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Review

Age-related hearing loss and tinnitus, dementia risk, and auditory amplification outcomes

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ABSTRACT

Age-related hearing loss (ARHL) or presbycusis, as the third leading cause of chronic disability in older adults, has been shown to be associated with predisposing cognitive impairment and dementia. Tinnitus is also a chronic auditory disorder demonstrating a growth rate with increasing age. Recent evidence stands for the link between bothersome tinnitus and impairments in various aspects of cognitive function. Both ARHL and age-related tinnitus affect mental health and contribute to developing anxiety, stress, and depression. The present review is a comprehensive multidisciplinary study on diverse interactions among ARHL, tinnitus, and cognitive decline in older adults. This review incorporates the latest evidence in prevalence and risk factors of ARHL and tinnitus, the neural substrates of tinnitus-related cognitive impairments, hypothesized mechanisms concerning the association between ARHL and increased risk of dementia, hearing amplification outcomes in cases with ARHL and cognitive decline, and preliminary findings on the link between ARHL and cognitive impairment in animal studies. Given extensive evidence that demonstrates advantages of using auditory amplification in the alleviation of hearing handicap, depression, and tinnitus, and the improvement of cognition, social communication, and quality of life, regular hearing screening programs for identification and management of midlife hearing loss and tinnitus is strongly recommended.

1. Introduction

Among all sensory deficits associated with aging, deterioration in hearing is the most impressive decline in humans (Howarth and Shone, 2006). Population studies estimate the prevalence of significant hearing loss (average of pure-tone thresholds $_{0.5–4.0\,kHz} > 25$ dB HL) of those aged 60–80 years at 21–27% (Cacciatore et al., 1999; Dalton et al., 2003; Gopinath et al., 2009a; Hogan et al., 2009; Lohler et al., 2019). In the Baltimore study on adults aged 70 years and older, the prevalence of significant age-related hearing loss (ARHL) in the better ear was 63.1% (Lin et al., 2011c). A large body of evidence demonstrates ARHL to be detrimental to physical and mental health, cognition, independence, social interaction, and quality of life in the elderly and that it can precipitate the early landmarks of dementia and Alzheimer's disease (AD) (Cherko et al., 2016; Cosetti and Lalwani, 2015; Taljaard et al., 2016). Even mild levels of hearing loss may increase the long-term risk of developing cognitive decline and dementia (Albers et al., 2015; Fortunato et al., 2016). Hearing ability provides communication through speech, informs warning of potentially injurious events occurring outside the visual field, and develops our feelings and realization of music and nature. The stronger impact of hearing loss is manifested by profound consequences on verbal communication, and the social, functional, and psychological well-being of the person (Howarth and Shone, 2006; Lee, 2015; Swords et al., 2018). Even though the complex etiology of the dementia is not fully understood, modifiable risk factors related to lifestyle characteristics, environmental risks, and diseases were shown as the underlying reasons in 35% of cases (Livingston et al., 2017). Hearing loss, which is the third most challenging disability in older adults, also acts as the most effective risk factor associated with dementia (Livingston et al., 2017; Loughrey et al., 2018).

Dementia is a progressive neurodegenerative disorder associated

Abbreviations: Aβ, amyloid-beta; AD, Alzheimer's disease; ARHL, age-related hearing loss; CAEPs, central auditory evoked potentials; CAPD, central auditory processing disorder; CI, cochlear implant; fMRI, functional magnetic resonance imaging; GABA, gamma-aminobutyric acid; GRM7, glutamate receptor, metabotropic, 7; HA, hearing aid; HINT, hearing in noise test; IGF, insulin-like growth factor 1; IL-1β, interleukin-1β; MCI, mild cognitive impairment; RCT, randomized controlled trials; SNHL, sensory-neural hearing loss; WHO, World health organization

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with cognitive impairment, neuropsychiatric symptoms, sensory and physical disabilities, dependency, caregiver burden, substantial health care expenditures, and premature death (Fiest et al., 2016; Fischer et al., 2016; Luo et al., 2018). Sensorineural systems play a crucial role in the diagnosis, treatment, and management of diverse neurological disorders (McGilton et al., 2016; Panza et al., 2019). Recent evidence indicates that sensory and motor changes may precede the cognitive symptoms of dementia by several years and may increase the risk of developing AD (Albers et al., 2015). The function of the ear and eye represents a unique pathway for exploring various conditions in cognitive decline or dementia. Vision impairment (low vision with visual acuity < 20/70) and ARHL were reported in 18% (Crews and Campbell, 2004) and 50% to two-thirds (Albers et al., 2015; Cruickshanks et al., 1998b; Fortunato et al., 2016) of individuals aged 70 years or over respectively. Notably, the prevalence of such sensory impairments among adults with dementia is estimated to be higher than in those who are cognitively intact (Fischer et al., 2016; Fortunato et al., 2016; Uhlmann et al., 1991).

ARHL is linked to an increased risk of the onset of dementia 5 to 10 years later (Albers et al., 2015). A case-control study on older adults with AD or other forms of cognitive impairments demonstrated a significant hearing loss in more than 90% of cases compared to age-matched controls (Gold et al., 1996). Extensive evidence links midlife hearing loss to the more rapid progression of cognitive decline and incidental dementia (Davies et al., 2017; Fortunato et al., 2016; Golub et al., 2017), hence a mild hearing loss is equivalent to the effect of brain aging by 6.8 years (Lin et al., 2011a). The severity of peripheral hearing loss is also related to an increased loss of performance in both verbal and nonverbal cognitive tests and accelerated development of dementia (Albers et al., 2015; Lin, 2011; Lin et al., 2011a,b; Lin et al., 2011c; Peracino and Pecorelli, 2016). As many aspects of daily living are associated with good hearing, studies suggest that the reduction of auditory inputs affect the quality of life, social relationships, motor skills, psychological functioning, and morphology and function of specific brain regions (Fortunato et al., 2016). For example, studies demonstrate the relationship between the severity of hearing loss and the reduction of signals in functional magnetic resonance imaging (fMRI) across all major neural components along the auditory neural pathways (Peelle et al., 2011). Hearing loss is also linked to compensatory recruitment of regions in the frontal and temporoparietal cortex that functions to maintain speech-language processing in older adults (Wingfield and Grossman, 2006). The cognitive load resulting from hearing loss could, therefore, result in the reduction of cognitive resources available for other cognitive functions, which leads to a diminished cognitive reserve and a predisposition to the occurrence of dementia symptomatology (Albers et al., 2015; Stahl, 2017; Swords et al., 2018).

The present review is a comprehensive multidisciplinary study on diverse interactions among ARHL, tinnitus, and cognitive decline in older adults. We hypothesized that a neuroscientific view in describing the basic and new concepts linked to this subject from diverse but associated fields of studies (e.g., gerontology, neurology, otology, audiology, and neuroscience) could synergistically improve the general knowledge in this area and stimulate the emergence of novel ideas for future research. The review begins with a detailed description of the epidemiology and risk factors of ARHL and its link with mental health symptoms. In this section, we also have a new look at tinnitus (phantom perception of sound) as one of the most challenging disorders of the auditory system that is related to hearing loss in its chronic form and worsens with increasing age (Aazh et al., 2017; Konig et al., 2006; Schecklmann et al., 2014). Then, the review is followed by an extensive overview of the latest evidence supporting the idea that the increased cognitive load resulted from ARHL can enhance the risk of developing cognitive decline or dementia. The hypothesized mechanisms underlying the association between ARHL and increased cognitive decline are also discussed. Given existing treatment options for auditory amplification in ARHL, we have also reviewed the latest evidence regarding the impact of aural rehabilitation services, (i.e., hearing aids or cochlear implants), as the most low-risk treatment option nowadays for improving memory, cognitive function, and mental health. The review ends by a brief report of a few preliminary studies in rodents exploring the neurobehavioral alterations supporting the relationship between ARHL and increased risk of cognitive impairment, as well as some conclusions and suggestions for future studies.

2. Prevalence and risk factors of age-related hearing loss (ARHL)

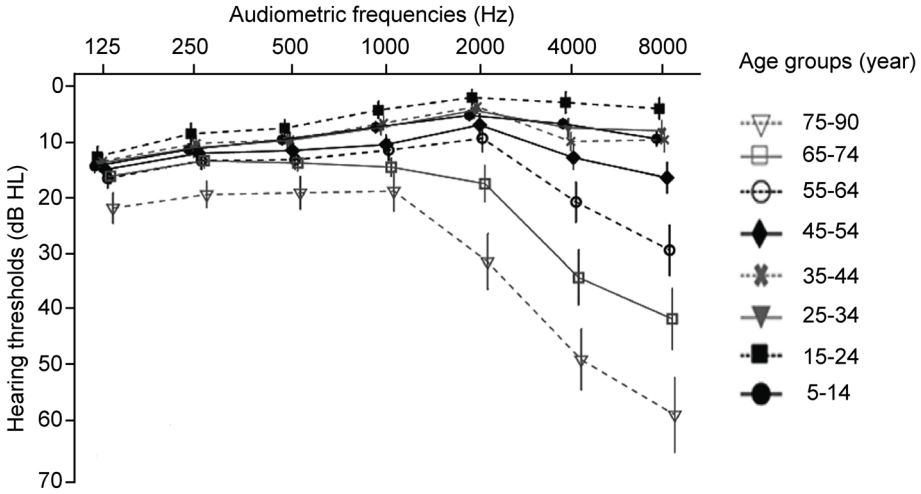
2.1. ARHL: peripheral and central

ARHL (presbycusis), a gradually progressive bilateral symmetrical sensory-neural hearing loss (SNHL), is mild to moderate in nature that affects the audiometric mid to high frequencies (2–8 KHz) resulting from the aging process (Fig. 1A). ARHL is a complex phenomenon characterized by audiometric threshold shift, degradation in speech-understanding, and speech-perception difficulties in adverse listening conditions such as reverberant and noisy environments or speech in noise (Gates and Mills, 2005; Howarth and Shone, 2006; Lee, 2013). ARHL is basically classified into six categories (i.e., sensory, neural, metabolic or strial, cochlear conductive, mixed, and indeterminate types), according to the audiometric tests' results and temporal bone pathology (Fig. 1B). These categories often combine in the aging ear, and the metabolic type is the pivot of ARHL types (Gates and Mills, 2005; Howarth and Shone, 2006). Overall, the prevalence of hearing loss entirely increases with every age decade from 5 to 10% at age 40 to about 80–90% at age 85. The incidence of new cases of hearing loss also rises sharply from about 2% at age 40 to 6% at age 65 (Eggermont, 2017).

The aging process of the auditory system, which manifests by the loss of receiving auditory inputs from the periphery (Fig. 1C), can also result from damage to the central parts of the auditory processing (Fig. 1D) (Pickles, 2015). Deteriorations in peripheral organs are partially driven by the loss of hair cells as well as the dysfunction of the stria vascularis (Ouda et al., 2015). Current evidence, however, suggests that central presbycusis may run independently of physiological deterioration of the peripheral organs (Gates and Mills, 2005; Ouda et al., 2015). The cascade of processing meaningful auditory stimuli, such as vocal sounds in animals and speech comprehension in humans, is a complex phenomenon that comprises both peripheral and central auditory pathways, as well as the auditory cortex and its interaction with many other parts of the brain (Hickok et al., 2011; Hickok and Poeppel, 2007; Ouda et al., 2015; Skipper et al., 2017) (Fig. 2). For instance, MRI studies using voxel-wise and region of interest (ROI) analyses demonstrate age-related vulnerabilities of the neural speech system after controlling for peripheral hearing loss (Bilodeau-Mercure et al., 2015). Thus, any age-related or pathological circumstances in the auditory system and the associations of the auditory cortex with other cortical areas can impact the quantity and quality of the auditory processing (Basner et al., 2014; Lin et al., 2011a). It is expected that the findings of functional neuroimaging studies with complex auditory tasks in humans can shed more light on our understanding of the central brain regions contributing to the perception of auditory stimuli and may also lead to updates in classifying ARHL.

Although some studies suggest central auditory dysfunction as a harbinger of AD (Gates et al., 2011; Panza et al., 2015; Swords et al., 2018; Warren and Bamiou, 2018), research on diverse fields of hearing science may not be on the same page given the nature of central presbycusis. Central auditory dysfunction is distinct from peripheral hearing loss. Deficits in central auditory processing are characterized by difficulties in understanding speech in noise that are not explained by cochlear peripheral (cochlear) hearing loss and do not improve with using hearing amplification systems (Gates, 2012). The development of a central hearing impairment that follows the onset of AD is rare, at 2%

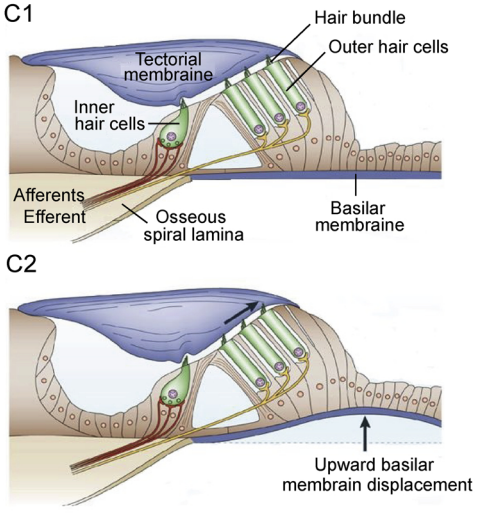
A Progress of age-related hearing loss (ARHL)



B Basic categories of ARHL (presbycusis)

Cochlear lesion	Pathology	Audiometric configuration
Sensory	Reduction of sensory cells in basal turn of cochea	Abruptly sloping high frequency hearing loss above the speech frequency range
Neural	Loss of cochlear neurons	Progressive loss of speech discrimination in the presence of stable pure-tone thresholds
Strial	Metabolic and vascular changes within cochlea	Slowley progressive hearing loss with flattening of audiogram and good speech discrimination
Conductive	Changes in the conduction or resonance of the cochlear duct	Linear descending pattern on audiogram
Mixed	Combination of above	Mild to moderate high frequency hearing loss
Intermediate	None of the above charactristics, the likelihood of cellular impairment	Flat or abrupt high frequency hearing loss

C Cellular structure of the organ of Corti



D The main ascending auditory neural pathway

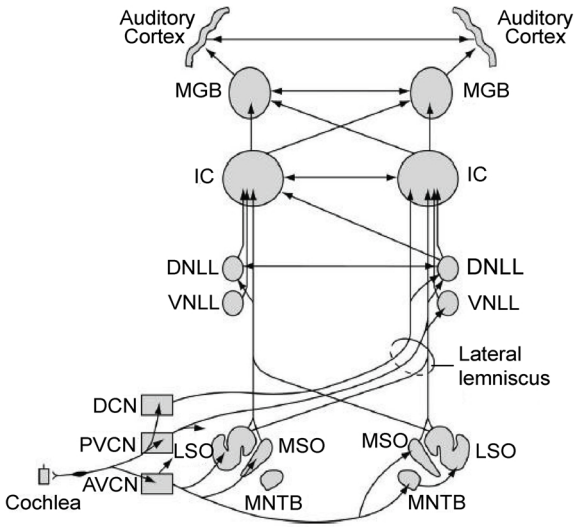


Fig. 1. Age-related hearing loss (ARHL) and the peripheral and central parts of the auditory system. A) Mean and 95% confidence interval of hearing thresholds per age group (reproduced by permission from Taylor & Francis, International Journal of Audiology, Rodríguez Valiente, et al., 2015). B) Pathologic-based categorization of ARHL (Howarth and Shone, 2006; Gates and Mils, 2005). C) The cellular structure of the organ of Corti. C1) Cross-section of the organ of Corti (~150 μm wide) through a middle turn of the cochlea, commonly three rows of outer hair cells and one row of inner hair cells. C2) The tectorial membrane is above the cells which can move in response to pressure variations in the fluid-filled tympanic and vestibular canals. Signals from each inner hair cell are relayed to the brain via 10 to 20 afferent fibers of the eighth cranial nerve. Outer hair cells have both sensory and motor capabilities and possess electromotility that underlies the cochlear amplifier (reproduced by permission from Nature Publishing Group, Nature Reviews Neuroscience, Fettiplace and Hackney, 2007). D) The main ascending auditory neural pathways in humans (reproduced by permission from Elsevier, Handbook of Clinical Neurology, Pickles, 2015). Abbreviations: AVCN, anteroventral cochlear nucleus; DCN, dorsal cochlear nucleus; DNLL, dorsal nucleus of the lateral lemniscus; IC, inferior colliculus; LSO, lateral superior olive; MGB, medial geniculate body; MNTB, medial nucleus of the trapezoid body; MSO, medial superior olive; PVCN, posteroventral cochlear nucleus; VNLL, ventral nucleus of the lateral lemniscus.

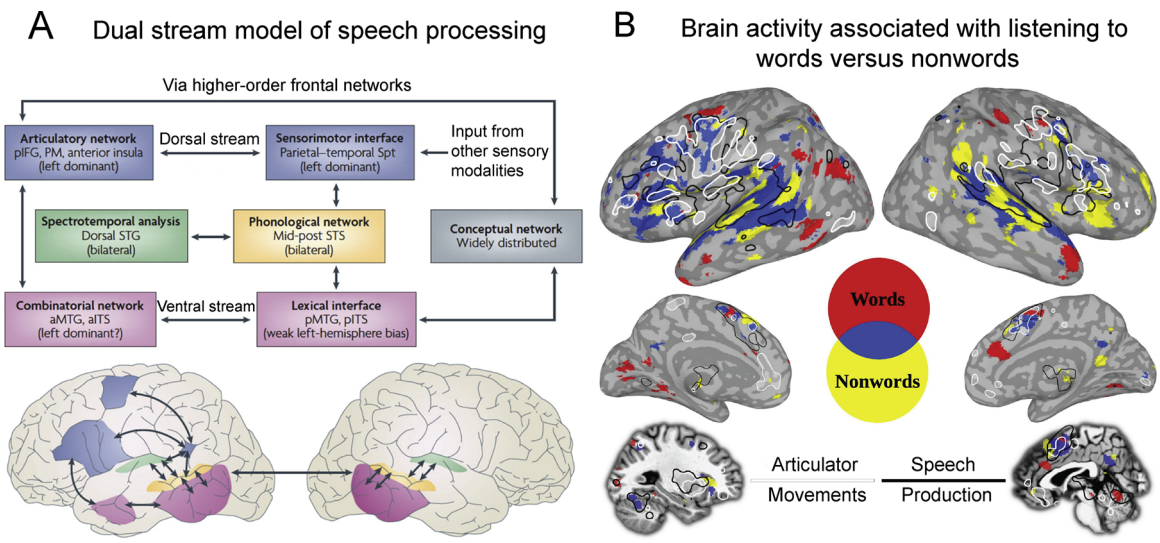


Fig. 2. Brain areas underpinning language processing. A) The dual-stream model holds that early stages of speech processing occur bilaterally in auditory regions on the dorsal STG (green) and STS (yellow) and then diverge into two broad streams: a temporal lobe ventral stream supports speech comprehension (lexical access and combinatorial processes; pink) whereas a strongly left dominant dorsal stream supports sensory-motor integration and involves structures at Spt and frontal lobe. The conceptual-semantic network (gray box) is largely distributed throughout the cortex. (reproduced by permission from Nature Publishing Group, Nature Reviews Neuroscience, Hickok and Poeppel, 2007). B) Neuroimaging meta-analyses of non-speech related movement of the vocal articulators, speech production, and natural or "passive" listening. Red and yellow colors demonstrate brain activity associated with listening to words versus non-words relative to high-level control conditions (e.g., matched stimuli or tasks) respectively. Blue points to the overlap of this activity. The outlined regions refer to activity patterns underlying speech production (black outlines) and moving the articulators without producing speech (white outlines) relative to high-level control conditions. Similar results comprising subcortical regions like the cerebellum have been presented in sagittal sections (reproduced by permission from Elsevier, Brain & Language, Skipper et al., 2017). Abbreviations: aITS, anterior inferior temporal sulcus; aMTG, anterior middle temporal gyrus; pIFG, posterior inferior frontal gyrus; PM, premotor; pITS, posterior ITS; pMTG, posterior MTG; Spt, Sylvian parietal-temporal; STG, superior temporal gyrus; STS, superior temporal sulcus.

of the older population (Livingston et al., 2017). Therefore, it is less likely that central auditory processing deficits (CAPD) play a significant contribution in the association between hearing loss and age-related mental diseases, i.e., dementia and AD (Gates et al., 2002; Livingston et al., 2017). In addition, from an audiological point of view, auditory cognitive impairments due to secondary changes in the central parts of the auditory nervous system that are driven by an enduring peripheral SNHL may not be classified as central presbycusis (Humes et al., 2012). Namely, the central auditory processing is not only affected by aging, but also by the reduction of auditory inputs from peripheral auditory organs. It has also been shown that the current tools are not sufficient for a reliable central auditory assessment, particularly in cases with peripheral hearing loss (Warren and Bamiou, 2018). Thus, future research is suggested to further elucidate the nature of the central presbycusis, as well as its likely contribution in predisposing cognitive decline and dementia.

2.2. Risk factors of ARHL

From an overall view, risk factors for ARHL can be divided into the modifiable (preventive) and non-modifiable (not or less preventive) risk, which points to the likely brain pathways involved. Risk factors also can generally be classified into four categories: cochlear aging, environmental risks (environmental and/ or occupational noise exposure, ototoxic medications), genetic predisposition, family history (sex, race, specific genetic loci/genes), and health co-morbidities (hypertension, diabetes, stroke, AD, atherosclerosis, cigarette smoking) (Cruickshanks et al., 2003; Fransen et al., 2008; Gates and Mills, 2005; Yamasoba et al., 2013). Studies demonstrate the higher risk of developing hearing loss with increasing age, sex (higher risk in males), and race (higher risk in African Americans). Genetic phenotype also accounts for a substantial portion of hearing loss risk, i.e., heritability indices of 0.35-0.55 (Yamasoba et al., 2013). For instance, a population-based study on data collected in six European countries demonstrated that common alleles of the GRM7 (glutamate receptor, metabotropic, 7) gene contribute to an individual's risk of developing ARHL, which suggests a possible role for glutamate toxicity in the pathophysiology of the disease (Friedman et al., 2009). Smoking has been shown to be associated with the increased risk of hearing loss with some controversial results of the dose effect (Cruickshanks et al., 1998a; Fransen et al., 2008). Noise exposure is also a known risk factor of hearing loss that can drive both auditory (hearing loss) and non-auditory effects (noise-induced sleep disturbance and annoyance, increased ischemic heart disease, and cognitive impairment, respectively) (Fritschi L et al., 2011; Jafari et al., 2018). It has been shown that 16% of disabling hearing loss in adults is attributed to occupational noise exposure (Eggermont, 2017). Noise-induced hearing loss and noise-induced tinnitus are auditory effects of noise that can be created by only a single exposure to an intense impulse sound (such as a sudden loud blast sound) or by a long-lasting exposure with moderate sound pressure levels (e.g., daily exposure with heavy construction equipment noise) (Basner et al., 2014).

2.3. ARHL and mental health symptoms

ARHL, depression, and anxiety are considered as the leading causes of disability worldwide (World Health Organization (WHO, 2017a), and can promote the occurrence of one another (Jayakody et al., 2018). ARHL is associated with a multitude of health outcomes, similar to those identified for depression, anxiety, and stress, such as increased risk of cognitive impairment and dementia, reduced quality of life, low level of activity, frailty, social isolation, and poor general health (Khalsa, 2015; Livingston et al., 2017). Dysfunction in social communication can be seen in individual's inability in coping with stressful situations and in managing personal, interpersonal, or geographic environments (Lozupone et al., 2018). ARHL, which is a source of stress and mental fatigue, can lead to social isolation and subsequent depression that may predispose individuals to cognitive decline (Mener et al., 2013; Peelle and Wingfield, 2016). A recent study demonstrated that hearing loss is a causative factor for clinically significant

depression, anxiety, and stress symptoms, and the severity of hearing impairment was linked to the severity of mental health symptoms (Jayakody et al., 2018). In line with the association between ARHL and mental health detriments in humans, recent animal studies also indicate that exposure to chronic stress, especially noise exposure, can precipitate the early landmarks of cognitive impairments, anxiety-like behavior, and AD-like neuropathological changes during the lifespan (Jafari et al., 2018; 2019).

3. Prevalence and risk factors of age-related tinnitus (ART)

3.1. Tinnitus and hyperacusis

Studies indicate an increased rate of hearing loss, tinnitus, and hyperacusis with increasing age, and their association has been discussed in many research papers (Aazh et al., 2017; Konig et al., 2006; Schecklmann et al., 2014). Tinnitus derived from the Latin word *tinnire* meaning "to ring," is the sensation of sound without any external acoustic sound source (phantom perception of sound) (Chari and Limb, 2018; Omidvar et al., 2018; Shargorodsky et al., 2010). Hyperacusis is also a kind of decreased sound tolerance that is characterized by negative reactions to the physical characteristics of certain daily sounds (e.g., spectrum and intensity) (Jastreboff and Jastreboff, 2015). It has been suggested that the emergence of hyperacusis is associated with the dysfunction of a unconscious part of the auditory pathways that produce significant distress and impairment in social, occupational, and recreational activities (Aazh et al., 2017; Jastreboff and Jastreboff, 2015). Tinnitus and hyperacusis can both be diagnosed with audiological tests and self-assessment questionnaires (Aazh et al., 2017; Aazh and Moore, 2017; Oiticica and Bittar, 2015; Park et al., 2017). The epidemiological studies estimate the prevalence of tinnitus to be 10–15% in the adult population (Gopinath et al., 2010; Lasisi et al., 2010; Shargorodsky et al., 2010) (Table 1). Distress from tinnitus interferes with quality of life and psychological behavior in severely affected individuals, which is approximately 1–2% of tinnitus patients (Ahmad and Seidman, 2004; Baguley et al., 2013; Fujii et al., 2011; Lasisi et al., 2010). The incidence rate (Martinez et al., 2015) and the prevalence of tinnitus increase by age (Fujii et al., 2011; McCormack et al., 2016; Oiticica and Bittar, 2015) up to approximately 70 years (Møller, 2011). For instance, from 10 to 19% prevalence in the general adult population to 24–45% in older adults (Sindhusake et al., 2003). Overall, there is a large variability in tinnitus prevalence estimation ranging from 5.1% to 42.7% resulting from a widespread inconsistency among studies in the clinical definition and reporting tinnitus (McCormack et al., 2016). The similar trend of age impact has been shown for hyperacusis (Adams and Marano, 1995; Paulin et al., 2016).

Whereas the prevalence of tinnitus is not directly related to the prevalence of hearing loss in the standard audiometric frequency range (125–8000 Hz) (Eggermont, 2017), chronic tinnitus is frequently accompanied by a hearing impairment. Nevertheless, it is still unknown whether hearing loss can lead to the development of tinnitus (Konig et al., 2006). Although the link between the pitch of the tinnitus sensation and the edge frequency of the audiogram (the frequency at which hearing loss worsens relatively abruptly) (Moore and Vinay, 2010) suggests a functional connection between tinnitus and hearing loss in individuals with high-frequency hearing loss, tinnitus also is seen in people with normal audiometric hearing. Many people with hearing loss do not also present symptoms of tinnitus (Eggermont, 2017; Konig et al., 2006). A steep audiogram (a sharp decrease in hearing levels after mid audiometric frequencies), however, can predispose the occurrence of tinnitus that results from an abrupt discontinuity in the activity along the tonotopic axis. In a steep audiogram, tinnitus pitch is also frequently matched to frequencies above the audiogram edge (Konig et al., 2006).

Despite the widespread prevalence of tinnitus as one of the most common disorders of the auditory system, there is little consensus on its underlying mechanisms and management approaches. Tinnitus is generally classified as subjective or objective. Most tinnitus is subjective insofar as it is heard only by the patient (Bauer, 2018; Chari and Limb, 2018). Objective or somatic tinnitus, i.e., a sound produced within the body by blood flow, muscle contractions, or spontaneous cochlear emissions, which can be detected and measured by an external observer, is uncommon (Bauer, 2018; Omidvar and Jafari, 2019). Tinnitus may be unilateral or bilateral, pulsatile or non-pulsatile, and intermittent or constant (Ferreira et al., 2009). Tinnitus can be perceived as inside or outside the head or mainly in one or both ears. It may be described qualitatively as a cicada-like sound, humming, tonal ringing, hissing, buzzing, whistling, static, roaring, or variable combinations of these descriptions (Chari and Limb, 2018). Studies suggest the contribution of increasing age (Fujii et al., 2011; Martinez et al., 2015; Nondahl et al., 2010; Oiticica and Bittar, 2015; Shargorodsky et al., 2010), loud noise or occupational noise exposure (Fujii et al., 2011; Shargorodsky et al., 2010), history of smoking (Nondahl et al., 2010; Shargorodsky et al., 2010), as well as health conditions such as hearing loss (Gopinath et al., 2010; Nondahl et al., 2010; Shargorodsky et al., 2010; Sindhusake et al., 2003), hypertension (Lasisi et al., 2010; Shargorodsky et al., 2010) or ischemic heart disease (Fujii et al., 2011), head injury (Lasisi et al., 2010; Nondahl et al., 2010), arthritis (Nondahl et al., 2010), otitis media (Lasisi et al., 2010), symptomatic dizziness (Gopinath et al., 2010), and steroid or antihypertensive medication (Fujii et al., 2011) as likely risk factors of developing and/ or accelerating tinnitus in older adults (Table 1). A histopathological study in a small group of aged individuals with and without prolonged tinnitus (mean duration of 20.3 years) indicated that atrophy of the stria vascularis and loss of outer hair cells is more common in individuals with tinnitus than those without tinnitus (Terao et al., 2011). Although cochlear abnormalities created by known risk factors could be the initial source of tinnitus, the concomitant neural alternations including 1) changes in level of spontaneous neural activity in the central auditory system, 2) alterations in the temporal pattern of neural activity, and 3) reorganization of tonotopic maps are more likely to be involved in initiating a long-term bothersome tinnitus (Adjamian et al., 2009; Baguley et al., 2013).

For those patients with bothersome tinnitus who seek treatment, no decisive treatment option exists. The lack of a crucial treatment for tinnitus results from diversity in clinical characteristics of patients and the low consistency in outcome measurements, at least in part (Bauer, 2018; Chari and Limb, 2018). For patients with no symptoms of a distinct disease process, current remediation strategies are generally aimed to reduce the severity of tinnitus and improve the quality of life (Chari and Limb, 2018). Common treatment options include auditory stimulation (sound therapy, hearing amplification devices such as hearing aid and cochlear implant), psychological approaches (tinnitus retraining therapy, cognitive behavioural therapy, counselling), medications (antidepressants, anxiolytics, anticonvulsants, herbal supplements such as Ginkgo Biloba), and brain stimulation must be tailored according to the patient profile and the severity of the tinnitus (for more information refer to Chari and Limb, 2018, and Bauer, 2018) (Bauer, 2018; Chari and Limb, 2018). Tinnitus patients can demonstrate serious associated morbidities consisting lifestyle detriment, emotional difficulties, increased risk for depression (Gopinath et al., 2010), anxiety (Pattyn et al., 2016; Shargorodsky et al., 2010), sleep disturbance and insomnia (Aazh et al., 2017; Crocetti et al., 2009; Ferreira et al., 2009; Folmer and Griest, 2000), and lower quality of life (Ferreira et al., 2009; Gopinath et al., 2010; Lasisi et al., 2010). These symptoms, which affect psychological behavior and emotional well-being, demonstrate significant variability among patients with tinnitus that can impact the outcomes of treatment plans (Adjamian et al., 2009). Whereas tinnitus might be tolerable for some people, it could be intolerable to others leading to the activation of the limbic system and resulting in other comorbid psychological symptoms of tinnitus (Tyler and Baker, 1983). Fig. 3 illustrates suggested brain networks and auditory and non-

Table 1
Characteristics of studies exploring tinnitus in older adults.

Authors, Year	Participants	Methodology	Major aim	Measurements	Main findings
Aazh et al. (2017)	184 adults ≥60 year	Retrospective cross-sectional study	Factors related to tinnitus and hyperacusis handicap	PTA, ULL; and self-assessment questionnaires: HADS, HQ, ISI, THI, VAS	A strong association was shown between tinnitus annoyance and tinnitus handicap. The depression level also predicted both hyperacusis handicap and insomnia score.
Aazh et al. (2017)	573 patients aged 7-95 years (mean 55 years) from both genders	Retrospective cross-sectional study	Uncomfortable loudness levels in patients with tinnitus and hyperacusis	PTA, ULL; and self-assessment questionnaires: HADS, HQ, ISI, THI, VAS	Hyperacusis can be diagnosed by applying appropriate cut-off values for ULLmin (≤77) dB HL and HQ score (≥22). Large interaural asymmetry and major across-frequency variations in ULLs were linked to higher HQ scores.
Park et al. (2017)	Older (n = 76) and younger (n = 64) adults from both genders	Retrospective cross-sectional study	Effect of age on tinnitus and its psychological aspects	PTA, tinnitus matching, THI, and psychometric questionnaires (BDI, BEPSI).	No age effect on subjective tinnitus severity, depressive symptoms, and stress levels.
Oiticica and Bittar (2015)	1960 people aged 18-65 years and older from both genders	Cross-sectional study	Tinnitus prevalence in the city of São Paulo	PTA, tinnitus matching, THI, and psychometric questionnaires (BDI, BEPSI).	The prevalence of tinnitus was 22%. Tinnitus affected more women (26%) than men (17%) and increased with age.
Martinez et al. (2015)	4.7 million residents of England under 85 years of age of both genders	Observational study	Ten-year incidence of tinnitus and its burden on the UK health service	Including patients with clinically significant tinnitus (sigT) diagnosed at the hospital	The new incidence rate and the 10-year cumulative incidence of sigT were 5.4 and 58.4 cases per 10,000 residents, respectively. The incidence rate increased with age, peaking at 11.4 per 10,000 at age 60-69 years.
Fujii et al. (2011)	14,423 adults aged 45 to 79 years from both genders	Population-based cohort study	Prevalence of tinnitus in community-dwelling Japanese adults	Case history and asking questions related to tinnitus experience	11.9% prevalence of tinnitus that increased with age. History of occupational noise exposure, ischemic heart disease or hypertension, and antihypertensive or steroid medication were identified as likely risk factors.
Terao et al. (2011)	18 temporal bones of subjects with ARHL with or without tinnitus aged 64-93 years from both genders	Cross-sectional study	Exploring tinnitus-induced cochlear changes in presbycusis	PTA, histopathologic assessments	A more severe degeneration of outer hair cells and stria vascularis was shown in the tinnitus group.
Gopinath et al. (2010)	1214 people ≥49 years from both genders	Longitudinal cohort study (Blue Mountains Hearing Study)	The predictors and impacts of tinnitus in older adults	PTA, assessment of the quality of life (SF-36) and depression (CES-D)	Symptomatic dizziness and hearing loss were significant risk factors for incident tinnitus. The tinnitus people exhibited a lower quality of life and a higher risk of developing depression.
Lasisi et al. (2010)	1302 elderly Nigerians ≥65 years from both genders	Longitudinal cohort study	The prevalence and correlates of tinnitus and its impact on the quality of life	Face-to-face interviews, ADL, chronic physical and pain conditions, and transient ischemic attack, WHOQoL-Bref, blood pressure measures	The tinnitus prevalence was 14.1%. It was associated with health conditions such as otitis media, head injury, rhinosinusitis, hypertension, and quality of life.
Nondahl et al. (2010)	2922 adults aged 48-92 years not reporting tinnitus at baseline from both genders	Epidemiological study	Ten-year incidence and risk factors of tinnitus among older adults	PTA, taking health history including tinnitus	The 10-year cumulative incidence of tinnitus was 12.7%. The risk of developing tinnitus was associated with the history of arthritis, head injury, smoking, hearing loss, and age.
Shargorodsky et al. (2010)	14,178 people ≤81 years from both genders	Retrospective study	Prevalence and risk factors of tinnitus among US adults	Participants from the NHANES 1999-2000, 2001-2002, and 2003-2004 surveys were included.	The prevalence of tinnitus was highest among older adults, non-Hispanic whites, former smokers, and adults with loud noise exposure, hearing loss, hypertension, or generalized anxiety disorder.
Ferreira et al. (2009)	100 tinnitus patients 0 > 60 years from both genders	Cross-sectional study	Tinnitus characteristics among old people	Otolaryngology examination, PTA, case history	Tinnitus was mostly non-pulsatile, permanent, and bilateral with impacts on concentration, sleep, and emotional and social life.
Sindhusake et al. (2003)	2015 adults aged 55-99 years from both genders	Longitudinal cohort study (Blue Mountains Hearing Study)	The prevalence and characteristics of prolonged tinnitus	PTA and case history	30.3% report of tinnitus experience, with a higher degree of hearing loss in tinnitus patients. Tinnitus had a gradual onset and was mildly-extremely annoying.

ADL, activity daily living; BDI, Beck depression inventory; BEPSI, brief encounter psychosocial instrument; CES-D, center for epidemiologic studies depression scale; HADS, hospital anxiety and depression scale; HQ, hyperacusis questionnaire; ISI, insomnia severity index; NHANES, national health and nutrition examination survey; PRA: pure-tone audiogram; SF-36, short-form 36-item health survey; THI, tinnitus handicap inventory; ULL, uncomfortable loudness level; VAS, visual analogue scale; WHOQoL-Bref, the world health organization quality of life brief version.

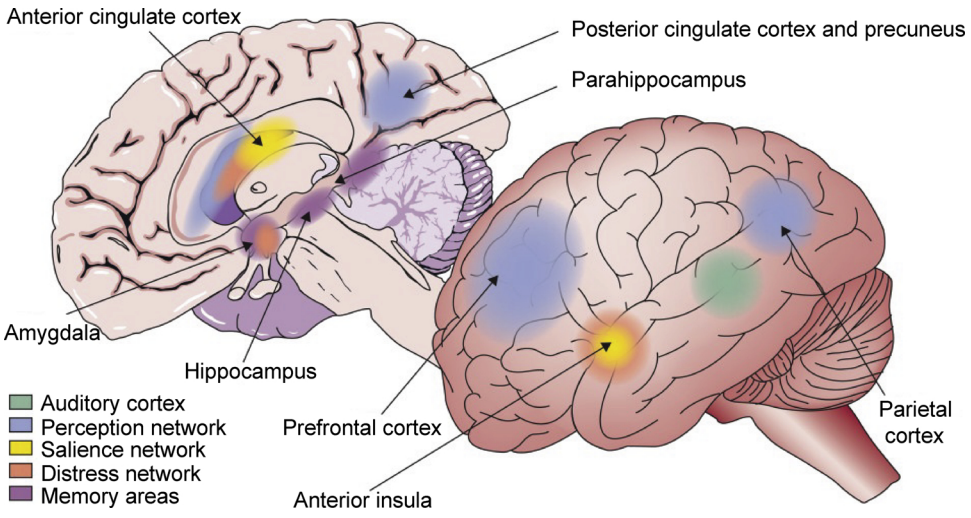


Fig. 3. Brain networks involved in tinnitus (phantom) perception. Increased activity in the auditory cortex (green) because of auditory deprivation is essential, but not sufficient, for tinnitus perception. Tinnitus reaches to the conscious level if the auditory activity is connected to a larger coactivated awareness network consisting the subgenual and dorsal anterior cingulate cortices, posterior cingulate cortex, precuneus, parietal cortex, and prefrontal cortex (blue). Salience to the phantom percept is shown by activation of the dorsal anterior cingulate cortex and anterior insula (yellow). Tinnitus annoyance is related to the coactivation of a non-specific distress network comprising the anterior cingulate cortex (subgenual and dorsal anterior cortical cortices), anterior insula, and amygdala. Memory mechanisms consisting the parahippocampal area, amygdala, and hippocampus have a major role in the persistence of the phantom perception (reproduced by permission from Elsevier, The Lancet Neurology, Langguth et al., 2013).

auditory brain areas involved in tinnitus perception (De Ridder et al., 2011; Langguth et al., 2013). The involvement of limbic system (hippocampus, amygdala, hypothalamus, and cingulate gyrus) in affective processing through its regulation on the endocrine and the autonomic nervous systems, as well as its connections to the prefrontal cortex, is considered to significantly contribute to the negative emotions associated with tinnitus as well as the success rate of remediation approaches (Adjamian et al., 2009). It is expected that future randomized controlled trials (RCTs) of tinnitus treatments could reduce the risk of bias and further clarify the outcome measures by choosing homogenous samples of individuals with tinnitus in etiology, severity, age, and years of affliction. They also require the application of standardized assessments, long posttreatment follow-ups, and acceptable statistical powers (Adjamian et al., 2009; Baguley et al., 2013; Bauer, 2018; McCormack et al., 2016).

3.2. Tinnitus-related cognitive impairments

Current evidence cumulatively stands for the link between bothersome tinnitus and cognitive impairment in adults (ranging from young adults to older people) (Gudwani et al., 2017; Hallam et al., 2004; Rossiter et al., 2006; Tegg-Quinn et al., 2016; Vanneste et al., 2016). This association results from the fact that tinnitus is not only an aberrant auditory sensory perception but also linked to a variety of non-auditory symptoms leading to frustration, inability to relax, and difficulty concentrating (Trevis et al., 2016; Wineland et al., 2012). In the two reviews published in 2016, the association between chronic tinnitus and impairments in diverse aspects of cognitive function, especially the executive control of attention (Tegg-Quinn et al., 2016) and working memory (Mohamad et al., 2016) were demonstrated, whereas the hearing loss was accounted for as a covariate. Recent studies also indicate structural and functional changes in the brain of people with invasive tinnitus associated with their cognitive impairments (Chen et al., 2018; Hong et al., 2016; Mannarelli et al., 2017; Wang et al., 2018). For instance, neuroimaging studies of tinnitus demonstrate reduced gray matter in the ventromedial prefrontal cortex (Leaver et al., 2012), impaired arcuate fasciculus connected with the auditory and frontal regions (Lee et al., 2007), changes in hippocampal activity, as well as insular activity, and anterior cingulate activity (Vanneste et al., 2016), enhanced functional connectivity of the posterior cingulate cortex (Chen et al., 2018b), and abnormalities in late auditory evoked potentials (Chen et al., 2018; Mannarelli et al., 2017) and top-down processing (Mannarelli et al., 2017). Cholinergic hypofunction also was proposed as a major contributor to age-related tinnitus (Ruan et al., 2018). Overall, studies suggest tinnitus-related cognitive impairment as a primary feature of tinnitus and not a secondary response to the manifestation of the disease (Wang et al., 2018).

Tinnitus affects people differently (Henry et al., 2015). Based upon Dobie's (2004) three-level pyramid analogy, the base of the pyramid contains nearly 80% of people with tinnitus who are not annoyed by tinnitus. The next higher level contains people whose tinnitus is bothersome, ranging from mild to severe. The tip of the pyramid also includes those few individuals who are debilitated by their tinnitus. Whereas there is a known relationship between bothersome tinnitus and symptoms of cognitive impairments (Gudwani et al., 2017; Hallam et al., 2004; Rossiter et al., 2006; Tegg-Quinn et al., 2016; Vanneste et al., 2016), the contribution of tinnitus in the link between ARHL and cognitive decline is not well-understood. Given that tinnitus shows a high probability of comorbid hearing loss (Schecklmann et al., 2014; Schilder et al., 2014), it is difficult to specify how much of the non-auditory effects independently result from tinnitus. Behavioral studies, however, demonstrate that individuals with both tinnitus and hearing loss have more severe reactions to tinnitus than those with tinnitus and normal hearing (Mazurek et al., 2010; Savastano, 2008). Thus, further studies are needed to clarify the distinct contribution of tinnitus, hearing loss, and their comorbidity in developing cognitive decline in physiological aging and as a risk in predisposing the landmarks of dementia.

4. ARHL, cognitive load, and dementia

4.1. Sensory and cognitive impairments in dementia

Age-associated cognitive decline or normal cognitive aging drives changes in brain structure-function that are non-pathological, within normative age-appropriate values (Deary et al., 2009). Whereas a little age-associated decline is seen in some mental functions (e.g., verbal ability, some numerical abilities, and general knowledge), the decline in other mental abilities such as aspects of attention, memory, executive functions, processing speed, and reasoning (known as fluid mental abilities) starts from middle age or even earlier (Aghamolaei et al., 2018; Deary et al., 2009; Harada et al., 2013; Jafari et al., 2013). Besides the progressive loss of cognitive function as the phenotypic impairment presented in AD, clinical AD studies also have a general consensus on changes in sensory and motor systems at the early stages of AD in many people (Albers et al., 2015; Fischer et al., 2016; Luo

et al., 2018). Such studies suggest that changes in hearing, olfaction, and even walking speed may precede the onset of cognitive impairments and dementia by 5 to 15 years as the strong risk factors for AD dementia (Devanand et al., 2008; Lin et al., 2011b; Murphy et al., 2002; Verghese et al., 2007). Whereas ample research indicates that specific sensory or motor changes may be early noninvasive biomarkers for AD, current clinical measures are not distinct to AD and can be seen in association with other types of neurological disorders such as Parkinson's disease or distinct non-AD types of dementia; or non-neurologic impairments of sensory or musculoskeletal systems (Albers et al., 2015). Thus, future research in age-associated sensory and motor decline and AD-associated sensory and motor decline are required to differentiate between these two in normative sensory, motor, and cognitive data. It is also essential to clarify the neuropathological deficits in sensory and/or motor processing that are specifically associated with AD compared to other chronic diseases in older adults.

4.2. ARHL as a modifiable risk factor for dementia

Dementia is the major worldwide challenge for health and social care in the current century. Alzheimer's disease (AD) is a progressive neurological disorder that impairs memory and other cognitive abilities in the elderly populations and accounts for 60–80% of dementia cases (Marcello et al., 2015). The morphological features of AD include the extracellular deposition of amyloid-beta (Aβ) peptide, the formation of intracellular neurofibrillary tangles of hyperphosphorylated tau protein, as well as neuronal and synaptic loss in the cerebral cortex and hippocampus (Cui and Li, 2013; Marcello et al., 2015). The amyloid cascade and tau production are the two prominent hypotheses of the underlying molecular mechanisms describing the AD pathogenesis (Shen et al., 2018). Whereas the complex etiology of the AD is not well-realized, recent reviews and multidisciplinary studies emphasize the contribution of lifestyle characteristics, environmental factors, and diseases in predisposing the risk of developing AD (Khalsa, 2015; Livingston et al., 2017; Marcello et al., 2015). Besides well-known risk factors related to mental disease and dementia, hearing loss has shown a strong association with cognitive impairment and the development of dementia and AD (Davies et al., 2017; Ford et al., 2018; Fortunato et al., 2016; Golub et al., 2017; Martini et al., 2014; Wei et al., 2017). In a meta-analysis (Livingston et al., 2017) on a life-course model of the contribution of modifiable risk factors to dementia and AD (35% compared to 65% potentially non-modifiable risk factors), midlife hearing loss (9%) demonstrated the highest contribution among other well-known risk factors like less education in early life (8%), smoking (5%), depression (4%), physical inactivity (3%), social isolation (2%), hypertension (2), obesity (1%), and diabetes (1%). It was also suggested that the midlife hearing loss might be a consequence of preclinical neurodegeneration rather than a cause (Kivimaki and Singh-Manoux, 2018; Warren and Bamiou, 2018). Hearing loss as an effect or a cause associated with dementia, however, is a reversible sensory deficit (Panza et al., 2015). Current research demonstrates advantages of hearing amplification devices in at least partially restoring hearing ability and improving overall cognitive performance in older adults (Cherko et al., 2016; Katz et al., 2015; Mamo et al., 2016; Martini et al., 2014; Pichora-Fuller, 2015) (Table 2, refer to Section 6, auditory amplification for improving cognition and social interaction, for further information).

4.3. Auditory deprivation and cognitive decline

Hearing loss is the most frequent sensory deficit in human populations, affecting more than 360 million people worldwide (World Health Organization (WHO, 2017b). Approximately one-third of adults older than 65 years experience a disabling hearing loss (Cacciatore et al., 1999; Dalton et al., 2003; Hogan et al., 2009; Loughrey et al., 2018). Changes in auditory and speech neural pathways subsequent to peripheral hearing losses appear as the major auditory deficit accounts for the association with AD (Fortunato et al., 2016). A large body of evidence indicates that ARHL is detrimental to physical and mental health, cognition, verbal communication, independence, social interaction, and quality of life in the elderly (Chen et al., 2015; Cherko et al., 2016; Deal et al., 2017a, b; Lin and Albert, 2014; Lin et al., 2014, 2011c; Lin et al., 2013). The cohort studies imply that even hearing loss in mild level predisposes the long-term risk of cognitive decline in those who are cognitively intact but hearing-impaired at baseline (Deal et al., 2017b, 2015; Fritze et al., 2016; Gallacher et al., 2012; Gurgel et al., 2014; Lin, 2011; Lin et al., 2011a, b; Valentijn et al., 2005; Wei et al., 2017). It appears that the ARHL is not only more prevalent in individuals with dementia than in age-matched controls, but also independently associated with the incidence of dementia resulting from degradation of auditory inputs to the brain (Albers et al., 2015; Deal et al., 2017b; Ford et al., 2018; Gallacher et al., 2012; Golub, 2017; Gurgel et al., 2014; Lin et al., 2011a, b; Lin et al., 2011c, 2013; Taljaard et al., 2016; Yuan et al., 2018). For instance, functional and structural neuroimaging studies demonstrate the age-related dysfunction of the main inhibitory neurotransmitter system in central auditory pathways, e.g., gamma-aminobutyric acid (GABA) (Gao et al., 2015), the link between the degree of hearing impairment and the loss of brain auditory signals (Peelle et al., 2011), the association between the disruption of cortical spontaneous neural activity and specific cognitive performance, and speech-language processing (Chen et al., 2018a), as well as the recruitment of regions in the frontal and temporoparietal cortex to make up and/or support speech-language processing in older adults (Wingfield and Grossman, 2006). Thus, the onset of presbycusis may trigger a need for increased cognitive resources during speech comprehension, which might lead to auditory and cognition-related cortical reorganization (Ren et al., 2018). This process can lead to the reduction of cognitive resources available for other cognitive functions and subsequently to the decline of cognitive reserve and the acceleration of preclinical landmarks of dementia (Albers et al., 2015; Stahl, 2017). In a recent MRI study in aged people without a central nervous system involvement, severe cardiac disease, pulmonary disease, or metastatic cancer, peripheral hearing loss was independently linked to accelerated declines in whole brain volume and temporal lobe atrophy (Qian et al., 2017). Cohort studies indicate that ARHL precedes the onset of clinical dementia by 5 to 10 years (Albers et al., 2015). In fact, for every 10 dB increase in hearing loss over 25 dB, there is a 20% increased risk of developing dementia (Lin et al., 2011b). The mean time for developing dementia also has been reported to be 10.3 years in adults over 65 years of age with hearing loss at baseline versus 11.9 years in those with normal hearing (Gurgel et al., 2014). A recent cohort study of 37,898 older men with a mean follow-up of 11.1 years, as well as a systematic review and meta-analysis of prospective studies, demonstrated that mid-life hearing loss might account for up to 9.1% of global dementia cases (Ford et al., 2018). This result is similar to one that was reported in the Lancet International Commission on Dementia, Prevention, Intervention, and Care (Livingston et al., 2017).

Although the consequences of auditory deprivation are not as readily apparent as the loss of other sensory modalities such as vision (Luo et al., 2018), and so are often under-recognized or considered less severe, their effects are quite impressive given that audition is essential for spoken language, the core of human interaction (Cherko et al., 2016; Martini et al., 2014). Hearing and cognition rely on shared neurocognitive resources and relate to each other in several different ways (Wayne and Johnsrude, 2015). It has been proposed that increasing the cognitive load on a vulnerable brain (McCoy et al., 2005; Stahl, 2017), which can affect a person's ability to understand explanations, follow directions, and correctly interpret interpersonal communication (Gopinath et al., 2009; Huang et al., 2010; McGilton et al., 2016), are prominent impacts of hearing loss that can accelerate brain atrophy (Lin and Albert, 2014; Qian et al., 2017) and cognitive impairment (Bernabei et al., 2014). Given some methodological

Table 2
Characteristics of studies exploring the outcomes of hearing aid usage on cognitive performance among older adults.

Authors, Year	Participants	Methodology	Major aim	Measurements	Main findings
Karawani et al. (2018)	32 older adults aged 62-82 years with SNHL from both genders	Cohort study, half of the participants used bilateral RIC HAs for six months	Effect of HA usage on cognitive and neural function	The NIH toolbox was used to test working memory, attention, and processing speed. The CAEP P1, N1, and P2 peaks were recorded in quiet and noise in response to speech syllables.	The relationship between working memory function and cortical response amplitudes suggested a mechanism for the association between hearing loss and cognitive decline.
Johnson et al. (2017)	45 older adults aged 61-81years with SNHL from both genders	A cohort study to test the impact of two premium-feature and two basic-feature mini BTE HAs	Effect of HA usage on sound localization	Testing unaided and aided localization ability in quiet and noise with a 24 loudspeaker array, and self-report of everyday life localization by SSQ	Improved localization performance only in self-reported everyday situations.
Giroud et al. (2017)	30 older adults aged 60-77 years with SNHL and 13 controls from both genders	Cohort study, 2/3 of participants with previous experience of using HAs were fitted with new RIC HAs for three months	Impact of using new HAs in auditory plasticity	EEG recording	The HA group displayed higher processing effort (GFP) compared to those with normal hearing. The GFP improved in HA users after acclimatization to new HAs.
Deal et al. (2017a,b)	40 older adults aged 70-84 years with SNHL	RCT, half of the participants received bilateral ITE HAs and aural counseling, and the other half received a healthy aging program	Effect of HA usage in reducing cognitive decline	Self-assessment questionnaires: HHIE-S, Cohen social network index, UCLA loneliness scale, a depression scale, short-form 12 questionnaire, and a detailed battery for testing memory, language, and executive function	A clear efficacy of the hearing intervention was reported in perceived hearing handicap and memory function.
Mamo et al. (2017)	20 dementia cases aged 76.9 years with SNHL from both genders	Cohort study, participants used a HA for one month	Short-term outcomes of using HA in cases with dementia	HEARS program: receiving 2 hours communication strategies for patients suspected to dementia and their caregivers and provision of a simple OTC HA	Caregivers reported improvements in patients' engagement and their neuropsychiatric symptoms.
Yamada et al. (2017)	105 older adults aged 60-90 years with SNHL from both genders	Cohort study	Effect of HA experience on the quality of life	The association between the daily hours of HA usage and social relations with changes in the WHOQOL-OLD total score were determined 2 and 6 months afterward.	HA usage was associated with an improvement in QOL likely due to enhanced communication opportunities.
Castiglione et al. (2016)	Older adults with SNHL (n = 85), and controls with normal hearing (n = 20) aged 65-89 years from both genders	Cross-sectional study	Effect of using HA or CI on cognitive function and depression	Using memory and depression questionnaires: MoCA, GDS, DST, Stroop test	Using HA or CI was effective for different degrees of hearing loss and led to improvements in cognitive performance, social isolation, and depression.
Dawes et al. (2015)	A subsample of the UK Biobank data set (n = 164,770) of adults aged 40-69 years	Prospective study	Effect of HA on cognitive performance	Structural equation modeling of associations between hearing loss, cognitive performance, social isolation, depression, and HA usage was conducted.	Improvement in cognitive function, social isolation, and depression.
Deal et al. (2015)	1889 older adults aged 70-79 years from both genders	Prospective cohort study	The incidence of dementia in hearing impaired and self-reported HA users (n = 174)	Five years follow up including CVA cognitive assessments, hearing tests, and determining dementia risk	The estimated effect of HA usage was in the direction of reduced dementia risk but not statistically significant due to a wide confidence interval.
Lavie et al. (2015)	Older adults with (n = 36) and without HA (n = 11) aged 64-88 years	Prospective cohort study	Effect of HA experience on unaided speech perception	Speech perception was evaluated by dichotic listening and SIN tests before and 4, 8, and 14 weeks after HA fitting	Even a short-term HA usage derives changes in the processing of auditory perceptual tasks suggesting the potential for subsequent neuroplasticity in older adults.
Acar et al. (2011)	34 older adults aged 65-82 years with SNHL from both genders	Prospective cohort study	Cognitive and psychological benefits of using HAs	Comparing the scores of MMSE and GDS before and three months after HA fitting	Improvements in cognitive and depression scores after HA usage.
Choi et al. (2011)	Older adults with HA (n = 188), and controls with normal hearing (n = 11) aged 69.5 years	Prospective cohort study	Effect of HA on cognitive performance	The VVLT and WIN tests were performed before and six months after HA fitting.	Improvement in speech-related cognitive performance after HA usage.
van Hooren et al. (2005)	Older adults with (n = 55) and without HA (n = 46) aged ≥60 years	Prospective cohort study	Effect of HA on cognitive performance	Cognitive tests, including SCWT, CST, LDST, and VVLT were performed before and 12 months after HA fitting.	No improvement in cognitive tests compared with the control group.
Tesch-Romer (1997)	Older adults with (n = 70) and without HA (n = 42), and a group with normal hearing (n = 28) from both genders	Prospective cohort study	Effects of HA on psychological behavior	Using questionnaires or behavioral measures of cognition, communication problems, social activities, and psychosomatic well-being	Long-term use of HA improved self-perceived hearing handicap.

BTE, behind the ear; CAEP, cortical auditory evoked potentials; CI, cochlear implant; CST, concept shifting task; DST, digit span test; EEG, electroencephalography; GDS, Geriatric depression scale; GFP, global field power; HA, hearing aid; HHIE-S, hearing handicap inventory for the elderly-screening version; LDST, letter-digit substitution test; MMSE, mini-mental state examination; MoCA, Montreal cognitive assessment, NIH, national institute of health; OTC, over the counter; RCT, randomized controlled trial; RIC, receiver in the canal, SCWT, Stroop color-word test, SNHL, sensory-neural hearing loss; SSQ, speech, spatial, and qualities of hearing scale; UCLA, University of California Los Angeles, VVLT, visual-verbal learning test; WIN, word in noise test.

limitations such as the lack of homogeneous sample sizes, age-appropriate normative data, applying convenient diagnostic tests, or ethical restrictions, it might be difficult to mechanistically investigate the neural substrates underlying the relationship between hearing and cognition in humans. Experimental animal studies, however, could be a proper solution to afford part of these research limitations (refer to section 8, preliminary findings in animal studies, for further information).

5. Hypothesized mechanisms on the link between ARHL and cognitive decline

Whereas a growing body of research confirms the relationship between hearing loss and cognitive impairment, little neurophysiological mechanistic evidence exists to support this association. Studies have not identified which one comes first (i.e., hearing loss or cognitive impairment), whether hearing loss drives cognitive decline, whether cognitive decline results in hearing loss, or whether they are both created by other factors (Fortunato et al., 2016; Gallacher et al., 2012; Golub, 2017; Mudar and Husain, 2016; Wayne and Johnsrude, 2015). Thus, several potential hypotheses have been suggested in the literature including: 1) the cognitive load on perception hypothesis; 2) the information-degradation hypothesis; 3) the sensory-deprivation hypothesis; and, 4) the common-cause hypothesis (Uchida et al., 2019) (Fig. 4), which are briefly discussed in turn.

The “cognitive load on perception hypothesis” proposes the adverse impacts of the age-related cognitive decline on auditory perception (Humes et al., 2013; Kiely et al., 2012; Lindenberger and Baltes, 1994), but there is limited evidence supporting this hypothesis (Wayne and Johnsrude, 2015). In contrast, “the information-degradation hypothesis” suggests that the loss of auditory inputs and consequently increased reliance on cognitive resources drives cognitive decline in older adults (Pichora-Fuller, 2003). Thus, a high processing load during auditory perception can interfere with encoding and lead to an impairment in cognitive performance that manifests as impaired memory (Akeroyd, 2008; Zekveld et al., 2007). This effect is stronger in effortful listening conditions (degraded speech signal) or during adverse listening situations (noisy environments) (Amichetti et al., 2013; Wingfield and Tun, 2007). Whereas this hypothesis assumes that changes in cognition performance could be potentially reversible by improving the quality of the speech communication, the sensory-deprivation hypothesis proposes that neuroplastic changes in cognitive resources resulting from ARHL are permanent over time (Humes et al., 2013; Lin and Ferrucci, 2012). Few mechanistic physiological studies, however, support the idea that potential deafferentation and atrophy in the auditory system leads to long-lasting neuronal reorganization resulting from chronic auditory deprivation (Wayne and Johnsrude, 2015). There is, however, a little supportive evidence of cortical reorganization as a consequence of reduced sensory input. For instance, increased activation in frontal and posterior parietal working memory and attention networks in older adults compared with younger individuals during the speech in noise tasks (Wong et al., 2009), as well as a negative relationship between peripheral hearing and gray matter density in primary auditory cortical areas (Eckert et al., 2013; Peelle et al., 2011) indicate that hearing loss precedes the onset of clinically significant cognitive decline. The “sensory-deprivation hypothesis” is also contradicted by findings demonstrating the insignificant impact of long-term hearing impairments on overall cognitive performance in younger adults (Vernon, 2005). There is also a growing body of current evidence that suggests the positive effect of hearing amplification systems in improving cognitive performance, especially memory, in aging people (Deal et al., 2017a; Giroud et al., 2017). According to “the common-cause hypothesis”, a shared mechanism underlies both age-related changes in cognition and hearing through widespread neural degeneration that is not only limited to the auditory modality (Yamasoba et al., 2013). Ample evidence supports systematic age-related central nervous system pathology, including widespread brain atrophy and reduced dendritic spine densities in multiple cortical regions, particularly in the temporal lobe (Qian et al., 2017) and prefrontal regions (Park and McDonough, 2013; Wayne and Johnsrude, 2015). Among these four potential hypotheses, the information-degradation and common-cause hypotheses are well-supported by the relevant evidence (Lin et al., 2013; Park and McDonough, 2013). The information degradation and sensory-deprivation hypotheses, however, can be considered as the ‘sensory hypothesis’, as they rely on the role of downstream demands, auditory inputs, on cognitive resources (Wayne and Johnsrude, 2015).

6. Auditory amplification for improving cognition and mental health

Audiology has been faced with enormous technological advancements in hearing amplification devices, overall hearing aids, hearing implants, and assistive listening devices (Katz et al., 2015; Vaisbuch and Santa Maria, 2018). This section briefly reviews current evidence of improvements in hearing handicap, cogitative function, and social communication resulting from using hearing aids or cochlear implants. Despite significant technological progress in hearing amplification services, a successful aural rehabilitation program is a multi-stage approach that begins with counseling and identifying communication needs based on hearing and speech test results, interview and self-assessment questionnaires, communication situations, physical and mental health, and individual and family expectations (Cherko et al., 2016; Dillon, 2012; Katz et al., 2015; Mamo et al., 2016; Martini et al., 2014; Pichora-Fuller, 2015).

6.1. Hearing aids

Today’s hearing aids incorporate technological inventions in diverse aspects of sound signal processing, convenient usage, and physical appearance (Vaisbuch and Santa Maria, 2018). Improvements in wireless technology, frequency-specific amplification, background noise cancellation, directionality in conversation with multiple speakers, acoustic feedback cancellation, and decreased artifacts have led to impressive outcomes in speech perception in both quiet and noisy environments for adults (Vaisbuch and Santa Maria, 2018). Through wireless technology, hearing aids can be connected to other devices such as Smartphones, TV, and music streaming devices, and also help to interact with appliances, doorbells, and smoke detectors that promote older adults’ independence (Domingo, 2012). The same technological progress has been implemented in assistive listening devices. For instance, the frequency modulation system (FM) has shown to be beneficial in improving communication abilities in older adults (Chisolm et al., 2007; Dillon, 2012).

Cohort studies, with the exception of one research paper (van Hooren et al., 2005v), demonstrate that increased auditory experience through hearing aid usage can lead to auditory plasticity (Giroud et al., 2017; Lavie et al., 2015), improvements in cortical auditory evoked potentials (CAEPs) and working memory function in quiet and noise (Karawani et al., 2018), enhanced overall cognitive performance and reduced depression (Acar et al., 2011; Castiglione et al., 2016; Choi et al., 2011; Tesch-Romer, 1997), better quality of life (Dawes et al., 2015; Said, 2017; Yamada et al., 2017), reduced self-perceived hearing handicap (Deal et al., 2017a; Tesch-Romer, 1997), and diminished dementia risk (Deal et al., 2017b) (Fig. 5A, Table 2). Studies also demonstrate the benefits of hearing aids in auditory localization performance in both laboratory tests and self-reported everyday situations (Johnson et al., 2017). In a recent RCT using detailed self-assessment questionnaires and a neurocognitive battery for testing memory, language, and executive function in older adults with mild to moderate hearing loss, estimates of 6-month outcomes were consistent with improvement or no change only in the hearing intervention group

Hypotheses	Possible associations between ARHL and cognitive decline	
Cognitive load on perception	Increased cognitive load due to aging	→ Reduced auditory perception
Information degradation	Reduced auditory inputs (hearing loss)	→ Reduced cognitive performance driven by increased reliance on cognitive resources
Sensory deprivation	Reduced auditory inputs (hearing loss)	→ Cognitive decline driven by neuroplastic changes in cognitive resources
Common-cause	General age-related neuropathological changes in brain	→ Auditory impairment and cognitive decline

Fig. 4. The major hypotheses underlying the association between loss of auditory inputs resulting from age-related hearing loss (ARHL) and cognitive impairment.

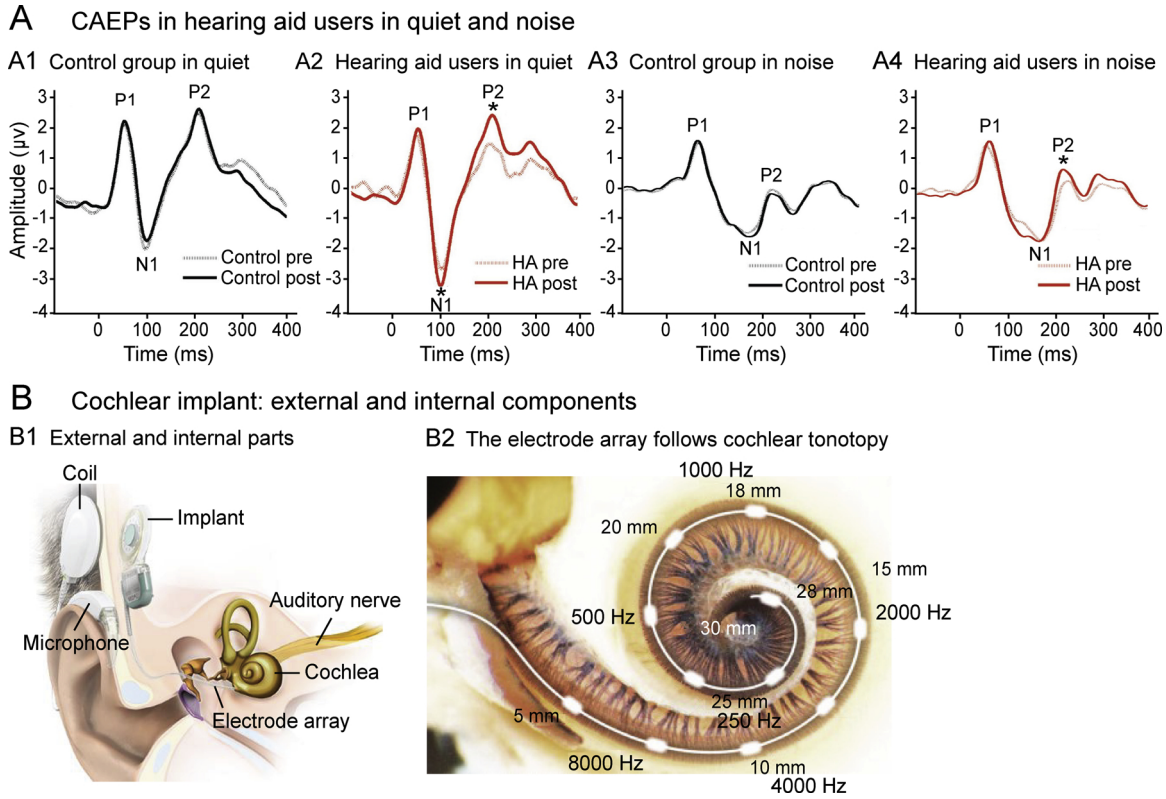


Fig. 5. Hearing aid and cochlear implant. A) Grand average of CAEPs in quiet and noise in older adults with ARHL with and without hearing aid experience. A1) Control group in quiet in the first and second (after 6 months) recordings. A2) Hearing aid users in quiet in the first and second (6 months after HA experience) recordings. A3) Control group in noise in the first and second (after 6 months) recordings. A4) Hearing aid users in noise in the first and second (6 months after HA experience) recordings. Significant improvements in CAEPs in both quiet and noise were shown only in the hearing aid group compared with the control group (reproduced by permission from Elsevier, Neuropsychologia, Karawania et al., 2017). B) A schematic representation of CI. B1) External and internal components of CI. The microphone on a sound processor collects sound waves, and the processor converts them into digital information that is transferred through the coil to the implant just under the skin. Electrical signals are transferred down to the electrode array inserted into the cochlea. Hearing signals are captured by auditory nerve fibers and projected to the brain, which provide a sense of hearing. B2) The electrode array inserted to both apical and basal regions of the cochlea stimulates auditory nerve fibers in line with the cochlear tonotopy (reproduced by permission from MED-EL Corporation, Canada). Asterisks indicate *P < 0.05. ARHL, age-related hearing loss; CAEPs, cortical auditory evoked potential; CI, cochlear implant.

(receiving bilateral in-the-ear hearing aids and aural counseling). This finding demonstrated clear efficacy in perceived hearing handicap and memory function. In contrast, in the successful aging group (including a protocol developed for promoting healthy aging), estimates of 6-month outcomes were consistent with no change or worsening of function (Deal et al., 2017a). The hearing intervention also is beneficial for older adults diagnosed with cognitive decline and dementia. For instance, in a recent hearing care intervention including fitting a hearing aid (HEARS program: receiving two hours communication strategies for patients suspected to dementia and their caregivers and provision of a simple over the counter hearing aid), caregivers believed that the program was advantageous in improving patients' engagement and reducing their neuropsychiatric symptoms (Mamo et al., 2017). This study, however, had several scientific limitations such as a low sample size, non-homogeneity in the degree of cognitive impairment that was only based on the mini-mental state examination (MMSE) score, poor inclusion criteria, no appropriate control group, and a short intervention period.

Current accomplishments in the field of hearing amplification for ARHL result from the fact that hearing loss is not only a sensory deficit. ARHL gradually leads to specific challenges for speech understanding and subsequently social interaction resulting from reduced sensory inputs contribute to episodic memory, processing speed, and working memory function (Karawani et al., 2018; Peelle et al., 2011). Further than losing auditory cues, which lead to changes in understanding the hearing environment, ARHL degrades the speech signals delivered to the auditory cortex and associated cognitive and linguistic higher-order cortical areas and leads to extensive neuroplastic changes in many

associated brain regions (Humes et al., 2012). Current neurophysiological evidence demonstrating improved working memory performance, enhanced cortical amplitudes (Karawani et al., 2018), and reduced perceptual efforts (Giroud et al., 2017), as well as behavioral evidence of improvements in diverse aspects of speech (Choi et al., 2011; Lavie et al., 2015), memory, and social communication (Dawes et al., 2015; Deal et al., 2017a) suggest hearing aids as successful sensory devices in producing an experience-dependent plasticity and restoring some aspects of both sensory and cognitive functions. Overall, whereas existing findings are in line with significant advantages of long-term use of hearing aids, further studies, however, are suggested to understand neuronal changes underlying sustained use of hearing amplification, and demonstrating the impact of years of hearing deprivation, the degree of cognitive decline, and advancing age on hearing aids' outcomes. It should also be noticed that research findings, especially in laboratory conditions, might not be directly translated to applications for clinical practice and everyday life (Johnson et al., 2017). Hearing aid rehabilitation, therefore, should be set up individually for each older adult.

6.2. Cochlear implants

The cochlear implant (CI) is one of the most successful neuroprosthetic devices in neurorehabilitation (Kuchta, 2007; Lim et al., 2009). The CI priority to other sensory implants partly results from the fact that the perception of auditory information is largely based on temporal processing, which can be well-transmitted by only a few electrodes. Other senses such as vision are dependent, however, on high-resolution spatial processing implicating many more individual channels to transmit information (Kuchta, 2007). The CI was originally developed to replace the function of the profoundly impaired inner ear, and its candidacy was limited to those with bilateral profound SNHLs. Today candidacy criteria for CI in adults include an acquired bilateral moderate-to-profound SNHL with limited benefit from properly fit hearing aids, and a scoring of 50% or less on a test of open-set sentence recognition (e.g., hearing in noise test (HINT) sentences). The CI also has been shown to be helpful in restoring hearing ability and speech perception in quiet and noise in older adults with single-sided deafness (Arts et al., 2012; Friedmann et al., 2016; Mertens et al., 2018), unilateral (Firszt et al., 2012b), and asymmetrical (Firszt et al., 2012a) hearing impairments. The CI includes a surgically implanted device and an externally worn speech processor (Fig. 5). The internal processor takes advantage of the tonotopic organization of the basilar membrane and transfers processed information to electrodes located at different positions within the cochlea. Stimulation of these electrodes provides localized excitation of cochlear nerve fibers leading to discriminate corresponding pitch information used to comprehend speech (Fig. 5B2). A microphone, speech processor, connecting cables, and a transmitter coil are external components of the CI that have the role of collecting, processing, and transmitting auditory inputs to the internal components (Katz et al., 2015) (Fig. 5B1).

Systematic reviews on the clinical effectiveness of CI demonstrate a significant improvement in speech understanding after cochlear implantation without an increased surgical risk in older adults (Berrettini et al., 2011; Boisvert et al., 2016; Budenz et al., 2011; Hilly et al., 2016; Savvas and Rudack, 2017). Aged people, however, require a longer aural rehabilitation period to cope with speech understanding in adverse listening conditions compared to the younger adults. This longer period likely results from age-related neuronal loss and degenerative processes in the peripheral and central auditory systems as well as associated cortical areas (Cosetti and Lalwani, 2015). Whereas advanced age has been shown not to be a contraindication in CI candidacy (Chiesa Estomba et al., 2017; Garcia-Iza et al., 2018), shorter duration of hearing deprivation, pre-implant use of hearing aids (Castiglione et al., 2015, 2016; Mosnier et al., 2014), and right-side implantation in cases of unilateral CI (Budenz et al., 2011; Mosnier et al., 2014; Sharpe et al., 2016) are effective predictive factors that positively influence the outcomes (Garcia-Iza et al., 2018). Overall, given that vision problems, reduced proprioception or motor function, and dexterity difficulties are more common in older individuals and can affect CI outcomes, CI candidacy is suggested to be based on individual characteristics in the aspect of overall health and cognitive status of recipients (Berrettini et al., 2011; Savvas and Rudack, 2017).

In respect to cognitive outcomes after cochlear implantation in older adults, most studies agree on the significant cognitive improvements after CI experience (Castiglione et al., 2016; Claes et al., 2018b; Jayakody et al., 2017; Murillo-Cuesta et al., 2017). For instance, in two recent studies with 12 months post-implantation follow up, a significant improvement in overall cognition mainly associated with the immediate and delayed memory domain, working memory, processing speed, and sustained attention (Claes et al., 2018b), as well as cognitive flexibility, attention, paired associated learning and simple reaction time tasks (Jayakody et al., 2017) were reported. The results generally rely upon the impact of improved post-implantation hearing and speech perception scores on reducing cognitive load on working memory and executive functions in long-term users of CI (Castiglione et al., 2016; Jayakody et al., 2017). Studies also indicate the contribution of CI experience in improving quality of life and reducing depression symptoms and social isolation (Crowson et al., 2017; Knopke et al., 2016; Murillo-Cuesta et al., 2017). Systematic reviews, however, emphasize the use of more appropriate cognitive assessment tools, control for practice effects by applying alternate forms of cognitive tests, as well as applying appropriate statistical tests to control risks of bias in future studies (Claes et al., 2018a; Miller et al., 2015).

6.3. Hearing aids and cochlear implants in tinnitus management

Given the high incidence of concurrent hearing loss in older adults with tinnitus, hearing aids are often the first suggested treatment option in these cases (Bauer, 2018; Chari and Limb, 2018). The masking effect of amplified sound could be effective at tinnitus frequencies within the amplification range of hearing aids, i.e., less than 6000 Hz (Baguley et al., 2013; Chari and Limb, 2018). Current evidence also suggests that CI has a suppressive effect on tinnitus in most CI candidates, namely more than 80 percent of cases (Bovo et al., 2011; Holder et al., 2017; Pan et al., 2009; Valles-Varela et al., 2013). Several likely underlying mechanisms such as habituation, acoustic masking, direct electrical nerve stimulation, and cortical reorganization have been discussed for this pacifying effect after CI (Bovo et al., 2011). There are, however, a few studies that report tinnitus appearance after CI, likely resulting from newly formed aberrant neuroplastic changes in the auditory pathways by CI stimulation (Akdogan et al., 2009; Ramakers et al., 2017). Further research to clarify the neurophysiological mechanisms underpinning the suppressing effect of CI on tinnitus, thus, is required before suggesting CI as a treatment option for tinnitus.

7. Further evidence of brain plasticity (reserve) in older adults

The ultimate goal of all non-pharmacological, neurorehabilitation, or cognitive technology-based programs in improving cognitive performance is linked to the concept of "reserve" that accounts for differences among individuals in susceptibility to age-related brain changes and pathology, such as that is seen in AD (Stern, 2012). By definition, "reserve" is classified into two main features: "brain reserve" and "cognitive reserve". Brain reserve stands for a quantitative or passive view of the brain, such as the number of neurons or synapses available to be lost, which differs among individuals with AD. By contrast, cognitive reserve is an active form of reserve in which brain function rather than brain morphology matters most (Stern, 2009). According to the concept of cognitive reserve, the brain actively copes with pathology by using preexisting cognitive-processing approaches or compensatory mechanisms (Stern, 2002, 2009) (Fig. 6A). Thus, with

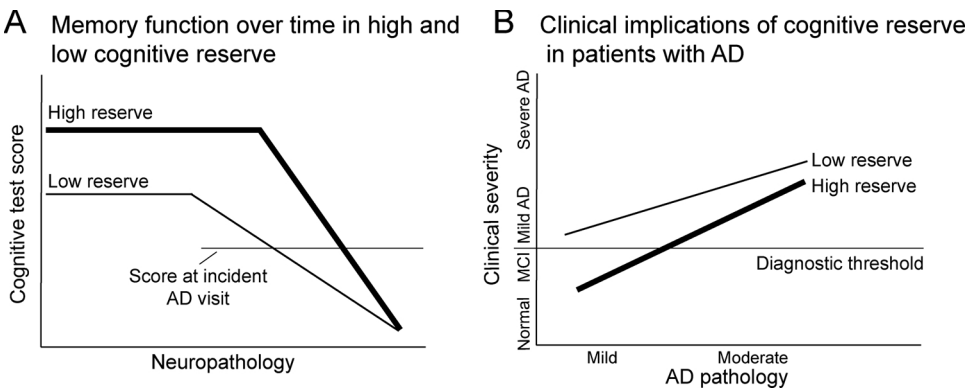


Fig. 6. Cognitive reserve in AD. A) Hypothesized change in memory function over time in individuals with high and low cognitive reserve. The AD pathology begins to advance before changes in memory performance are observed. The decline is seen later in individuals with high cognitive reserve because pathology is tolerated longer than by people with low cognitive reserve. B) Clinical implications of cognitive reserve in patients with AD. Individuals with low cognitive reserve might seem to be clinically demented when AD pathology is mild, whereas those with higher cognitive reserve might remain clinically normal. At higher levels of pathology, both groups might appear to be clinically demented. Still, those with a higher reserve will appear to be less clinically severe than those with a lower reserve. AD, Alzheimer's disease; MCI, mild cognitive impairment (reproduced by permission from Elsevier, The Lancet Neurology, Stern, 2012).

the same brain size, an individual with high cognitive reserve would have a better functional outcome with the same amount of pathology compared to an individual with low cognitive reserve (Stern, 2012) (Fig. 6B). For instance, at age 60 or older, people with less than 8 years of education had a 2.2 times higher risk of developing dementia than those with more years of education. Individuals with low lifetime occupational attainment were also at a 2.25 times greater risk of developing dementia than those with high lifetime occupational attainment (Stern et al., 1994). In the aging process, the brain's response to the reduction of physical and cognitive abilities is interpreted as neuroplasticity. This neuroplasticity is produced by modulations in neural connectivity and brain function in response to changing demands and environments during the lifespan (Kraft, 2012; Park and Bischof, 2013). Research in the enhancement of experience-dependent plasticity in older adults through physical activity programs (e.g. aerobic, resistance, and coordination training; dance and movement interventions; or sport, Tai Chi, and martial arts), cognitive training approaches (computer-based training, video games), or social engagement activities also has attracted considerable attention in recent publications (Ballesteros et al., 2015).

Life-course music training also can ameliorate age-related cognitive decline (Leon and Woo, 2018). Studies demonstrate the link between early or prior musical experience and enhanced ability to process speech in older adults (Bidelman and Alain, 2015). Interestingly, even moderate amounts of early music training can produce a persistent effect on maintaining the cognitive ability of older adults, even long decades after their musical experience (White-Schwoch et al., 2013). Lifelong bilingualism also provides a strong cognitive reserve that delays the onset of dementia by 4–5 years (Bialystok et al., 2007; Craik et al., 2010; Jafari et al., 2015; Perani and Abutalebi, 2015). Neuroimaging studies suggest that cognitive reserve driven by bilingualism is associated with increased gray and white matter densities in brain attention and executive control circuits rather than the direct impact on memory circuits initially affected in AD (Anderson et al., 2018). It also has been shown that enduring activation of the executive control circuits can protect a range of neuronal, glial, and synaptic functions within frontostriatal and frontoparietal networks (Anderson et al., 2018; Gold, 2015; Perani and Abutalebi, 2015).

8. Preliminary findings in animal studies

Whereas current human evidence cumulatively demonstrates the predisposing impact of hearing loss as a risk to exacerbate the burden of cognitive decline and dementia, there is little mechanistic evidence that unveils neuropathological changes underpinning this association. This lack of evidence mainly results from a combination of methodological limits and ethical restrictions. Experimental studies in animals have a history of providing a way to further clarify the mechanisms of disorders. Recent studies of rodents have begun to probe the neurobehavioral alterations relying upon the link between ARHL and pathological landmarks of cognitive impairments (Table 3). Studies in wild-type mice (C57BL/6 J) demonstrate the precedence of a significant hearing loss (at 6 months) before a significant memory impairment (at 15 months) (Dong et al., 2018), or their origination at the same time (at 6 months) (Yu et al., 2011). They also point to the possible role of changes in the expression levels of matrix metalloproteinase (MMP)-9 in the auditory cortex and hippocampus in the association between ARH and cognitive impairment (Dong et al., 2018). MMP-9 is a member of a large family of zinc-dependent endopeptidases that plays a major contribution in synaptic plasticity and cognitive processing (Lei et al., 2011) through cleaving extracellular matrix and numerous cell surface receptors necessary for synaptic and circuit-level reorganizations (Tang et al., 2014). A recent longitudinal study also demonstrated a greater loss of auditory inputs resulting from both reduced inner and outer hair cells at the apical and basal turns of the basilar membrane in the AD mice compared to the wild-type mice, as well as auditory dysfunction in behavioral hearing tests (O'Leary et al., 2017). A subsequent study affirmed the same results and suggested the beneficial impact of antioxidant treatment in delaying both ARHL and memory impairment (Marie et al., 2018). Given the extreme vulnerability of the cochlea to oxidative stress, it has been suggested that treatment with the antioxidants N-acetylcysteine can reduce the potential increase of the cochlear oxidative stress in different types of hearing loss, including ARHL (Kopke et al., 2015).

Studies also demonstrate the role of an age-dependent reduction in insulin-like growth factor 1 (IGF-1) and its underlying contribution in the association between sensory impairments and cognitive decline in older adults. The IGF-1 could be effective in hindering cell death through its neuroprotective impact in maintaining cellular metabolism, and activating cell growth, proliferation, and differentiation (Riquelme et al., 2010). The IGF-1 deficiency also is shown in SNHL in both rodents and humans (Rodriguez-de la Rosa et al., 2017). Current evidence suggests that inflammasomes, which cleave precursors of interleukin-1β (IL-1β) and IL-18 to generate their active forms, also play a leading role in the inflammatory response in the central nervous system and AD pathogenesis, as well as the pathological process of ARHL (Shi1 et al., 2017).

9. Conclusions and future directions

The inevitable deterioration in hearing ability that occurs with age is a multifactorial process that can vary in severity from mild to substantial. Tinnitus is also a known auditory disorder that elevates with increasing age. Both age-related hearing loss and tinnitus affect mental health and psychological well-being and contribute to developing cognitive decline, anxiety, stress, and depression. In recent decades,

Table 3
Characteristics of studies exploring the association between ARHL and cognitive impairment in rodents.

Authors, Year	Animals	Methodology	Major aim	Measurements	Main findings
Dong et al. (2018)	Male C57BL/6 J mice at three ages 3, 6, and 15 months	Cross-sectional study	The association between ARHL and cognitive decline	ABR, MWT, transmission electron microscopy, and western blot analysis	The precedence of a significant hearing loss (6 months) than memory decline (15 months) was observed. The MMP-9 expression in the auditory cortex and hippocampus may be linked to the relationship between ARHL and cognitive decline.
Marie et al. (2018)	Female SAMP8 mouse model of ARHL at 1-4 months	Interventional cohort study	Effect of N-acetylcysteine (an antioxidant) treatment on ARHL	ABR, DPOAE, and cochlear morphology	The N-acetylcysteine delays the aging process by slowing the ARHL, protecting the cochlear hair cells, and improving memory.
O'Leary et al. (2017)	Double transgenic 5xFAD mouse model of AD and wild-type mice at 3-16 months from both sexes	Longitudinal cohort study	The association between ARHL and AD	The PPI of the ASR, ABR, and cochlear morphology	The AD mice displayed a significant ARHL due to the loss of cochlear hair cells compared to the wild-type mice.
Yu et al. (2011)	Male C57BL/6 J mice at 2, 4, and 6 months (testing group), and CBA/CaJ mice (control group)	Cross-sectional study	The association between ARHL and synaptic changes in the hippocampus	ABR, MWT, transmission electron microscopy, and immunohistochemistry	ARHL at 6 months was accompanied with the degeneration of synapses in the hippocampal CA3 region of C57BL/6 J mice.

ABR, auditory brainstem response; AD, Alzheimer's disease; ARHL, age-related hearing loss; DPOAE, distortion product otoacoustic emission; (MMP)-9, matrix metalloproteinase; MWT, Morris water task; PPI of the ASR, prepulse inhibition of the acoustic startle reflex.

ARHL has been a hot research topic in the multidisciplinary field of aging studies. It is not only because ARHL is one of the most common health detriments affecting older adults, but also because of its association with cognition. Current epidemiological research demonstrates the widespread implications of midlife hearing loss for the mental and physical health of older adults. Structural brain imaging studies indicate the reduction of whole brain volume and temporal lobe atrophy in ARHL. fMRI studies also demonstrate that speech understanding in older adults with ARHL is more cognitively demanding and leads to accessibility to fewer brain resources for understanding conversational content or making memories. Ample evidence from epidemiological and experimental studies shows a strong association between ARHL and cognitive decline, and it is estimated that midlife hearing loss accounts for up to 9.1% of global dementia cases (Ford et al., 2018; Livingston et al., 2017). Although there is no consensus on the underlying causal links between auditory and cognitive decline, several theoretical mechanistic pathways are proposed, and future research should lead to further clarification. Similarly, during recent decades, structural and functional brain studies indicate the relationship between bothersome tinnitus and impairments in diverse aspects of cognitive function, especially executive control of attention and working memory. Given the high comorbidity of tinnitus with hearing loss, it is difficult, however, to differentiate how much of cognitive decline is resulting from tinnitus in different individuals. With respect to 1) current remarkable technological developments in hearing amplification devices; 2) extensive experimental, epidemiological, and clinical evidence that supports advantages of auditory amplification (as a non-pharmacological intervention) in reducing hearing handicap and depression, suppressing tinnitus, and improvements in cogitative function, social communication, and quality of life; 3) very low risk of aural rehabilitation treatments in age-related hearing loss and tinnitus; 4) a high rate of morbidity of dementia; and, 5) the absence of an effective treatment for dementia, regular hearing screening programs for identification and rehabilitation management of hearing loss and tinnitus is strongly recommended.

Despite current studies that cumulatively identify a link between midlife hearing loss and increased risk of developing neuropathological changes linked to cognitive decline or dementia, little mechanistic causal evidence has been found to explain this association. Future research will have to clarify whether there is a causal relationship between hearing loss and cognitive deterioration, or if these two are simply complementary dependent measures of a common neurological decline. Further clarification is also suggested to discriminate between age-related hearing loss and AD-related hearing loss with respect to differential diagnosis and normative behavioral data. Future research is also required to specify the neuropathological deficits in auditory processing that specifically result from AD compared to other chronic diseases in older adults. There are also a few recent preliminary laboratory animal studies in the relationship between ARHL and increased risk of cognitive impairment. It is expected that future advancements in this emerging field of study will be promising in response to many fundamental and methodological questions in human studies.

In the field of hearing amplification, with the exception of a few recent electrophysiological studies, there is little objective evidence that demonstrates neuronal changes subsequent to long-term use of hearing aids or CIs. The influence of factors such as years of hearing deprivation, the degree of cognitive decline, and stage of dementia on auditory amplification outcomes also have not been specified yet. In tinnitus studies, the homogenity in tinnitus severity, etiology, age, gender, hearing loss, anxiety, depression, and years of affliction are also suggested to decrease the risk of bias in future research, as well as to further clarify the outcome measures in tinnitus treatment interventions. It is expected that future neuroimaging and functional studies will have a direct impact on the development of the next generation of hearing aids in ARHL by unveiling the neural circuitry underpinning

the link between ARHL and cognitive impairment, as well as providing further convincing evidence concerning brain plasticity following long-term use of hearing amplification.

Declaration of Competing Interest

The authors claim no conflict of interest.

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