CHAPTER TWENTY-ONE

Longitudinal Changes in Hearing and Speech Perception in Older Adults

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Introduction

Since 1987, the Hearing Research Program at the Medical University of South Carolina (MUSC) in Charleston has conducted basic and clinical studies of presbyacusis. In this program, parallel experiments include an animal model of age-related hearing loss and large numbers of adults of various ages, whose hearing ranges from normal to severe sensorineural hearing loss. In establishing the focus of this program, age-related hearing loss was considered a significant area of research because of its high prevalence and complex etiology. Currently, about 75% of the ~30 million hearing-impaired individuals in the United States are ≥ 55 years of age. When thresholds at higher frequencies are considered, nearly all individuals over 80 years of age have significant hearing loss. Indeed, presbyacusis is the most prevalent of the chronic conditions of aging among males 65 years and older and the fourth most prevalent condition among older females, after arthritis, cardiovascular diseases, and visual impairments (Collins, 1997). From now until 2050, the number of individuals with hearing loss will substantially increase, due to the growth in the number of individuals who are older than 65, 75, and 85 years of age. These changing demographics make age-related hearing loss a significant scientific issue, given the lack of a strong evidence base for prevention methods, treatment approaches, and rehabilitation protocols.

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In addition to its high prevalence, age-related hearing loss was considered a significant area of scientific focus because of its complex etiology. Many factors contribute to age-related hearing loss in older humans, including genetic and aging factors; a lifetime of exposures to noise and ototoxic drugs; diet; trauma; and otologic and other diseases. As a result of these multiple, complex factors, it is not feasible in older humans to determine the unique contribution of age-related changes to the auditory system, independent of the accumulated effects due to environmental and other ototoxic factors. To determine the magnitude and effects of an aging component, research on age-related hearing loss has been conducted with laboratory animals raised under strict experimental control. At MUSC, the gerbil animal model has been used extensively, due, in part, to audiometric profiles in older animals that are similar to audiograms of 65- to 70-year-old human males and females (Mills et al., 1990). In this model, gerbils are raised during their three-year lifespan in a controlled environment, whereby noise and ototoxic drug exposures are kept to a minimum, and humidity, nutrition, and diet are carefully monitored. Under these conditions, hearing loss observed in older gerbils relates only to changes due to age or genetic factors. Age-related changes observed in the gerbil's auditory anatomy and physiology contribute to our understanding of age-related hearing loss in older humans, for whom environmental and other ototoxic factors cannot be controlled or even monitored over the lifespan. An initial focus of the program at MUSC has been the audiometric configuration typical of older adults who have not experienced long-term exposures to noise. This configuration is characterized by a relatively flat loss of 10–40 dB HL in lower frequencies, coupled with a gradually sloping loss in the higher frequencies (e.g., Jerger et al., 1993), a pattern of hearing loss

also seen in older gerbils raised in quiet. Thus, it may be possible to reveal the underlying mechanisms responsible for this configuration in humans by assessing (in quiet-aged gerbils) age-related changes in the anatomy and physiology of sensory cells, the cochlear lateral wall (stria vascularis, spiral ligament), and the auditory nerve.

In designing a large-scale study of age-related hearing loss in older humans, an important consideration was the selection of a cross-sectional or longitudinal study design. In a cross-sectional study of aging, large numbers of subjects of various ages are recruited and evaluated at the same time. Mean results for specific variables of interest (e.g., hearing levels, speech-recognition scores) at one point in time are compared between subgroups of subjects who have similar ages or age ranges. Many cross-sectional studies of auditory function in older adults, including speech recognition, report age-related differences in performance (e.g., Jerger, 1973, 1990, 1992; Mościcki et al., 1985; Gates et al., 1990; Wiley et al., 1998). Some experimental designs attempt to account for differences in pure-tone thresholds across groups by stratifying subjects by degree of hearing loss, or by forming subgroups with the goal of minimizing group differences in magnitude of hearing loss. Despite these controls, the interpretation of results of cross-sectional studies is complicated by hearing loss that increases in older subjects and rates of threshold change that may vary among individuals. Results are also inconsistent with regard to the contributions of age, gender, and other demographic variables. These inconsistencies may be attributed to differences in sampling methods, sample sizes, procedures, or statistical methods. Most importantly, without controls for age-related threshold changes, it is not possible to determine the extent to which age-related differences in speech recognition relate to differences in audibility alone, or whether additional factors should be considered, such as dysfunction in the peripheral auditory system (other than elevated thresholds), central-auditory changes, or cognitive declines.

In a longitudinal study of aging, repeated measures of the same variables in the same subjects are obtained over a long period of time. With subjects serving as their own controls, effects of uncontrollable factors that differ among subjects and within subject subgroups, such as noise history, occupation, nutrition, and pre-existing health conditions, are minimized. Longitudinal studies can measure age-related changes in hearing levels and speech recognition for groups and for individuals, whereas cross-sectional studies provide measures of age-related changes for groups only. The major disadvantages of longitudinal studies of older persons include difficulty in recruitment and retention and high cost. Data collection takes many years, making it necessary to retain subjects in good general health over long periods of time. This raises concerns about "selective attrition" in longitudinal studies of aging, wherein healthier or higher performing older participants may remain in the study longer. Only a few large-scale longitudinal studies of hearing have been conducted, including the Baltimore Longitudinal Study of Aging (Brant and Fozard, 1990; Pearson et al., 1995), the British Medical Research Council's epidemiologic studies in the United Kingdom and Denmark (Davis et al., 1991), the Framingham Heart Study (Gates & Cooper, 1991), and the Beaver Dam Epidemiology of Hearing Loss study (Cruickshanks et al., 2003). In the longitudinal study of age-related hearing loss at MUSC, subjects 18 years and older who are in good general health are recruited and scheduled to come to the laboratory approximately once per month for a total of 3 to 6 visits to complete an extensive test battery, which includes audiologic measures (behavioral and self-assessment questionnaires), biologic/medical data, cognitive testing, and brain imaging studies.

Many of the large-scale longitudinal studies of hearing listed above included measures of speech recognition but none have reported longitudinal changes. The few studies that have assessed longitudinal changes were limited by small sample sizes of older subjects, only 1–2 repeated measurements, and short time spans (Møller, 1981; Pedersen et al., 1991; Hietanen et al., 2004; Divenyi et al., 2005). Most importantly, none of these studies assessed changes in speech recognition over time while controlling for concurrent changes in pure-tone thresholds. In the MUSC longitudinal study of age-related hearing loss, recognition of isolated monosyllabic words in quiet was measured in a large sample of older persons. Repeated measures were obtained yearly or every 2–3 years. To control for changes in pure-tone thresholds and speech levels occurring over the same time period, speech-recognition scores were adjusted using an importance-weighted speech-audibility metric (articulation index, AI).

This report will feature four main topics: (1) results from the gerbil animal model that provide a biological explanation of age-related hearing loss as indicted by the audiogram and a comparison to audiograms of older humans; (2) an overview of the MUSC longitudinal

study of age-related hearing loss; (3) cross-sectional and longitudinal changes in hearing in older adults; and (4) longitudinal changes in speech recognition in older adults, independent of changes in hearing.

The Gerbil Animal Model of Presbyacusis

As reviewed earlier, at MUSC, gerbils are raised so that every aspect of their environment is controlled (noise exposure, drugs, diet, humidity). Under those conditions, the main findings related to age-related changes in auditory anatomy and physiology are: (1) only scattered outer hair cell loss (sensory presbyacusis), which is usually limited to the extreme basal and apical regions of the cochlea, and a generally normal population of inner hair cells (Tarnowski et al., 1991); (2) primary degeneration of spiral ganglion neurons (neural presbyacusis) (Mills et al., 2006); and (3) systematic degeneration of the cochlear lateral wall (metabolic presbyacusis), which is the most prominent of the anatomical changes seen in aging gerbils (Spicer and Schulte, 1991; Schulte and Schmiedt, 1992). The lateral wall is responsible for production and maintenance of the endocochlear potential (EP). The EP is the 80–100 mV potential between scala media and scala tympani, which is present across the outer hair cells and provides voltage to the "cochlear amplifier." The cochlear amplifier is dependent on an active process located in the outer hair cells to physically increase traveling wave vibrations along the basilar membrane (e.g., Davis, 1983). An important factor linking this outer hair cell function to the normal audiogram is that the maximum gain of the normal cochlear amplifier varies along the basilar membrane. That is, in the apical region of the cochlea, which responds to lower frequencies, the gain is ~20 dB, but in the basal region of the cochlea, which is tuned to higher frequencies, the gain can be as large as 50–60 dB (Ruggero & Rich, 1991; Cooper & Rhode, 1997; Robles & Ruggero, 2001).Thus, with an age-related decline in the EP, the voltage available to the cochlear amplifier is reduced, which can reduce the cochlear amplifier gain by as much as 20 dB in the lower frequencies and as much as 60 dB in the higher frequencies.

In a study by Schmiedt et al. (2002), neural thresholds (i.e., thresholds of the compound action potential of the auditory nerve) and EP were measured in large numbers of older gerbils raised in quiet. At lower frequencies, the decline in EP (relative to younger animals) was typically 40–50 mV, whereas the corresponding neural threshold shift (relative to younger animals) was only ~20 dB. At higher frequencies, a somewhat larger decline in EP corresponded to a ~60 dB increase in neural thresholds. This resulted in a relatively flat hearing loss at lower frequencies coupled to a sloping hearing loss at higher frequencies (metabolic presbyacusis), similar to the audiometric profile of many older humans. To test the hypothesis that the decline in EP resulted in threshold shifts in older gerbils because it reduced the voltage available to the cochlear amplifier, younger gerbils were treated chronically with furosemide, a loop diuretic, which artificially produces a systematic decline in the EP (Sewell, 1984). In the furosemide-treated gerbils, neural threshold shifts at higher frequencies were well ordered by the amount of EP loss, whereas the neural threshold shift at lower frequencies was largely independent of EP loss. As a result, the audiometric configuration resulting from the furosemide-produced reduction in EP was very similar to hearing losses seen in quiet-aged gerbils who exhibit an age-related decline in EP, supporting the hypothesis that the EP declines resulted in the characteristic audiogram of older gerbils.

To summarize, metabolic presbyacusis features a flat 10–40 dB low-frequency hearing loss with thresholds at higher frequencies gradually increasing to ~60 dB, preservation of (but reduced) cochlear nonlinearities, and primary degeneration of spiral ganglion neurons. Age-related losses of outer and inner hair cells are rarely seen, except in the most apical and basal regions of the cochlea, where high-frequency thresholds may exceed 60 dB. In contrast to changes due to aging, threshold elevations resulting from sensory cell loss (e.g., due to noise or drug exposure) feature a steeply sloping high-frequency hearing loss, loss of cochlear nonlinearities, and secondary neural degeneration associated with injury to inner hair cells (Schmiedt et al., 1990). These results and others suggest that, in the absence of other damage, age-related hearing loss should be viewed as a vascular, metabolic, neural hearing loss rather than a sensory hearing loss.

The MUSC Longitudinal Study of Age-Related Hearing Loss

In the longitudinal study of age-related hearing loss at MUSC, participants are 18 years of age and older who are in good general health. Subjects are excluded if they show evidence of conductive hearing loss or active otologic or neurologic diseases. Subjects' hearing ability

can range from normal to severe hearing loss, but hearing must be good enough to provide measurable results on most tests. All subjects are screened with the Mini-Mental State Exam. Table 1 lists the entire test battery. The audiometric test battery includes the following: pure-tone air-conduction thresholds at conventional frequencies (repeated at every visit) and extended high frequencies; speech-recognition thresholds (SRT) using the Auditec recording of the CID W-1 spondaic word lists (Hirsh et al., 1952); several measures of speech recognition in quiet and in noise using a variety of recorded test materials; middle-ear measurements; otoacoustic emissions; upward and downward spread of masking; and auditory brainstem responses. The cognitive test battery includes standardized measures of abstract reasoning, attention, inhibition, intelligence, perceived workload, processing speed, and working memory. A subset of subjects undergoes structural and function brain imaging (MRI) while listening to and understanding low-pass-filtered speech as a function of low-pass cutoff frequency and/or speech in background babble at various signal-to-babble ratios. Medical/biologic measures include blood draws for clinical chemistries, including serum estradiol and progesterone levels for female subjects, blood draws to extract and store DNA to identify and characterize genes that are under- or over-expressed with age, and an otologic examination. Over the course of the study, some blood chemistry measures have been discontinued (e.g., electrolytes, immunoglobulins, thyroid function) after determining there were no associations with hearing in older persons (Lee et al., 1998). In addition, subjects provide oral and written responses to questionnaires on hearing and medical history, tinnitus, smoking, handedness, medication use, occupational and non-occupational noise history, hearing-aid use, self-evaluation of hearing handicap and outcomes of health conditions, and undergo memory screenings. Finally, a family pedigree for hearing loss is obtained by interview with a genetics counselor.

After competing the test battery, subjects are scheduled annually to update their contact information, to update medical and hearing histories and medication information, and for measurement of thresholds at conventional frequencies and monosyllabic word-recognition scores. To obtain additional longitudinal data, a portion of the test battery is repeated every 2 to 3 years (see test measures identified with asterisks in Table 1).

To retain a nearly constant number of subjects actively involved in the longitudinal study, approximately 50 new subjects have been enrolled each year since the start of the study in 1987; this enrollment is based on average attrition rates. Ideally, the number of active subjects is maintained in the range of 325–350. This number of subjects is appropriate for the staff and testing facilities available daily. Increasing the number of active subjects increases the wait time for return testing, which may lead to rising subject drop-out rates. Subjects have voluntarily withdrawn from the study due to non-study-related illnesses or death, moving from the area, no longer perceiving a benefit of participation, and increased time constraints. Subjects have been discontinued from the study due to difficulty scheduling, non-aging-related changes in hearing or otologic or neurologic conditions, and poor test reliability. Of the older persons screened but not enrolled, 72% had evidence of middle-ear disease; 18% had fluctuating, asymmetric, or profound hearing loss, or hearing loss associated with Meniere's disease or acoustic neuroma; and 8% gave unreliable responses during hearing testing. To date, more than 1,000 subjects have participated in the program; of these, some longitudinal data covering at least a 3-year period are available from more than 450 subjects. Table 2 includes age and gender distributions of study participants as of November, 2009, including currently active subjects and subjects for whom longitudinal data are available. The numbers of subjects under 60 years of age are relatively small because, in most years of the program, emphasis was placed on recruiting large numbers of older adults and smaller numbers of younger (18–30 years) "control" subjects with normal hearing. In more recent years, subjects are recruited throughout the lifespan, including subjects in the "middle ages" from 31–59 years. Additional details of subject selection and test administration are included in previous publications reporting results from the MUSC longitudinal study of age-related hearing loss (e.g., Dubno et al., 1995; Dubno et al., 1997; Lee et al., 2005; Mills et al., 2006).

Figure 1 of Dubno et al. (2008) displays mean (±1 SD) pure-tone thresholds (in dB HL) as a function of audiometric frequency mea-sured most recently for 835 female and male subjects, compared to female and male subjects of similar ages from the Framingham Heart Study cohort (Gates et al., 1990) and the Beaver Dam cohort (Cruickshanks et al., 1998). Mean thresholds of our female subjects are very similar to those of both community-based, epidemiological studies of age-related hearing loss. Mean thresholds of our male subjects are very similar to 70–79 year olds from the Beaver Dam study, but somewhat poorer than those from the Framingham

Audiometric Measures
Hearing for pure tones, including extended high frequencies*
Ability to understand speech in quiet and in noise (SRT, NU6, SPIN, SSW)*
Otoacoustic emissions*
Upward and downward spread of masking
Middle ear function*
Auditory brainstem responses
Cognitive Measures
Abstract reasoning (Wisconsin Card Sort Test - WCST)
Attention (Visual Search and Attention Test, WCST)
Inhibition (Stroop Neuropsychological Screening Test)
Intelligence (Wechsler Abbreviated Scale of Intelligence)
Perceived workload (NASA Task Load Index)
Processing speed (Connections Test; Purdue Pegboard Test)
Working memory (Abbreviated Wechsler Memory Scale)
Brain Imaging (MRI)
Structural and functional neuroimaging while listening to and understanding
Low-pass filtered speech
Speech in background babble
Medical/Biological Measures
Clinical chemistries from blood
Lipid profile*
Hematology panel
Hormones (Estradiol, Progesterone – Female subjects only)
C-reactive protein*
DNA extracted from blood and stored
Otologic examination
Questionnaires
Medical history*
Prescription and over-the-counter drugs*
Noise history
Hearing-aid history*
Hearing handicap (HHIE or HHIA)*
Memory screening (SPMSQ and MMSE)*
Self-report outcomes of health conditions (PROMIS)*
Tinnitus
Smoking*
Handedness (Edinburgh Handedness Inventory)
Family pedigree for hearing loss (with genetics counselor)

Table 1. Human subject protocol.

Note: An asterisk (*) following the name of the test indicates that measures are obtained longitudinally (yearly or more frequently, or every 2–3 years). Abbreviations: SRT: Speech Recognition Threshold; NU6: Northwestern University Auditory Test #6; SPIN: Speech Perception in Noise Test; SSW: Staggered Spondaic Word Test; HHIE: Hearing Handicap Inventory for the Elderly; HHIA: Hearing Handicap Inventory for Adults; SPMSQ: Short Portable Mental Status Questionnaire; MMSE: Mini-Mental State Exam; PROMIS: Patient-Reported Outcomes Measurement Information System.

	Total with any data		Total with longitudinal data		Currently Active	
Age Range	18-59	60-98	18-59	60-95	18-59	60-93
Female	85	483	10	235	14	201
Male	76	385	12	200	15	125
Total	161	868	22	435	29	326
Grand Total	1,029		457		355	

Table 2. Age and gender distributions of participants in the MUSC longitudinal study of age-related hearing loss (as of November, 2009).

Note: Age and gender information for currently active subjects and for subjects with longitudinal data (data over at least a 3-year time span) are listed separately.

study, possibly because the mean age of our subjects (74 years) is at the upper end of the comparison age range (70–74 years). The mean audiograms of the female subjects are similar to those described earlier as attributed to metabolic presbyacusis, namely a flat loss of ~20 dB in the lower frequencies coupled with a gradually sloping loss in the higher frequencies. The mean audiograms of the male subjects are similar to those of the female subjects in the lower frequencies, but show more steeply sloping loss in the higher frequencies. Male subjects in the MUSC study report a higher percentage of significant noise exposure than female subjects. For occupational noise, 14–18% of females vs. 60–68% of males report significant exposures, depending on age range. Similarly, for noise from firearms, 6–9% of females vs. 58–66% of males report significant exposures. This suggests that hearing loss profiles for males may be a consequence of the combined effects of metabolic and sensory presbyacusis.

Age-related Changes in Hearing in Older Adults Measured Cross-sectionally

Figure 4 of Schmiedt (2010) displays mean audiograms of ears of female and male subjects at the time of their enrollment in the longitudinal study, organized cross-sectionally by age. The audiograms of female subjects show the progression of a generally constant hearing loss at lower frequencies to a gradually sloping loss at higher frequencies; thresholds increase steadily with age, but more so in higher than lower frequencies. In these female subjects with limited noise exposure, audiometric configurations are consistent with an age-dependent progressive degeneration of the lateral wall, systematic decline in the EP, and the frequency-dependent loss of gain of the cochlear amplifier (metabolic presbyacusis). In contrast, audiograms of male subjects of increasing age (many with a history of noise exposure) show some evidence of metabolic presbyacusis in the lower frequencies combined with a pattern consistent with sensory cell loss in the higher frequencies, with losses that increase with age at a slower rate. There is a marked decline in thresholds at all frequencies except around 4.0 kHz in males older than 85 years of age. This is consistent with threshold changes in very old quiet-aged gerbils, which show a 50% or greater loss of viable stria vascularis (Schulte & Schmiedt, 1992). These gender- and frequency-related differences have been confirmed in a study of longitudinal changes in thresholds of older subjects from our database (Lee et al., 2005; 2006), which is described in the next section.

Longitudinal Changes in Hearing in Older Adults

Pure-tone thresholds for conventional and extended high frequencies from the MUSC human subject database were analyzed for longitudinal changes and to determine the effects of initial thresholds, age, gender, and noise history on these longitudinal changes. At the time of entry into the study, subjects' ages ranged from 60 to 81 years (mean = 68.1). Subjects had between 2 and 21 visits (mean = 9.8) over a period of 3 to 11.5 years (mean = 6.4). Conventional pure-tone thresholds from 0.25 to 8.0 kHz were measured during most visits. Extended high-frequency thresholds from 9.0 to 18.0 kHz were measured every 2–3 years. This large number of repeated measurements allowed thresholds at each frequency from each subject to be fit with separate linear regressions, increasing the accuracy of the estimation for the rate of change in hearing thresholds. Better accuracy in the estimation makes it possible to detect associations among variables even when the effects were small.

Overall, the average rate of change in thresholds was 0.7 dB/year at 0.25 kHz, increasing gradually to 1.2 dB/year at 8.0 and 12.0 kHz (see Figure 2 in Lee et al., 2005). Rate of threshold change increased significantly with age at 0.25 to 3.0, 10.0, and 11.0 kHz for females and at 6.0 kHz for males. Figure 6 in Lee et al. (2005) displays mean

threshold change (in dB/year) as a function of frequency for females and males. After adjusting for age, females had a significantly slower rate of change than males at 1.0 kHz but a significantly faster rate of change than males from 6.0 to 12.0 kHz. This effect was due to higher thresholds at high frequencies for males at their entry into the study, which was also seen in our cross-sectional data. These longitudinal changes in pure-tone thresholds are consistent with the hypothesized relationship between metabolic and sensory presbyacusis and age-related declines in thresholds as seen on the audiogram.

What is the evidence that these changes underlie the characteristic gradually sloping audiogram of aging gerbils and humans? First, age-related declines in the EP and related shifts in thresholds and reduced amplitudes of the compound action potential of the auditory nerve can be temporarily reversed by current injections into scala media (Schmiedt, 1993), consistent with a presumed role of the EP in maintaining synchronized neural firing and neural viability (Suryadevara et al., 2001). Second, as reviewed earlier, age-related declines in the EP can be reproduced in younger animals by the chronic application of furosemide, which artificially reduces the EP (Schmiedt et al., 2002). Third, threshold shifts in neural thresholds due to furosemide-induced changes in the EP are similar to audiometric threshold shifts in non-noise-exposed subjects from our longitudinal study (Mills et al., 2006) and a human subject sample reported by Jerger et al. (1993). There is a quantitative match between gerbil and human data at 1.0 kHz and below (dashed horizontal line), i.e., a 20–40 mV loss of voltage throughout the cochlea with a 20–dB loss in threshold. From 1.0–3.0 kHz, the match is ±5 dB (solid line). At 4.0 kHz and above, some of the human data exceed gerbil data; however, this disparity may reflect the possibility that the cochlear amplifier gain in the base of the cochlea is greater in humans than in gerbils. The correspondence between threshold shifts produced in gerbil (by furosemide-induced changes in the EP) and audiometric configurations of aging humans (from our database and others) suggests a common mechanism, a reduction in the EP (metabolic presbyacusis), which effectively reduces the voltage available to the cochlear amplifier. Thus, age-related hearing loss as shown by the audiogram can be best explained by age-related pathology of the cochlear lateral wall, which deprives the cochlear amplifier of its essential power supply (voltage). This hypothesis predicts that age-related declines in hearing as indicated by the audiogram are largely explained by pathology of the auditory periphery.

Longitudinal Changes in Speech Recognition in Older Adults

The MUSC longitudinal study of age-related hearing loss includes longitudinal measures of SRT, word recognition in quiet (NU#6), maximum word recognition in quiet (NU#6), recognition of low- and high-context sentences in noise (SPIN), and binaural word recognition (SSW). This section will focus on longitudinal changes in word recognition in quiet. Using procedures developed for estimating rates of change in pure-tone thresholds, word-recognition scores were analyzed for longitudinal changes and to determine the effects of initial thresholds, age, gender, and noise history on these longitudinal changes.

As noted earlier, assessing longitudinal changes in speech recognition of older subjects is not straightforward because pure-tone thresholds change with increasing age and rates of change vary among subjects and for different frequencies. Adding complexity is that speech presentation levels in our protocol increased with age because scores were obtained with speech at fixed sensation levels. Accordingly, longitudinal changes in word-recognition scores were examined independently of changes in pure-tone thresholds and speech levels by adjusting scores using predictions from an importance-weighted speech-audibility metric, as estimated by the AI (ANSI, 1969; 1997). Briefly, we used the AI to predict word recognition scores for each subject at each time point and then compared measured and predicted scores at each time point. Similar to procedures used to estimate longitudinal changes in pure-tone thresholds, linear-regression slope was then used to estimate the rate of change in adjusted speech-recognition scores.

The rationale for comparing observed and predicted scores was as follows. Increasing age results in higher pure-tone thresholds, which lowers speech audibility and the computed AI, corresponding to a lower predicted score. If declines in word recognition over time are similar to predicted declines, poorer hearing (reduced audible speech) accounts for these changes, rather than increasing age or age-related factors. If declines are faster than predicted, poorer hearing does not entirely account for declines in word recognition; the remainder may be attributed to other factors, such as increasing age. Thus, the difference between observed and predicted scores at different time points measures how word recognition changed with increasing age while accounting for changes in speech audibility. Additional details of methods and results are included in Dubno et al. (2008).

Recognition of isolated monosyllabic words in quiet from NU#6 (Tillman & Carhart, 1966) was measured in both ears of 256 older persons (128 males and 128 females); a minimum of 3 scores was obtained from each ear of each subject over a range of 3–15 years. At the time of their first measure, these subjects ranged in age from 50–82 years (mean = 67.6 years). At the time of their last measure, their ages ranged from 60–91 years (mean = 75.0 years). As described earlier, the protocol of the longitudinal study called for yearly measures of pure-tone thresholds and word-recognition scores in quiet. In addition, scores for the NU#6 were obtained at 2–3-year intervals. As a result, subjects had between 3–18 NU#6 scores (mean = 7.2 scores) over a period of 3–15 years (mean = 7.3 years). A total of 3,683 scores from 512 ears were analyzed.

The average rate of change in NU#6 scores for 512 ears was –1.04%/year ($p<0.0001$). Although this suggests that word-recognition scores declined significantly over time, some of the change may be attributed to changes in speech audibility resulting from threshold or speech-level changes occurring during the same time span. The average rate of change in adjusted NU#6 scores was –0.74%/year ($p<0.0001$). Thus, word recognition declined significantly with increasing age even when accounting for age-related changes in speech audibility.

Effects of Initial Hearing Loss and Age

Rate of decline in word recognition increased by a small, but significant, amount as initial hearing loss increased, even while taking into account hearing-level-related differences in speech audibility (see Figure 4 in Dubno et al., 2008). Thus, rate of decline in word recognition was significantly faster for individuals with more severe hearing loss. This effect of degree of hearing loss suggests that with more severe injury to the peripheral and/or central auditory system, impairments to auditory and/or cognitive function other than elevated thresholds (reduced audibility) resulted in faster declines in word recognition as subjects aged. Reduction in simple audibility due to elevated thresholds was eliminated as a factor by evaluating differences between observed scores and scores predicted by importance-weighted speech audibility (AI).

The absence of an effect of initial age suggests that, among older subjects, the rate of decline in word recognition did not accelerate with increasing age. That is, the rate of decline in word recognition was not faster for subjects in their 70s or 80s than for subjects in their 60s. This finding, together with the significant effect of initial hearing loss, suggests that the changes in function that accompanied higher thresholds and resulted in faster declines in word recognition were not increasing with age. Taken together, these age-related declines in word recognition were more consistent with underlying changes in auditory, rather than cognitive, function resulting from peripheral, rather than central, auditory system pathology. Additional discussion of these issues and the possibility that a single nervous-system factor underlies observed age-related changes is included in Dubno et al. (2008).

Effects of Gender and Serum Hormone Levels

Declines in adjusted word recognition were significantly faster for females (–0.92%/year) than for males (–0.57%/year), even while taking into account gender-related differences in speech audibility due to their threshold differences. It is possible that different etiologies underlie the hearing loss observed in older females and males. As discussed earlier, threshold elevation in males may result from combined effects of noise and aging (plus other exogenous factors) whereas threshold elevation in females may have a smaller noise component. These patterns are consistent with faster rates of pure-tone threshold changes in the higher frequencies for females than males (Lee et al., 2005) and may relate to the faster declines in adjusted word recognition seen here. Thus, gender-related differences in the etiology of cochlear injury in older persons, and mechanisms underlying presybacusis, could have implications for age-related changes in auditory function, such as speech recognition.

Hormones levels in the blood may represent another gender-related factor that co-varies with age and may explain the faster decline in word recognition for females than males. Females with higher levels of progesterone in their blood had faster declines in word recognition than females with lower levels of progesterone (see Figure 5 in Dubno et al., 2008). This result is consistent with the negative effect of hormone therapy that includes progestin reported by Guimaraes et al. (2006) and a biochemical mechanism that relates progesterone to activation of inhibitory neurotransmittors, such as γ-aminobutyric acid (GABA) in the aging auditory system. Nevertheless, with the exception of exogenous ototraumatic factors (such as noise exposure) and potential effects of hormone replacement therapy and serum hormone levels, biological explanations for gender differences in presbyacusis remain unclear.

Longitudinal Changes in Observed and Predicted Word-recognition Scores

To assess changes in observed and predicted word-recognition scores over time, we grouped data according to laboratory visit and plotted mean scores against subjects' mean ages at each visit. Figure 6 (top) in Dubno et al. (2008) presents mean (±1 SE) observed word-recognition scores (filled) and mean (±1 SE) predicted scores (open) for laboratory visits 1–13 plotted against mean subject age during those visits. The larger variance for scores at older mean ages is due to smaller sample sizes.

Scores at younger ages were better than predicted and scores at older ages (beginning ~age 74) were worse than predicted. The lower panel plots the difference between observed and predicted scores. The observed-predicted difference function (solid line) has a negative slope, so that as subjects aged, their observed scores became poorer than predicted at a rate of –0.8% per year ($p<0.0001$), consistent with the average regression slope. The linear fit of these data further suggests that this decline does not accelerate with age. That is, the rate of decline in word recognition was not faster for subjects in their 70s or 80s than for subjects in their 60s. Thus, in contrast to the assumption that word recognition difficulties of older subjects are accounted for by elevated thresholds, word recognition declined significantly with age more than would be predicted by changes in speech audibility associated with declines in pure-tone thresholds.

Summary and Impact on Clinical Practice

The main conclusions of the work presented in this report are the following: (1) In the absence of noise exposure, audiometric configurations for older humans are consistent with the effects of metabolic presbyacusis as seen in the gerbil animal model of age-related hearing loss, whereby declines in the endocochlear potential reduce the voltage available to the cochlear amplifier and reduce the cochlear amplifier gain more in higher than lower frequencies. These changes result in the characteristic audiogram of older gerbils and humans, i.e., a flat 10–40 dB hearing loss in lower frequencies coupled with a gradually sloping hearing loss at higher frequencies. (2) In older adults, pure-tone thresholds increase with age by an average of 1 dB/year (10 dB/decade). (3) The rate of decline in high-frequency hearing increases for older females but decreases for older males. (4) Word recognition in quiet declines with age, even after accounting for reductions in audible speech due to poorer hearing. (5) The rate of decline in word recognition is faster for older individuals with more severe hearing loss. (6) The rate of decline in word recognition is faster for older females with higher levels of progesterone in their blood. (7) Audiogram shapes and longitudinal changes in hearing in humans and in the gerbil animal model are consistent with the view of age-related hearing loss as a metabolic, vascular, neural disorder rather than a sensory disorder.

The clinical implications of these findings are significant. Rates of declines in hearing and word recognition as patients grow older will vary from patient to patient, which impacts decisions related to amplification and other forms of rehabilitation. Because of their generally better hearing due to limited noise exposure at early ages, women will likely have more rapid declines in high-frequency hearing as they age than men. In future decades, as more women spend significant time in the workplace and individuals continue to work through their 60s and 70s, the gender distinction between metabolic (female) and metabolic/sensory (male) presbyacusis may not be as clear.

More rapid changes in high-frequency hearing status as female patients get older may require yearly (rather than biennial) checks of hearing and confirmations of the appropriateness of hearing-aid selections and prescriptive fittings. Frequent checks of hearing-aid status and changing needs for auditory rehabilitation may be especially important for some patients, given that more rapid declines may be seen in individuals with more severe hearing loss.

Finally, a clearer understanding of the underlying mechanisms of age-related hearing loss may lead to better audiologic care for older patients. For example, patients who may be classified with the metabolic phenotype (mild to severe) are those with negative noise histories, flat hearing loss in the lower frequencies ranging from 10–40 dB HL, and gradually sloping hearing loss in the higher frequencies with slopes ranging from 10 to 20 dB/oct. These individuals may be primarily older female patients, but may also include male patients who have not experienced significant noise exposure. Patients who may be classified with the sensory phenotype are those with positive noise histories, thresholds in the lower frequencies $\leq$10 dB HL and steeply sloping hearing loss in the higher frequencies with slopes >20 dB/oct. Patients classified with the metabolic/sensory

phenotype are those with positive noise histories, characteristics of metabolic presbyacusis in the lower frequencies (flat loss ranging from 10–40 dB HL) and characteristics of sensory loss in the higher frequencies (steeply sloping loss with slopes >20 dB/oct). Moreover, because cochlear nonlinearities may be preserved (but reduced) in metabolic presbyacusis but absent in sensory presbyacusis, patients whose audiograms are consistent with the metabolic phenotype may perform better on certain measures of auditory function relative to patients whose audiograms are consistent with the sensory phenotype. For example, for a given amount of hearing loss, otoacoustic emissions (an index of cochlear nonlinearities) may be more robust for patients with metabolic than sensory presbyacusis. Word recognition (after adjusting for effects of reduced audibility) may be better for patients in the metabolic category than for those with evidence of sensory loss (sensory, metabolic/sensory), which may predict larger hearing-aid benefit and success or more tolerance of background noise. Although these assumptions must be confirmed through additional research, an understanding of the underlying mechanisms that produce specific audiogram shapes and changes in auditory function with age may ultimately provide more detailed diagnostic information that will lead to "personalized" audiologic care with more attention to factors specific to an individual patient.

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