorder.

Clinical Case Studies

Other structural MRI-related studies have been reported for individuals with hyperacusis associated with lesions in the central nervous system. Khalil et al. (2002) reported a case of a 35-year-old man with an intracranial aneurism of the middle cerebral artery on the right side measuring 4 × 3 cm. Episodic hyperacusis was the primary symptom. In those episodes, which lasted 5–10 min and were associated with nausea, sounds were described as “accelerated, exaggerated, and very loud” in both ears. Pure-tone audiometry and tympanometry were reported as normal, but no psychoacoustic measures of loudness hyperacusis were reported. The authors postulated that turbulent blood flow and pressure effects of the aneurism “irritated” the auditory cortex, resulting in loudness hyperacusis, which the authors believed was consistent with the intermittent and brief nature of the symptoms. The patient was treated with a Guglielmi detachable coil embolization that resulted in complete resolution of the symptoms.

In a patient with multiple sclerosis, Cohen, Rudge, Robinson, and Miller (1988) reported damage to the pontine olivocochlear bundle, with prominent symptoms such as intolerance of loud sounds, distorted perception of speech, and music being reported. Also noted were subtle abnormalities of stapedius reflex thresholds, reduced masking level differences for a 500-Hz tone, and lowered ULLs on the same side as the lesion. The auditory effects described above were thought to be permanent and were interpreted as removal of inhibition from the hair cells in the cochlea.

H. Lee et al. (2003) reported two cases in which migraine headaches associated with multiple bilateral infarcts in the cerebellum and the pons (documented by MRI) resulted in acute auditory symptoms. In a 25-year-old woman (Patient 2 of their report), initial symptoms included right-sided tinnitus, hyperacusis, vertigo, right-sided hearing loss, diplopia, quadriparesis, and right-sided hemibody numbness. These symptoms extended over a 3-day period and were characterized by blurred vision; dysarthria; incapacitating headaches with bifrontal, bitemporal, and bioccipital foci; and severe hyperacusis, in which “the wind sounded like an airplane.” A family history of migraine headache in both

parents and a paternal grandfather was also reported. This report emphasizes the importance of considering *migrainous infarction* when acute auditory other neurological symptoms are manifest. Fukutake and Hattori (1998) described a 49-year-old man without psychiatric or epileptic disturbance with a small lesion in the right inferior thalamus (medial geniculate body), characterized as a hemorrhagic infarction. He experienced hyperacusis and palinacusis (the phenomenon whereby a sound appears to continue after the physical stimulus has terminated) on the side contralateral to the lesion. Other case reports support the view that hyperacusis can be observed in cases of pontine hemorrhage (E. Lee, Sohn, Kwon, & Kim, 2008).

Weber et al. (2002) described a central effect of fear hyperacusis in cases of multiple sclerosis. MRI showed brain stem lesions primarily in the pontine area, and electrophysiological measures (auditory brain stem responses) showed abnormal increased interpeak latencies (see also Fukutake & Hattori, 1998, noted above). Weinberg and Rowe (1941) described a case of multiple cranial lesions with hyperacusis and porropsia (visual distortion in which stationary objects appear to be moving away). This case was complicated by metastatic osteomyelitis of the skull with chronic subdural hematoma. Surgical extirpation of the infected bone and drainage of the hematoma relieved the unusual auditory and visual symptoms. Previous to this time, only one other case with these symptoms had been reported (Higier, 1934).

Overall, these case studies suggest that lesions in the brain stem likely contribute to what is clinically observed as hyperacusis in some patients.

How Hyperacusis Affects People

People with hyperacusis can have very different levels of distress, and our clinical experience is that they often are more handicapped than those with tinnitus. Hyperacusis can influence emotional well-being, hearing, sleep, and concentration. This is the basis for Tinnitus Activities Treatment (Tyler, Noble, Coelho, Haskell, & Bardia, 2009), which is also applied to hyperacusis patients (see Treatments section in Part II). Jüris, Andersson, Larsen, and Elselius (2013) studied a group of 62 patients with hyperacusis and reported that about 47% fitted the diagnosis of having an anxiety disorder. Some patients complain that their hyperacusis interferes with speech perception, particularly in noise. How hyperacusis affects the coding of speech and separating speech from noise at these higher levels is unknown. Because many people with hyperacusis also have hearing loss, it is difficult to isolate peripheral and central effects. Furthermore, we should not forget that many with hyperacusis appear to have normal hearing thresholds. Some people with hyperacusis report that they are awakened from sleep by sounds or that they do not sleep well because of the anticipation of a loud or annoying sound. Some report that they have difficulty concentrating in anticipation of a loud or annoying sound. A particular problem for those with hyperacusis, and one that is not always appreciated, is that they

often have to move around in different areas with varying noise levels throughout the day. Some areas might be quiet, some might have moderate noise levels, and some might have high enough levels that noise protection is warranted. This might naturally lead to fear hyperacusis.

It would be of interest to apply the World Health Organization categorization of Functional Impairments as has been done for tinnitus (Tyler, 1993; Tyler et al., 2009). For example, the primary functions impaired could be emotions, hearing, sleep, and concentration. This would limit activities of socialization, work, and education and would have an economic impact.

Many with severe hyperacusis, notably fear hyperacusis, experience dire emotional problems (notably anxiety and depression). Juris et al. (2013) reported that 56% of patients (35 of 62) with hyperacusis met criteria for a psychiatric disorder. Most had a social phobia and/or a generalized anxiety disorder. A common perspective among clinical otologists and audiologists is that hyperacusis is primarily a psychological disorder. One can imagine at least two scenarios. Auditory system abnormalities could lead to hyperacusis. This could lead to anxiety and depression. Another scenario is that brain abnormalities could lead to mental illness and dysfunction (and, therefore, a psychiatric disorder) and that hyperacusis is one symptom resulting from this. This distinction will likely be important in understanding mechanisms. Counseling and sound therapy management addressing both the hyperacusis and the psychological issues resulting from hyperacusis could (at present) be applied regardless of the underlying mechanisms.

Summary

In Part I, we have proposed what we believe is a straightforward summary of the different forms of hyperacusis (common adjectives that are distinct and easy to understand by patients and professionals): loudness, annoyance, fear, and pain. We have provided a broad background of the symptoms that are often related to hyperacusis. We have also emphasized the importance of perceived environmental issues related to hyperacusis, which extends the scope beyond the link to hearing loss and tinnitus. A wide range of etiologies have been associated with hyperacusis, which highlights the likelihood of many different subtypes and mechanisms and likely the need for many different treatments. We believe that there are several areas that have the potential to help researchers understand these different types of hyperacusis, including pain, touch, vision, and smell. We believe that this broader perspective will assist future researchers. Functional and structural neuroimaging studies have begun to explore the role of the brain in hyperacusis, but more work is needed. In Part II, we explore mechanisms, treatments, and future research areas.

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