

Age-Related Hearing Loss and the Development of Cognitive Impairment and Late-Life Depression: A Scoping Overview

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ABSTRACT

Age-related hearing loss (ARHL) has been connected to both cognitive decline and late-life depression. Several mechanisms have been offered to explain both individual links. Causal and common mechanisms have been theorized for the relationship between ARHL and impaired cognition, including dementia. The causal mechanisms include increased cognitive load, social isolation, and structural brain changes. Common mechanisms include neurovascular disease as well as other known or as-yet undiscovered neuropathologic processes. Behavioral mechanisms have been used to explain the potentially causal association of ARHL with depression. Behavioral mechanisms include social isolation, loneliness, as well as decreased mobility and impairments of activities of daily living, all of which can increase the risk of depression. The mechanisms underlying the associations between hearing loss and impaired cognition, as well as hearing loss and depression, are likely not mutually exclusive. ARHL may contribute to both impaired cognition and depression through overlapping mechanisms. Furthermore, ARHL may contribute to impaired cognition which may, in turn, contribute to depression. Because ARHL is highly prevalent and greatly undertreated, targeting this condition is an appealing and potentially influential strategy to reduce the risk of developing two potentially devastating diseases of later life. However, further studies are necessary to elucidate the mechanistic relationship between ARHL, depression, and impaired cognition.

KEYWORDS: presbycusis, age-related hearing loss, depression, dementia, cognitive decline

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Presbycusis, or age-related hearing loss (ARHL), is a highly prevalent and undertreated condition, affecting more than two-thirds of adults older than 70 years.¹ In recent years, researchers have identified an independent association between ARHL and both cognitive impairment and incident dementia. ARHL also is correlated with an increased risk of late-life depression; however, this relationship is less studied.²⁻⁸

Both depression and cognitive impairment pose a major burden to worldwide healthcare systems. Dementia affects approximately 46.8 million people worldwide. Studies project that the prevalence will increase to 74.7 million by 2030 and to 131.5 million by 2050.⁹ The worldwide costs of dementia were estimated to be about \$818 billion in 2015, and was projected to surpass \$1 trillion by 2018.¹⁰ Depression has a 12-month and lifetime prevalence of 10.4% and 20.6%, respectively, and affects more than 2 million of the 34 million Americans older than 65 years.¹¹ Studies have projected that this condition will be the major cause of increased health care costs in middle-to-higher income countries by the year 2030.¹²

The relationship between ARHL and conditions of aging raises the exciting possibility that hearing loss, a common and undertreated condition, could be a modifiable risk factor. Though no causal mechanisms have been definitively established, plausible mechanisms link ARHL to both depression and cognitive impairment. Targeting ARHL could potentially reduce the prevalence, burden, or healthcare costs for these difficult-to-manage diseases of late life.¹³ Treatment is available for all levels of ARHL, ranging from hearing aids for mild-to-moderate hearing loss to cochlear implants (CIs) for severe-to-profound hearing loss.¹⁴ Certain rare forms of hearing loss can be improved with minor surgery. However, despite the overwhelming high prevalence of ARHL in the population, available treatments are grossly underutilized. This review summarizes the associations between ARHL, cognition, and depression, and highlights the importance and potential benefits of further investigating these relationships.

BACKGROUND OF AGE-RELATED HEARING LOSS

ARHL is inherent in human aging; given a long enough life, nearly everyone will develop hearing loss. ARHL is characterized as a gradual, progressive, and bilateral symmetric sensorineural hearing loss that initially affects higher frequencies (pitches). It is the second most common condition in the geriatric population. ARHL is a multifactorial condition that manifests due to a combination of intrinsic factors, such as genetic predisposition, and extrinsic factors, such as environmental noise exposures, cardiovascular disease, and ototoxic medications. The pathophysiology is attributed to degenerative changes of inner ear, including loss of cochlear inner and outer hair cells, degradation of spiral ganglion cells, or atrophy of the stria vascularis.¹⁵ However, the underlying trigger of this degenerative process remains unknown. Unfortunately, ARHL is irreversible and treatments solely aim to maximize remaining function (hearing aids) or completely bypass the inner ear and directly stimulate the hearing nerve (CIs).

ARHL initially presents as increased hearing thresholds, meaning that sounds are heard at a decreased volume. The quietest level (in decibel hearing level, or dB) at which the subject can hear the sound is termed the hearing threshold. Hearing is tested and hearing thresholds are identified through pure tone audiometry, where tones of a specific frequency are presented in a soundproof booth. The tones progressively increase in intensity (i.e., loudness) and the individual notes when he/she can hear the sound. Once pure tone hearing thresholds are obtained, type, degree, and configuration of hearing loss can be determined.

ARHL initially affects higher frequencies but progresses to involve midrange and lower frequencies over time. Speech primarily falls within the midrange of frequencies. Certain parts of words, such as the consonant /t/ in the word "right," fall among high frequencies. With ARHL, consonants are mostly affected, and can be misheard or not heard at all. While this may seem like a clarity problem, this issue stems from lack of volume. Hearing aids are an effective treatment, as they can be manipulated

to preferentially increase the loudness of certain frequencies.

Over time, the clarity of sound also will decrease. This can be tested with speech audiometry, where a individual is asked to repeat words at a comfortable level of loudness. The word recognition score (sometimes called the “speech discrimination score”) is the percent of correctly repeated words. When clarity and word recognition are affected, individuals with ARHL particularly struggle with conversations in background noise and music enjoyment. The challenge of understanding speech in background noise is significant, as most speech in the real world occurs in the presence of some type of competing sound. These difficulties may decrease participation in social activities¹⁶ and reduce quality of life.¹⁷

Hearing loss is a major burden for the elderly population. Over two-thirds of patients older than 70 years are afflicted, and the prevalence will only increase as the population ages.¹ Evidence shows that hearing interventions (i.e., hearing aids and CIs) improve both hearing-specific quality of life as well as overall quality of life. However, despite the high prevalence of hearing loss in the U.S. population, fewer than 20% of adults with hearing loss use any treatment.¹⁴

AGE-RELATED HEARING LOSS AND COGNITION

Dementia, the most concerning form of cognitive impairment, is a debilitating condition with extraordinary societal costs and no known treatment. There is great effort to identify and target modifiable risk factors of dementia, which could reduce or delay the burden of the disease later in life. These include smoking, cardiovascular disease, diabetes, and obesity. Hearing loss is a relatively new recognized modifiable risk factor.¹⁸ Multiple cross-sectional studies have identified associations between ARHL and both cognitive impairment and dementia, controlling for several potentially confounding risk factors.¹⁹ Similarly, longitudinal studies have identified an independent association between hearing loss and incident dementia, also after controlling for potential confounders. One noteworthy study found that

the risk of dementia over a 12-year period was 1.9 times higher among those with mild hearing loss compared with those with normal hearing. The risk among those with severe hearing loss increased by nearly five times.³

The potential impact of treating hearing loss is substantial, as was illustrated by using population-attributable fractions (PAFs). This metric can be used to estimate the percent reduction in incident dementia over a given time if a specific risk factor was removed. The unweighted PAF of hearing loss for dementia was recently calculated to be 23%. This is higher than all other PAFs of other modifiable risk factors, such as low education, depression, social isolation, hypertension, diabetes, and smoking.¹⁸ Considering the prevalence of hearing loss in the elderly, as well as the availability and accessibility of treatment options, targeting hearing has recently become an attractive strategy for potentially reducing the risk or delaying the onset of dementia.

In addition to dementia, several cohort studies and meta-analyses have noted a relationship between hearing loss and cognitive impairment. Specifically, ARHL measured through pure tone audiometry has been associated with worse scores on a wide range of neuropsychological tests assessing several cognitive domains, including memory, language, and executive function.²⁰ This has been consistently observed in both small and large observational studies^{21–23} as well as cross-sectional²⁴ and longitudinal population-based studies.²⁵ One newer study showed that there was no hearing threshold above which the hearing–cognition relationship begins. Subclinical hearing loss, defined as imperfect hearing (> 0 dB) that is better than the 25-dB threshold for mild hearing loss, was still a risk factor for impaired cognition.²⁶

Several preliminary noncontrolled treatment trials have suggested an improvement in cognition with hearing loss treatment. Studies reported better scores in a wide range of neurocognitive functions associated with both memory and executive function.^{27,28} While these studies have several flaws, including potential confounding, their results are encouraging and provide evidence for a positive impact of hearing loss treatments on cognitive function.

The association between ARHL and both cognitive impairment and dementia has been increasingly substantiated by a growing literature; however, the mechanism behind this connection is uncertain. Several plausible mechanisms elucidating the hearing loss–cognition relationship have been suggested. These mechanisms can be broadly divided into causal (ARHL causes cognitive impairment) or common (factors that cause both ARHL and cognitive impairment) mechanisms.^{29,30}

Casual Mechanisms

Causal mechanisms indicate that ARHL, through various potential mediating pathways, increases the risk of cognitive impairment or dementia. Several of these potential pathways have been proposed (Fig. 1, pathways A–C).

COGNITIVE LOAD

Hearing loss can lead to a greater cognitive load (Fig. 1, Pathway A), as cognitive resources are expended from processing a degraded auditory signal. Consequently, cognitive reserve can be depleted.³¹ Individuals with better cognitive reserve have an easier ability activating and reallocating compensatory processes when suffering from abnormal brain function. This phenomenon is thought to occur in patients with brain damage from trauma or stroke, as those with less cognitive reserve are less effectively able to maintain function of the damaged region compared with those with more cognitive reserve.³²

This idea may extend to other pathologies that increase the brain's cognitive load, such as hearing loss. Those who experience hearing loss may consume cognitive resources from other brain regions while struggling to understand speech. This could lead to cognitive dysfunction if cognitive reserve is not abundant in the affected individual. Several meta-analyses and systematic reviews have shown that ARHL impacts a wide range of cognitive domains, including executive function, word understanding, attention, processing latency, short- and long-term memory, and working memory.³³ Brain activity changes on functional magnetic resonance imaging (fMRI) in postlingually hearing-impaired adults. Increased activation of frontal and prefrontal cortical regions coupled with decreased activation in the temporal region (commonly associated with auditory processing) on speech-stimulated EEG supports the idea of increased recruitment of other brain regions to aid speech perception. In these studies, the process of resource allocation in individuals with hearing loss likely results in increased cognitive load, as those with hearing loss are redirecting finite cognitive resources to decode speech, which previously (i.e., prior to hearing loss) was not a major consumer of the brain's cognitive reserve.¹⁹ As a result, there are not enough cognitive resources left to devote toward other higher-level processes such as memory and executive function. This could contribute to cognitive decline.

Anecdotally, direct experiences of hearing-impaired older adults support this theory. In challenging listening environments, understanding

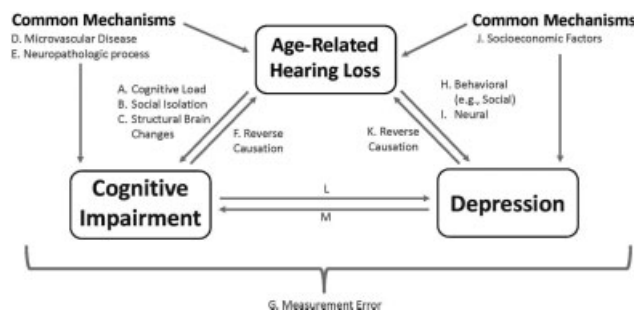


Figure 1 Proposed mechanistic relationship between age-related hearing loss, cognitive impairment, and depression. Common mechanisms are also called confounders. Factors that appear along an arrow between hearing loss and cognitive impairment (cognitive load, social isolation, brain changes) or between hearing loss and depression (behavioral, neural) are also called mediators.

words a speaker is saying can require greater cognitive effort. For example, the speaker may have said “cat” or “rat” but based on the subsequent sentence, neither makes sense. “Bat” becomes the likely word in this scenario. Though by the time, the listener has processed this, the speaker is three sentences ahead and the entire purpose of the story is lost.³⁴

SOCIAL ISOLATION

Social isolation (Fig. 1, Pathway B) is another possible mediator that could explain a causal relationship between ARHL and cognitive impairment.^{35,36} Social connectedness includes many different factors, including living arrangements, depth and size of social networks, participation in social gatherings, and engagement in community activities.³⁷

Hearing loss may adversely affect socialization. Those suffering from hearing loss require more cognitive energy for verbal conversation^{38,39} and thus communication may suffer. Relationships can be negatively affected and activities that were once enjoyed, such as interacting in groups or attending social events, may no longer be pleasant. Those affected by hearing loss may feel that they are burdening others, as conversations require more patience from those who are not. Additionally, hearing loss has been shown to reduce an individual’s ability to feel self-confident and independent, which can hamper interactions with less familiar, outside communities. The combination of these various factors can result in a feeling of loneliness, disconnection from previously strong social circles, and a reduction in social engagement.

Poor social engagement is independently associated with a higher risk of cognitive decline.⁴⁰ Promoting social engagement allows the older individual to better cope with the aging process. Diminished social networks and engagement increase the rate of cognitive decline through reduced brain stimulation. Additionally, people who feel disconnected from their community are less likely to participate in activities such as physical exercise and routine healthcare visits.⁴¹ This might also adversely affect cognitive function. Treating hearing loss, primarily through hearing aids, has already been shown in both cross-sectional and longitudinal

studies to improve feelings of loneliness and quality of life.^{42,43}

STRUCTURAL BRAIN CHANGES

ARHL may lead to changes in brain structure (Fig. 1, Pathway C) which in turn may increase the risk of cognitive impairment and dementia. This association has primarily been observed through the measurement of brain volumes on MRI.²⁹ Cross-sectional studies have noted decreased volume of the primary auditory cortex (i.e., in the temporal lobe) on MRI in patients with ARHL. This is likely a result of reduced activation of the region due to the lack of stimulation from the afferent auditory system.^{44,45} Longitudinal studies also have found that individuals with hearing loss had an increased rate of brain volume reduction compared with those who did not suffer from hearing loss.⁴⁶ Notably, the rate of brain volume decline in patients with ARHL was elevated for the entire cerebral cortex and the temporal lobe, which is responsible for speech and language processing. Atrophy of the temporal lobe is also seen in early stages of Alzheimer’s disease, as this region is responsible for different forms of memory and sensory transmission between different structures.⁴⁷ It is possible that ARHL accelerates cognitive decline by contributing in an additive manner to the atrophy of the temporal lobe and other regions commonly associated with Alzheimer’s. Prospective cohort studies have identified a relationship between midlife hearing impairment and reduced brain volume trajectories of the temporal lobe.⁴⁸

Common Mechanisms

Another possibility is that ARHL is related to cognitive impairment but does not cause it. Instead, confounding processes may contribute to the development of both ARHL and cognitive impairment. Two possible mechanisms are microvascular disease and neuropathologic processes.

Microvascular disease (Fig. 1, Pathway D) has been implicated as a cause of both ARHL and dementia. Chronic damage to the microcirculation of the cochlea can result in hearing impairment.⁴⁹ Disease of small vessels results in diminished cochlear blood flow, which

subsequently leads to ischemic intracochlear injury. The stria vascularis, which is responsible for regulation of endolymph (an inner ear fluid) is fundamental for proper cochlear physiology and is the most notable location of ischemic injury.⁵⁰ Clinical studies have found associations between stroke and acute sensorineural hearing loss, as well as chronic ARHL, likely because microvascular disease causes both.⁵¹

Microvascular cochlear damage is analogous to vascular dementia, in which periodic ischemic damage to the major regions of the brain due to diseased small vessels leads to cognitive decline. This is secondary to both local damage of major brain regions supplied by damaged vasculature and induction of neurodegenerative changes in distant regions. This inevitably leads to derangements in structural connectivity which results in impaired communication between cortical and subcortical brain regions.^{52–54}

Recent studies that have shown an association between ARHL and impaired cognition have adjusted for vascular risk, because of the obvious confounding potential of vascular disease. Conditions such as hypertension, smoking, and diabetes have been controlled for in multivariable regression. Since the relationship between ARHL and impaired cognition persists even after accounting for this known common cause, then vascular disease cannot entirely account for the relationship.^{5,7}

Basic neuropathologic processes could, hypothetically, cause both dementia and ARHL (Fig. 1, Pathway E). Classic histopathologic features underlying Alzheimer's include senile plaques (i.e., β -amyloid deposits) and neurofibrillary tangles (i.e., hyperphosphorylated tau protein aggregates) on autopsy specimens of the brain. The presence of these features on pathology specimens is tightly connected to dementia.⁵⁵ In theory, amyloid and tau buildup also could cause ARHL by depositing in key auditory structures, such as the central auditory cortex, cochlear nuclei, inferior colliculi, and thalamus.⁵⁶ However, ARHL is a peripheral phenomenon diagnosed by pure tone audiometry and such deposits have yet to be identified in the peripheral auditory system. Neuroimaging studies have shown that poorer hearing is associated with poorer cognitive function, but

not with amyloid deposition.⁵⁷ Though further studies are needed to confirm, this may suggest that the mechanism is independent of amyloid-related brain changes.

A possibility remains that undiscovered factors cause both ARHL and dementia (Fig. 1, Pathway E). Because they are undiscovered, they cannot be controlled for in observational studies. For example, it is theoretically possible that some unknown neurodegenerative process causes both ARHL and dementia, a phenomenon known as residual confounding. A randomized controlled trial would be needed to eliminate the possibility of residual confounding.

Reverse Causation

Scenarios where impaired cognition or dementia cause accelerated hearing loss (Fig. 1, Pathway F) are theoretically possible, but unlikely. This could occur if cognitively impaired individuals tend to be exposed more frequently to excessively loud noise or ototoxic substances than individuals without cognitive impairment. A lower level of health literacy is associated with cognitive decline,⁵⁸ meaning those with cognitive impairment may not as effectively understand how to preserve hearing through avoidance of perpetual noisy environments or avoidance of medications. However, longitudinal studies have shown that hearing loss increases the risk of later cognitive impairment and dementia.³ This temporal association is incompatible with reverse causation.

Measurement Error

There is also the concern that hearing loss is associated with inaccurate diagnosis of poor cognition. Poor performance on the cognitive test may be due to instructions not being heard (Fig. 1, Pathway G). Many cognitive tests, including the commonly used screening Mini Mental Status Exam (MMSE) and Montreal Cognitive Assessment (MoCA), rely on the patient's ability to hear, as instructions are usually verbally communicated. An inability to hear the instructions may lead to an artificially low score on cognitive testing, and therefore the extent of cognitive impairment may be

overestimated. This is unlikely, as subjects are usually tested by a trained examiner in a quiet room where instructions, unless the individual has severe hearing loss, are likely audible. The association between hearing loss and poor cognition persists even when those with severe hearing loss are eliminated. One recent study found an association between cognitive impairment and subclinical hearing loss.²⁶ Moreover, studies have been conducted using nonverbal cognitive tests and have found an association between ARHL and reduced cognitive functioning.⁵⁹

Cognitive impairment could make it difficult to appropriately and reliably perform a hearing test. This could result in an artificially low hearing test score that is unrelated to actual hearing ability. This is unlikely due to the simplicity of the clinical audiometric battery, which consists of raising a hand when a tone is heard or repeating words. Examiners are trained to adjust the speed of the test, which allows subjects to have ample time to process each step. Pure tone audiometry, the primary hearing measure in most current epidemiologic studies, is designed to test peripheral hearing. Higher cortical processes that would normally be diminished in individuals with dementia, however, are not assessed by pure tone audiometry.⁶⁰ As a proof of point, pure tone audiometry can be completed in children as young as 3 years old. Patients who experience severe dementia might struggle with audiometry testing. For this reason, previous longitudinal studies have excluded those with severe dementia at baseline.⁶¹

Other Limitations

While studies have shown enough evidence to strongly hypothesize a causal relationship between ARHL and dementia, it is likely that the relationship is multifactorial, involving several different mechanisms that could act in an additive manner. The ability to make concrete conclusions is limited by the difficulties found in studying cognition and hearing loss. For example, in studies using exposure and outcome measures which are not necessarily ideal, it is possible that there is overdiagnosis of dementia in those with hearing loss, or vice versa. Hearing loss may give the illusion of cognitive decline in

those affected. As a result, family members or health care providers may more aggressively screen for dementia and therefore identify the disease earlier and more frequently than those not affected with hearing loss. However, this phenomenon has not been formally explored.

Additional Considerations

In addition to hearing loss, other sensory impairments have been associated with cognitive decline, including both visual and olfactory impairment.^{62,63} The visual–cognition mechanism may resemble the hearing–cognition mechanism. Visual impairment could lead to social isolation, as well as reallocation of cognitive resources, due to a lack of stimulation of the primary visual cortex.

The olfaction–cognition relationship, particularly olfaction–dementia, may operate in the reverse direction, such that dementia is the cause as opposed to the effect. This theory is primarily supported by the presence of neurofibrillary tangles in the olfactory bulb in both Alzheimer’s and degenerative diseases of the brain.⁶⁴ This is in contrast to the peripheral auditory mechanisms, where such pathology has not been seen. Further studies exploring the effect of confounding sensory impairment, as well as causation, will need to be conducted before concrete conclusions can be made.

Vestibular function and balance also have been associated with cognitive function. Cross-sectional studies and longitudinal studies have illustrated that poorer balance is associated with worse performance on cognitive testing after controlling for confounders, including hearing loss.^{65,66} The exact nature of this relationship requires further study.

The relationship between the other senses, such as taste and touch, and cognitive decline remain largely unstudied.

AGE-RELATED HEARING LOSS AND DEPRESSION

Elderly individuals experiencing hearing loss have higher levels of depression and score worse on geriatric depression scales compared with their normal hearing counterparts.^{8,67} There are multiple theories that may explain why hearing

loss is associated with late-life depression. Individuals who have difficulty hearing also have difficulty following conversations. This can be frustrating when interacting with family and friends, and can diminish their enjoyment of social activities and relationships.

Hearing loss also makes it difficult for those affected to participate in leisure activities, primarily because they feel less comfortable physically navigating through their environment without hearing. This could lead to the development of depressive symptoms. Studies suggest that those with significant hearing loss report lower and impaired physical activity as well as slower gaits.⁶⁸ Symptoms such as decreased leisure activity, slowed gait, and poor physical performance are related to frailty, a condition of generalized physiologic decline associated with increased morbidity and mortality risk exhibited by elderly adults. Interestingly, such symptoms of the frailty phenotype also are exhibited by individuals with late-life depression. Researchers have proposed that there is a bidirectional association with characteristics of frailty and late-life depression.⁶⁹

There are not as many high-quality studies that concretely establish the relationship between hearing loss and depression as there are in the cognitive literature. Studies examining the relationship between depressive symptoms and hearing loss have demonstrated mixed results. This may be attributed to the variability in measurement strategies as well as the weakness in study designs. One study identified a relationship between mild hearing loss and depression, but not moderate or severe hearing loss.⁷⁰ Interestingly, another study identified a linear relationship between the degree of depression and greater hearing deficit.⁷¹ Yet another found an association between pure-tone audiometry hearing thresholds and depression, but not with self-reported hearing loss.⁷² There have been consistent findings of an association between hearing aid use and a reduced odds of depression or depressive symptoms.^{73,74} This phenomenon also has been described in individuals with cochlear implants.⁷⁵

While results have varied, there are several potential mechanisms by which hearing loss may contribute to the development of

depression. These can be divided into behavioral factors and neural pathways.

Causal Mechanisms

BEHAVIORAL MECHANISMS

Behavioral mechanisms elucidating an association between hearing loss and depression are relatively intuitive (Fig. 1, Pathway H). Hearing is fundamental to communication via spoken language; thus, hearing loss is inextricably related to social dysfunction. Individuals with hearing impairment are more likely to withdraw from society, experience social isolation, and have reductions in social networks. These factors, in turn, have been independently associated with depression.^{76–78} This social isolation primarily stems from an impairment in communication. Without effective communication, individuals are less able to maintain relationships, social activities, and leisure activities.⁷⁹

Social isolation is highly correlated with depression, in addition to poor quality of life and increased mortality and morbidity.^{80–82} As outlined earlier, reduced social interaction is associated with an increased risk of incident dementia, which has been linked, in turn, to the development of depressive symptoms, independent of other confounders such as hearing loss and other sensory impairment.^{40,83} Self-reported loneliness, a common component of the social isolation, also has been a reported predictor of the development of Alzheimer's disease in longitudinal studies.⁷⁶

Hearing loss also has been associated with poor physical functioning and activity. This includes slower gaits and substandard execution on measures of physical performance.^{68,84,85} Additionally, studies have identified an independent inverse relationship between hearing and postural control, which can be associated with difficulty walking and a higher risk of falls.^{86,87} A relationship between falls and hearing loss has been well-documented. In fact, a systematic review found that the odds of falling were 2.39 times greater for elderly patients with hearing loss.⁸⁸ This review, however, admits the statistic is limited by potential publication bias. Furthermore, the important confounding effect of poor vestibular function (i.e., since hearing

and vestibular function are often related) was generally not controlled for. This is an important consideration, as hearing aids rehabilitate the cochlear portion of the inner ear, not the vestibular portion. The fear of falling has been associated with social isolation, anxiety, a reduced level of independence, and depression.⁸⁹ Finally, decreased physical activity and impaired gait are part of the syndrome of frailty. Researchers have proposed that there is a bidirectional relationship between frailty syndrome and late-life depression.

Auditory impairment is closely associated with tinnitus, an unwanted and often bothersome sound most commonly described as ringing.⁹⁰ While the etiology of tinnitus is complex, hearing loss is partly causative. Indeed, hearing loss is diagnosed in more than 90% of patients with tinnitus.⁹¹ The reported prevalence of bothersome tinnitus in individuals older than 60 years ranges from 8 to 20%.⁹² Chronic tinnitus is associated with depression and anxiety symptoms, and is likely a component of the mechanisms underlying hearing loss and depression. Bidirectional, or circular, association is probable as tinnitus can cause worsening anxiety or depression, which increases the annoyance of tinnitus. Chronic tinnitus has been associated with suicide attempts, although this relationship is still under investigation.⁹³

NEURAL MECHANISMS

Neuroimaging studies support a relationship between ARHL and depression (Fig. 1, Pathway I). As described previously, hearing loss is associated with several brain changes in both the peripheral and central auditory pathways, as well as other related structures of the prefrontal cortex over time.⁹⁴ In studies using MRI imaging, the brains of patients with ARHL have demonstrated diminished volumes of many brain regions, including the temporal and frontal cortices, amygdala, hypothalamus, and primary auditory cortex.^{44,45,95,96} Many mental health symptoms, including those seen in depression, have been linked to the neuronal connectivity of these brain regions.⁹⁷ Therefore, pathophysiological changes of neurological pathways and atrophy of key structures due to ARHL may contribute to the development of depression.

In addition to brain volume changes, fMRI studies have shown functional changes in the brains of depressed patients. Based on these functional changes, some believe it is possible to subclassify depression based on activity differentials.⁹⁸ Reductions in activity of the thalamus, temporal lobe, cerebellar posterior lobe, insula, and occipital lobe have been observed in depressed patients relative to healthy patients.⁹⁹ Studies have shown that these functional abnormalities persist even after treatment.¹⁰⁰ Therefore, hearing loss may contribute to the development of late-life depression through compensatory recruitment of other areas of the brain, such as those necessary for emotional stability, to support effortful listening. These can lead to overtaxing the cognitive network's capacity and cause executive dysfunction, which is a classic characteristic of depression in the elderly. Diminished executive function predicts a poorer response to antidepressant medications, and is associated with a higher rate of relapse and recurrence of major depression.¹⁰¹ Studies have suggested that individuals with greater cognitive reserve may be better equipped to devote more energy toward brain regions that are responsible for regulating emotion.¹⁰² Therefore, as described earlier, depletion of cognitive reserve due to hearing loss can contribute to the development of depression in a similar manner to dementia.³² Notably, studies have shown deactivations in limbic structures in those with hearing loss. These structures are highly relevant for the experience of emotionality, and normally have strong neural connections with the auditory processing centers of the brain.¹⁰³ Dysregulation of these limbic structures in ARHL patients may result in downstream effects (i.e., emotional to the idea that hearing loss could have a direct mechanism with depression).

Common Causes

Certain factors may contribute to the development of both depression and ARHL independently. For example, both lower socioeconomic status (Fig. 1, Pathway J) and low education level are risk factors for the development of depression.¹⁰⁴ These factors also could contribute to ARHL, in theory, if these patients are

more likely to be exposed to noisier environments and more ototoxic medications. However, high-quality studies have attempted to control for such sociodemographic factors with multivariable regression and the hearing–depression relationship has persisted. Yet, residual confounding, whereby confounders that we are not aware of or cannot control for, is still possible. To fully control for confounders, a randomized control trial is needed.

Reverse Causation

Depression could contribute to poorer hearing in a reverse mechanism. This would be the case if those who were depressed were more likely to expose themselves to environments with excessive noise, or expose themselves to more ototoxins than those who are not depressed. This is unlikely through the noise-induced pathway, as studies looking at hearing loss in individuals with depression do not observe the classic hearing loss at a frequency of 4 kHz seen in those with noise-induced hearing loss.¹⁰⁵ Furthermore, ARHL is only partly due to environmental factors (i.e., preventable), as opposed to intrinsic or genetic hearing loss.

Measurement Error

Substandard performance on depression testing may not reflect depression in an individual, but rather could be a result of inability to hear the testing instructions. In a similar fashion to tests of cognition, those with hearing loss may artificially do worse on depression testing due to the inability to hear questions or instructions. This is unlikely, as several of the common screening tests for depression, such as the PHQ-9, are written tests. Furthermore, the relationship between hearing and depressive symptoms persists even if individuals with severe hearing loss are excluded.

Finally, individuals with depression may do worse on a hearing test not because of worse hearing, but because they were more apathetic and did not expend enough effort on the test. Hearing tests are reliable and relatively easy to complete. As described earlier, patients as young as 3 years can complete hearing assess-

ments, illustrating the degree of effort necessary to complete the test.

Other Limitations

Many of the studies listed earlier utilize self-reported data for both hearing and depression. This can introduce bias due to the stigma associated with functional impairment, preventing patients from consciously or subconsciously choosing to report their conditions. Additionally, studies vary greatly in how they choose to measure depression, as some do not use quantitative scales. Some studies utilize depressive symptom inventories; however, this measures depressive symptoms as opposed to clinically diagnosed depression. Few studies use psychometrically valid assessments.

Studying depression in the older adults can be difficult, as it can manifest in ways that may not be measured using standard depression inventories. For example, depression can commonly manifest as somatic symptoms in older patients. Lethargy, one of the most common symptoms of depression, may not be picked up by conventional screening methods.¹⁰⁶ Another key consideration is the temporal variability of depressive symptoms. Unlike dementia, which is generally irreversible and progressive, depression can be episodic. Symptoms will fluctuate depending on treatment with antidepressants, interpersonal or social support, and unknown factors. This makes it difficult to sensitively capture depression, especially when using cross-sectional designs. Due to the variability of depression presentation, it would be methodologically beneficial to limit studies to a relatively uniform population. For example, this could be done by studying ARHL in patients with clinically diagnosed depression who receive selective serotonin reuptake inhibitor treatment, as patients must have a certain intensity of symptoms to indicate medical treatment.¹⁰¹

Some have attempted to study how the treatment of hearing loss is related to depression. However, it is difficult to establish causality between hearing devices and depression, especially with cross-sectional studies, as those obtaining hearing aids or CIs are more motivated and less likely to be depressed. One study showed the opposite of an expected effect, in

which hearing aid use was associated with an increased risk of social isolation. The author notes that the study was limited by a questionnaire for social isolation with a low sensitivity, which is not an uncommon problem in many studies.⁴² The authors speculate that hearing aids discourage engagement in social activities due to the amplification of background noise in busy locations, as well as the stigma associated with wearing the device. Fortunately, hearing aids are immediately reversible, and individuals can always remove them if they negatively affect hearing ability, or perceived cosmesis, in certain situations.

THE NEXUS OF ARHL, DEPRESSION, AND COGNITION

Hearing loss has been independently associated with both depressive symptoms and cognitive impairment. However, these relationships do not act in silos. Depression is a risk factor for cognitive impairment, while cognitive impairment is a risk factor for depression. Thus, a cycle could be feasible where depression exacerbates cognitive function which further exacerbates depression (Fig. 1, Pathways L–M).

As previously described, the hearing–cognition and hearing–depression relationships share mediators, including social isolation (Fig. 2). Treating hearing loss would likely have a beneficial effect on socialization because of this common mechanistic pathway. This treating hearing loss, in turn, could have a downstream effect on both cognition and depression.

Likewise, structural brain changes are also a common mediator.³³ Brain volume changes

have been seen in both depression and dementia.^{107,108} Reduction in volume of several major cortices such as the postcentral cortex, insula, parietal, occipital, hippocampus, amygdala, and orbitofrontal lobes have been seen in patients diagnosed with major depressive symptoms.^{109,110} Similarly, dementia is associated with several brain changes throughout the cerebral cortex, including regions of memory and emotional processing, such as the prefrontal, temporal, and parietal lobes; anterior cingulate gyrus; limbic structures; and insula.^{46,108} In theory, hearing loss could contribute to both dementia and depression via brain volume changes, as many structures commonly atrophied in both conditions are not mutually exclusive.

Finally, hearing loss could cause both depression and dementia through a common mediating mechanism of depletion of cognitive reserve; fMRI studies have shown decreased activity in multiple cortical regions in patients diagnosed with depression, dementia, and hearing loss.¹¹¹ Similar to brain volume changes, the regions shown to change in activity in both dementia and depression are not mutually exclusive. By devoting more cognitive energy to hearing, cognitive reserve devoted to both cognition and emotional regulation could get depleted, which would result in both depressive symptoms and cognitive decline. However, it is still unclear whether depression and dementia are the causes or consequences of brain changes.¹¹²

If mechanisms underlying ARHL and dementia, as well as ARHL and depression, exist, then clinicians may be able to target both at once.

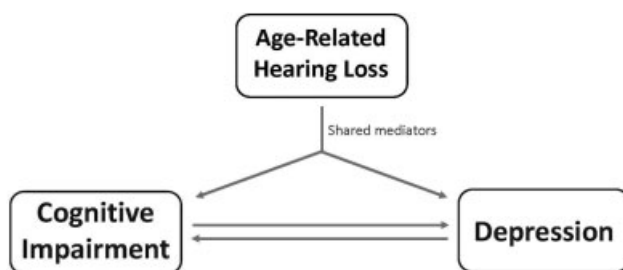


Figure 2 Additional mechanistic detail showing the interrelationship between age-related hearing loss, cognitive impairment, and depression.

FUTURE DIRECTIONS

ARHL has been independently associated with both cognitive impairment and depression. While the mechanism between the associations is unclear, studies have identified hearing loss as a potential modifiable risk factor for these highly prevalent and burdensome conditions.

Considering the high prevalence and undertreatment of ARHL, further exploring the effect of hearing loss treatment on depression and cognition should be expedited. Studies have suggested that hearing loss treatment, including hearing aids and CIs, may be effective for the treatment of both dementia^{113,114} and depression.^{42,73,75} While promising results may be found, these studies must be approached with caution because of design limitations.

Current evidence suggests it is possible that aggressive utilization of hearing aids could have substantial health and cost–benefit advantages. These advantages could include the treatment of ARHL and quality of life as well as the symptoms of dementia and depression.¹¹⁵ Medicare does not currently cover hearing aids, but modeling suggests that utilization of hearing aids would reduce Medicare spending.¹¹⁶ With that said, hearing aids are accessible, and devices will be less expensive due to the recent passage of the US Over the Counter Hearing Aid Act of 2017. This new regulatory change will allow individuals with perceived mild-to-moderate hearing loss to purchase hearing aids over the counter in the United States, without a prescription.¹¹⁷

Further studies must be conducted before treatment guidelines can be firmly established, primarily through randomized clinical trials, as these are needed to infer causation. The evidence base today is largely from cross-sectional and longitudinal studies. The use of neuroimaging can be a strong tool for observing modifications in cortical activity and structure as aural rehabilitation technology is used.

As further evidence implicates hearing loss in impaired cognition and depression, strategies to expand access to hearing loss treatment and technology would be beneficial. Healthcare workers who are not otolaryngologists or audiologists largely ignore hearing loss. They must be educated about the relationships between ARHL, cognitive impairment, and depression.

By doing so, primary care physicians may begin to routinely recommend hearing testing and treatment for their older patients. Likewise, psychiatrists may consider targeting hearing loss as a manageable component of depression.

CONCLUSION

Age-related hearing loss is a potential risk factor for cognitive impairment, dementia, and late-life depression. It is a highly prevalent and undertreated condition that is a potential target and modifiable risk factor in preventative strategies for both dementia and depression. Additional research, particularly randomized control trials and large prospective studies incorporating more neuroimaging modalities, are needed to further elucidate possible causal mechanisms behind the associations observed, and to comprehensively inform treatment guidelines.

CONFLICTS OF INTEREST

J.S.G. received travel expenses for industry-sponsored meetings (Cochlear, Advanced Bionics, Oticon Medical) and consulting fees or honoraria (Oticon Medical, Auditory Insight, Optinose, Abbott, Decibel Therapeutics), and also the department received unrestricted educational grants (Storz, Stryker, Acclarent, 3NT, Decibel Therapeutics).

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