

Chapter 14

Hearing impairment

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14.1 Introduction

A typical normal-hearing person can process sound information over at least a 120-dB dynamic range, from detecting nanometre vibrations to understanding speech in the noisy background of a loud concert. Under controlled conditions, a listener can discriminate a one-thousandth difference in pitch while processing timing information from tens of microseconds to hundreds of milliseconds. These sharp sensitivities are accomplished by delicate and exquisite mechanical, electrical, and neural mechanisms in the normal auditory system. Unfortunately, the sharp sensitivities are also susceptible to genetic and environmental impacts, from abnormal genes and the normal aging process to exposure to ototoxic drugs and noise, resulting in hearing impairment that affects one out of every ten people on earth. This hearing impairment not only lowers personal life quality but also increases the global health burden.

Here we deal with the perceptual and functional consequences of hearing impairment at the system level. Figure 14.1 illustrates this system approach to hearing impairment. Sound, the input to the auditory system, goes through a series of processing and transformations from the outer ear to the cortex, with its output being the perceived quality, meaning, and context of that sound. Specifically, the sound vibration is shaped by the outer and middle ears to produce maximal responses at 1–2 kHz, frequencies that are important to speech recognition. The cochlea, or the inner ear, adaptively amplifies the sound via outer hair cell motility and converts mechanical vibration into electric impulses via chemical transmission from the inner hair cell to the auditory nerve fibers. The electric impulses are further processed, coded, and interpreted by the auditory brainstem and cortex to form an auditory object of the sound vibration. In addition to this forward-feeding pathway, there are backward-feeding pathways from the auditory brainstem to the auditory nerve, the cochlea, and the middle ear that modulate the forward-feeding activities.

Damage to any part or parts of the auditory system will affect normal processing and produce hearing impairment. Depending upon the degree and the site of damage, different physiological processes may be disrupted, producing not only different degrees of hearing impairment but also different perceptual and functional deficits. The remainder of this chapter will discuss the types of hearing impairment, linking structural damages to physiological changes and functional consequences. While the focus will be the perceptual and functional consequences of hearing impairment, this chapter will also briefly discuss the diagnosis and treatment of hearing impairment.

14.2 Causes

Clinically, hearing impairment is classified into two major categories: conductive loss and sensorineural loss. Both types of hearing impairment can be congenital or acquired. Congenital hearing loss is typically identified at birth via hearing screening or from the family history. It may have a genetic or non-genetic origin. Most forms of congenital hearing loss are not syndromic and are

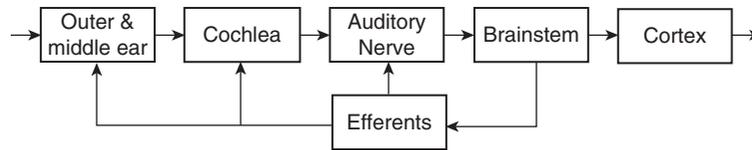


Fig. 14.1 A system approach to hearing impairment.

associated with autosomal recessive transmission: for example Alport's syndrome or Potter's syndrome may present with a family history of kidney disease. Additional causes of congenital hearing loss that are not hereditary include maternal infection, kernicterus, trauma during birth, and medication toxicity (e.g. Gurtler and Lalwani, 2002).

Although there is a genetic component, acquired hearing loss is usually related to environmental factors. Noise exposure, ototoxic medications, and presbycusis (a general term used to describe hearing loss due to aging), are the leading causes for acquired sensorineural loss. Other forms of acquired sensorineural loss include autoimmune disorders, sudden sensorineural hearing loss, head trauma, or an acoustic neuroma. The main causes for acquired conductive hearing loss include otosclerosis, otitis media, obstruction of the ear canal, tympanic membrane perforation, cholesteatoma, or tympanosclerosis (e.g. Zadeh and Selesnick, 2001).

Here we describe the symptoms and diagnosis of several major types of hearing impairment. First, in noise-induced hearing loss, a temporary loss of hearing may occur which usually resolves after 24 hours, but a permanent hearing loss will occur with repeated exposure to loud noises. High-pitched tinnitus frequently accompanies noise-induced hearing loss. A history of noise exposure and an audiogram that demonstrates a worsened threshold at frequencies near 4 kHz typically confirms the diagnosis (Conference, 1990).

Ototoxic drugs include the following common medications: aminoglycoside antibiotics, platinum-based chemotherapeutic agents (i.e. cisplatin, carboplatin), and loop diuretics. Non-steroidal anti-inflammatory drugs (NSAIDs) cause a sensorineural hearing loss as well as tinnitus, which sometimes reverse after stopping the medication. Close monitoring of a patient's hearing and dosing can reduce the risk of ototoxicity during the use of known deleterious drugs (e.g. Rybak and Ramkumar, 2007).

Autoimmune disorders, specifically polyarteritis nodosa, systemic lupus erythematosus, and Wegener's granulomatosis may cause hearing loss. Metabolic disorders such as diabetes, hypothyroidism, renal failure, and hyperlipidemia may also cause hearing loss in extreme situations. Autoimmune inner ear disorders are characterized by a progressive bilateral sensorineural hearing loss that is responsive to steroid treatment. The rate of hearing loss can be rapid (over weeks) or slower (over years). Speech understanding is generally significantly poorer than would be expected based on the degree of hearing loss (e.g. Ryan *et al.*, 2001).

Ménière's disease is characterized by episodic vertigo, tinnitus, fluctuating hearing loss, and aural pressure. There is no universally accepted cause, but histopathologic evidence shows increased hydraulic pressure in the affected inner ear's endolymphatic system. The etiology is multifactorial, as both genetic and environmental factors play a role. Treatment includes lifestyle changes such as reduced sodium intake, elimination of caffeine and alcohol from the diet, and stress reduction. Intratympanic steroids and aminoglycoside antibiotics have been used for treatment. Surgical therapy is used as a last resort (e.g. Paparella and Djalilian, 2002).

Sudden sensorineural hearing loss is a medical emergency, defined as the loss of greater than 30 dB at three or more adjacent audiometric frequencies. This loss may occur over a period of three days or less and is typically unilateral. While spontaneous recovery rates are cited to be

between 32% and 70%, only 10–15% of cases are discovered to have a specific etiology. Reversible causes include perilymphatic fistula, trauma to the inner ear or ossicular chain, or the presence of an acoustic neuroma. Most sudden hearing loss cases are irreversible and may be due to an autoimmune process, or a viral or vascular etiology (e.g. Conlin and Parnes, 2007).

Acoustic tumors, or more accurately, vestibular schwannomas, often produce a unilateral, asymmetric, or sudden hearing loss. Other common symptoms include unilateral tinnitus, vertigo, or imbalance. In rare cases, acoustic tumors can occur as a familial form in neurofibromatosis type-2 with bilateral vestibular schwannomas (e.g. Daniels *et al.*, 2000). A loss resulting from an acoustic tumor is also referred to as a ‘retrocochlear loss’ in the literature.

14.3 Diagnosis

A diagnostic method can be subjective or objective. Subjective methods include pure-tone audiometry and speech audiometry. A pure-tone audiogram illustrates a relative measure of hearing against the averaged young and healthy subjects’ hearing level (HL) by depicting the softest level that a person can hear as a function of pure-tone frequency from 250 Hz to 8000 Hz. Hearing levels are grouped in ranges of 20 dB HL to differentiate those with normal hearing from those who have a mild, moderate, severe, or profound hearing loss.

Figure 14.2 shows three audiograms from a person with normal hearing (top-left panel), a person with conductive hearing loss (top-right panel), and a person with sensorineural hearing

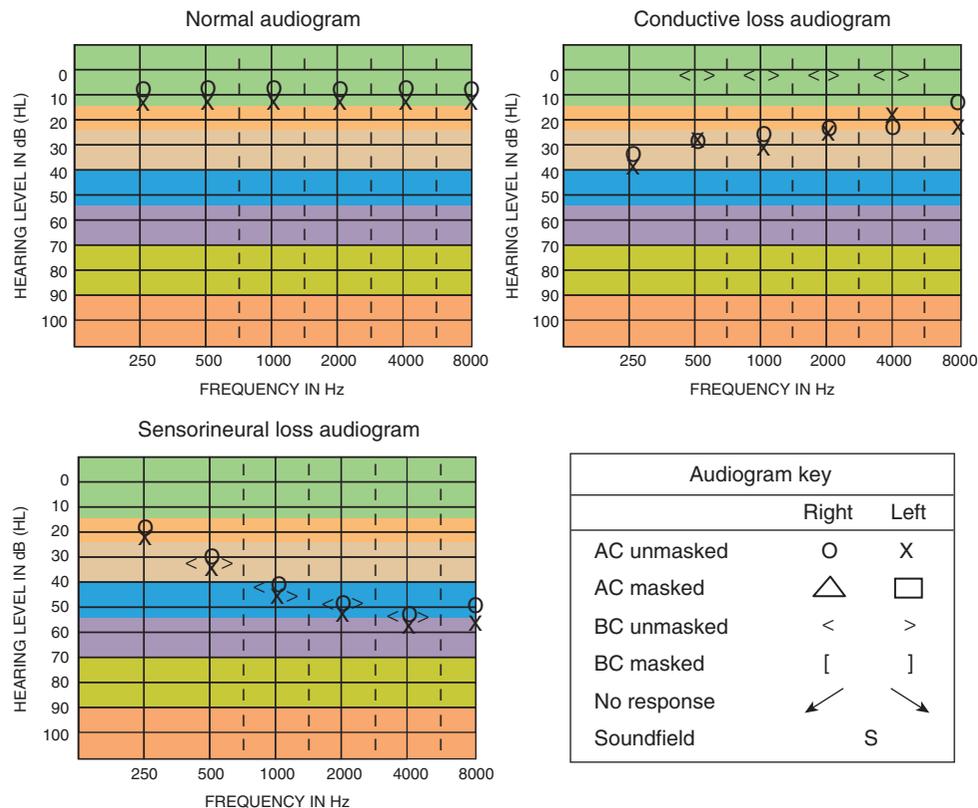


Fig. 14.2 Audiograms of normal and impaired hearing.

loss (bottom-left panel). A person with pure-tone thresholds less than 20 dB HL is considered to have normal hearing. A person with conductive loss can be identified by a >15-dB air–bone gap between air and bone conduction thresholds. In this typical case, the air–bone gap decreases from 30 dB at low frequencies to 20 dB at high frequencies. On the other hand, a person with typical sensorineural loss will have similar air and bone conduction thresholds at low and high frequencies. All three audiograms show symmetrical hearing. In the cases of unilateral hearing loss, masking is required in the better ear to prevent cross-hearing (i.e. hearing the sound in the good ear when testing the bad ear).

Because pure-tone audiograms may not always predict true hearing impairment, speech audiometry is also used. For example, the speech reception threshold (SRT) measures the lowest level at which a patient can identify 50% of spondee words (a set of double-syllabic words). This threshold should be within ± 5 dB of the pure-tone average thresholds. Speech recognition scores over 90% are considered to be within normal ranges when single-syllable words are presented at 30–40 dB above the speech reception threshold. In patients with neural and central losses, there are often inconsistent results between the pure-tone audiogram and speech audiometry.

Various objective methods can also be used to differentially diagnose the integration and function of the external ear, the middle ear, the inner ear, and the auditory nervous system. First, tympanometry measures the reflection of sounds from the eardrum and can be used to measure the eardrum and middle ear function. For example, a flat tympanogram indicates that acoustic compliance does not change as a function of the ear pressure, usually signaling middle ear effusion or eardrum perforation.

Second, the acoustic reflex method measures contraction of the stapedius muscle in response to a loud controlled sound. The measure is the least intense sound level that can be administered to give a response, and the presence of the response indicates normal function of the cochlea, the auditory nerve, the ventral cochlear nucleus, the facial nerve, and the stapedius muscle. Damage to any part or parts of this feedback loop may produce absent acoustic reflexes.

Third, otoacoustic emissions (OAE) are tiny sounds generated from the cochlear outer hair cells that can be measured by placing a sensitive, low-noise microphone in the ear canal. The presence of OAE indicates normal cochlear amplification function, whereas absence can be due to either damaged outer hair cells (origin) or an obstructed middle ear (pathway). Because OAE testing is rapid and does not require subject cooperation, it has been widely used in infant hearing screening as well as in identifying malingerers who want to feign a hearing loss. The top panel of Fig. 14.3 shows a typical OAE waveform.

Fourth, the auditory brainstem response (ABR) measures the evoked potentials, recorded by surface electrodes placed at the vertex of the head and the mastoids, in response to a click or tone pip through an air transducer or bone oscillator. The normal ABR has well-identifiable waveform peaks. The bottom panel of Fig. 14.3 shows a typical normal ABR waveform, with Wave I corresponding to activities generated at the distal auditory nerve, Wave II to the proximal auditory nerve, Wave III to the cochlear nucleus, and Wave V to the lateral lemniscus/inferior colliculus (Wave IV, not shown, corresponds to the superior olive). Abnormalities in ABR can occur due to conditions such as auditory neuropathy or tumors involving the internal auditory canal (e.g. vestibular schwannoma and Meningioma).

14.4 Classification

Recent advances in our understanding of these hearing disorders have allowed us to more accurately classify hearing impairment according to its anatomy and pathophysiology. To reflect these

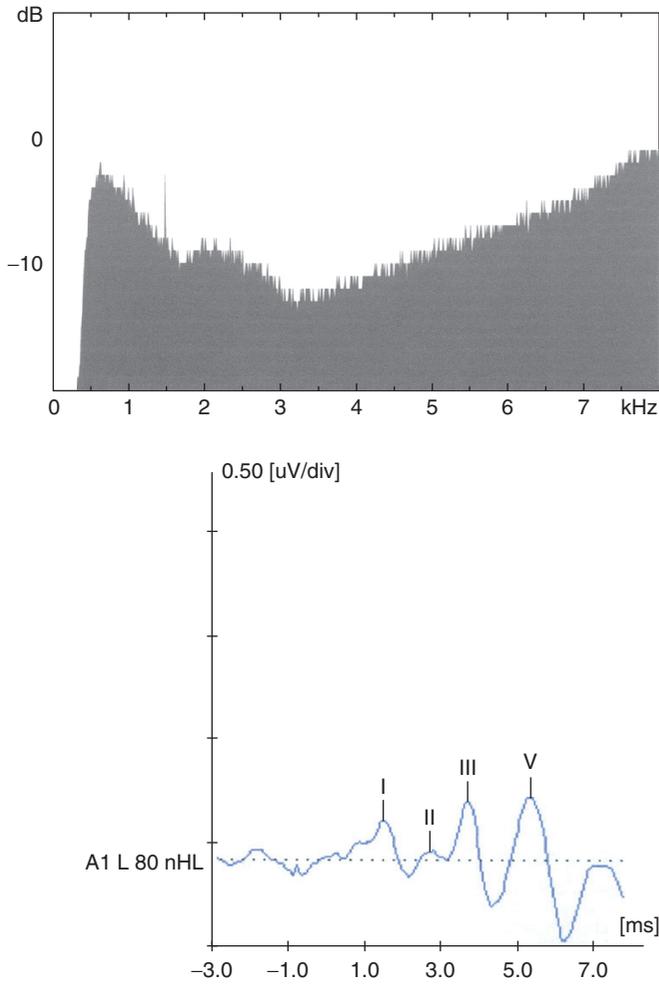


Fig. 14.3 Sample otoacoustic emission (top panel) and auditory brainstem response (bottom panel) recordings. Otoacoustic emission is spontaneously recorded from a young, normal-hearing ear, showing a peak of -3 dB SPL at 1.5 kHz. Auditory brainstem response is generated by a click sound and recorded from the same young, normal-hearing ear, showing wave I, II, III, and V.

advances in both diagnosis and knowledge, here we classify hearing impairment according to the following five categories:

- 1 Conductive loss (damage to the outer and/or middle ears)
- 2 Cochlear loss (damage to the inner ear)
- 3 Neural loss (damage to the auditory nerve)
- 4 Feedback loss (damage to the backward-feed pathway)
- 5 Central loss (damage to the brainstem and the cortex)

Table 14.1 lists diagnosis and symptoms on each of these different types of hearing impairments. Patients with conductive loss typically have elevated thresholds with air conduction compared to bone conduction, particularly at low frequencies. The middle ear function can be affected and measured by positive results in tympanograms. Acoustic reflex and OAE should not be affected, but may not be measured because of the disrupted mechanic pathway rather than

Table 14.1 Diagnosis and symptoms of different hearing impairments

Type	Origin	Audiog	Tymp	AR	OAE	ER	Imag	Sp
1	Conductive	+	+	—*	—*	—	—	—
2a	Cochl.—OHC	+	—	—*	+	—	—	—*
2b	Cochl.—IHC	—*	—	+	—	+*	—	+
3	Neural	—*	—	+	—	+	—	+
4	Feedback	—	—	+	—	—	—	—*
5	Central	—	—	—	—	+*	+*	+

Notes and abbreviations: Cochl., cochlear; OHC, outer hair cell (damage); IHC, inner hair cell (damage); Audiog, audiogram; Tymp, tympanogram; AR, acoustic reflex; OAE, otoacoustic emission; ER, evoked responses; Imag, brain imaging, including PET, MRI and fMRI techniques; Sp, speech recognition in quiet and in noise. +, positive or abnormal result; —, negative or normal result; *, see notes in the text.

damaged neural processing. Patients with outer hair cell damage typically have elevated thresholds with both air and bone conduction, particularly at high frequencies. The OAE may disappear but the middle ear and the nerve function should be normal. Speech recognition can be compensated for with properly fitted hearing aids. Patients with inner hair cell damage could have normal thresholds, normal middle ear, and normal OAE function, but demonstrate abnormal acoustic reflex, ABR and speech recognition that are disproportionate to the hearing loss suggested by the audiogram. Patients with neural loss (e.g. auditory neuropathy) have essentially the same symptoms as those with inner hair cell damage, which needs fine diagnostic measures to differentiate them. Patients with feedback loss may have normal function in quiet but impaired function in noise. Patients with central loss have normal peripheral function but abnormal central function, as reflected by evoked potentials, brain imaging, and speech recognition.

The next five sections focus on the perceptual consequences of these hearing impairments.

14.5 Conductive loss

Conductive hearing loss can be caused by any process that impedes the conduction of sound from the auricle to the cochlea. For example, cerumen impaction or a foreign body in the ear canal is a common cause of ear canal obstruction. In addition, congenital malformations of the ear canal, as well as collapse of the ear canal can cause a conductive hearing loss of up to 30 dB.

However, the most common cause of conductive hearing loss is typically fluid accumulation in the middle ear. This fluid is generally caused by a dysfunctional Eustachian tube, a ventilation path between the middle ear and throat. If this fluid is secondarily infected, as frequently occurs in children, then it becomes a common condition called ‘otitis media’. The fluid in the middle ear impedes vibration of the tympanic membrane, reducing the efficiency of sound conduction. Other similar conductive losses may involve perforation, tympanosclerosis (thickening of the fibrous layer), or atelectasis (loss of the fibrous layer) of the tympanic membrane.

Conductive loss can occur as a result of disruption of sound transmission in other parts of the middle ear or even the inner ear. For example, chronic infections of the middle ear may permanently disrupt the ossicular chain function. Overgrowth of bones in the stapes region, namely ‘otosclerosis’, reduces mobility of the stapes. Finally, if there is an opening into the inner ear that is uncovered, then some of the sound-induced volume velocity will be shunted away from the cochlea, creating a conductive hearing loss.

Generally, conductive loss can be corrected medically, producing nearly normal perceptual performance after correction (e.g. Snik *et al.*, 1991). The exception to this rule is auditory deprivation in early life secondary to conductive loss, which can cause abnormal development and significant hearing impairment including temporal and speech processing. However, there is evidence that prompt and proper training can correct these problems (Gravel *et al.*, 1996; Moore *et al.*, 2003).

14.6 Cochlear loss

Cochlear loss usually refers to structural damage in the inner ear, ranging from disarrayed stereocilia to the loss of outer and inner hair cells (Liberman, 1990). While the physiological responses to these structural damages have been systematically documented, their perceptual consequences are yet to be totally delineated. Here, we consider mainly the different effects between selective loss of outer hair cells and selective loss of inner hair cells on hearing.

The main cause of cochlear loss is damage to the outer hair cells. Outer hair cells provide non-linear amplification to an incoming sound. Non-linear amplification involves amplifying a soft sound up to 1000 times (60-dB gain) while gradually decreasing gain as the sound gets louder, causing the cochlea eventually to become a linear system that provides no gain to a loud sound (Ruggero, 1992). At high frequencies the gain is also frequency-specific, such that the gain is applied only to frequencies close to the best frequency of each place on the basilar membrane. This non-linear amplification is critical to solving the dynamic range problem (Chapter 3 of this volume) and sharp frequency selectivity (Chapter 2 of this volume). Damage to outer hair cells, therefore, has a fundamental impact on the perception of sound.

The most apparent consequence of outer hair cell damage is loss of sensitivity (an inability to hear soft sounds). Most cochlear-impaired subjects in this category have elevated thresholds at high frequencies because there is some evidence that high-frequency hearing behaves more non-linearly than low-frequency hearing.

Outer hair cell damage also produces significant changes in suprathreshold measures, particularly in the intensity and frequency domains. Loudness recruitment is a well-known manifestation of the perceptual changes in intensity as a result of the outer hair cell damage. The top-left panel of Fig. 14.4 demonstrates this phenomenon by contrasting loudness growth as a function of sound intensity between a normal-hearing ear and a cochlear-impaired ear. Loudness grows as a power function of sound intensity in the normal ear, over at least a 100-dB dynamic range (Stevens, 1961). In the impaired ear, the dynamic range is reduced because of the loss of sensitivity to low levels rather than insufficient loudness perception at high intensities. As a consequence, loudness appears to grow more steeply near threshold but catches up at high intensities. However, the loudness recruitment function does not necessarily require a change in the slope of the loudness function. It may also be accounted for, at least in part, by an increased loudness baseline value at the threshold in the impaired ear (Buus and Florentine, 2002).

At the physiological level, outer hair cell damage makes the basilar membrane behave more like a linear system. Behavioral measures using on- and off-frequency forward-masking techniques have confirmed the linearization of the basilar membrane vibration in the impaired ear (Oxenham and Plack, 1997). The top-right panel re-plots the Oxenham and Plack data, showing non-linear compression (roughly a 5 dB : 1 dB slope in the off-frequency masking growth function) in the normal ears, as opposed to the linear masking growth function in the impaired ears.

Outer hair cell damage also reduces frequency selectivity in the impaired ear. Frequency selectivity can be measured as psychophysical tuning curves, in which a pure tone is presented at a fixed level while the masker level is varied as a function of masker frequency, such that the masker

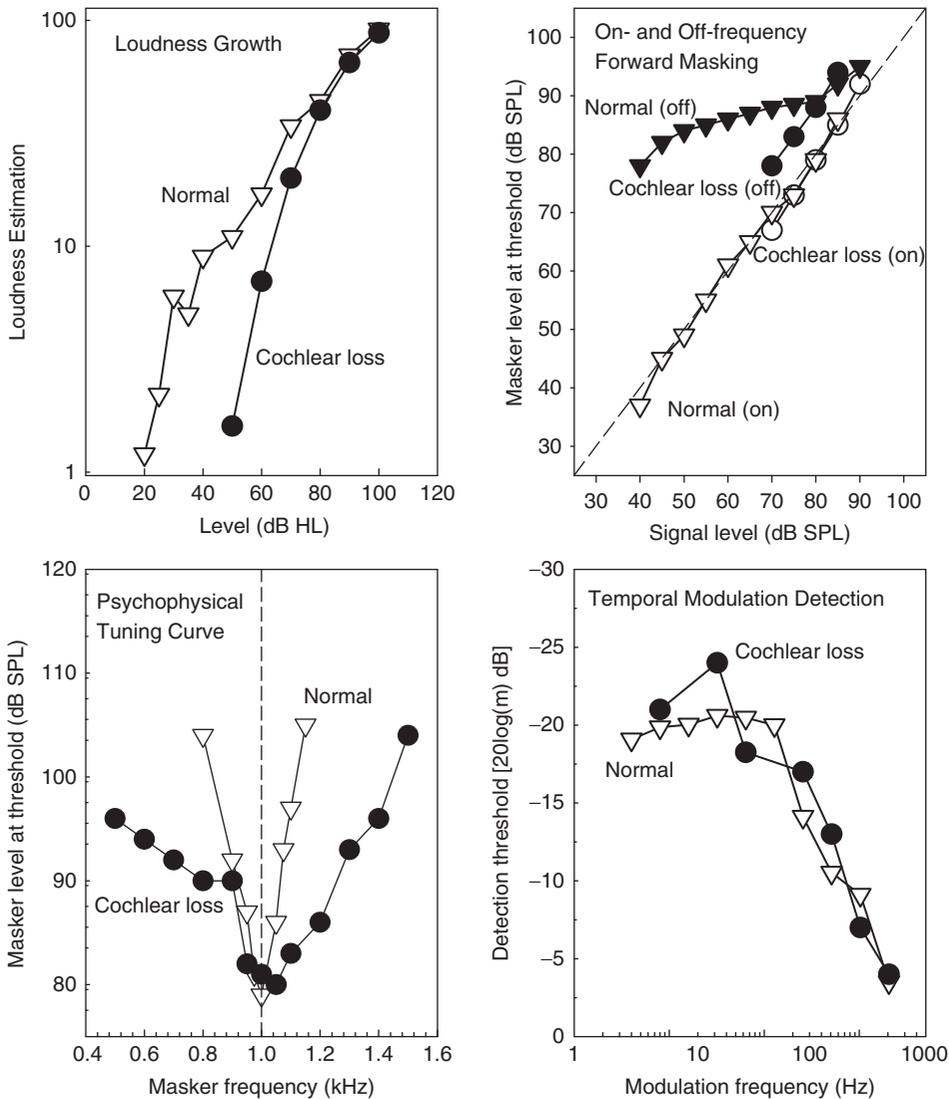


Fig. 14.4 Perceptual consequences of cochlear hearing loss (damage to outer hair cells). Top-left panel: Loudness growth from a unilaterally cochlear-impaired listener in the normal ear (open inverted triangles) and the impaired ear (solid circles). Unpublished data collected by Zeng. Top-right panel: Behavioral measurements of basilar membrane non-linearity in normal-hearing listeners (inverted triangles) and cochlear-impaired listeners (circles). The degree of compression is illustrated by the slope difference in the growth of masking function between 6-kHz on-frequency (open symbols) and 3-kHz off-frequency (solid symbols) forward maskers for a 6-kHz signal frequency. Data are re-plotted from Oxenham and Plack (1997). Bottom-left panel: Psychophysical tuning curve from a unilaterally cochlear-impaired listener in the normal ear (open inverted triangles) and the impaired ear (solid circles). Data are re-plotted from Fig. 8 in Moore and Glasberg (1986), who used a forward-masking procedure and a similar signal level in a unilaterally impaired subject PM. The signal was a 1-kHz pure tone presented at 72 and 84 dB SPL in the normal (threshold at 1 kHz = 24 dB SPL) ear and the impaired (threshold = 69 dB SPL) ear, respectively. Bottom-right panel: Temporal modulation transfer functions in normal-hearing listeners (open inverted triangles) and a cochlear-impaired listener (solid circles). Data are re-plotted from Zeng *et al.* (1999).

just makes the signal inaudible. Although the shape of psychophysical tuning curves is greatly influenced by the choice of signal level, masker type (pure tone vs. noise) and procedure (forward vs. simultaneous masking) (e.g. Ryan *et al.*, 1979; O'Loughlin and Moore, 1981; Nelson, 1991), there is strong evidence for broadening of the tuning curve, particularly the loss of the sharp tuning curve tip, in the cochlear impaired ear (e.g. Moore and Glasberg, 1986). The bottom-left panel shows psychophysical tuning curves at 1-kHz frequency between the normal ear and the impaired ear in a unilaterally cochlear-impaired subject. Compared with the sharp tuning curve (Q10 dB bandwidth = 128 Hz) in the normal ear, the impaired ear had essentially the same characteristic frequency or tip but a three to four times wider Q10 dB bandwidth. This broadened tuning curve does not necessarily worsen frequency discrimination because the cochlear-impaired listeners may utilize a temporally based cue, such as phasing locking in the auditory nerve, in frequency discrimination (e.g. Tyler *et al.*, 1983).

Indeed, outer hair cell damage may produce a relatively minor effect on temporal processing. The bottom-right panel of Fig. 14.4 shows essentially normal temporal modulation detection in a cochlear-impaired listener (adapted from Zeng *et al.*, 1999), but similar data have been obtained in larger subject populations and different audiogram configurations (Bacon and Gleitman, 1992; Moore *et al.*, 1992). There is a known non-linear interaction between intensity and temporal processing (e.g. Penner and Shiffrin, 1980), making direct assessment of temporal processing in cochlear-impaired listeners somewhat tricky. It is generally accepted that, after taking elevated thresholds, reduced non-linear compression, and loudness recruitment into account (Oxenham and Bacon, 2003), cochlear damage usually does not impair temporal processing such as the temporal integration function (Florentine *et al.*, 1988; Plack and Skeels, 2007), temporal gap detection (Florentine and Buus, 1984; Nelson and Thomas, 1997), the temporal window (Plack and Moore, 1991), and forward and backward masking (Nelson and Freyman, 1987).

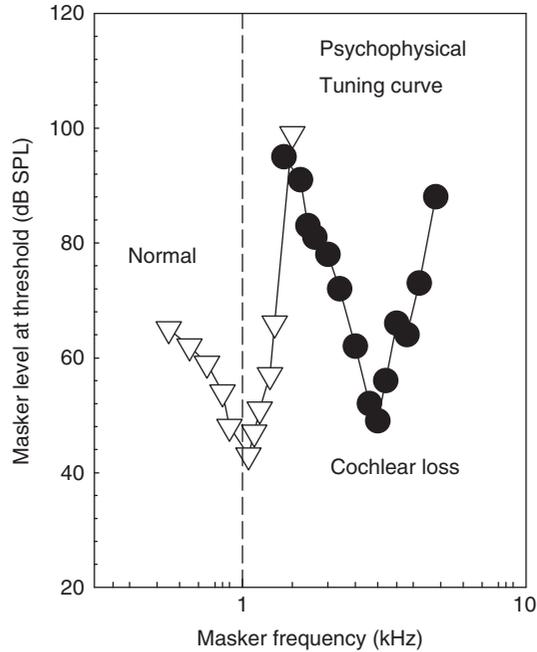
Similarly, after taking audibility and asymmetric hearing loss into account, outer hair cell damage typically has little or no effect on binaural tasks, such as sound localization using interaural level and timing differences (Hawkins and Wightman, 1980; Hausler *et al.*, 1983; Hall *et al.*, 1984; Smoski and Trahiotis, 1986). Although outer hair cell damage impairs intensity and frequency processing as well as speech recognition, particularly in noise and reverberation situations, its impairment can be remedied to a large extent by properly fitted hearing aids with dynamic range compression.

On the other hand, selective inner hair cell loss, such as that induced by the anti-cancer ototoxic drug carboplatin (Wake *et al.*, 1993), produces totally different physiological responses. As long as the outer hair cells are largely intact, significant selective loss of inner hair cells could produce relatively normal thresholds and tuning at the auditory nerve level (Wang *et al.*, 1997; Salvi *et al.*, 2000). Perceptually, selective inner hair cell loss has been studied as 'dead regions' (i.e. regions with no inner hair cell activity) in the cochlea (Moore, 2004).

The most significant difference between outer and inner hair cell damage has been the shifted tip of the psychophysical tuning curve. Figure 14.5 re-plots the Florentine and Houtsma data (1983), showing relatively unchanged tuning but an almost 2-octave shift in the tuning curve tip from 1 kHz in the normal ear to 4 kHz in the impaired ear that is indicative of inner hair cell loss. Because of the selective inner hair cell loss in the affected frequency region, signal detection relies on intact inner hair cells whose characteristic frequencies are outside the dead region (Moore and Alcantara, 2001).

Another manifestation of the presence of dead regions in the cochlea is the significantly increased threshold for detection of pure tones in suprathreshold noise. The idea is simple, because one would expect only a 3–6-dB increase in threshold, had the hearing loss been solely related to outer hair cell damage that increases the auditory filter bandwidth by a factor of 2–4. If the detection threshold is increased by 10 dB or more, then it is more likely that the inner hair

Fig. 14.5 Perceptual consequences of cochlear loss (damage to inner hair cells). Psychophysical tuning curve from a unilaterally cochlear-impaired listener in the normal ear (open inverted triangles) and the impaired ear (solid circles). Data are re-plotted from Florentine and Houtsma (1983).



cells at the signal frequency are lost, and that detection of the signal has to evoke responses by inner hair cells outside the dead region. For clinical convenience, Moore and his colleagues proposed to use ‘threshold equalizing noise’ (TEN) to probe the dead region, because TEN can overcome the difficulty with different audiogram configurations that may be due to either loss of sensitivity as a result of the damaged outer hair cells or the presence of dead regions associated with the selective inner hair cell loss (Moore *et al.*, 2000).

Although the presence of dead regions in the cochlea certainly affects place-based frequency perception (Huss and Moore, 2005), its associated dramatic change in psychophysical tuning curve position does not necessarily change the affected subject’s pitch perception, nor does it necessarily worsen frequency discrimination (Turner *et al.*, 1983). In fact, frequency discrimination at the edge of dead regions may be enhanced compared with normal performance (Thai-Van *et al.*, 2003). This relatively unaffected, or even improved, pitch performance suggests either the usage of a temporally based pitch perception cue or cortical plasticity induced by cochlear damage.

Intensity and temporal processing have not been studied in listeners with dead regions, but they may be relatively normal as long as they can use intact inner hair cells outside the dead region to process the intensity and temporal information. The problem with this ‘apparent’ normal processing is that the relevant intensity and temporal information is processed in the wrong place, resulting in abnormal processing of complex temporal–spectral patterns that are typically associated with speech and music perception (see Chapters 8–10). Indeed, there is some evidence that hearing aids that amplify the sound above audibility in the dead region do not improve, and may decrease, speech intelligibility (e.g. Hogan and Turner, 1998).

14.7 Neural loss

Auditory neurons receive information from the inner hair cells via chemical synapses, and send electric information to the brainstem for further processing. Neural loss ranges from dysfunctional

synapses to demyelination, axonal loss, or even cell death. Clinically, neural loss is often referred to as ‘auditory neuropathy’ (Starr *et al.*, 1996) or ‘auditory dys-synchrony’ (Berlin *et al.*, 2003). The signature of auditory neuropathy is the presence of a normal cochlear amplification function with absent or abnormal auditory brainstem responses. Functionally, neural loss differs from cochlear loss in that neural loss produces significant temporal processing deficits, which, in turn, lead to significant speech perception difficulty that cannot be accounted for by the degree of audibility (Zeng *et al.*, 1999, 2005).

Figure 14.6 shows the same sample perceptual measures in people with auditory neuropathy and in those with cochlear impairment, providing contrast between the two types of hearing impairment. The top-left panel shows nearly normal loudness-growth function in a neuropathy subject who has a normal audiogram. Intensity discrimination is also relatively normal in neuropathy subjects (Zeng *et al.*, 2005).

The top-right panel shows behavioral measures of basilar membrane non-linearity in neuropathy subjects. Similar to the Oxenham and Plack data (1997), the open inverted triangles show linear on-frequency forward-masking growth function while the solid inverted triangles show highly compressive off-frequency forward-masking growth function in normal-hearing subjects (Bai *et al.*, unpublished data). The neuropathy subjects show a similarly linear on-frequency masking function (open circles) and compressive off-frequency masking function (solid circles below 90 dB SPL). However, neuropathy subjects are 20–40 dB more susceptible to the masker, particularly for the off-frequency masker. The excessive masking has been observed in other types of masking, including simultaneous, forward, backward, onset, and steady-state masking (Zeng *et al.*, 2005). Although both neuropathy subjects and the subjects with dead regions show excessive masking, the underlying mechanisms can be totally different. The dead regions lack signal-carrying inner hair cells, while neuropathy produces temporal jitters in nerve discharge, effectively removing the phase-locking cue that is important in the detection of tones in noise.

The bottom-left panel shows psychophysical tuning curves from a normal-hearing subject (Kluk and Moore, 2004) and a neuropathy subject (Vinay and Moore, 2007). The neuropathy subject produced a slightly wider psychophysical tuning curve (a factor of 1.7 in bandwidth) than the normal-hearing subject but the same tip at 4 kHz. These tuning curve parameters are important to help differentiate between cochlear loss and neural loss. On the one hand, the neural damage and the outer hair cell damage do not change the tuning curve position, but the latter produces much wider tuning curves. On the other hand, neural damage and the inner hair cell damage produce similarly wide tuning curves, but the latter changes the tuning curve position.

The bottom-right panel shows temporal modulation transfer functions measured in a group of normal subjects and a group of neuropathy subjects (Zeng *et al.*, 1999). On average, the neuropathy subjects require an approximately 30% amplitude modulation to reach detection threshold, and their transfer functions have a bandpass characteristic. In comparison, the normal subjects require only 10% modulation for detection, and their transfer functions have a low-pass characteristic with a significantly higher low-pass cut-off frequency.

Extensive psychophysical measures (Starr *et al.*, 1996; Kraus *et al.*, 2000; Rance *et al.*, 2004; Zeng *et al.*, 2005) have shown that neural damage has minimal effects on intensity-related perception, such as loudness discrimination, frequency discrimination at high frequencies, and sound localization using interaural level differences. In contrast, neural damage significantly impairs timing-related perception, such as frequency discrimination at low frequencies, temporal integration, gap detection, temporal modulation detection, backward and forward masking, signal detection in noise, binaural beats, and sound localization using interaural time differences. These perceptual consequences are the opposite of what is typically observed in cochlear-impaired subjects, who have impaired intensity perception but relatively normal temporal processing after taking

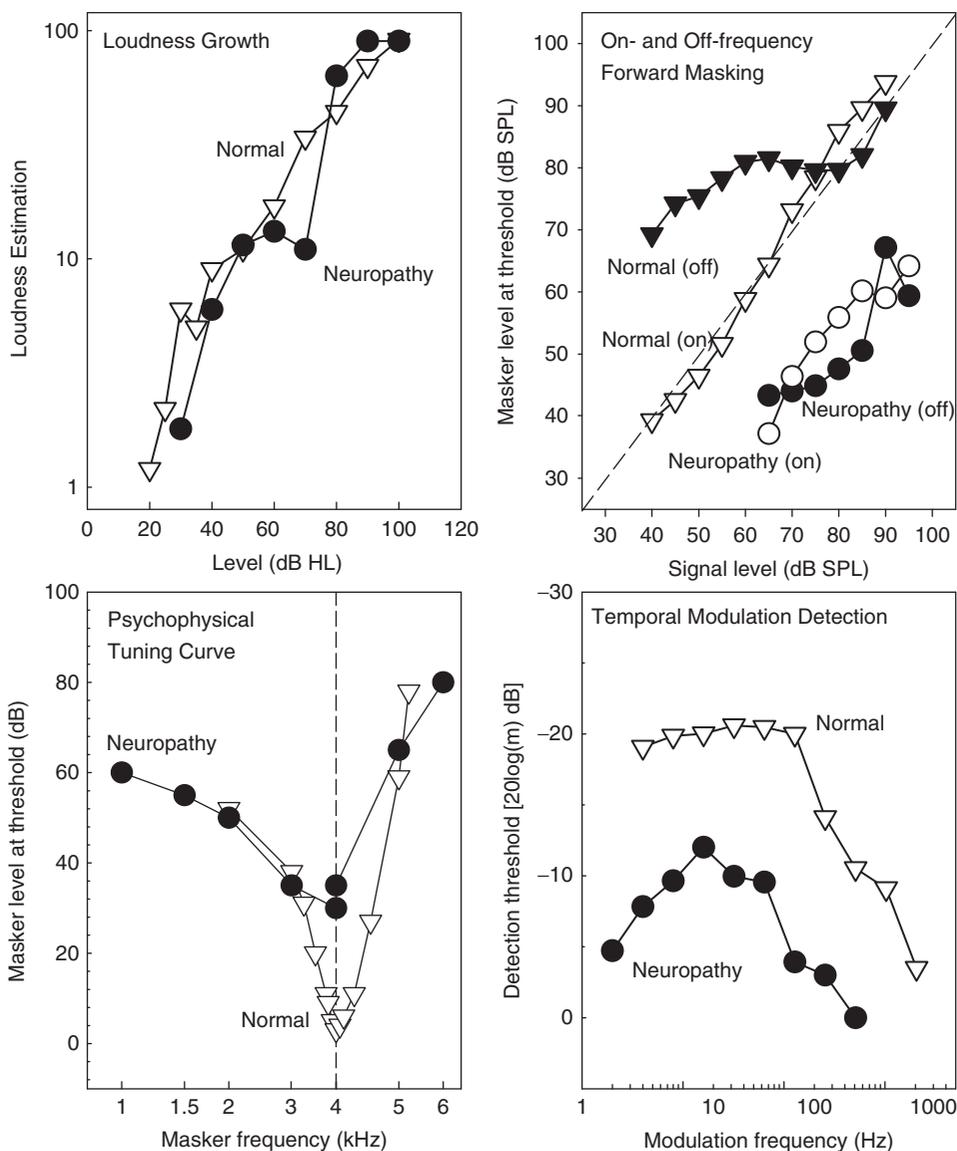


Fig. 14.6 Perceptual consequences of neural loss (auditory neuropathy, AN). Top-left panel: Loudness growth in a normal ear (open inverted triangles) and an AN ear (solid circles). Unpublished data collected by Zeng. Top-right panel: Behavioral measurements of basilar membrane non-linearity in normal-hearing listeners (inverted triangles) and AN listeners (circles). The degree of compression is illustrated by the slope difference in the growth of masking function between 6-kHz on-frequency (open symbols) and 3-kHz off-frequency (solid symbols) forward maskers. Unpublished data from Zeng, Bai, and Starr. Bottom-left panel: Psychophysical tuning curve in normal-hearing listeners (open inverted triangles) and an AN listener (solid circles). The normal data are from Kluk and Moore (2004, mean data in their Fig. 4 using a 10-dB SL, 4-kHz pure-tone signal and a 320-Hz wide masker), with permission; while the AN data are from Vinay and Moore (2007, S8 left ear data in their Fig. 8 using a 10-dB SL, 4-kHz pure-tone signal and a third-octave noise masker), with permission. Bottom-right panel: Temporal modulation transfer functions in normal-hearing listeners (open inverted triangles) and AN listeners (solid circles). Data are re-plotted from Zeng *et al.* (1999).

their impaired intensity perception into account. Studying perceptual differences between cochlear loss and neural loss also sheds light on the mechanisms underlying basic auditory processing. Different neural codes are used: a suboptimal spike count code for intensity processing, a synchronized spike code for temporal processing, and a duplex code for frequency processing.

14.8 Feedback damage

In addition to the ascending pathway, the auditory system has a descending pathway that uses feedback loops to control information flow and processing (see Chapters ?? and ?? in Volume 2). Damage to the feedback control can also impair auditory processing, but relatively little attention has been paid to this impairment. Here we consider two feedback loops: the middle ear or the stapedius muscle reflex, and the olivocochlear efferent reflex.

Physiological studies have demonstrated an anti-masking role for both the stapedius reflex and the efferent reflex, but these two reflexes work at different intensities and frequencies (e.g. Liberman and Guinan, 1998). The stapedius reflex is activated by loud sounds and attenuates the sound input to the cochlea up to 20–30 dB at low-to-middle frequencies (below 1 kHz, the solid line in Fig. 14.7). On the other hand, the efferent reflex can be activated by soft sounds and attenuates the mechanical transmission up to 30 dB at middle-to-high frequencies (2–10 kHz, the dashed line in Fig. 14.7). Damage to these reflexes can cause significant hearing impairment.

Borg and Zakrisson (1973) measured speech intelligibility as a function of speech level from 30 to 127 dB SPL in seven subjects with unilateral Bell's palsy and paralysed stapedius muscles. In the normal ears, speech intelligibility maintained a high performance level at ~90% correct up to 120 dB SPL; whereas in the affected ears with paralysed stapedius muscles, performance started to deteriorate at 100 dB SPL and dropped to 30% correct at 120 dB SPL. This roll-over performance-intensity function was replicated in a large patient population with Bell's palsy and may be related to excessive upward spread of masking from low-frequency components of speech to intelligibility-bearing

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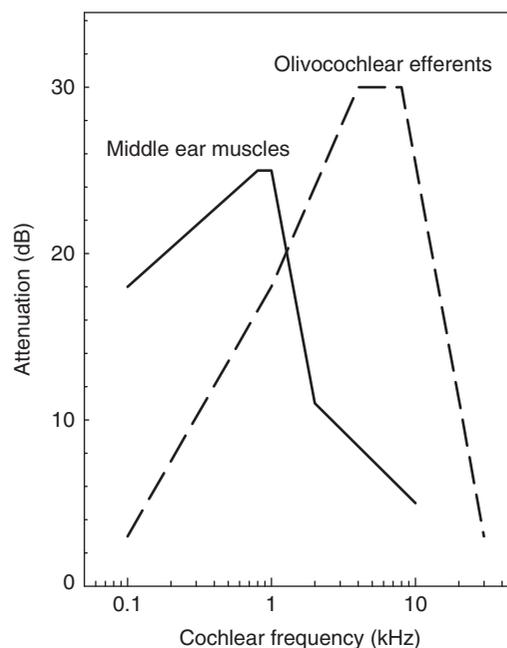


Fig. 14.7 Attenuation as a function of cochlear frequency caused by middle ear muscle contraction (the solid line) or by electrical stimulation of the medial olivocochlear efferents (the dashed line). The original middle ear muscle data were taken from Pang and Peake (1986) with permission, and the original olivocochlear efferent data were taken from Guinan and Gifford (Guinan and Gifford, 1988) with permission. The figure was modified according to Liberman and Guinan's (1998) Figure 2 with the y-axis converted into dB values.

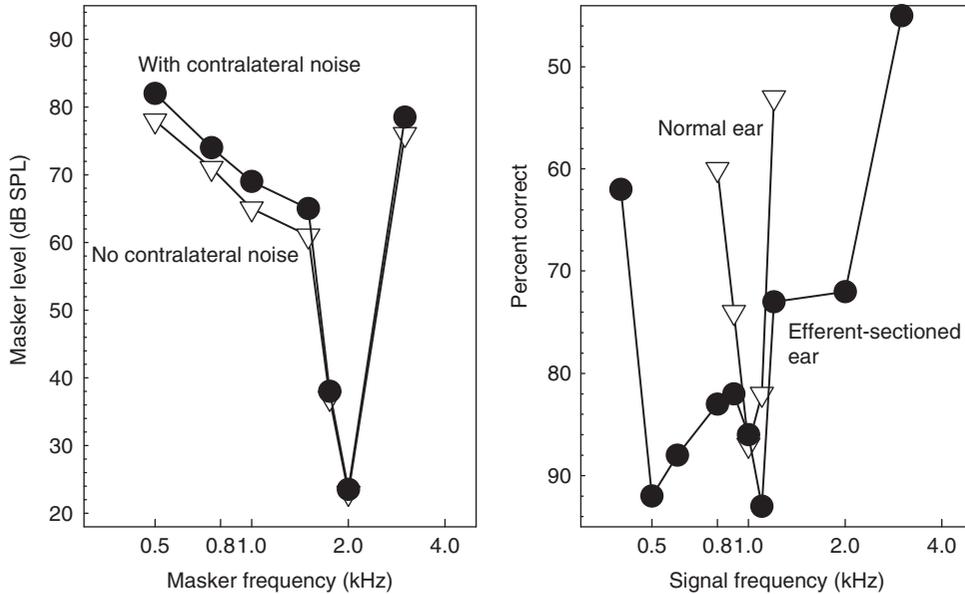


Fig. 14.8 Role of olivocochlear efferents in hearing. Psychophysical tuning curves (left panel) measured in the absence (control, open inverted triangles) and presence (solid circles) of contralateral noise. Attention filters (right panel) measured before (control, open inverted triangles) and after (solid circles) efferent section.

middle- and high-frequency components (Wormald *et al.*, 1995). The impaired stapedius muscle reflex reduces the auditory operating range by 15–20 dB at high levels.

Activation of the efferent reflex enhances frequency selectivity, whereas an impaired efferent reflex reduces frequency selectivity, impeding auditory performance in noise (Zeng *et al.*, 2000; Guinan, 2006). The left panel of Fig. 14.8 shows that activation of the efferent reflex via contralateral noise sharpens the psychophysical tuning curve, mostly by increasing the slope of the low-frequency side (Kawase *et al.*, 2000). The overall effect of the efferent reflex is relatively small, but may contribute to the changes in frequency selectivity caused by cochlear loss and neural loss. The right panel of Fig. 14.8 shows that surgical removal of the efferent reflex widens the attention filter by more than one order of magnitude (Scharf *et al.*, 1994). There are also multiple backward-feeding pathways from the cortex to the auditory brainstem, which are not discussed here because their perceptual significance has not been clearly identified (for a review, see Suga *et al.*, 2000).

14.9 Central loss

With few exceptions, hearing impairment related to central loss has no clearly defined physiopathology and is usually associated with, or sometimes the main culprit responsible for, symptoms such as central auditory processing disorder, language impairment, learning disability, autism, and attention deficits. Here we define central loss as hearing impairment unrelated to any apparent problems in the peripheral auditory system from the external ear to the inner ear, including the auditory nerve. This is an emergent area of research that is closely tied to aspects of neuroscience such as brain imaging and cortical plasticity. We present several hearing impairment cases related to central loss to shed light upon the common and different aspects between peripheral and central hearing impairments.

Levine *et al.* (1993) measured electrophysiological and psychophysical performance in 38 patients with multiple sclerosis (MS), a demyelinating disease in the brain. They compared these results with brain imaging data, being able to pinpoint specific abnormal performance to central lesion sites. They found that both abnormal brainstem auditory evoked potentials and abnormal interaural timing differences (see Chapter 6) using high-frequency carriers (>4000 Hz) are tightly coupled with the auditory brainstem lesion, whereas interaural level differences and interaural timing differences using low-frequency carriers (<1000 Hz) may not be tightly coupled with the auditory brainstem lesion. In contrast to neural loss in the periphery, relatively simple temporal processing such as gap detection may not be affected in patients with MS unless the degree and scope of the demyelination are extensive (Hendler *et al.*, 1990).

Auditory processing impairment has been suggested to be the main culprit causing specific language impairment in 3–6% of children who are otherwise unimpaired (e.g. Tallal and Stark, 1981). The hearing impairment is not related to audibility, as in the case of traditional sensorineural hearing loss, but related to the inability to process rapidly varying temporal information, such as detection and discrimination of brief sounds in the presence of competing sounds (e.g. Wright *et al.*, 1997). Because there are no apparent lesions in the auditory periphery in these affected children, their inability to process brief sounds is most likely to have a central origin. There have been reports that intensive and structured training in processing brief sounds can lead to improved language learning in these children, but whether temporal processing deficits are the culprit for language impairment and whether these training programs are effective are still subjects of controversy (Bishop *et al.*, 1999; Gillam *et al.*, 2008).

A final example that shows centrally related hearing impairment is autism—which typically involves the affected subjects' inability to filter out irrelevant background information. Again, children with autism typically show normal peripheral audition from pure-tone audiogram, middle ear function, acoustic reflex to otoacoustic emission (Gravel *et al.*, 2006). However, children with autism have difficulty processing suprathreshold information, including abnormal loudness perception, frequency processing, attention, and cortical processing of complex sounds such as voices (Ceponiene *et al.*, 2003; Gage *et al.*, 2003; Gervais *et al.*, 2004; Khalifa *et al.*, 2004).

14.10 Summary of perceptual consequences of hearing impairment

Table 14.2 summarizes the perceptual consequences of various hearing impairments. Conductive loss would linearly reduce loudness growth but should have negligible effects on all other perceptual functions. The three asterisks on temporal, binaural, and speech processing associated with conductive loss may indicate temporary difficulties due to deprivation of early auditory experience and unilateral loss.

Outer hair cell (OHC) damage produces loudness recruitment, linear basilar membrane response, and reduced frequency resolution and selectivity, but otherwise relatively normal perceptual functions if the elevated thresholds are properly compensated for.

Inner hair cell (IHC) damage will likely not affect loudness growth and basilar membrane non-linearity. The two signatures of the inner hair cell damage, or the presence of dead regions, are the shifted psychophysical tuning curve position and excessive masking (>10 dB than normal or outer hair cell damage). The dead region can occur anywhere in the cochlea. As long as the adjacent inner hair cells are intact, frequency discrimination and binaural differences do not have to be compromised. However, the 'wrong place' pitch can produce a significant problem in speech and music perception.

Recall that clinical audiological diagnosis in Table 14.1 cannot differentiate between inner hair cell damage and neural damage. Here the perceptual consequences of these two impairments can

Table 14.2 Perceptual consequences of hearing impairments

Type	Origin	L	BM	FDL	PTC	tMTF	Mask	Bin	Sp
1	Conductive	+	–	–	–	–*	–	–*	–*
2a	Cochlear —OHC	+	+	+	Wide	–*	–	–	–*
2b	Cochlear —IHC	–*	–?	–*	Shift	–?	+	–?	+
3	Neural	–*	–*	+Low	–*	+	+	+ITD	+
4	Feedback	–	–	–	–*	+	+	+ITD	–*
5	Central	–	–	–	–	+	?	+	+

Notes and Abbreviations: L, loudness growth; BM, basilar membrane non-linearity; FDL, frequency discrimination limen; PCT, psychophysical tuning curve; tMTF, temporal modulation transfer function; Mask, masking; Bin, binaural hearing; ITD, interaural time difference; Sp, speech recognition. +, positive result; –, negative result; *, see notes in the text.

be differentiated because the neural damage explicitly affects spike synchrony, whereas the inner hair cell damage does not. Spike synchrony is essentially a low-frequency effect, specifically affecting frequency discrimination at low frequencies, temporal modulation transfer function, and only interaural time differences but not interaural level differences. The psychophysical tuning curve does not shift position nor does it significantly increase its breadth, especially at high frequencies. The excessive masking and speech recognition deficits are a result of impaired temporal processing.

Feedback loss produces relatively subtle changes in perception. The known effects include a 10–20-dB reduction in dynamic range as a result of the damaged middle ear muscle reflex, a reduced anti-masking function and broadened attention filters as a result of the sectioned efferent pathway.

Except for well-identified pathological conditions such as MS, where specific lesions relate to perceptual consequences, most cases of central auditory processing disorders lack correlation between structural changes and (dys)functions. Improved functional measures and brain imaging techniques are needed to provide such correlation.

The above examples are more like ‘pure’ cases involving only one type of hearing impairment. In reality, there are at least two difficulties challenging the diagnosis and treatment of hearing impairment. First, a patient may have mixed losses involving several types of hearing impairment. Second, different hearing impairments may produce similar perceptual consequences. For example, impaired temporal processing may be observed in patients with auditory neuropathy, multiple sclerosis, central auditory processing disorder, or specific language impairment. Systematic and strategic diagnosis is required to differentiate the origin of these hearing impairments. For example, auditory neuropathy and multiple sclerosis both produce abnormal auditory brainstem responses, but auditory neuropathy will have normal brain imaging whereas multiple sclerosis will not. Central auditory processing disorder may have auditory specific impairment, whereas language impairment may accompany impairment in other modalities. Proper diagnosis is important because it will lead to proper treatment.

14.11 Simulations of hearing impairment

It has always been an intriguing question: What does sound sound like to a hearing-impaired person? Simulations of hearing impairment are important not only to allow a normal-hearing

person to appreciate the difficulty a hearing-impaired person faces in daily life, but also to help understand mechanisms and perceptual consequences of hearing loss. Over the years, researchers have developed audio-simulations of various hearing impairments, which are briefly summarized here.

To simulate conductive loss, the simplest way is to use fingers to plug up both ear canals. One would experience either loudness reduction (about 20 dB) for an external sound source or loudness increment for an internal sound source (e.g. chewing crunchy potato chips, the so-called 'occlusion effect').

To simulate the effect of sloping high-frequency hearing loss, low-pass filters with different cut-off frequencies can be implemented (Fig. 14.9), see: <http://www.neurophys.wisc.edu/animations/>

Notice the differential effects of high-frequency hearing loss on speech and music: the low-pass filtering greatly reduces speech intelligibility but has no effect on melody recognition. To further simulate suprathreshold distortions such as loudness recruitment and spectral smearing that are typically associated with cochlear loss (Moore and Glasberg, 1993), the reader is referred to the sound samples, including speech, music, and environmental sounds under quiet and more realistic listening situations, on the Phonak website: <http://www.phonak.com/consumer/hearing/hearinglossdemo.htm>

To simulate auditory neuropathy, different degrees of temporal smearing using actually measured modulation transfer functions are applied to speech sounds (Zeng *et al.*, 1999), see: <http://www.ucihs.uci.edu/hesp/Simulations/simulationsmain.htm>

Notice in the waveforms that the natural fluctuations in amplitude are gradually flattened as the severity of auditory neuropathy is increased.

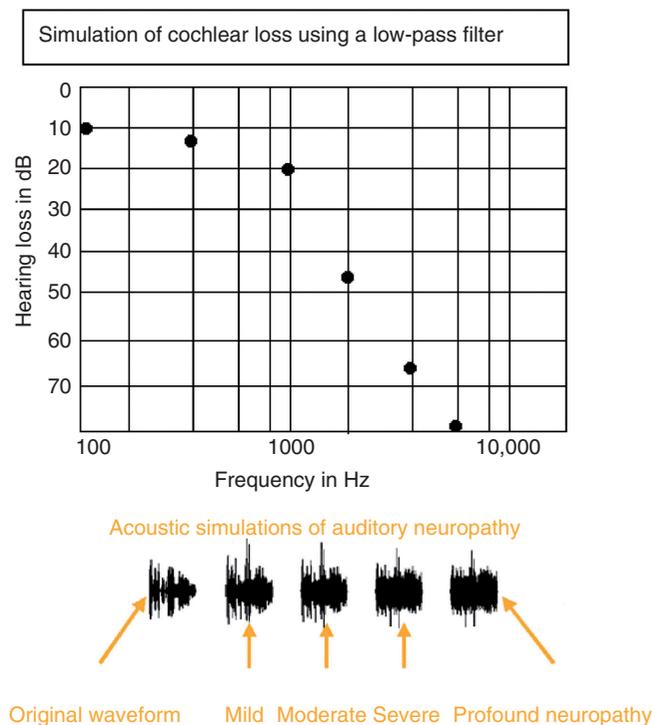


Fig. 14.9 Simulations of hearing impairment: Cochlear loss (top panel) and auditory neuropathy (bottom panel).

Finally, simulation of information overload in autism can be viewed at: <http://www.youtube.com/watch?v=BPDTEuotHe0>

14.12 Treatment

Depending upon the type and severity of hearing impairment, three treatment options are available, including hearing aids, middle ear implants, and cochlear implants. These devices all use a microphone to pick up acoustic signals, but use different signal processing techniques, and most importantly have totally different output signals (Fig. 14.10).

A hearing aid is essentially an acoustic transducer that has a sound input and a sound output. According to the degree and frequency region of hearing loss, the hearing aid selectively amplifies the sound to make otherwise inaudible frequency components of a sound audible, while at the same time ensuring that the sound is not amplified too much as to overstimulate the hearing-impaired listener. A multichannel, wide-dynamic compression circuit is typically implemented to achieve these two seemingly conflicting goals. Acoustic feedback (a loud ringing) resulting from the direct acoustic path between the microphone and the speaker can be an annoying problem for hearing-aid users who require a great deal of amplification (>40–60 dB); automatic feedback cancellation (e.g. reverse filtering at the ringing frequency) can be used to alleviate this problem. Hearing aids are most effective for hearing-impaired listeners with mild-to-severe cochlear loss.

A middle ear implant can avoid the feedback problem by bypassing air conduction altogether. The middle ear implant stimulates the cochlea via mechanic vibration delivered to either the middle ear bones or the mastoid bone. Because no speaker is needed, the implant can maintain relatively high fidelity, particularly at high output levels. Bone-conduction hearing aids are traditionally used for patients with conductive and mixed loss hearing loss, chronic infections of the ear canal or the middle ear, ear canal atresia or stenosis, and single-sided deafness. One major difference between traditional bone-conduction hearing aids and middle ear implants is that traditional bone-conduction hearing aids do not require surgery but middle ear implants do.

If the hearing-impaired listener has no functional inner hair cells, then no matter how loud a sound is amplified, the impaired listener cannot hear any sound. A cochlear implant is therefore needed to replace the function of the damaged inner ear by directly stimulating the residual auditory nerve with electric currents. The cochlear implant has two main components: an external processor, and an internal receiver and stimulator. The external sound processor takes sound, processes it digitally, breaks it down into a number of frequencies (typically 16–22) and sends the

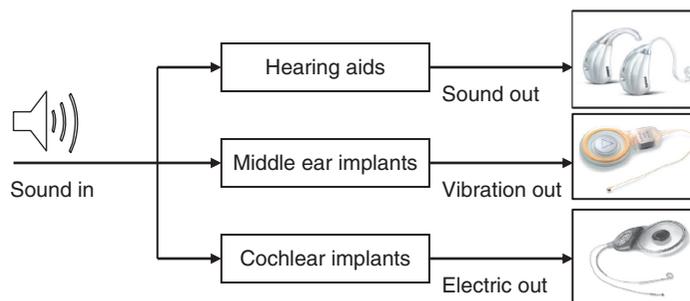


Fig. 14.10 Treatment of hearing impairment using hearing aids, middle-ear implants, and cochlear implants. The hearing aids shown are Exélia micro from Phonak (www.phonak.com). The middle-ear implant shown is Soundbridge from Med-El (www.medel.com). The cochlear implant shown is Nucleus-24 from Cochlear (www.cochlear.com).

frequencies via a radiofrequency signal to the implanted part. The internal receiver and stimulator decode the radiofrequency signal into patterned electric pulses and send them to different electrodes to stimulate the adjacent spiral ganglion cells in the cochlea.

Cochlear implants have been used by more than 100 000 hearing-impaired persons worldwide as of 2008, more than half being deaf children who have since developed normal language. Previously, a cochlear-implant candidate needed to be profoundly deaf to be eligible for implantation. At present, a person can receive a cochlear implant even if he or she has a normal audiogram but less than 50% speech intelligibility. Some success has been reported for using cochlear implants to treat patients with auditory neuropathy (e.g. Miyamoto *et al.*, 1999; Shallop *et al.*, 2001; Zeng and Liu, 2006). However, to treat patients with sectional auditory nerve and a totally deformed or ossified cochlea, a brainstem implant with electrodes placed in the cochlear nucleus or inferior colliculus would be used (e.g. Brackmann *et al.*, 1993; Lenarz *et al.*, 2006).

In addition to the device approach, there has been a strong effort towards the regeneration of hair cells for the biological treatment of hearing impairment. It is well known that hair cells can be regenerated from basal cells in birds, but recent results have demonstrated hair cell regeneration in mammals (Izumikawa *et al.*, 2005; White *et al.*, 2006). Future treatment of hearing impairment may incorporate, or combine, both engineering and biological approaches.

14.13 Concluding remarks

Hearing impairment may arise from genetic deficits or environmental assaults, affecting one part or many parts of the normal auditory process from the external ear to the brain. Hearing impairment has been traditionally classified into conductive loss and sensorineural loss. However, recent advances in genetics, physiology, and psychology have allowed the differentiation of at least five types of hearing impairment according to lesion site and perceptual consequences:

- 1 Conductive loss (elevated thresholds)
- 2 Cochlear loss (loudness and pitch abnormalities)
- 3 Neural loss (temporal processing impairment)
- 4 Feedback loss (anti-masking and attention deficits)
- 5 Central loss (temporal and complex processing deficits)

Conductive loss can be treated by either surgery or bone-conduction hearing aids. Cochlear loss, particularly that due to outer hair cell damage, can be treated with hearing aids, but cochlear loss with inner hair cell damage may require cochlear implantation. Neural loss cannot be treated effectively with hearing aids, but can be partially compensated for by cochlear implants. Feedback loss produces relatively subtle perceptual changes, which may not require aggressive intervention. Central loss can be permanent, e.g. multiple sclerosis, or temporary, such as plasticity-based changes, which may be ameliorated by training and learning. Hearing impairment may also produce other symptoms such as tinnitus and dizziness, which have no wholly effective treatment at present.

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References

- Bacon, S. P. and Gleitman, R. M. (1992). Modulation detection in subjects with relatively flat hearing losses. *Journal of Speech and Hearing Research* 35:642–53.

- Berlin, C. I., Hood, L., Morlet, T., Rose, K., and Brashears, S. (2003). Auditory neuropathy/dys-synchrony: diagnosis and management. *Mental Retardation and Developmental Disabilities Research Reviews* 9: 225–31.
- Bishop, D. V., Carlyon, R. P., Deeks, J. M., and Bishop, S. J. (1999). Auditory temporal processing impairment: neither necessary nor sufficient for causing language impairment in children. *Journal of Speech and Hearing Research* 42:1295–310.
- Borg, E. and Zakrisson, J. E. (1973). Stapedius reflex and speech features. *Journal of the Acoustical Society of America* 54:525–7.
- Brackmann, D. E., Hitselberger, W. E., Nelson, R. A., Moore, J., Waring, M. D., Portillo, F., et al. (1993). Auditory brainstem implant: I. Issues in surgical implantation. *Otolaryngology and Head and Neck Surgery* 108:624–33.
- Buus, S. and Florentine, M. (2002). Growth of loudness in listeners with cochlear hearing losses: recruitment reconsidered. *Journal of the Association for Research in Otolaryngology* 3:120–39.
- Ceponiene, R., Lepisto, T., Shestakova, A., Vanhala, R., Alku, P., Naatanen, R., et al. (2003). Speech-sound-selective auditory impairment in children with autism: they can perceive but do not attend. *Proceedings of the National Academy of Sciences USA* 100:5567–72.
- Conference, N. C. (1990). Noise and hearing loss. *Journal of the American Medical Association* 263:3185–90.
- Conlin, A. E. and Parnes, L. S. (2007). Treatment of sudden sensorineural hearing loss: I. A systematic review. *Archives of Otolaryngology and Head and Neck Surgery* 133:573–81.
- Daniels, R. L., Swallow, C., Shelton, C., Davidson, H. C., Krejci, C. S., and Harnsberger, H. R. (2000). Causes of unilateral sensorineural hearing loss screened by high-resolution fast spin echo magnetic resonance imaging: review of 1,070 consecutive cases. *American Journal of Otology* 21:173–80.
- Florentine, M. and Buus, S. (1984). Temporal gap detection in sensorineural and simulated hearing impairments. *Journal of Speech and Hearing Research* 27:449–55.
- Florentine, M. and Houtsma, A. J. (1983). Tuning curves and pitch matches in a listener with a unilateral, low-frequency hearing loss. *Journal of the Acoustical Society of America* 73:961–5.
- Florentine, M., Fastl, H., and Buus, S. (1988). Temporal integration in normal hearing, cochlear impairment, and impairment simulated by masking. *Journal of the Acoustical Society of America* 84: 195–203.
- Gage, N. M., Siegel, B., Callen, M., and Roberts, T. P. (2003). Cortical sound processing in children with autism disorder: an MEG investigation. *Neuroreport* 14:2047–51.
- Gervais, H., Belin, P., Boddaert, N., Leboyer, M., Coez, A., Sfaello, I., et al. (2004). Abnormal cortical voice processing in autism. *Nature Neuroscience* 7:801–2.
- Gillam, R. B., Loeb, D. F., Hoffman, L. M., Bohman, T., Champlin, C. A., Thibodeau, L., et al. (2008). The efficacy of Fast ForWord Language intervention in school-age children with language impairment: a randomized controlled trial. *Journal of Speech, Language, and Hearing Research* 51:97–119.
- Gravel, J. S., Wallace, I. F., and Ruben, R. J. (1996). Auditory consequences of early mild hearing loss associated with otitis media. *Acta Oto-laryngologica* 116:219–21.
- Gravel, J. S., Dunn, M., Lee, W. W., and Ellis, M. A. (2006). Peripheral audition of children on the autistic spectrum. *Ear and Hearing* 27:299–312.
- Guinan, J. J., Jr. (2006). Olivocochlear efferents: anatomy, physiology, function, and the measurement of efferent effects in humans. *Ear and Hearing* 27:589–607.
- Guinan, J. J., Jr and Gifford, M. L. (1988). Effects of electrical stimulation of efferent olivocochlear neurons on cat auditory-nerve fibers. III. Tuning curves and thresholds at CF. *Hearing Research* 37:29–45.
- Gurtler, N. and Lalwani, A. K. (2002). Etiology of syndromic and nonsyndromic sensorineural hearing loss. *Otolaryngologic Clinics of North America* 35:891–908.
- Hall, J. W., Tyler, R. S., and Fernandes, M. A. (1984). Factors influencing the masking level difference in cochlear hearing-impaired and normal-hearing listeners. *Journal of Speech and Hearing Research* 27:145–54.

- Hausler, R., Colburn, S., and Marr, E. (1983). Sound localization in subjects with impaired hearing. Spatial-discrimination and interaural-discrimination tests. *Acta Oto-Laryngologica* **400** (Suppl.):1–62.
- Hawkins, D. B. and Wightman, F. L. (1980). Interaural time discrimination ability of listeners with sensorineural hearing loss. *Audiology* **19**:495–507.
- Hendler, T., Squires, N. K., and Emmerich, D. S. (1990). Psychophysical measures of central auditory dysfunction in multiple sclerosis: neurophysiological and neuroanatomical correlates. *Ear and Hearing* **11**:403–16.
- Hogan, C. A. and Turner, C. W. (1998). High-frequency audibility: benefits for hearing-impaired listeners. *Journal of the Acoustical Society of America* **104**:432–41.
- Huss, M. and Moore, B. C. (2005). Dead regions and pitch perception. *Journal of the Acoustical Society of America* **117**:3841–52.
- Izumikawa, M., Minoda, R., Kawamoto, K., Abrashkin, K. A., Swiderski, D. L., Dolan, D. F., *et al.* (2005). Auditory hair cell replacement and hearing improvement by Atoh1 gene therapy in deaf mammals. *Nature Medicine* **11**:271–6.
- Kawase, T., Ogura, M., Hidaka, H., Sasaki, N., Suzuki, Y., and Takasaka, T. (2000). Effects of contralateral noise on measurement of the psychophysical tuning curve. *Hearing Research* **142**:63–70.
- Khalfa, S., Bruneau, N., Roge, B., Georgieff, N., Veuillet, E., Adrien, J. L., *et al.* (2004). Increased perception of loudness in autism. *Hearing Research* **198**:87–92.
- Kluk, K. and Moore, B. C. (2004). Factors affecting psychophysical tuning curves for normally hearing subjects. *Hearing Research* **194**:118–34.
- Kraus, N., Bradlow, A. R., Cheatham, M. A., Cunningham, J., King, C. D., Koch, D. B., *et al.* (2000). Consequences of neural asynchrony: a case of auditory neuropathy. *Journal of the Association for Research in Otolaryngology* **1**:33–45.
- Lenarz, T., Lim, H. H., Reuter, G., Patrick, J. F., and Lenarz, M. (2006). The auditory midbrain implant: a new auditory prosthesis for neural deafness—concept and device description. *Otology and Neurotology* **27**:838–43.
- Levine, R. A., Gardner, J. C., Stufflebeam, S. M., Fullerton, B. C., Carlisle, E. W., Furst, M., *et al.* (1993). Binaural auditory processing in multiple sclerosis subjects. *Hearing Research* **68**:59–72.
- Lieberman, M. C. (1990). Quantitative assessment of inner ear pathology following ototoxic drugs or acoustic trauma. *Toxicologic Pathology*, **18**(1, Pt 2):138–48.
- Lieberman, M. C. and Guinan, J. J., Jr. (1998). Feedback control of the auditory periphery: anti-masking effects of middle ear muscles vs. olivocochlear efferents. *Journal of Communication Disorders* **31**:471–82; quiz 483; 553.
- Miyamoto, R. T., Kirk, K. I., Renshaw, J., and Hussain, D. (1999). Cochlear implantation in auditory neuropathy. *Laryngoscope* **109**(2, Pt 1):181–5.
- Moore, B. C. (2004). Dead regions in the cochlea: conceptual foundations, diagnosis, and clinical applications. *Ear and Hearing* **25**:98–116.
- Moore, B. C. and Alcantara, J. I. (2001). The use of psychophysical tuning curves to explore dead regions in the cochlea. *Ear and Hearing* **22**:268–78.
- Moore, B. C. and Glasberg, B. R. (1986). Comparisons of frequency selectivity in simultaneous and forward masking for subjects with unilateral cochlear impairments. *Journal of the Acoustical Society of America* **80**:93–107.
- Moore, B. C. and Glasberg, B. R. (1993). Simulation of the effects of loudness recruitment and threshold elevation on the intelligibility of speech in quiet and in a background of speech. *Journal of the Acoustical Society of America* **94**:2050–62.
- Moore, B. C., Shailer, M. J., and Schooneveldt, G. P. (1992). Temporal modulation transfer functions for band-limited noise in subjects with cochlear hearing loss. *British Journal of Audiology* **26**:229–37.
- Moore, B. C., Huss, M., Vickers, D. A., Glasberg, B. R., and Alcantara, J. I. (2000). A test for the diagnosis of dead regions in the cochlea. *British Journal of Audiology* **34**:205–24.

- Moore, D. R., Hartley, D. E., and Hogan, S. C. (2003). Effects of otitis media with effusion (OME) on central auditory function. *International Journal of Pediatric Otorhinolaryngology* 67(Suppl. 1):S63–67.
- Nelson, D. A. (1991). High-level psychophysical tuning curves – forward masking in normal-hearing and hearing-impaired listeners. *Journal of Speech and Hearing Research* 34:1233–49.
- Nelson, D. A. and Freyman, R. L. (1987). Temporal resolution in sensorineural hearing-impaired listeners. *Journal of the Acoustical Society of America* 81:709–20.
- Nelson, P. B. and Thomas, S. D. (1997). Gap detection as a function of stimulus loudness for listeners with and without hearing loss. *Journal of Speech, Language, and Hearing Research* 40:1387–94.
- O’Loughlin, B. J. and Moore, B. C. (1981). Off-frequency listening: effects on psychoacoustical tuning curves obtained in simultaneous and forward masking. *Journal of the Acoustical Society of America* 69:1119–25.
- Oxenham, A. J. and Bacon, S. P. (2003). Cochlear compression: perceptual measures and implications for normal and impaired hearing. *Ear and Hearing* 24:352–66.
- Oxenham, A. J. and Plack, C. J. (1997). A behavioral measure of basilar-membrane nonlinearity in listeners with normal and impaired hearing. *Journal of the Acoustical Society of America* 101:3666–75.
- Pang, X. D. and Peake, W. T. (1986). How do contractions of the stapedius muscle alter the acoustic properties of the ear? In *Peripheral Auditory Mechanisms* (ed. J. L. H. J. Allen, A. Hubbard, S. I. Neely, and A. Tubis), pp. 136–43. New York, NY: Springer-Verlag.
- Paparella, M. M. and Djalilian, H. R. (2002). Etiology, pathophysiology of symptoms, and pathogenesis of Meniere’s disease. *Otolaryngologic Clinics of North America* 35:529–45, vi.
- Penner, M. J. and Shiffrin, R. M. (1980). Nonlinearities in the coding of intensity within the context of a temporal summation model. *Journal of the Acoustical Society of America* 67:617–27.
- Plack, C. J. and Moore, B. C. (1991). Decrement detection in normal and impaired ears. *Journal of the Acoustical Society of America* 90:3069–76.
- Plack, C. J. and Skeels, V. (2007). Temporal integration and compression near absolute threshold in normal and impaired ears. *Journal of the Acoustical Society of America* 122:2236–44.
- Rance, G., McKay, C., and Grayden, D. (2004). Perceptual characterization of children with auditory neuropathy. *Ear and Hearing* 25:34–46.
- Ruggero, M. A. (1992). Responses to sound of the basilar membrane of the mammalian cochlea. *Current Opinion in Neurobiology* 2:449–56.
- Ryan, A., Dallos, P., and McGee, T. (1979). Psychophysical tuning curves and auditory thresholds after hair cell damage in the chinchilla. *Journal of the Acoustical Society of America* 66:370–8.
- Ryan, A. F., Keithley, E. M., and Harris, J. P. (2001). Autoimmune inner ear disorders. *Current Opinion in Neurology* 14:35–40.
- Rybak, L. P. and Ramkumar, V. (2007). Ototoxicity. *Kidney International* 72:931–5.
- Salvi, R. J., Ding, D., Wang, J., and Jiang, H. Y. (2000). A review of the effects of selective inner hair cell lesions on distortion product otoacoustic emissions, cochlear function and auditory evoked potentials. *Noise and Health* 2:9–26.
- Scharf, B., Magnan, J., Collet, L., Ulmer, E., and Chays, A. (1994). On the role of the olivocochlear bundle in hearing: a case study. *Hearing Research* 75:11–26.
- Shallop, J. K., Peterson, A., Facer, G. W., Fabry, L. B., and Driscoll, C. L. (2001). Cochlear implants in five cases of auditory neuropathy: postoperative findings and progress. *Laryngoscope* 111(4, Pt 1):555–62.
- Smoski, W. J. and Trahiotis, C. (1986). Discrimination of interaural temporal disparities by normal-hearing listeners and listeners with high-frequency sensorineural hearing loss. *Journal of the Acoustical Society of America* 79:1541–7.
- Snik, A. F., Teunissen, E., and Cremers, C. W. (1991). Frequency resolution after successful surgery in congenital ear anomalies. *Scandinavian Audiology* 20:265–7.
- Starr, A., Picton, T. W., Sininger, Y., Hood, L. J., and Berlin, C. I. (1996). Auditory neuropathy. *Brain* 119:741–53.

- Stevens, S. S. (1961). To honor Fechner and repeal his law: A power function, not a log function, describes the operating characteristic of a sensory system. *Science* 133:80–6.
- Suga, N., Gao, E., Zhang, Y., Ma, X., and Olsen, J. F. (2000). The corticofugal system for hearing: recent progress. *Proceedings of the National Academy of Sciences USA* 97:11807–14.
- Tallal, P. and Stark, R. E. (1981). Speech acoustic-cue discrimination abilities of normally developing and language-impaired children. *Journal of the Acoustical Society of America* 69:568–74.
- Thai-Van, H., Micheyl, C., Moore, B. C., and Collet, L. (2003). Enhanced frequency discrimination near the hearing loss cut-off: a consequence of central auditory plasticity induced by cochlear damage? *Brain* 126:2235–45.
- Turner, C., Burns, E. M., and Nelson, D. A. (1983). Pure tone pitch perception and low-frequency hearing loss. *Journal of the Acoustical Society of America* 73:966–75.
- Tyler, R. S., Wood, E. J., and Fernandes, M. (1983). Frequency resolution and discrimination of constant and dynamic tones in normal and hearing-impaired listeners. *Journal of the Acoustical Society of America* 74:1190–9.
- Vinay, [S. N.] and Moore, B. C. (2007). Ten(HL)-test results and psychophysical tuning curves for subjects with auditory neuropathy. *International Journal of Audiology* 46:39–46.
- Wake, M., Takeno, S., Ibrahim, D., Harrison, R., and Mount, R. (1993). Carboplatin ototoxicity: an animal model. *Journal of Laryngology and Otology* 107:585–9.
- Wang, J., Powers, N. L., Hofstetter, P., Trautwein, P., Ding, D., and Salvi, R. (1997). Effects of selective inner hair cell loss on auditory nerve fiber threshold, tuning and spontaneous and driven discharge rate. *Hearing Research* 107:67–82.
- White, P. M., Doetzlhofer, A., Lee, Y. S., Groves, A. K., and Segil, N. (2006). Mammalian cochlear supporting cells can divide and trans-differentiate into hair cells. *Nature* 441:984–7.
- Wormald, P. J., Rogers, C., and Gatehouse, S. (1995). Speech discrimination in patients with Bell's palsy and a paralysed stapedius muscle. *Clinical Otolaryngology and Allied Sciences* 20:59–62.
- Wright, B. A., Lombardino, L. J., King, W. M., Puranik, C. S., Leonard, C. M., and Merzenich, M. M. (1997). Deficits in auditory temporal and spectral resolution in language-impaired children. *Nature* 387:176–8.
- Zadeh, M. H. and Selesnick, S. H. (2001). Evaluation of hearing impairment. *Comprehensive Therapy* 27:302–10.
- Zeng, F. G. and Liu, S. (2006). Speech perception in individuals with auditory neuropathy. *Journal of Speech, Language, and Hearing Research* 49:367–80.
- Zeng, F. G., Oba, S., Garde, S., Sininger, Y., and Starr, A. (1999). Temporal and speech processing deficits in auditory neuropathy. *Neuroreport* 10:3429–35.
- Zeng, F. G., Martino, K. M., Linthicum, F. H., and Soli, S. D. (2000). Auditory perception in vestibular neurectomy subjects. *Hearing Research* 142:102–12.
- Zeng, F. G., Kong, Y. Y., Michalewski, H. J., and Starr, A. (2005). Perceptual consequences of disrupted auditory nerve activity. *Journal of Neurophysiology* 93:3050–63.

