

REVIEW

A review of new insights on the association between hearing loss and cognitive decline in ageing

Ipoacusia e declino cognitivo: revisione della letteratura

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SUMMARY

Age-related hearing loss (ARHL) has a multifactorial pathogenesis and it is an inevitable hearing impairment associated with reduction of communicative skills related to ageing. Increasing evidence has linked ARHL to more rapid progression of cognitive decline and incidental dementia. Many aspects of daily living of elderly people have been associated to hearing abilities, showing that hearing loss (HL) affects the quality of life, social relationships, motor skills, psychological aspects and function and morphology in specific brain areas. Epidemiological and clinical studies confirm the assumption of a relationship between these conditions. However, the mechanisms are still unclear and are reviewed herein. Long-term hearing deprivation of auditory inputs can impact cognitive performance by decreasing the quality of communication leading to social isolation and depression and facilitate dementia. On the contrary, the limited cognitive skills may reduce the cognitive resources available for auditory perception, increasing the effects of HL. In addition, hearing loss and cognitive decline may reflect a 'common cause' on the auditory pathway and brain. In fact, some pathogenetic factors are recognised in common microvascular disease factors such as diabetes, atherosclerosis and hypertension. Interdisciplinary efforts to investigate and address HL in the context of brain and cognitive ageing are needed. Surprisingly, few studies have been addressed on the effectiveness of hearing aids in changing the natural history of cognitive decline. Effective interventions with hearing aids or cochlear implant may improve social and emotional function, communication, cognitive function and positively impact quality of life. The aim of this review is to overview new insights on this challenging topic and provide new ideas for future research.

KEY WORDS: Hearing loss • Dementia • Elderly • Cochlear implant • Cognitive impairment

RIASSUNTO

La perdita dell'udito legata all'età o presbiacusia è un deficit correlato al processo irreversibile di invecchiamento che riconosce una patogenesi multifattoriale. Crescenti osservazioni hanno collegato la presbiacusia a una rapida progressione del declino cognitivo e incidentalmente con la demenza. Molti aspetti della vita quotidiana degli anziani sono stati collegati alle loro capacità uditive, mostrando che la perdita uditiva incide sulla qualità della vita, i rapporti sociali, le capacità motorie, gli aspetti psicologici, la funzione e la morfologia di specifiche aree cerebrali. Studi epidemiologici e clinici confermano l'ipotesi di un legame tra queste condizioni e questo lavoro ha lo scopo di fare il punto sui meccanismi patogenetici che sostengono tale associazione. Lo sforzo di un lavoro congiunto tra otorinolaringoiatri, audiologi, neurologi e cognitivisti è quello di chiarire gli aspetti comuni, le possibilità di diagnosi e di intervento precoce al fine di ridurre gli effetti dell'uno sull'altro di questi processi degenerativi. Le osservazioni sperimentali e cliniche si concentrano su differenti aspetti: in primo luogo la privazione uditiva per lungo tempo può avere un impatto negativo sulle prestazioni cognitive diminuendo la qualità della comunicazione che porta all'isolamento sociale e la depressione e quindi facilitare la demenza. Al contrario, le capacità cognitive limitate possono ridurre le risorse cognitive disponibili per la percezione uditiva, aumentando così gli effetti della perdita dell'udito. Inoltre, questa associazione può rappresentare la conseguenza di una 'causa comune' nella patogenesi del deficit uditivo e del sistema nervoso centrale. Infatti, molti dei fattori eziopatogenetici sono comuni, quali le cause microvascolari della malattia (es. diabete, aterosclerosi, ipertensione). La sfida di questi anni è quella di aumentare le conoscenze sui rapporti tra invecchiamento cerebrale e cognitivo ed ipoacusia, grazie anche ai progressi del neuroimaging. Sorprendentemente pochi dati sono stati pubblicati sull'utilità delle protesi acustiche nel cambiare la storia naturale di declino cognitivo. La protesizzazione e gli impianti cocleari possono migliorare le attività sociali e la sfera emotiva, la comunicazione e quindi più in generale la funzione cognitiva, con un globale impatto positivo sulla qualità della vita. Lo scopo di questo lavoro è quello di fornire le informazioni attualmente disponibili in letteratura su rapporto tra declino cognitivo e deficit uditivo nell'anziano, fornendo nuovi spunti di ricerca per il futuro.

PAROLE CHIAVE: Ipoacusia • Demenza • Deficit cognitivo • Impianto cocleare • Anziani

Introduction

It is well known that both hearing loss (HL) and cognitive impairment are associated with ageing. The first report on the independent relationship between hearing impairment and cognitive dysfunction appeared about 30 years ago¹, suggesting the hypothesis that age-related hearing loss (ARHL) may contribute to dementia. Probably the lack of interaction among ENT specialists, audiologists, neurologists, epidemiologists and cognitive scientists has limited the possibility to better recognise their correlation and impact on elderly people. More recently, growing epidemiological, neurobiological and neuroimaging evidence opened a new interest in this field and an increasing number of reports have focused on the relationship and effects of both HL and cognitive decline on the quality of life and rehabilitative perspectives². ARHL can be defined as a progressive, bilateral, symmetrical HL that reduces an individual's communicative skills due to age and can be considered a multifactorial complex disorder, with both environmental and genetic factors contributing to the aetiology of the disease³. Cognitive impairment generically refers to a wide range of conditions ranging from mild cognitive impairment to severe dementia, while different degrees of hearing loss can impact the communicative impairment and quality of life. The increasing prevalence of cognitive decline^{4,5} and the devastating impact of dementia on affected individuals and the burden imposed on families and society has made prevention and treatment of dementia a public health priority. Many aspects of daily living of elderly people have been linked to hearing abilities, showing that ARHL affects the quality of life, social relations, motor skills, psychological aspects, function and morphology in specific brain areas. On the basis of clinical evidence, it has been suggested that ARHL is linked with more rapid progression of dementia. The potential public health impact of ARHL in the context of dementia is substantial given the high worldwide prevalence of HL in older adults and the ready availability of existing hearing rehabilitative interventions, which remain risk free and underutilised. Until now, in the literature there are no studies demonstrating the utility of hearing rehabilitation in changing the natural history of dementia. Interdisciplinary efforts to investigate and address ARHL in the context of brain and cognitive impairment in older subjects are challenging. Despite the increasing attention, the relationship between cognitive status and HL is still controversial, and in particular it remains to be investigated whether HL is involved in the causal mechanisms of dementia or whether there is an independent relationship in which ARHL might enhance the effects of dementia. The aim of this paper is to focus on the new insights on epidemiological aspects, prevention, assessment and intervention strategies for older adults with HL who are at risk of developing dementia.

Epidemiology of hearing loss and dementia

Hearing loss affects approximately one-third of adults from 61 to 70 years of age and more than 80 percent of those older than 85 years. After hypertension and arthritis, it is the most common health disorder in older patients. More than 90% of HL in older patients can be classified as ARHL, while few patients are effected by conductive or mixed hearing loss. The impact of ARHL will increase due to the ageing of baby boomers and it is reasonable to assume a further escalation because of the constant growth of average lifespan in industrialised countries. In the US, 26.7 million adults older than 50 years suffer from ARHL and only 3.8 million use hearing aids⁶, while, in UK 8.1 million suffer from HL, of whom 1.4 million use hearing aids^{4,7}. According to the United Nations, the global population will grow from 6.9 billion in 2010 to 9.3 billion in 2050. The proportion of the population aged 60 or older will nearly double in the same period, reaching 21% of the total population in 2050, or nearly 2 billion of people in 2050. Males demonstrate a higher incidence of presbycusis with earlier onset compared to women. Among European Countries, in Italy, 1 in 6 of people suffer some form of HL, in Finland 1 of 7, while in Sweden and Denmark 1 of 10 people are affected by ARHL. For the WHO, in Europe about 70 million people are affected by ARHL, even if the statistics include also slight hearing levels with threshold greater than 25 dB. Only about 20% of people 65 years or older with moderate to profound ARHL perceive themselves as hearing impaired and about 70% of people with ARHL refuse hearing aids (www.actiononhearingloss.org.uk/your-hearing/aboutdeafness-and-hearing-loss/statistics.aspx). Interestingly, costs for hearing aids are lower than the cost of the untreated HL with an expense cost of € 213 billion per year in Italy and France, about € 22 billion in UK and € 30.2 billion in Germany^{5,6}. In developed countries, hearing loss (HL) is very prevalent; although in African and South East Asian regions preventable causes of hearing impairment such as otitis media, sensorineural damage due to nutritional deficiencies, noise-induced hearing loss, ototoxicity and genetic hearing loss from consanguinity are more commonly reported in the literature than ARHL even if they can contribute to this condition⁸. Epidemiological evidence⁷⁻⁹ supports the association between ARHL and late-life cognitive disorders suggesting that hearing impairment is a modifiable factor that, with appropriate treatment, could facilitate activities of daily living, decrease isolation and loneliness of aged subjects and slow down cognitive decline. Similar to ARHL, there are gradual and age-related losses in cognitive processing including speed of information processing, memory and attention. Beyond normal age-related cognitive changes, clinically mild cognitive impairment (MCI) increases with age and about one fifth of

people have some degree of cognitive loss by the age of 70 years¹⁰. The prevalence of dementia increases from 5% in those 71 to 79 years to 37% in those 90 years and older, with an overall prevalence of approximately 14% for those over 70 years of age⁹. Moreover, a continuum between MCI and dementia has been recognised^{12,13} and patients with MCI are at an intermediary stage that often, but not always, progresses to Alzheimer's disease (AD), which is the most common form of dementia. It is suggested that the rate of conversion from MCI to AD is about 10% to 15% per year, which increases to 80% after 6 years, and it is higher than the rate of 1-2% per year observed in the general population¹⁴. Numbers of dementia are impressive: in 2005, 24.3 million people were estimated to have dementia, with 4.6 million new cases of dementia every year (one new case every 7 patient). This number is expected to double every 20 years to 8.1 million people by 2040^{4,5}.

Altogether, given the high prevalence of both hearing loss and cognitive decline in older adults that increases in prevalence with age⁸⁻¹⁵, it is reasonable to assume that cognitive disorders are common in many of the oldest adults who have ARHL. Therefore, epidemiological evidence supports the hypothesis that there is a link between ARHL and dementia.

The hypotheses on the relationship between age-related hearing loss and cognitive decline

Even if epidemiological, audiological and auditory central testing corroborate the association between HL and incidental dementia^{16,17}, different relationships are debated. Major evidence supports the hypothesis that cognitive decline can reduce the cognitive resources available for auditory perception manifesting as hearing loss and reduced understanding of speech, also indicated as "cognitive load on perception hypothesis". In contrast, it has been shown that the risk of developing dementia is higher in individuals affected by ARHL^{11-13,17} suggesting that hearing loss leads to cognitive decline because of degradation of inputs to brain (Fig. 1). Lin et al.¹¹ demonstrated that for every 10 dB increase in HL over 25 dB HL there was a 20% increased risk of developing dementia. More recently, Gurcel et al.¹⁸ showed that in adults over 65 years of age the mean time for developing dementia was 10.3 years in those with hearing loss at baseline *versus* 11.9 years for counterparts with normal hearing. Thus, ARHL has been found to be independently associated with poorer cognitive function and incident dementia; in particular, normal hearing individuals, compared to mild, moderate, and severe hearing loss patients had a two, three, and five-fold increased risk of incident all-cause dementia, respectively^{13,19}. It has also been demonstrated that ARHL impacts several domains of healthy aging including social engagement, physical mobility and activity, falls, vitality and even dementia, in addition to cognitive dysfunction

^{15,20}. Moreover, it has been demonstrated that scores from several cognitive tests generally declined linearly with increasing levels of HL^{12,17}. A strong association has been observed between HL and measures of memory and executive function. Furthermore, a significant association between severe HL and poorer cognitive function has been found administering both verbal and non-verbal cognitive tests to older patients²¹⁻²⁵. More recently, Dupuis and colleagues²⁶ confirmed Lin's data, but focused attention on the influence of HL or other sensory deficits on the results of cognitive tests. Nevertheless, this datum is still debated, and previous studies have been prone to exclude this relationship^{24,25}.

All efforts should be made to establish the relationship between HL and cognition in older patients undergoing to clinical evaluation. In some cases, cognitive losses may be misdiagnosed or conversely over-diagnosed when the sensory abilities of patients are not considered. This matter is especially important when a diagnosis of dementia is based on orally administered evaluation using tests environment in which there may be varying levels of ambient noise. A recent study by Jorgensen et al.²⁷ indicates that in only 13% of patients in a primary care clinic who were affected by memory loss was hearing status investigated. In summary, the association between ARHL and cognitive impairment is now well established by several cross-sectional and longitudinal studies, and it is unquestionable that hearing loss is more common in patients affected by dementia than in healthy older adults.

Interestingly, it has been postulated that ARHL may act as a "second hit" on the brain, thus adversely affecting cognitive performance and increasing the risk of dementia by adding to brain injuries derived from other disorders (e.g., amyloid-beta accumulation, neurofibrillary tangles and microvascular disease). For example, cross-sectional neuroimaging studies have demonstrated that peripheral hearing impairment is associated with reduced cortical volumes in the primary auditory cortex and variation in the integrity of central auditory white matter tracks as described in the following paragraph^{28-32,37-40}. Longitudinal data from animal models^{33,34} also demonstrated that cochlear impairment may precipitate changes in cortical reorganisation and brain morphometry. Accordingly, confirmation for a link from HL and cognitive impairment is also derived by the evidence that both conditions are sequelae of an underlying pathology such as hypertension, diabetes and/or atherosclerosis (Fig. 1). As previously mentioned, ARHL is a complex multifactorial disorder with both environmental (i.e. noise, ototoxic drugs, atherosclerosis, diabetes, hypertension) and genetic factors (i.e. genetic susceptibility) that contribute to its aetiology. As experimentally shown^{3,33,34}, the aged cochlea shows degeneration of stria vascularis, sensorineural epithelium and neurons in the spiral ganglion and auditory cortex of the central auditory pathways related to exogenous factors

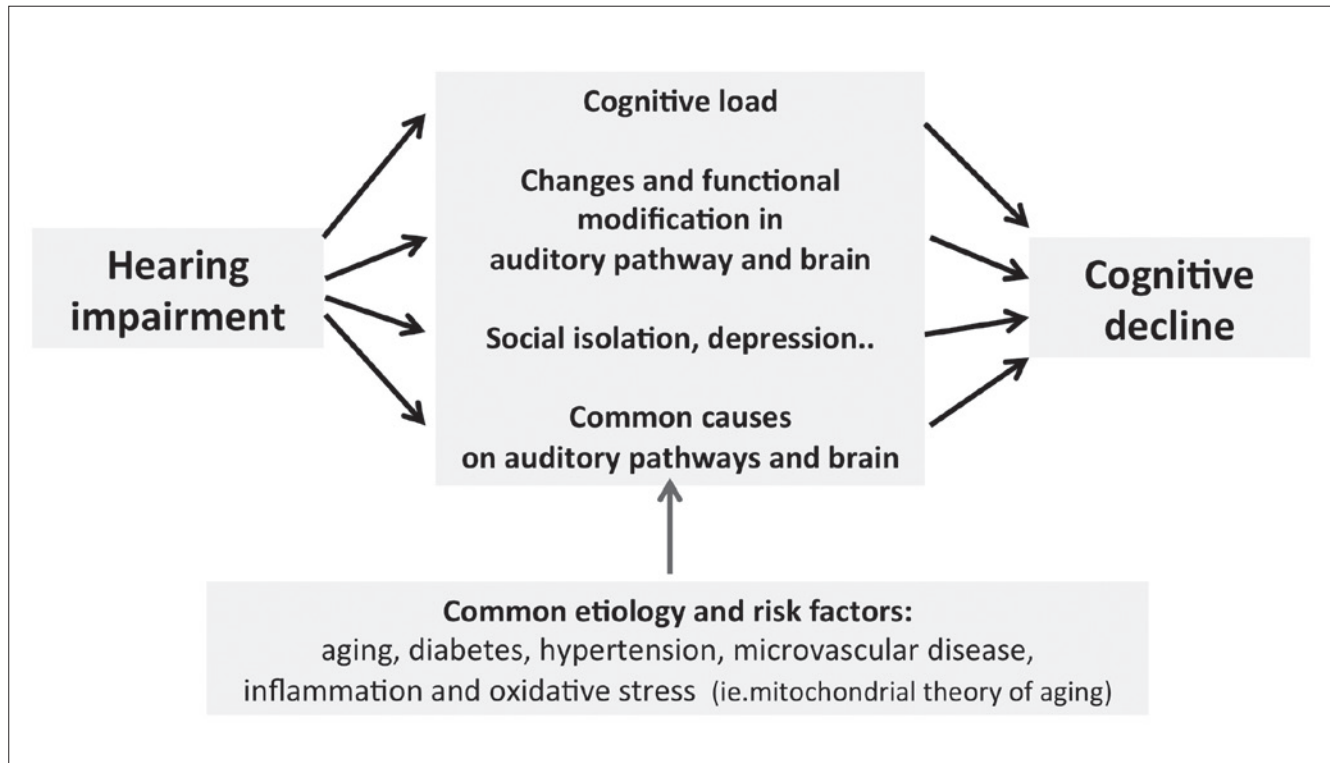


Fig. 1. Conceptual model of the association of hearing loss with cognitive decline (adapted from Lin ²).

(e.g. noise and ototoxic drugs, vascular risk factors) inducing oxidative stress pathways (including the “mitochondrial theory of ageing”) and inflammation; some of these mechanisms are common to neurodegenerative diseases including AD. Experimentally, the role of microvascular damage in the pathogenesis of AHRL has been clearly demonstrated together with the evidence that spiral ganglion deafferentation is associated with altered dendritic architecture of auditory pyramidal neurons ³³. Thus, common factors could underlie a simple correlation between hearing and cognition including age, vascular risk factors and social factors (e.g. education) ^{2,11-13}.

Alternatively, mechanistic hypotheses have been proposed that argue for a causal association between ARHL and cognitive decline, including increased social isolation and loneliness, increased cognitive load and changes in brain structure ³⁵. Further studies will be needed to clarify this association.

All epidemiological and clinical evidence has been organized in the following four hypotheses (Fig. 2): first, cognitive decline may reduce the cognitive resources that are available for auditory perception, increasing the effects of hearing loss, also referred as “cognitive load on perception hypothesis”. When the inputs are poor, either through degraded stimuli or impaired perception, additional cognitive resources are required to understand the signal. For the “information degradation hypothesis”, an additional effort is required either

because the stimuli are degraded, for example in noisy environment, because the perception is decreased, and therefore cognitive resources used for the signal codification are not available for cognitive roles ²⁸. In contrast, as previously mentioned, the “sensory-deprivation hypothesis” described by Lin and colleagues ¹¹⁻¹³, suggested that hearing loss causes cognitive decline that is permanent or potentially remediable after rehabilitation. According to this hearing impairment increases cognitive effort in patients with cognitive defects and depressive symptoms ³⁵. A plausible mechanism may be that impaired perception could lead to worsening cognition over time and social isolation which in turn leads to cognitive decline. Finally, a fourth mechanism takes inspiration by the evidence that some common factors cause both declines, also called the “common cause hypothesis”, in fact the clinical demonstration is that multiple sensory modalities and cognition appear to decline concurrently in the older patients. As summarised by Lin et al. ² in a convincing model (Fig. 1, 2), there is a common aetiology for ARHL and cognitive decline, even dementia, that is based firstly, on microvascular and ageing risk factors, and secondly hearing impairment affects different domains such as social isolation, loneliness, increased cognitive load and changes in brain structure that may contribute to the onset of cognitive decline and dementia ².

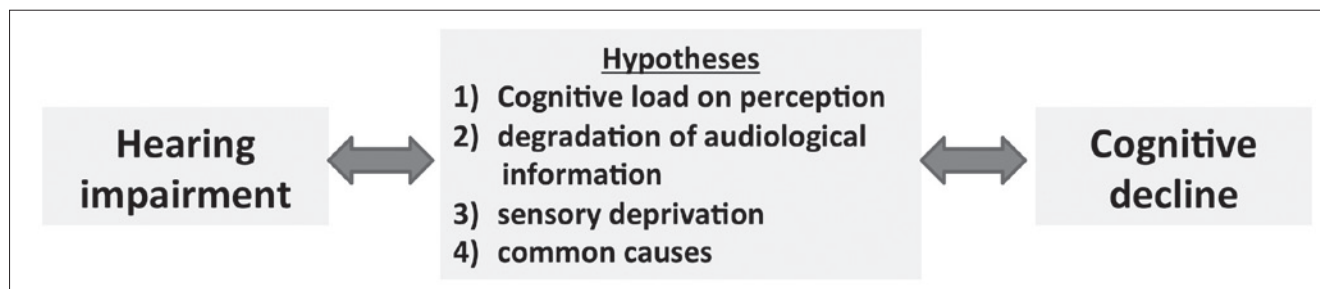


Fig. 2. The epidemiological and clinical evidence is summarised in the following hypotheses on the relationship between HL and cognitive decline.

Peripheral and central origin of ARHL: a link between central auditory processing disorders and cognitive decline

Traditionally, cochlear damage, including hair cell loss and damage of stria vascularis and spiral ganglion neurons, was considered to be the main cause for ARHL according to Schuknecht topology, which correlated the patterns of hearing loss with the location of the hearing defect. Temporal bone studies suggested three main types of presbycusis: *sensory presbycusis* with high frequencies HL caused by hair cell loss and subsequent neural degeneration, *neural presbycusis* characterised by the loss of word discrimination caused by the primary degeneration of cochlear neurons and *metabolic/strial presbycusis* characterised by a flat pure-tone audiometry caused by the atrophy of stria vascularis³⁶. Additional types have been described: *mechanical* (cochlear/conductive hypothetical) with changes in the basilar membrane affecting its properties and function, and *mixed and indeterminate* when multiple influences interact³⁷. However, sound perception depends not only on normal cochlea but also on the function of the auditory pathway, which may explain the fall of discrimination, in particular in noisy environments, and increasing evidence supports a pivotal role of central auditory processes (CAP) in presbycusis. The role of CAP is well established in several behavioural phenomena such as sound localisation and lateralisation, auditory discrimination, temporal aspects of audition (temporal resolution, masking, integration and ordering), auditory performance with competing acoustic signals and auditory performance with degraded signals. Even if the simplest auditory tasks are influenced by higher-level, non modality-specific factors as attention, learning, motivation, memory and decision processes and higher level contextual information influence the perceptual analysis of the acoustic signal; while various knowledge sources interact and support the auditory processing of spoken language and other complex acoustic signals. Briefly, central auditory process disorders (CAPDs) concern an auditory perceptual dysfunction that cannot be explained on the basis of peripheral hearing loss and refer to impairment in central auditory pathways, such as neural transmission, feature extraction

deficit, or information processing problems that lead to impaired speech understanding. CAPD can affect all people at any age (even children or young adults) as a consequence of brain focal injuries, or neurological and genetic disorders³⁸⁻⁴².

The existence of ARHL decline in CAPD is well established, but the mechanism and effects are still controversial. While the presence of a pure CAPD seems to be uncommon in older patients, the evaluation of comorbidity between central and peripheral damage using central auditory testing in these patients may be challenging. The prevalence of ARHL and CAPD in a population older than 65 years was 64.1 and 14.3%, respectively⁴³. Furthermore, studies on the association between CAP dysfunction and MCI or AD are limited⁴⁴. Many authors identified these disorders in the auditory portions of the central nervous system without clear lesions³⁹. The pathophysiology of CAPD is not fully understood, probably involves interhemispheric interaction and *corpus callosum* function. CAPD tests typically require extracting auditory signals in noise or competing signals and the diagnosis of a CAPD can be very tricky in older patients even affected by cognitive decline^{39,41}. Gates et al.^{16,45} investigated the relationship between CAPD and dementia. In a first study they found that CAPD was evident in subjects with mild AD, whereas peripheral auditory function was not different from control subjects. A link between CAPD and cognitive dysfunction is also explained by the observation that older patients with CAPD seem to be more prone to experience dementia than those without CAPD. Furthermore, in older people with mild, amnesic, single domain cognitive impairment (MCI), severe CAPD is more prevalent than in people with normal cognitive status and the presence of CAD is more likely to be associated with an increased risk of dementia diagnosis in the follow-up period^{46,47}. Gates et al.⁴⁵ in a 3-year follow-up study showed that severe CAPD was predictive for the risk of subsequent diagnosis of AD. Moreover, as recently reviewed by Panza et al.⁴⁴, longitudinal studies also confirmed that the peripheral ARHL is associated with decline of several cognitive domains and accelerated cognitive decline. As previously mentioned, diagnosis of CAPD is clinically argue and results of auditory central testing controversial.

From 2009 to 2011, the America Academy of Audiology Task Force on Central Presbycusis reviewed 145 papers to understand the evidence on age-related changes in auditory portions of the central nervous system and the impact of such changes on everyday communication and function. Based on this review of the literature, the authors concluded that the evidence for the existence of central presbycusis in the isolated entity is insufficient⁴⁸. On the other hand, recent findings support the existence of central presbycusis as a multifactorial condition that involves age- and/or disease-related changes in the auditory system and brain⁴⁴.

Age-related changes in the human central auditory system: morphological and neuroimaging evidence

In the last years, increasing interest has been focused on neuroplasticity of the brain which indicates the changes of its structure and function in response to environment and experience occurring in both synaptic, network and anatomical levels. It is common sense that an “active” life is beneficial for the mind and brain. In fact, it is well known that both physical and intellectual activity have a positive influence on the incidence of neurodegenerative disorders and cognitive decline. Recently, it has been described that enriched environment improves learning, enhances neurogenesis and branching, synapse formation and activity of neurotrophic factors^{33,34}.

In principle, ageing causes cortical atrophy, which is accompanied by shrinkage of grey and white matter volumes and enlargement of the cerebrospinal fluid space⁴⁹. Post-mortem analyses have shown a decline in the number of dendrites, synapses and neuronal fibres without direct loss of neurons⁵⁰. Thus, as also discussed in the previous paragraph, lifestyle and environment can modulate neuroplasticity even in aged adults, who can be affected by neurobiological and anatomical changes. Major modifications include white matter de-myelination and grey matter shrinkage, altered neurotransmission and neural atrophy that can be enhanced by visual and hearing deprivation involving neural connectivity and brain organisation. In this field, studies are still ongoing. However, growing contributions by neuroimaging and neurobiological findings suggest a cortical and neuronal reorganisation after hearing loss in consequence of adaptive or maladaptive plasticity observed in neurodegenerative diseases and HL induced by exogenous factors or ageing^{33,34}.

It has been recently demonstrated by MRI that subjects with hearing impairment have accelerated rates of whole brain atrophy as well as specific volume declines in the right superior, middle and inferior temporal gyri over a mean 6.4 years of follow-up¹⁷. These findings extend the discussion on whether peripheral hearing impairment has broader implications for brain structure and function. Pri-

or cross-sectional neuroimaging studies demonstrated that greater audiometric hearing impairment is associated with reduced volumes in the primary auditory cortex and temporal lobe²⁸⁻³⁰. Other studies, using diffusion-tensor imaging of central auditory pathways, demonstrated decreased fractional anisotropy in the lateral lemniscus and inferior colliculus in individuals with hearing impairment versus those with normal hearing^{31,50}. The temporal regions are intriguing because they are important not only for spoken language processing, but also for semantic memory and sensory integration, and are involved in the early stages of mild cognitive impairment or early AD⁵². A shared neuropathological or intrinsic cellular ageing process leading to both cochlear and brain ageing is a mechanistic option. Hearing impairment may also be potentially associated with brain volume changes through reduced neural stimulation of the auditory cortex by impoverished auditory signals²⁸. New insights on the biochemical changes in the auditory cortex have been detected by MR spectroscopy, which is an interesting tool for studying cortical mechanisms. In a recent report⁵³ it was demonstrated that ARHL is accompanied by the reduction of the excitatory activity in the auditory cortex. By using MR spectroscopy, the authors examined metabolite levels in the auditory cortex of subjects older than 65 years either with mild or severe presbycusis, demonstrating significant lower concentrations of glutamate and N-acetylaspartate in aged subjects with increased levels of lactate. Significant differences were not found in other metabolites, including GABA, which is the most important inhibitory neurotransmitter. In summary, the older brain suffers not only from atrophy but also from changes in the content of some metabolites affecting both grey and white matter even if the morphological findings in neuroimaging are still controversial. We expect that in the future robust evidence will be obtained by improvements in neuroimaging techniques. In principle, there is substantial evidence supporting the hypothesis that the modifications observed in the brain in patients affected by ARHL depend more on ageing than on hearing impairment.

Impact of ageing and hearing loss on linguistic abilities

Evidence on the relationship among ageing, hearing loss and linguistic abilities is scarce, however the question of how hearing impairment affects linguistic abilities due to the consequences on the quality of life (i.e. social isolation, depression, etc.) remains an interesting feature. In principle, linguistic abilities do not seem to be affected by age. Although there is little loss of word knowledge, word retrieval during speaking becomes slower and more difficult⁵⁴. This can lead to more frequent occurrences of “tip-of-the-tongue” status, where a desired word or person’s name is known, but there is difficulty in its retrieval^{55,56}.

On the other hand, spoken language comprehension tends to be preserved, despite atrophy in the neural regions involved. Some functional MRI studies identified a two-component model of sentence comprehension: a core sentence-processing area located in the perisylvian region of the left cerebral hemisphere and an associated network of brain regions that support working memory and other resources needed for comprehension of long or syntactically complex sentences⁵⁷⁻⁵⁹. In fact, working memory is known to constrain the comprehension of sentences with complex syntactic structures⁶⁰ that result in adults in the alteration in producing syntactically complex utterances. The syntactic organisation represents a special burden on working memory⁶¹.

Although, there is a question of whether all aspects of language processing are constrained by a single working memory resource or by a complex of specialised resources⁶², there is no doubt that working memory limitations affect cognition in aging adulthood. It might be predicted by two observations: firstly, complex syntax and rapid speech rates operate in a multiplicative fashion in affecting sentence comprehension⁶³. Secondly, in spoken language comprehension, it is well known that recognition is superior for words heard within a meaningful sentence than for words heard in isolation. This longstanding observation reflects the general principle that the amount of sensory information needed for correct recognition of any stimulus will be inversely proportional to its probability within a constraining context⁶⁴.

This generality, although correct, overlooks the potential importance of the cognitive effort required for comprehension of speech that is syntactically complex⁶⁵.

This is important for word recognition because understanding the meaning of a sentence is the force that constrains the probability of a particular word in that context. The comprehension of syntactically complex speech may draw on working memory resources that are already limited in normal ageing⁶⁵; many studies have shown differential effects of syntactic complexity on older adults' comprehension relative to that of younger adults. This latter aspect has been investigated in older adults with hearing loss, because the decreased activation of specialised processing regions of brain, and limited ability to coordinate activity between regions, contribute to older adults' difficulty with sentence comprehension under difficult listening condition⁶⁶. In fact, it would be expected that when older adults with already limited working memory resources are further strained by perceptual effort attendant to even a mild hearing loss, the negative effects on sentence comprehension of age and syntactic complexity can be further multiplied⁵⁹.

Stewart and Wingfield⁶⁷ confirmed the common findings of better report accuracy for meaningful sentences than for words heard in isolation without a sentence context, but for older adults there was also a significant effect of

syntactic complexity of sentence stimuli. This effect was further increased by HL. These results are interpreted in terms of age-limited working memory resources that are impacted both by the resource demands required for comprehension of syntactically complex sentences and by effortful listening attendant to hearing.

An interesting study analysed the role of hearing acuity, age and verbal and cognitive ability in word recognition when words are heard in the absence of a linguistic context, or when heard preceded by varying degrees of contextual constraint. Results emphasise the importance of cognitive function in auditory performance⁵⁷⁻⁵⁸, showing in addition, that as the degree of contextual support from a linguistic context increases, the relative contributions of cognitive ability and hearing acuity are reversed. Specifically, in a neutral context there is a large role for hearing acuity on word recognition and a modest role for cognitive ability. By contrast, in the highest context condition, hearing acuity was no longer a significant predictor, but general cognitive ability played a significant role. These findings underscore the need to take into account the relationship of individual differences in cognitive ability and constraints of linguistic context, as well as hearing acuity.

Impact of hearing loss on physical activity and quality of life in the elderly

As previously adduced, maintaining an optimal level of physical functioning is a critical aspect of healthy aging, however, longitudinal studies on the association of hearing impairment with incident functional are not conclusive, with some studies demonstrating a positive association¹¹⁻¹³, and other contributions denying⁶⁸. This heterogeneity on results is likely explained by differences in how hearing (e.g. subjective self-report³ vs objective clinical audiometry) and physical functioning (e.g. activities of daily living, walking difficulty, falls) or other self-reported measures were quantified⁶⁸⁻⁷².

Chen and colleagues⁷³ reported that subjects with average greater hearing impairment had poorer short physical performance battery scores and slower gait speeds at two time points 10 years apart, which were also reflected in an increased risk of incident disability and requirement for nursing care in women. Moreover, Gispén et al.⁷⁴ showed that moderate or severe hearing impairment in older adults was independently associated with less physical activity as measured subjectively by the self-report and objectively according to accelerometry. Patients with moderate or severe hearing impairment had a 59% greater possibility of having lower levels of self-reported physical activity and 70% greater odds of having lower levels of accelerometer-measured physical activity than those with normal hearing. Interestingly, several studies have demonstrated associations between HL and poor physical functioning⁷⁵⁻⁸⁰, poor cardiorespiratory fitness, sedentary behaviour and slow

gait speed in older adults⁸¹. In contrast, other reports have indicated that there is no significant association between HL and physical functioning and activity⁸². Subjective measurement⁸³ or varying definitions⁸⁴ of hearing may explain the reported heterogeneity in study results.

Different mechanisms can explain the observed association between hearing and physical activity. Individuals with moderate or greater hearing impairment may perform less physical activity because they are socially isolated (and thus have less likelihood of exercise in a social setting) than those with normal hearing. Studies have also demonstrated that impaired hearing can contribute to cognitive load and therefore affect attentional and cognitive resources^{11 17} that are important for maintaining posture and balance⁸⁵. Impaired hearing can restrict the ability to monitor the auditory environment effectively (e.g., hearing footfalls and other auditory cues that provide orientation to the physical environment), thereby affecting the likelihood of performing physical activities. Alternatively, common pathological processes may underlie impairments in hearing and physical activity. Accordingly with the evidence for a link between presbycusis and cognitive impairment as described above, cardiovascular disease may contribute to HL⁸³ and poorer health and physical activity. In fact, HL in older patients is often associated with cardiovascular disease (e.g., congestive heart failure, coronary artery disease, angina pectoris, myocardial infarction, hypertension, smoking status, BMI). Alternatively, common neural degeneration affecting not only the cochlea but also the vestibular organ, involved in the balance control, can explain the relationship between HL and poor physical activity.

Growing findings indicate that in older patients *frailty* represents a clinical syndrome characterised by decreased physiologic reserve and weakness that causes an increased vulnerability to stressors⁸⁶. The prevalence of frailty is increased in the institutionalised population. Epidemiologic studies investigating the association of HL with frailty and physical functioning suggest that moderate to severe HL seems to be associated with increased risk of developing frailty, independently of age, demographic characteristics and cardiovascular risk factors². Further studies are needed to determine the pathogenesis of this association. It is interesting also to take into consideration the effects of *dual sensorial impairment* (i.e. hearing and visual loss, DSI) in older patients and their relationship with cognitive decline. Obviously the effects of late-onset DSI depend by the severity of sensorial impairments in both ears and eyes, however it is demonstrated that DSI affects physical, psychological, and psychosocial well-being⁸⁷. Furthermore, Lin et al.¹¹ reported that, patients affected by DSI had the greatest odds of cognitive and functional decline, although the risk was not different in patients with visual impairment alone suggesting that the presence of HL does not further decreased the effects on cognition. Nevertheless, more studies are needed to better understand the in-

teraction of visual and hearing impairment in older adults. Finally, as a consequence of all the aspects interfering with the good health of older patients, Genter et al.⁸⁴ found that HL was associated with a 34% increased risk of mortality compared with normal hearing in community-dwelling older adult aged 70-79. After adjustment for other demographic characteristics (sex, education, and study site) and cardiovascular risk factors (diabetes, stroke, and smoking), HL was associated with a 20% increased risk of mortality compared with normal hearing⁸⁴. Two studies examined the association of audiometric HL with mortality. The first paper performed in adults aged 70 and older found an association between HL and mortality after adjusting for demographic characteristics, but this association disappeared after adjusting for various health factors⁸⁸. A second study conducted in adults aged 50 and older used structural equation modeling and found an association between HL and mortality that was mediated through cognitive impairment and walking disability⁸⁹. Finally, in adults aged 67 and older an association between objective HL and increased cardiovascular mortality has been found, but not with all-cause mortality⁹⁰. In contrast with these findings, in others studies this association seems to be inconsistent, so we agree that additional studies are needed in proving the relationship between HL and overall mortality⁹¹⁻⁹⁴.

The impact of hearing aids and cochlear implant on elderly deaf patients

On the basis of “a cascade hypothesis” between HL and cognitive decline the natural consequence is that the use of hearing aids (HA) or cochlear implant should be associated with better cognitive performance. It is evident that older adults with untreated moderate to profound hearing loss may develop a cascade of conditions including communication difficulties, social isolation, depression, an association with falls and declines in physical functioning, decreased quality of life and even cognitive decline that could be counteracted by HA (Fig. 3). However, few studies investigated whether auditory amplification can reduce the risk of cognitive decline and dementia. A recent paper addressed the positive association of HA use on cognition that was independent of any positive association of hearing aid use on social isolation and depression. Therefore, the authors suggested that the effects of HA on cognition was not correlated to the reduction of the adverse effects of hearing loss on social isolation or depression and probably related to the direct impact on the hearing amplification on daily life⁹⁵. How HA impact on cognitive performance through a reduction of depression or social isolation or, as a direct consequence, remains controversial. Furthermore, the question how hearing aids might interfere with cognitive decline remains unexplained. Accordingly with the hypothesis suggested by the Dawes et al.⁹⁵ untreated hearing loss may increase

the effect of auditory deprivation on the brain resulting in increased cognitive decline. Moreover, cognitive decline can reduce social participation, increase isolation and depression thus reducing the interest for hearing rehabilitation. A randomised clinical trial of HL treatment⁹⁶ that examined outcomes beyond measures of speech perception and quality of life, demonstrated improved social and emotional function, communicative abilities and cognitive function in the treatment group. Unfortunately, the reported prevalence of HA users in older adults varies from 21.5% in UK, 11.0% in Australia and approximately 14% in the US with a level of satisfaction that is lower than in young and adult patients⁶⁹⁷. Possible explanations for the no-use of HA are the poor quality of amplified sound, the availability of technological solutions and the cost for hearing aids. Further research is needed to determine whether HA independently improves the quality of life of these patients.

An interdisciplinary approach and collaboration between otolaryngologists and neuro-psychologists is mandatory to investigate and address hearing loss in the context of brain and cognitive aging for a correct management of older patients and the decision for hearing aids or cochlear implant (CI).

In the last two decades, the literature has been enriched by several studies based on speech perception outcome, comparing younger and older adult CI recipients. Older adults underwent to CI achieve significant improvement in speech perception performance scores over preoperative performance with conventional amplification⁹⁸. Furthermore, older adults can continue to benefit from cochlear implantation with long-term use although psychosocial changes, hearing deprivation length, age at implantation, and reduced cognitive and learning abilities influence outcomes in elderly patients. A recent paper from Lin's Group² addresses the positive impact of both HA and CI on mental health quality of life. Interestingly, the authors found that patients who received CI had twice the gain in the mental component summary score compared to HA recipients at 6 and 12 months after amplification. Di Nardo et al.⁹⁸ compared auditory performances and several quality of life outcomes between under 60 years CI users and over 60 years recipients. They found a significant benefit on speech recognition tests compared to preimplantation condition, even if younger CI users scored significantly better in both bisyllabic words and sentences recognition test. No significant difference was found between the study and control group in physical and mental health status, conversation with an outsider, or use of TV and phone. Overall satisfaction derived from CI was higher in the older than in the younger patients. These findings indicate a high level of satisfaction and a dramatic improvement in quality of life and communication abilities after cochlear implantation in elderly people with postlingually bilateral severe-to-profound hearing

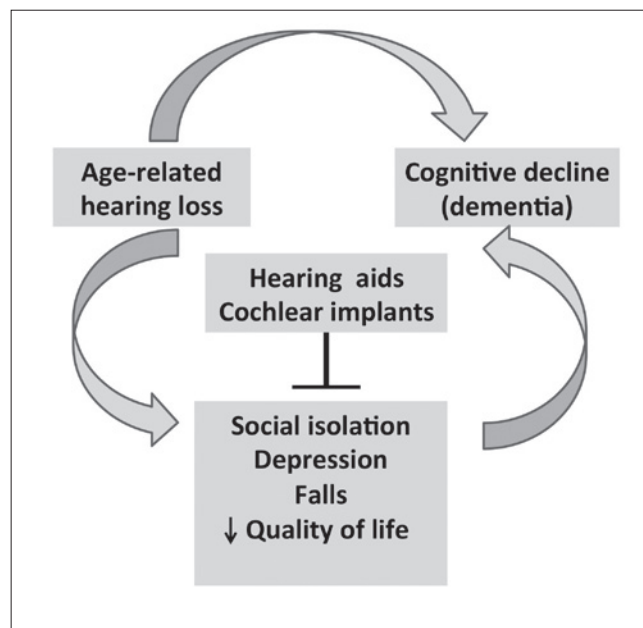


Fig. 3. Untreated moderate to profound hearing loss may develop a cascade of conditions including communication difficulties, social isolation, depression, falls and decreased quality of life that could be counteracted by hearing aids and cochlear implants.

loss that cannot be explained only by enhancements to auditory perception. More studies that demonstrate a link between CI rehabilitation and cognitive level will be challenging. In 2015, Miller et al.⁹⁹ reviewed 5057 articles and concluded that only 3 studies met the full criteria for this topic. The overall results were inconclusive in terms of cognitive benefit provided by cochlear implantation. Mosnier et al.¹⁰⁰ conducted a prospective study on impact of cochlear implant in old people and concluded that hearing rehabilitation using cochlear implantation is associated with an improvement in function in all cognitive domains as early as 6 months after implantation in elderly patients who had abnormal test scores at baseline. More than 80% of patients who had the poorest cognitive scores before implantation improved their cognitive function at the 1-year post implantation interval. In contrast, patients with the best cognitive performance before implantation demonstrated stable results. These preliminary results have never been confirmed in a trial with a larger and more representative cohort. Further research is thus needed to evaluate the long-term influence of hearing restoration on cognitive decline and its effect on public health.

Conclusions

Robust evidence suggests that HL in the elderly is independently associated with development of cognitive decline and dementia. Several hypotheses on the pathogenic relationship between HL and cognitive decline have been

postulated and summarized in a conceptual model in which the hearing impairment impacts cognitive load, changes in brain structure and function, leads to social isolation and depression related with a common aetiology (i.e. genetic and environmental factors).

HL and their putative effects on cognition are highly prevalent in older patients and their effects may be preventable and treatable with rehabilitative devices (i.e. hearing aids and cochlear implants) that remain widely underutilised. Further research is needed to understand if and how hearing aids and cochlear implants can change the natural history of these conditions and improve quality of life in the elderly.

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