Title

The Effects of Age-Related Hearing Loss on the Brain and Cognitive Function

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Abstract

Age-related hearing loss is a common problem for older adults, leading to communication difficulties, isolation, and cognitive decline. Recently, hearing loss has been identified as potentially the most modifiable risk factor for dementia. Listening in challenging situations, or when the auditory system is damaged, strains cortical resources, which may change how the brain responds to cognitively demanding situations more generally. Here, we review the effects of age-related hearing loss on brain areas involved in speech perception, from the auditory cortex, through attentional networks, to the motor system. We explore current perspectives on the possible causal relation between hearing loss, neural reorganisation, and cognitive impairment. Through this synthesis we aim to inspire innovative research and novel interventions for ameliorating hearing loss and cognitive decline.

The Ageing Ear: Tired of Listening?

Age-related hearing loss (ARHL), or presbycusis, is characterised by gradually developing high-frequency hearing loss, often accompanied by poor speech discrimination, and may begin to surface in the fourth decade of life [1]. The prevalence of ARHL increases with age, affecting more than 40% of people over 50 years old, rising to about 71% of people over 70 years [2]. For most, it is a relatively unremarkable part of the ageing process (see Box 1), but some individuals with ARHL experience effort and difficulties in speech understanding, hindering communication and socialisation [3]. Increased listening effort may lead older adults to avoid social interaction, exacerbating loneliness, depression, and reducing well-being [4]. Recent research further shows that hearing loss is associated with cognitive decline and dementia [5,6]. However, although there is reasonable evidence for hearing loss as a marker for risk of cognitive decline, it is not yet clear whether there is a causal effect of hearing loss on cognitive decline. Collating the most recent evidence on how ARHL affects the brain provides valuable information on possible underlying mechanisms and causal relations between hearing loss, neural changes, and dementia.

[Insert Text Box 1]

This review discusses the physiology of ARHL, from the peripheral auditory system to the auditory cortex, and to global neural changes that accompany ARHL. The review focuses on the impact of these cortical changes on cognitive functioning during ageing, while exploring the evidence for a possible causal relation between ARHL-related changes in neural functioning and cognitive decline.

The Peripheral and Subcortical Auditory System in Age-related Hearing Loss

ARHL is attributed to either sensory, metabolic, or neural changes in the peripheral auditory system, which affects hearing ability. Sensory ARHL is characterised by degeneration of outer and inner hair cells within the cochlea, of which the inner cells are responsible for the transduction of auditory signals. Atrophy originates in the basal end of the cochlea, and over time progresses to the apex. Basal atrophy manifests in the high-frequency hearing loss typical of sensory ARHL [7]. It has been suggested that degeneration of basal sensory receptor cells is often

a consequence of accumulated environmental noise exposure, rather than ageing [8]. Sensory ARHL is quantifiable using pure-tone audiometry. The audiogram showing sensory ARHL will display normal hearing thresholds in the lower frequencies, and a steep increase in thresholds at higher frequencies [9]. However, older adults with similar pure-tone thresholds can differ in their ability to understand degraded speech, even after the effects of age are controlled for [10]. The effect of ARHL on the wider auditory periphery, auditory cortices, and non-auditory neural systems has a greater effect on communication due to increased difficulty with speech perception.

Metabolic (or strial) ARHL is characterised by atrophy of the stria vascularis, on the outer wall of the cochlear duct, which is responsible for metabolic processes in the cochlea. Degeneration of this structure decreases the endocochlear potential (EP), impairing the EP-dependent cochlear amplifier. The entire cochlea is affected, but the amplifier is particularly necessary for the perception of high-frequency sounds [11]. The audiogram for metabolic ARHL will display a constant hearing loss at lower frequencies, with a gradual increase in threshold at higher frequencies due to the EP loss [9,12]. The flat loss at lower frequencies and gradual sloping loss at higher frequencies in metabolic ARHL, compared to the normal lower frequency thresholds and drastic sloping loss at higher frequencies in sensory ARHL, is key in differentiating these two sub-types of hearing loss [9].

Neural ARHL is characterised by atrophy of the spiral ganglion cells, the first afferent neurons in the neural pathway from the ear to the brain. The audiogram is not affected until a critical number of cells have degenerated (80-90%) [13]. This type of hearing loss may precede sensory hair loss and is accompanied by a dramatic decrease in speech discrimination ability [14]. This neural degeneration may provide insight into why older adults with similar hearing acuity (measured by pure-tone audiometry) differ in their speech-in-noise perception [15].

[Insert Figure 1]

Auditory perception involves not only peripheral ‘hearing’ and transduction of sounds, but also decoding and comprehension of the auditory message, which occurs in higher brainstem and cortical regions. Studies suggest that ageing may impact supra-threshold auditory processes (which cannot be identified by a clinical

audiogram), including temporal coding, which involves the synchronisation of neural firing to the temporal fine structure or temporal envelope of sound [16]. Animal models suggest that this temporal coding may be affected by age-related cochlear synaptopathy, the loss of connections between the sensory hair cells and the auditory nerve [17]. Brainstem temporal processing may also decline due to age-related demyelination [18], and a reduction in neural inhibition [19]. Brainstem neural function can be measured using the auditory brainstem response (ABR), a measure of synchronous activation of successive nuclei within the auditory pathway in response to a brief click or tone. Amplitudes of ABR waves are reduced in older listeners [20]. The frequency-following response (FFR) is a sustained brainstem potential reflecting neural synchronisation to the frequency components in a sound wave. The FFR can be used to measure the temporal precision of subcortical neural coding of musical pitch and speech [21]. Research has demonstrated stronger FFR responses in younger compared to older listeners in response to speech stimuli [22,23]; particularly speech in noise [24]. It is possible that age-related supra-threshold temporal processing deficits in the brainstem and midbrain account in part for the speech-in-noise perception difficulties facing older listeners, which are not well predicted by pure-tone audiometry [25].

When the auditory periphery is damaged, the cochlea is less effective in converting sound into neural activity. A reduction in the precision of subcortical neural coding can also impact on the representation of sounds. The resultant auditory signal is therefore diminished, which may significantly affect how the brain processes this information. One might hypothesise that this altered neural processing may in turn affect non-auditory cognitive processes due to atrophy, or cortical reorganisation, changing the way in which resources in the brain are allocated during perception and comprehension of speech.

The Auditory Cortex in Age-related Hearing Loss

The auditory cortex encompasses several brain regions in the temporal lobes which are organised in a functional hierarchy for the processing of sound. The primary auditory cortex, at the bottom of this functional hierarchy located on Heschl's gyrus, receives direct information from the cochlea via the ascending auditory

pathway. The wider auditory cortex, extending from Heschl's gyrus to the superior temporal gyrus, receives projections from the primary auditory cortex and is involved (among other functions) in sound localisation, as well as integration with other sensory networks.

Anatomical Changes

Evidence indicates that older adults with hearing loss show a constellation of changes in primary auditory cortex. For example, dysfunctional neurotransmission due to decreased gamma-aminobutyric acid (GABA) (see Glossary) concentration has been observed in older adults with hearing loss compared to normal hearing [26]. However, there is evidence for a general age-related decline in GABA concentration in the auditory cortex, independent of hearing loss [27]. As well as potential defective neurotransmission, there is evidence for diminished grey matter volume in the primary auditory cortex associated with poorer hearing [28]. However, global decreases in grey matter volume, as well as cortical thinning and increased cerebrospinal fluid are neural characteristics of general ageing [29,30]. An important question is whether deprivation of auditory input due to ARHL exacerbates the brain atrophy typical of ageing, and whether this has consequences for cortical organisation. Studies provide evidence for a link between changes in brain morphology and ARHL (assessed using audiometric thresholds), including cortical thinning [31], and reduced grey matter volume in the auditory cortices [32,33]. There are two proposed explanations for the changes in brain morphology in older adults who display age-related hearing threshold elevations. The first is that there is a direct causal relation between auditory impairment and declines in brain volume due to auditory deprivation (sometimes referred to as the auditory deprivation hypothesis) [33]. The second is that ageing leads to a concurrent decline in the auditory periphery and the central nervous system [34,35].

One longitudinal study provides evidence supporting the idea of a causal relation between ARHL (quantified as pure-tone average (PTA) >25 dB HL in older adult participants) and neural atrophy in support of the auditory deprivation hypothesis. Differences in brain volume between older adults with normal vs. clinically significant pure-tone hearing loss were not present in a baseline MRI scan. However, 6.4 years later, those with pure-tone hearing loss showed an accelerated decline in brain volume, especially in the right temporal lobe [36]. Others have contested the auditory

deprivation hypothesis. Indeed, a more recent longitudinal study found no evidence that clinically significant pure-tone hearing loss affected brain morphology [34]. These inconsistent findings could be explained by the different longitudinal time windows employed; 6.4 years in the former study compared to a shorter window stretching from approximately 1.3 to 5 years in the latter. It is possible that a causal relation between clinically significant pure-tone hearing loss and reduced grey matter in the auditory cortex does exist, but only presents after a longer time period (>5 years).

Functional Changes

In addition to structural changes in the cortex, older adults with clinically significant pure-tone hearing loss also display functional differences in auditory processing compared to younger adults with normal pure-tone thresholds. For example, functional Magnetic Resonance Imaging (fMRI) studies to determine age-related changes in the auditory cortex showed that the older adults with pure-tone threshold elevations exhibited increased activation in response to pink noise (i.e., 1/f noise) in the temporal lobes, particularly in the right hemisphere, compared to younger adults with normal audiometric thresholds who showed reduced activation and left lateralisation [37]. The authors suggested that this activation may be due to reduced inhibition associated with ageing, or potentially a compensatory mechanism for elevated audiometric thresholds [37]. However, there were no significant differences in activation between older adults with mild (audiometric thresholds > 20 dB HL at frequencies ≥ 4000 Hz) vs. moderate (audiometric thresholds > 20 dB HL at frequencies ≥ 1000 Hz) pure-tone hearing loss. The lack of effect of hearing loss severity on neural activity may be seen as casting doubt on the existence of a causal relation between pure-tone hearing loss and neural changes. Other researchers using more complex auditory stimuli, consisting of monosyllabic words, also found similar effects of age on auditory cortex activity, but age-related pure-tone hearing loss (PTA 26 – 40 dB HL) did not significantly affect activation [38]. These data can be interpreted to support the theory that general ageing, or indeed other sub-types of hearing loss not identified by the audiogram, rather than clinically significant pure-tone hearing loss, leads to functional changes in the auditory cortex.

The perception, and more so, comprehension, of auditory information is reliant on integration among brain networks to interpret auditory stimuli. Studies have found

important differences in functional connectivity among brain areas involved with auditory processing in older adults with ARHL, which may hinder speech perception [39]. Specifically, findings show reduced connectivity between visual and auditory sensory cortices in ARHL [40], as well as in the attention and default mode networks [41]. These data suggest that in individuals with hearing loss, there are changes in the organisation of cortical networks supporting speech perception.

Non-Auditory Cortical Reorganisation

In the following section of this review, cortical reorganisation observed in ARHL will be explored further. The section will focus on three brain networks known to support auditory perception; the attentional, visual, and motor networks. Evidence indicates that ARHL not only affects auditory brain areas, but also non-auditory regions. This is because non-auditory regions are potentially up-regulated to support speech perception after hearing loss. It is possible that this suggested reorganisation of resources causes complications for cognitive and neural functioning.

Attentional Networks

The cingulo-opercular network is suggested to be of importance for speech processing in both normal-hearing and hearing-impaired individuals [42–44]. The cingulo-opercular network involves a number of brain areas including the anterior insula, the anterior cingulate cortices, and thalamus, thought to be involved in attention, which is advantageous for speech perception [44,45]. Morphological data indicate that individuals with ARHL display reduced volume in the anterior cingulate cortex (ACC) [46]. Research has investigated the relation between ACC atrophy and cochlear amplifier function; the main component of which is the outer hair cell, and is responsible for sensitive frequency resolution. Dysfunction is measured by assessing the outer hair cell function of the cochlea receptor [46]. The researchers found that greater atrophy of the ACC was observed in individuals with ARHL (PTA >20 dB HL) who also displayed cochlear amplifier dysfunction (assessed using distortion-product otoacoustic emissions, a type of sound generated by the outer hair cells), and this atrophy was related to greater memory impairments [46].

Evidence also suggests increased functional connectivity between auditory cortex and cingulo-opercular network in resting state fMRI in ARHL, after controlling for

variance in both age and cognitive functioning [47]. This provides some insight into potential compensatory neural activation associated with ARHL. It has been suggested that impaired auditory processing in ARHL leads to more effortful listening, which depletes the limited resource capacity available for both listening and non-auditory cognitive functions [48]. Researchers have proposed that activation of neural networks involved in effortful listening could contribute to the observed neural degeneration of these areas in ARHL, including for instance due to glutamate excitotoxicity of cingulate neurons [46].

Visual Networks

Older adults with hearing loss (average PTA 38.4 dB HL) display a reduced ability to supress activity in other sensory brain areas during auditory processing than those without hearing loss [49]. For example, increased visual cortex activation occurs during auditory word recognition tasks when intelligibility is decreased (due to increased background noise) [49]. Furthermore, there is evidence from resting state fMRI for increased connectivity between auditory and visual cortices in ARHL (defined in terms of high frequency loss using PTA) [45]. It is likely that increased visual activation works to support the auditory system during interpretation of degraded auditory information. Individuals with ARHL also show increased activation in auditory areas during the presentation of visual stimuli [50], further highlighting the level of cortical reorganisation among visual and auditory areas associated with ARHL.

Motor Networks

There is accumulating evidence that the articulatory motor cortex is involved in speech perception in young adults, particularly when speech perception is challenging [51]. It is possible that when listening becomes more demanding, the individual relies on integration across numerous brain areas to understand the auditory message; for example, by recruiting the motor cortices to provide motor representations of speech. However, it is unclear how motor networks are utilised for speech perception in older adults with hearing loss. Two hypotheses have been suggested to account for auditory-motor integration during speech perception in ARHL. First, the motor compensation hypothesis suggests that activation of the motor networks compensates for impaired auditory processing in ARHL [52]. This

hypothesis assumes that the articulatory motor cortex is upregulated during speech perception in persons with auditory deficits, and that this process compensates for impaired auditory function to aid speech perception. Second, the motor-decline hypothesis suggests that the impaired auditory periphery provides a reduced input to the auditory cortex, and consequent deficits in auditory processing reduce the input to the articulatory motor cortex [53].

Researchers have used brain stimulation, specifically transcranial magnetic stimulation (TMS) in combination with electromyography to measure Motor Evoked Potentials (MEPs) recorded from the tongue, to investigate age- and hearing-related differences in excitability of the motor cortex [53]. The authors found that excitability of the articulatory motor cortex, involved with tongue control, was significantly reduced in older adults with ARHL compared to older and younger adults with normal hearing, in support of the motor decline hypothesis [53]. These results suggest that deficits in the auditory system may reduce the input available to the motor cortex. This provides evidence for a decline in auditory-motor processing, not only associated with age-related changes in neural functioning, but specifically associated with hearing loss. In contrast to these findings supporting the motor decline hypothesis, fMRI studies provided support for the alternative motor compensation hypothesis. Specifically, fMRI data indicate that older adults have increased activation of frontal speech motor areas in a listening task at signal-to-noise ratios ranging from -12 dB to 8 dB, compared to younger adults. The increased activity also correlated with improved performance on the listening task in older adults [52].

A possible explanation for the discrepancies between these studies could stem from their methodological differences. In part, in the fMRI study there was no comparison between older adults with and without hearing loss [52]. Although listening demand was manipulated artificially using signal-to-noise ratio, it is not possible to draw definitive conclusions about the effects of ARHL on motor activation. Furthermore, the different methods, TMS in combination with electromyography and MEPs, as opposed to fMRI (BOLD signal), reflect different types of neural activation. MEPs are signals recorded from peripheral muscles that quantify the cortical excitability of the motor cortex at the time of brain stimulation, whereas the BOLD signal provides a more indirect measure of neural activation,

influenced by changes in cerebral blood flow, volume, and oxygen extraction. Because of these differences, MEPs may be more reflective of momentary neural activity, whereas fMRI data reflect activation over a longer time period. The fMRI data also showed increased recruitment of frontal regions, as well as motor areas, during listening [52]. This may suggest generalised recruitment of compensatory cognitive resources as opposed to specific motor compensation. Indeed, cognitive compensation is a widely recognised model in the context of cognitive ageing. Evidence indicates cognitive compensation and neural upregulation across numerous sensory and motor domains [54], including sensory-motor ageing in Alzheimer's Disease [55].

Taken together, these findings indicate that the sensory deprivation associated with ARHL influences brain structure, function, and typical neural resource allocation. These changes may influence the cognitive and neural resources available to individuals with ARHL. It seems reasonable to hypothesise that changes in resource allocation may in turn affect daily cognitive processes and functioning beyond auditory processing.

The Relation Between Auditory and Cognitive Impairment

In recent years, the association between ARHL and cognitive decline has gained international recognition among leading medical organisations, who have identified ARHL as the largest potentially preventable risk factor for dementia [6,56]. Cumulative data from large cohort studies show that ARHL is associated with an increased rate of cognitive decline and an increased risk of developing dementia, with the likelihood increasing with the severity of hearing loss [57–60]. These developments underscore the need for research efforts directed towards understanding the causal relation between the damaged auditory system, neural changes observed in ARHL, and cognitive decline. In doing so, researchers can identify possible mechanisms underlying the association between hearing loss and increased cognitive decline, which may inform avenues for early intervention. Three dominant hypotheses exist in the ARHL and cognitive decline literature: 1) The common cause hypothesis; 2) The information degradation hypothesis; and 3) The

sensory deprivation hypothesis [5,61,62], which the following sections will explore in turn.

The Common Cause Hypothesis

The common cause hypothesis suggests that the comorbid manifestation of cognitive decline and ARHL is attributable to a common neurodegenerative pathology. This hypothesis is supported by evidence of parallel changes in several perceptual and cognitive domains in older adults; for example, reduced cognitive decline and reduced visual acuity [63]. Additionally, the brain atrophy observed in both ageing and ARHL [27,34] may suggest that the concurrent manifestation is due to biological ageing, which affects global functioning. However, there is also evidence that supports a causal relation, with ARHL exacerbating cognitive decline in ageing: both the information degradation and sensory deprivation hypotheses support this view.

The Information Degradation Hypothesis

The information degradation hypothesis postulates that degraded auditory input, due to the impaired auditory periphery, places an increased demand on limited processing resources. Numerous models of working memory and cognitive resources share the common idea that these information processing resources are limited in the amount of information that can be attended to, held in memory, and used at any particular time [64]. Situations wherein speech quality is degraded by environmental noise, or hearing loss, lead to increased ‘listening effort’ required for processing and comprehending the auditory signal. Therefore, limited cognitive resources are diverted from other cognitive tasks towards effortful listening [65,66], resulting in depleted cognitive resources. This resource reallocation has detrimental effects on cognitive functions, which could theoretically lead to cognitive decline [67]. Evidence suggests that older adults experience more effort during listening than younger adults, measured using a dual-task paradigm with poorer performance on the secondary task indicating increased effort allocated to difficult listening [68]. The findings suggest that when listening is more difficult, it requires additional cognitive resources to cope with the demand, which means resources for other cognitive processes are depleted. Further evidence in support of this hypothesis comes from studies on the effects of hearing aids which help to restore auditory perception and

thus reduce cognitive load. For example, a 6-month hearing aid intervention was found to significantly improve both perceived hearing disability and memory performance [59]. This hypothesis has also been explored as a 'cognitive load' hypothesis by other researchers [5,69].

The Sensory Deprivation Hypothesis

The sensory deprivation hypothesis shares some conceptual points with the information degradation hypothesis, but it distinctively emphasises that the chronic reallocation of cognitive resources towards auditory perception over time due to long-term sensory deprivation in ARHL leads to cognitive decline [61,67]. This hypothesis highlights that this extended deprivation leads to compensatory cortical reorganisation and neural alterations which hinder general cognitive and emotional processes in favour of auditory perception. Evidence supports the idea of cortical alterations in ARHL, including increased reliance on frontal brain regions during speech perception [52,70], as well as reduced grey matter in the auditory cortex with decreased hearing ability [34].

Researchers have expanded on the sensory deprivation hypothesis, suggesting that although deprivation affects cognition directly through inadequate sensory input; it may also affect cognition indirectly through decreased socialisation, communication, or increased depression [71,72]. The hypothesis proposes that reduced social interaction associated with social isolation and depression may mediate the causal relation between hearing loss and cognitive decline [72,73]. There is a significant association between depressive symptoms in those with ARHL, as well as increased social isolation, and reduced quality of life [4,72,74]. In line with this perspective, the neural changes that results from ARHL, such as decreased ACC activation may directly affect emotion and mood regulation [75]. Evidence also indicates that ACC volume is correlated with depressive symptoms in individuals with ARHL [46]. Researchers also suggest that ageism and stigma associated with ARHL and ageing may exacerbate depressive symptoms and reduce social interactions due to embarrassment or decreased self-perceptions of ability [76].

Concluding Remarks and Future Perspectives

In this review, we examined the evidence for the effects of ARHL on auditory and non-auditory brain areas, and the impact of these cortical changes on cognitive

functioning during ageing. We explored changes in the peripheral and subcortical auditory system, the auditory cortex, as well as in attentional networks and the motor system. We also discussed current perspectives on the potential causal relationships between hearing loss, neural reorganisation, and cognitive impairment.

Due to the potential life-changing impact of understanding the relation between ARHL and dementia, it is essential to invest in research using methods that can determine causality. This should focus on the causal relation between peripheral auditory demand, cortical reorganisation, and cognitive decline (see Outstanding Questions). There are limitations with the quantification of both hearing loss and cognitive ability in the current literature, which lead to ambiguity in interpretation of the relation between hearing loss and cognitive decline. ARHL is frequently quantified using pure-tone audiometry, which does not capture the difficulties older adults experience with speech in noise, or neural ARHL. This may lead to an underestimation of the link between hearing loss and cognitive decline, if the full effect of hearing loss on communication, and ability to function in daily life, is not captured [77]. Incorporating tests of speech understanding in noise into standard audiometric assessments may prove valuable in capturing speech understanding, as well as hearing acuity. Capturing the extent of communication difficulties in ARHL may help us to understand the potential contribution of such difficulties to cognitive function in ageing. There is evidence to suggest that extending the frequency range of clinical audiometry to assess hearing acuity above 8000 Hz may be beneficial in predicting ARHL in early life [78]. Furthermore, this extended high frequency hearing acuity may be related to the ability to understand speech-in-noise in older adults [78,79].

It is important to also note that undiagnosed or untreated hearing loss may result in the misdiagnosis or overestimation of the level of cognitive impairment [5]. The source of this misdiagnosis could be the reliance on verbal administration of cognitive assessments, which depends upon auditory processing. Therefore, it is possible that individuals with hearing loss misunderstand, or cannot fully hear the task instructions, causing them to perform poorly and result in a misdiagnosis of cognitive decline. Indeed research shows that when the audibility of test items is reduced, or when noise exists in the testing environment, the scores on cognitive assessments are poorer [80–82]. Since listening with auditory impairment is effortful,

older adults with hearing loss may perform worse on these auditory-based cognitive assessments because more cognitive resources are directed towards listening, leaving fewer resources available for the cognitive processing required to perform adequately. The hearing-dependant subtests within tests of cognitive function may significantly affect their sensitivity and specificity as a screening tool [83]. Research shows that omitting the hearing-dependant subtests in one example of these cognitive tests (the Montreal Cognitive Assessment) reduces the sensitivity in diagnosing mild cognitive impairment; this points at the potential consequences of testing individuals with untreated hearing loss, or testing in a noisy environment, on the accuracy of the these cognitive screening measures [83]. Of note, however, the relation between hearing loss and cognitive decline has been demonstrated even when non-auditory tasks are used to quantify cognitive abilities [84,85].

[Insert Text Box 2]

As the population ages more rapidly than ever, the effect of hearing loss and cognitive decline on well-being and health resources have never been a more critical matter. Research into the neural effect of hearing loss, and the causal links between cortical reorganisation and cognitive decline may prove invaluable in informing future intervention strategies for both ARHL and associated health issues. By identifying potential mediators or mechanisms underlying the association between hearing loss and cognitive decline, researchers can identify promising avenues for early intervention to mitigate the escalated cognitive decline observed alongside ARHL.

Glossary

Anterior Cingulate Cortex (ACC): The anterior part of the cingulate cortex, within the cerebral cortex. It is thought to be involved in a multitude of complex cognitive processes.

Functional Magnetic Resonance Imaging (FMRI): A technique based on measuring the blood oxygenation level dependent (BOLD) signal, which aims to indirectly infer changes in blood flow associated with changes in neural activity.

Gamma Aminobutyric Acid (GABA): The primary inhibitory neurotransmitter in the brain involved in regulation of the inhibitory-excitatory balance of neurons.

Motor Evoked Potential (MEP): An electrical potential measured from peripheral muscles elicited by non-invasive magnetic stimulation of the motor cortex. The MEP

is measured using electrodes places on the skin, which record the electrical activity in the muscle (a technique called electromyography (EMG)).

Pure-Tone Average (PTA): The outcome measure of hearing acuity, defined as the average of hearing thresholds at specified frequencies. PTA is obtained using pure-tone audiometry testing. During the test, pure tones of sound are presented to each ear, typically at frequencies from 500 to 4000 Hz. The level of each tone is varied until the level is found which is just perceptible. At each frequency, 0 dB HL is defined as the average for young people with normal hearing. Individuals with averages above 20 dB HL would qualify as having mild hearing loss.

Transcranial Magnetic Stimulation (TMS): A non-invasive brain stimulation technique that uses a rapidly changing magnetic field to induce an electrical current (via electromagnetic induction) in a specific brain region.

Box 1.

Defining Age-Related Hearing Loss in Terms of Hearing Thresholds

Hearing thresholds are usually measured using pure-tone audiometry, which estimates the lowest detectable levels of pure tones at a range of frequencies. The pure-tone average (PTA) is the average of hearing threshold levels at frequencies of 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz in the individual's better ear. The World Health Organisation (WHO) defines the onset of mild hearing impairment as a PTA of >20 dB HL [86]. Further hearing impairment categories are defined at subsequent 15 dB steps; a hearing threshold of >35 dB HL would quantify moderate hearing loss, >50 dB HL for moderately-severe loss, >65 dB HL for severe loss, and >80 dB HL for profound hearing loss [87]. A person with normal hearing can hear tones in the frequency range 500 Hz – 4000 Hz presented at 20 dB HL or softer. ARHL presents following cumulative effects of ageing on the sensory system [88] (see Figure I).

[Insert Figure I]

Pure tone audiometry remains the primary, gold-standard method for quantifying ARHL in practice and research. It is used to understand changes in cochlear function and structure. However, to understand hearing ability more generally, it is also necessary to evaluate ability to function and participate in daily life activities [77]. Pure-tone thresholds do not account well for speech comprehension, which is a major complaint in ARHL [76]. There are numerous potential causes of damage to the peripheral and central auditory system, which can be categorised into various sub-types of ARHL. The damages can manifest not only in high-frequency threshold elevations, but also in the perception of supra-threshold sounds [76].

Box 2.

The Conceptualisation of Age-Related Hearing Loss: Considerations.

Hearing loss is often considered to be an unavoidable part of the ageing process, or even a natural part of healthy ageing. However, ARHL doesn't affect us all; approximately 29% of people aged 70+ don't experience this sensory affliction [2]. Therefore, it may be pertinent to distinguish between age *per se* as a cause of hearing loss, and all cumulative causes of hearing loss that occur over the lifespan to affect hearing acuity in older age. Potentially, a lifestyle in which damaging noise exposure is avoided, could decrease the risk of developing hearing loss. Studies find that socio-economic position (consisting of education background, occupation, and income) is strongly associated with hearing loss, with those who have lower levels of income and education posed at a higher risk of hearing loss [89,90]. These socio-economic factors, as well as lifestyle variables (including increased body mass index, reduced physical activity, and increased smoking and alcohol intake), were just as strongly associated with risk of hearing loss as was age [89]. These data are essential in identifying the potentially modifiable risk factors for hearing loss. It also suggests that a large proportion of hearing loss in older age may be preventable through lifestyle factors and management of socio-economic and health inequality. To understand these complex age-related health issues fully, large longitudinal epidemiological studies are needed. Researchers have suggested the use of 'lifestyle-related hearing loss' as a more inclusive conceptualisation of the potentially preventable sensory deficit [89].

Figures and Figure Legends

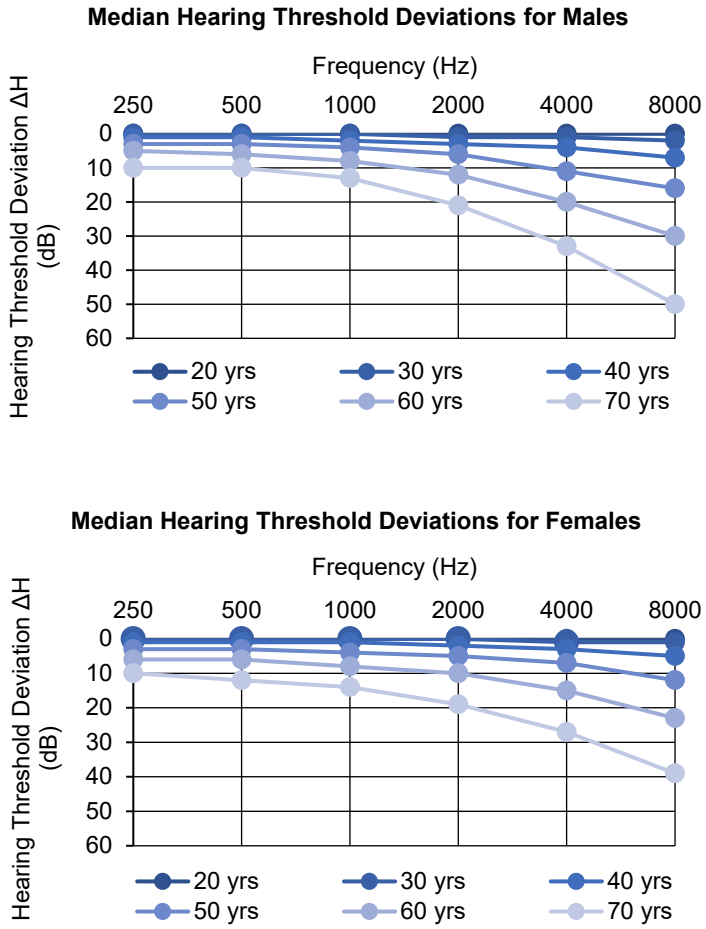
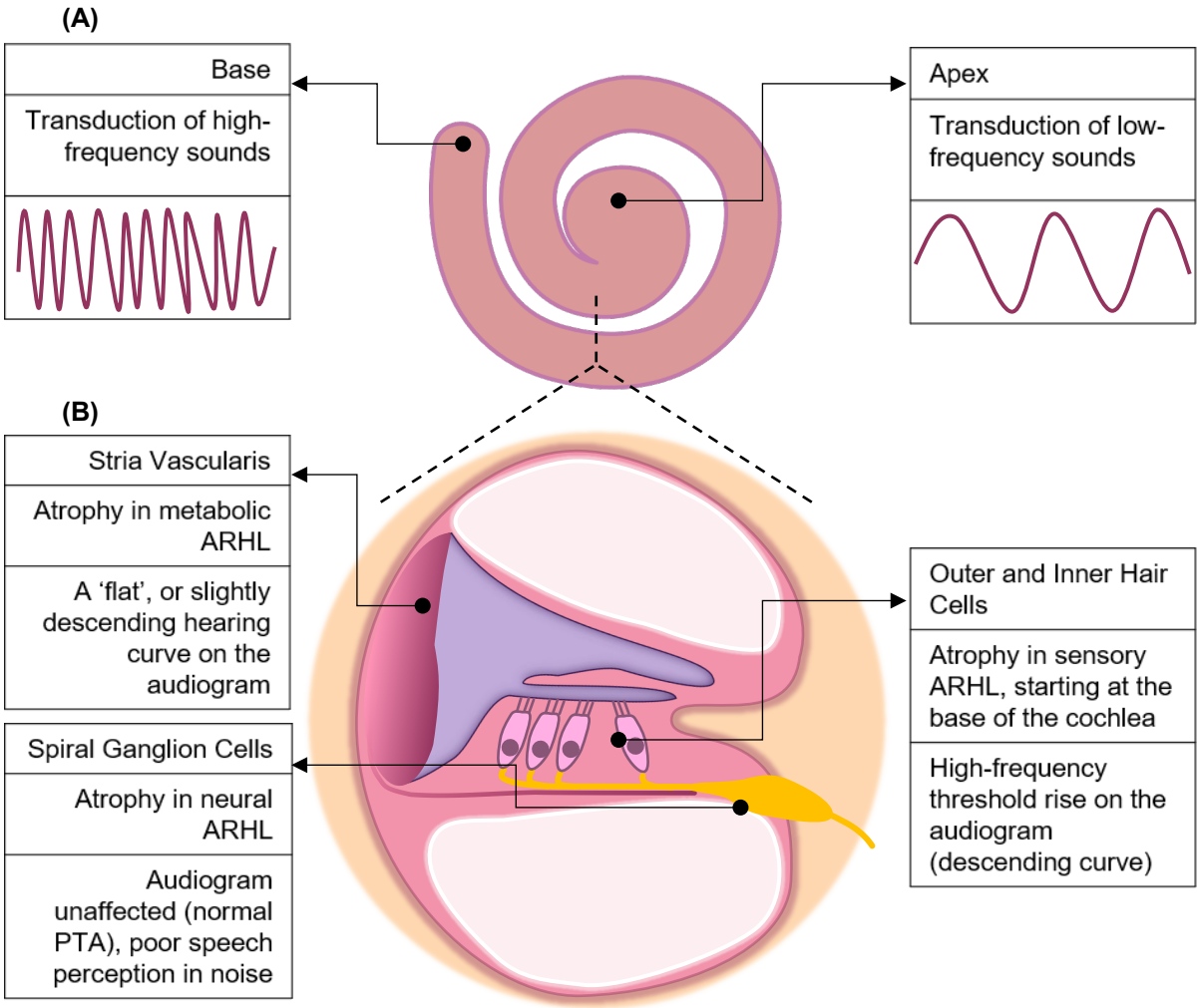


Figure I (Box 1).

A graphic of high-frequency threshold elevation as a function of age and gender on a pure-tone audiogram. The cumulative effects of ageing and lifestyle affect the perception of higher frequency sounds, meaning that the dB level of the sound needs to be higher for it to be successfully perceived. Data sourced from the International Standards Office document on Acoustics – Statistical Distribution of Hearing Thresholds Related to Age and Gender [91].



509 Figure 1.

510 There are three main types of ARHL, which manifest in different physical
511 characteristics in the peripheral auditory system. (A) A diagram of the cochlea,
512 indicating the tonotopic organisation of the transduction of sound. (B) A diagram of
513 the cross-section of the cochlea. Labels indicate the various atrophies within the
514 cochlea and the type of ARHL that manifests as a result, and how this can, or not, be
515 identified by standard audiometric testing.

516

Highlights

- Hearing loss has been identified as potentially the biggest modifiable risk factor for dementia and cognitive decline, but the causal link between these conditions affecting older adults is not clear.
- Age-related hearing loss presents as a constellation of dysfunctions that affect both the auditory periphery, the auditory cortex, and global cortical organisation.
- There is evidence for compensatory neural resource allocation, suggestive of cognitive compensation which may have a significant impact on cognitive functioning.
- Several hypotheses have been proposed to explain the potential relation between auditory and cognitive impairment: Some hypotheses suggest that the relation is underpinned by general neurodegeneration in ageing; others suggest that auditory impairment and sensory deprivation are causally linked to cognitive impairment.
- Limitations in the methods used for quantifying both age-related hearing loss and cognitive decline may lead to either over- or under-estimation of the association between age-related hearing loss and cognitive decline.

Outstanding Questions Box

- Age-related hearing loss has been associated with increased risk for cognitive decline. Is there a causal link between the two? And if so, what are the critical causal factors and mediators connecting age-related hearing loss and cognitive decline?
- Which, if any, additional cortical resources (e.g. motor cortices, or attentional networks) are recruited to compensate for impaired auditory processing in age-related hearing loss?
- Does potentially compensatory cortical reorganisation have a detrimental effect on cognitive functioning, due to reallocation of cognitive resources towards speech perception?
- Can interventions that focus on supporting potential compensatory cortical resources improve speech perception in noise, or cognitive function, in age-related hearing loss?

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