Aging Clin Exp Res (2014) 26:567–573
DOI 10.1007/s40520-014-0266-3

MINI REVIEW

Hearing loss and cognitive decline in older adults: questions and answers

Roberto Bernabei · Ubaldo Bonuccelli · Stefania Maggi · Alessandra Marengoni · Alessandro Martini · Maurizio Memo · Sergio Pecorelli · Andrea P. Peracino · Nicola Quaranta · Roberto Stella · Frank R. Lin · For the participants in the Workshop on Hearing Loss and Cognitive Decline in Older Adults

Received: 24 June 2014 / Accepted: 31 July 2014 / Published online: 4 October 2014

Abstract The association between hearing impairment, the diagnosis of dementia, and the role of sensory therapy has been proposed for some time, but further research is needed. Current understanding of this association requires the commitment of those experts who can integrate experience and research from several fields to be able to understand the link from hearing to dementia. A workshop whose panelists included experts from many areas, ranging from ear, nose and throat (ENT) to dementia's specialists, was promoted and organized by the Giovanni Lorenzini Medical Science Foundation (Milan, Italy; Houston, TX, USA) to increase the awareness of the relationship between hearing loss and dementia, and included questions and comments following a presentation from the clinical researcher, Frank Lin, who has been evaluating the relationship between hearing loss and cognitive decline since 2009.

Keywords Age-related hearing loss · Cognitive decline · Dementia · Interdisciplinary collaboration · Sensory therapy

Introduction

The clinical aspects of age-related hearing loss (ARHL) in many older adults are often perceived as an unfortunate but inconsequential part of aging. Researchers say hearing loss seems to speed up age-related cognitive decline, and think that treating hearing loss more aggressively could help delay cognitive decline and dementia. The devastating impact of dementia on affected individuals and the burden imposed on their families and society has made the prevention and treatment of dementia a public health priority. Interventions that could merely delay the onset of dementia

R. Bernabei
Department of Geriatrics, Neuroscience and Orthopaedics, Catholic University of the Sacred Heart, Rome, Italy

U. Bonuccelli
Neurology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

S. Maggi
Aging Branch, CNR Neuroscience Institute, Padua, Italy

S. Maggi
European Union Geriatric Medicine Society, Padua, Italy

A. Marengoni
Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

A. Martini
Department of Neuroscience and Sensory Organs, University Hospital of Padua, Padua, Italy

M. Memo
Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

S. Pecorelli
Rector of the University of Brescia, Brescia, Italy

A. P. Peracino (✉)
Fondazione Giovanni Lorenzini Medical Science Foundation, Milan, Italy
e-mail: andrea.peracino@lorenzinifoundation.org

A. P. Peracino
Fondazione Giovanni Lorenzini Medical Science Foundation, Houston, TX, USA

N. Quaranta
Otorhinolaryngology, Department of Basic Medical Science, Neuroscience and Sensory Organs, University of "A. Moro", Bari, Italy

by 1 year, from now, would lead to a more than 10 % decrease in the global prevalence of dementia in 2050. Unfortunately, there are no known interventions that currently have such effectiveness [1]. Frank Lin is the author of several recent studies which highlight the link between hearing and cognitive problems. The manifestations of age-related hearing loss (ARHL) in many older adults are subtle and thus hearing loss is often perceived as an unfortunate but inconsequential part of aging. Researchers say hearing loss seems to speed up age-related cognitive decline. Researchers think that treating hearing loss more aggressively could help delay cognitive decline and dementia. This paper highlights the questions and the relevant comments made during the workshop promoted and organized by the Giovanni Lorenzini Medical Science Foundation (Milan, Italy; Houston, TX, USA) to increase the awareness of the relationship between hearing loss and dementia and to stimulate interest and research in the field.

Questions and comments

What is the prevalence of hearing loss in the US and in Europe in adults and in those older than 70?

Hearing loss is an important public health concern with substantial economic costs and social consequences. Hearing impairment is the most frequent sensory deficit in human populations and affects newborns, children, adults, and the elderly [2]. In infants and children, hearing impairment retards the development of language and educational progress. In adults, it causes difficulties in both professional and social life, and as well as stigmatization. In the US [3], 26.7 million adults $\geq$50 years old suffer from hearing loss and 3.8 million use hearing aids. In England and Wales [4], 8.1 million suffer from hearing loss, of whom 1.4 million use hearing aids.

According to the United Nations, the overall global population will grow from 6.9 billion in 2010 to 9.3 billion in 2050. The proportion of the population aged 60 or older will nearly double in the same period, reaching 21 % of the total population in 2050, or nearly 2 billion people in 2050.

In 2008, the WHO estimated that over 360 million people (5.3 % of the global population) have disabling hearing loss, highest in developing regions (80 %) and lowest in high income regions [5].

These figures are expected to rise substantially in the future due to aging of the global population. There may be more than 700 million people with hearing loss worldwide by 2015 [6]. With the continued growth in the global population, this figure is expected to double to nearly 1.2 billion by 2050, most noticeably in people aged 60 and older.

In Europe, untreated hearing loss is estimated to cost € 213 billion a year [6, 7].

In 2025, it is estimated that 900 million people throughout the world will be hearing impaired; it is expected that around ten percent of these will be from Europe. In the next 100 years, hearing impairment is projected to affect about 30 percent of Europeans due to Europe's aging population. In Finland, 1 of 7 people deals with varying degrees of hearing loss; some form of hearing loss affects 1 in 6 Italians; and in Sweden and Denmark, 1 out of 10 people suffers from hearing loss. Medical costs (e.g. for hearing aids) account for only a small percentage of the overall cost. Untreated hearing loss costs in Europe are € 213 billion per year, about € 473 per year for each adult European. Sixteen percent of all adults in the whole Europe, more than 71 million people, suffer from a hearing loss greater than 25 dB, the definition of hearing loss recognized by the World Health Organization (WHO) [6]. In the European Union alone, more than 55 million people are hearing impaired, and the costs in the EU of unaided hearing impairment of all grades are 168 billion per year. Based on population statistics it is possible to calculate the yearly costs of untreated hearing loss in some European countries: Germany € 30,2 billion; France € 22,4 billion; United Kingdom € 22 billion; Italy € 21,3 billion; Spain € 16,3 billion; Poland € 14 billion; and the Netherlands € 6 billion.

In the USA hearing loss increases from 5 % for 40–49-year-olds to 75 % for those greater than 80 years of age [8].

What is the prevalence of worldwide dementia projected to be by 2050?

In 2005, 24.3 million people were estimated having dementia, with 4.6 million new cases of dementia every year (one new case every 7 s). This number was expected to double every 20 years to 8.1 million people by 2040 [9]. From some calculations the number of prevalent dementia cases in the year 2000 was 7.1 million, and in the next 50 years, this number will rise to about 16.2 million dementia sufferers [10]. Rates of increase are not uniform; numbers in developed countries were predicted to multiply by 100 % between 2001 and 2040, but by more than 300 %

R. Stella
Società Nazionale di Aggiornamento per il MMG-SNAMID and National Society for Medical Education in General Practice, Milan, Italy

F. R. Lin
Otolaryngology-Head and Neck Surgery, Geriatric Medicine, Mental Health, and Epidemiology, Johns Hopkins University, Baltimore, MD, USA

in India, China [9].The prevalence of dementia in the year 2000, in Europe, was 7.1 million, and was calculated to become about 16.2 million by 2050. Dementia, linked to expenditure on health and social care in Europe, is estimated to be responsible for 11,2 % of years of disability in people over 60 years of age, compared with 9.5 % for stroke, 5.0 % for cardiovascular disease, and 2.4 % for cancer. In Europe, the prevalence of Alzheimer disease (AD) increases exponentially with age [10].

Early detection of AD has a number of benefits to patients [11], their care-givers, and health and social care systems. Counseling and community services and support, lifestyle advice, cognitive training, and pharmacological therapy may all conserve cognition and function if the disease is detected early, thereby delaying institutionalization. Health and social care systems will also benefit financially from early detection of AD and delay in institutionalization [12].

Is hearing loss independently associated with accelerated cognitive decline, and incident cognitive impairment in community-dwelling older adults?

Some hearing researchers have concluded that most speech-understanding difficulties experienced by seniors are attributable to changes in peripheral hearing mechanisms rather than to age-related declines in cognitive abilities per se. Reduced speech understanding among seniors during more complex or noisy listening situations appear to involve additional factors not predictable from the audiogram. Such findings are consistent with cognitive models that describe an overall reduction in the speed of mental processing [13]. Many medical conditions are implicated in presbyacusis [14] such as: heredity (that may contribute up to 50 %), noise, history of chronic middle ear inflammation, and cardiovascular factors including diabetes, smoking and hypertension; additional relevant factors are hormones (including estrogen), exposure to ototoxic medication or chemicals and co-morbidities. As an example, ARHL seems to be more prevalent in patients with rheumatologic disease. Age-related hearing loss (ARHL) in humans is, in many occasions, due to: cochlear aging, environmental factors such as noise exposure, genetic predisposition, and health co-morbidities such as cigarette smoking and atherosclerosis. The primary pathology of ARHL includes the hair cells, stria vascularis, and afferent spiral ganglion neurons as well as the central auditory pathways. Genetic investigation has identified several putative associated genes, including those related to antioxidant defense and atherosclerosis. Exposure to noise is known to induce excess generation of reactive oxygen species (ROS) in the cochlea; cumulative oxidative stress can be enhanced by relatively hypoxic situations resulting from the impaired homeostasis of cochlear blood supply due to atherosclerosis, which could be accelerated by genetic and co-morbidity factors. Antioxidant defense systems may also be influenced by genetic backgrounds. These may explain the large variations of the onset and extent of ARHL among the elderly [15].

Considering cognitive function as an intellectual process that involves all aspects of perception, thinking, reasoning, recollecting, evaluating, etc., it is possible to understand the correlation between hearing loss and some modified brain perception activities.

One link between hearing loss and healthy aging presented by Frank Lin is through effects of hearing loss on cognitive load. Poorer hearing is associated with: (a) a reduced language-driven activity in primary auditory pathways [16], and (b) an increased compensatory language-driven activity in pre- frontal cortical areas [17]. Such a cognitive load could, therefore, affect an individual's performance in usual activities and cognitive tasks (among the criteria for the diagnosis of dementia).

Another link between hearing loss and healthy aging is through effects of hearing impairment on brain structure/function. In humans, hearing loss is associated in cross-sectional studies with: (a) reduced cortical volumes in primary auditory cortex [18], and (b) variation in central auditory white matter tract integrity on diffusion tensor imaging (DTI) [19]. A recent longitudinal study [20] has also demonstrated that hearing impairment is associated with accelerated atrophy in whole brain volumes and regions in the superior, middle, and inferior temporal gyri (regions critical for auditory processing but that also underlie other cognitive functions). Reduced stimulation from impoverished auditory signals from hearing impairment could plausibly contribute to alternations in brain structure/function. Alternatively, these associations could also be the result of a shared pathologic etiology such as from microvascular disease and Alzheimer's neuropathology [21].

Social isolation is a third possible link between hearing loss and healthy aging. Impaired communication from hearing loss could contribute to social isolation which is associated with poorer cognitive and physical functioning through: (a) upregulation of pro-inflammatory genes and increased inflammation [22, 23]; (b) poorer health behavioral pathways: smoking, adherence to medical treatment, diet, exercise, and (c) psychological pathways: self-esteem, self-efficacy, coping, sense of well-being.

In summary, hearing loss could impact several domains of healthy aging including social engagement, physical mobility and activity, falls, vitality, and dementia through several, non-mutually exclusive mechanistic pathways.

Is the use of standardized audiometric and cognitive tests effective in evaluating the association of hearing loss with cognitive trajectories and incident cognitive impairment?

Ongoing epidemiologic studies incorporating assessments of objective audiometric data and neurocognitive functioning will help to elucidate the association of hearing loss with cognitive trajectories and dementia. Current epidemiologic datasets that contain objective audiometric and neurocognitive data include: BLSA (Baltimore Longitudinal Study of Aging) [1], and the Health ABC (Health, Aging, and Body Composition) studies [24]. Hearing data have also begun to be collected in the USA in the ARIC (Atherosclerosis Risk in Communities Study: 7/1/1985–1/31/2016) and in Australia in the ASPREE (ASPirin in Reducing Events in the Elderly) clinical trial [25]; other previous Australian longitudinal studies (DYNOPTA; http://dynopta.anu.edu.au/) also have collected hearing data. Current/future longitudinal epidemiologic studies of older adults that are focused on cognition/dementia as possible outcomes should consider including audiometric assessments in the study protocol as routinely gathered data.

Are there independent associations between peripheral hearing impairment and brain structure/function?

Hearing impairment could potentially constitute a "second hit" on the brain and thereby adversely affect cognitive performance and increase the risk of dementia by adding to brain pathology resulting from other disorders (e.g., amyloid-beta accumulation, neurofibrillary tangles, and microvascular disease). For example, cross-sectional neuroimaging studies have demonstrated that peripheral hearing impairment is associated with reduced cortical volumes in the primary auditory cortex [16, 26, 27] and variation in the integrity of central auditory white matter tracks [19, 28]. Longitudinal data from animal models [29–31] also demonstrate that cochlear impairment may precipitate changes in cortical reorganization and brain morphometry. A recent neuroimaging study [21] using longitudinal MRI data from the BLSA demonstrated that individuals with hearing impairment had accelerated rates of whole brain atrophy as well as specific volume declines in the right superior, middle, and inferior temporal gyri over a mean 6.4 years of follow-up. These temporal regions are intriguing because they are important not only for spoken language processing [32], but also for semantic memory, sensory integration, and are involved in the early stages of mild cognitive impairment or early Alzheimer disease [33].

Could the hearing loss rehabilitative therapies moderate, delay, or prevent dementia?

Comprehensive hearing rehabilitative interventions that incorporate the use of sensory aids and rehabilitative counseling to maximize the audibility of speech signals and could plausibly lessen cognitive load [34], provide increased auditory stimulation, and promote social engagement. However, there has been no research that has investigated whether such therapies could actually reduce the risk of cognitive decline and dementia. There has only been one randomized clinical trial of hearing loss treatment [35] that has examined outcomes beyond measures of speech perception and quality of life. In this trial of 192 veterans performed more than two decades ago, individuals were randomized to immediate treatment (provision of a single monaural analog hearing aid *without* further training or counseling) versus no treatment. Outcomes at 4 months post-randomization demonstrated improved social and emotional function, communicative abilities, and cognitive function (as measured with a simple cognitive screening test [Short Portable Mental Status Questionnaire]) in the treatment group. These initial results have never been confirmed in a trial with a larger and more representative cohort, using more current hearing rehabilitative strategies (e.g., digital hearing aids, provision of rehabilitative counseling), and evaluating cognition comprehensively with longer periods of follow-up (to observe for reduced rates of cognitive decline over a several year period rather than an acute "improvement" in cognitive scores immediately post-treatment).

Results from observational epidemiologic studies of hearing loss and cognition have not found significant associations between hearing aid use and cognition [1, 24, 36, 37]. For example, in the Health ABC study, individuals using hearing aids versus those without hearing aids had lower rates of annual score declines on both the 3MS (-0.62 vs. -0.77 points/year, $p = 0.36$) and the DSST (-0.82 vs. -0.98 points/year, $p = 0.34$) [24], but these results were not significant. However, data on other key variables (e.g., years of hearing aid use, adequacy of hearing aid fitting and rehabilitation, etc.) that would affect the success of hearing loss treatment and affect any observed association were not available. Results obtained from observational studies must also be interpreted with caution because individuals choosing to use a hearing aid likely differ significantly from those individuals not using a hearing aid in both measured and unmeasured factors. Consequently, determining whether hearing rehabilitative strategies could affect cognitive decline will likely never be answered from observational studies and will require an RCT. Such a trial is currently being planned in conjunction

with the National Institute on Aging and using the existing infrastructure of the Atherosclerosis Risk in Communities Study in the United States.

Interdisciplinary collaboration

The association between not just hearing sensory impairment (but also of other senses, such olfactory, visual and touch), the diagnosis of dementia, and the role of sensory therapy has been suggested for a long time, but has not been the focus of concerted research; current understanding is patchy due to small numbers of underpowered and heterogeneous studies. With the aging population and rising prevalence of dementia, there is widespread interest in markers of early signs of dementia and tests to identify which patients with mild cognitive impairment (MCI) will progress to dementia. People with dementia are very sensitive to changes in environmental conditions [38]. Interdisciplinary collaborations among the experts are must not only under the scientific and clinical point of view but also of the social impact globally.

Conflict of interest Dr. Lin reports being on the scientific advisory board of Pfizer and Autifony, a consultant to Cochlear Ltd., and a speaker for Med El and Amplifon. The other authors have no conflicts of interest.

Appendix

From a Workshop promoted and coordinated by the Giovanni Lorenzini Medical Science Foundation (Milan, Italy and Houston, TX, USA) and held in Bologna, Italy, on April 15, 2014.

Participants

Roberto Bernabei - Department of Geriatrics, Neuroscience and Orthopaedics - Catholic University of the Sacred Heart - Rome, Italy

Stefano Berrettini - ENT Audiology and Phoniatrics Unit - Department of Neuroscience - University of Pisa - Pisa, Italy

Antonella Bertolotti - Cariplo Foundation - Research Area - Milan, Italy

Ubaldo Bonuccelli - Neurology Unit - Department of Clinical and Experimental Medicine - University of Pisa - Pisa, Italy

Andrea Canale - ENT Department 2 - AO Città della Salute e della Scienza of Turin - Turin, Italy

Alessandro Castiglione - Department of Neurosciences - Complex Operative Unit of Otorhinolaryngology and Otosurgery - University Hospital of Padua - Padua, Italy

Eliana Cristofari - Audiology Department - Ospedale di Circolo e Fondazione Macchi - Varese, Italy

Domenico Rosario Cuda - ENT Department - Guglielmo da Saliceto Hospital - Piacenza, Italy

Antonio De Caria - Audiologist - Mantova, Italy

Emanuela Folco - Fondazione Giovanni Lorenzini Medical Science Foundation - Milan, Italy and Houston, TX, USA

Carlo Gabelli - Regional Center for Brain Aging - Dept. of Internal Medicine - University of Padua - Padua, Italy

Elisabetta Genovese - ENT Department - University of Modena and Reggio Emilia, Modena, Italy

Enrico Ghidoni - Clinical Neuropsychology - Cognitive Disorders and Adult Dyslexia Unit-Neurology Department - S. Maria Nuova Hospital - IRCCS - Reggio Emilia, Italy

Carlo Antonio Leone - Department of Otolaryngology-Head-Neck Surgery - Monaldi Hospital - Naples, Italy

Frank R. Lin - Otolaryngology-Head & Neck Surgery, Geriatric Medicine, Mental Health, and Epidemiology - Johns Hopkins University - Baltimore, MD, USA

Stefania Maggi - CNR Neuroscience Institute - Aging Branch-Padua, Italy and President Elect - European Union Geriatric Medicine Society - Padua, Italy

Alessandra Marengoni - Department of Clinical and Experimental Sciences - University of Brescia - Brescia, Italy

Alessandro Martini - Department of Neuroscience and Sensory Organs - University Hospital of Padua - Padua, Italy

Marco Mauri - U.O. Neurology - Ospedale di Circolo Varese Italy - Assistant Professor - University of Insubria Varese - Varese, Italy

Maurizio Memo - Department of Molecular and Translational Medicine - University of Brescia - Brescia, Italy

Alessandro Padovani - Neurology Unit - Department of Clinical and Experimental Sciences University "Health and Wealth" of Brescia, Italy

Gaetano Paludetti - Surgical Sciences for Head and Neck Pathologies Department - Catholic University of the Sacred Heart - Rome, Italy

Sergio Pecorelli - Rector of the University of Brescia - Brescia, Italy

Andrea Peracino - Fondazione Giovanni Lorenzini Medical Science Foundation - Milan, Italy and Houston, TX, USA

Antonio Pirodda - Otorhinolaryngology at the University of Bologna - Chief of the ENT Unit - Policlinico S. Orsola Malpighi - Bologna, Italy

Alfredo Postiglione - Department of Clinical Medicine and Surgery, University "Federico II", Naples, Italy

Nicola Quaranta - Otorhinolaryngology - Department of Basic Medical Science, Neuroscience and Sensory Organs - University of "A. Moro" - Bari, Italy

Luca Oscar Redaelli De Zinis - Department of Otorhinolaryngology - Head and Neck Surgery University of Brescia - Spedali Civili Brescia - Brescia, Italy

Roberto Stella - Società Nazionale di Aggiornamento per il MMG-SNAMID and National Society for Medical Education in General Practice - Milan, Italy

Rosanna Tortelli - Unit of Neurodegenerative Diseases - Department of Clinical Research in Neurology - University of Bari "A. Moro" at Pia Fondazione Card. G. Panico, Tricase (Lecce), Italy and Department of Basic Medical Sciences, Neurosciences and Sense Organs - University of Bari "A. Moro" - Bari, Italy

References

1. Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrucci L (2011) Hearing loss and incident dementia. Arch Neurol 68:214–220
2. Mathers C, Smith A, Concha M (2000) Global burden of hearing loss in the year 2000 Geneva, World Health Organization. http://www.who.int/medicines/areas/priority_medicines/Ch6_21Hearing.pdf
3. Chien W, Lin FR (2012) Prevalence of hearing aid use among older adults in the United States. Arch Int Med 172:292–293
4. Taylor RS, Paisley S (2000) The clinical and cost effectiveness of advances in hearing aid technology. NICE Report. http://www.gserve.nice.org.uk/nicemedia/pdf/hearing_hta_report.pdf
5. Stevens G, Flaxman S, Brunskill E, Mascarenhas M, Mathers CD, Finucane M, On behalf of the Global Burden of Disease Hearing Loss Expert Group (2013) Global and regional hearing impairment prevalence: analysis of 42 studies in 29 countries. Eur J Public Health 23:146–152
6. Shield B (2006) Evaluation of the social and economic costs of hearing impairment. Hear-it. http://www.hear-it.org
7. Roth TN, Hanebuth D, Probst R (2011) Prevalence of age-related hearing loss in Europe: a review. Arch Otorhinolaryngol 268:1101–1107
8. Lin FR, Ferrucci L (2011) Hearing loss and falls among older adults in the United States. Arch Int Med 171:369–371
9. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, Hall K, Hasegawa K, Hendrie H, Huang Y, Jorm A, Mathers C, Menezes PR, Rimmer E, Scazufca M (2005) Alzheimer's Disease International. Global prevalence of dementia: a Delphi consensus study. Lancet 366:2112–2117
10. Wancata J, Musalek M, Alexandrowicz R, Krautgartner M (2003) Number of dementia sufferers in Europe between the years 2000 and 2050. Eur Psychiatry 18:306–313
11. Banerjee S, Willis R, Matthews D, Contell F, Chan J, Murray J (2007) Improving the quality of care for mild to moderate dementia: an evaluation of the Croydon Memory Service Model. Int J Geriatr Psychiatry 22:782–788
12. Todd S, Passmore P (2008) Alzheimer's disease—the importance of early detection European. Neurol Rev 3:18–21
13. Martin JS, Jerger JF (2005) Some effect of aging on central auditory processing. J Rehabil Res Dev 42:25–44
14. Huang Q, Tang J (2010) Age related hearing loss or presbycusis. Eur Arch Otorhinolaryngol 267:1179–1191
15. Yamasoba T, Lin FR, Someya S, Kashio A, Sakamoto T, Kondo K (2013) Current concepts in age-related hearing loss: epidemiology and mechanistic pathways. Hear Res 303:30–38
16. Peelle JE, Troiani V, Grossman M, Wingfield A (2011) Hearing loss in older adults affects neural systems supporting speech comprehension. J Neurosci 31:12638–12643
17. Grossman M, Cooke A, DeVita C, Chen W, Moore P, Detre J, Alsop D, Gee J (2002) Sentence processing strategies in healthy seniors with poor comprehension: an fMRI study. Brain Lang 80:296–313
18. Eckert MA, Kuchinsky SE, Vaden KI, Cute SL, Spampinato MV, Dubno JR (2013) White matter hyperintensities predict low frequency hearing in older adults. J Assoc Res Otolaryngol 14:425–433
19. Chang Y, Lee SH, Lee YJ, Hwang MJ, Bae SJ, Kim MN, Lee J, Woo S, Lee H, Kang DS (2004) Auditory neural pathway evaluation on sensorineural hearing loss using diffusion tensor imaging. Neuroreport 15:1699–1703
20. Lin FR, Ferrucci L, An Y, Goh JO, Doshi J, Metter EJ, Davatzikos C, Kraut MA, Resnick SM (2014) Association of hearing impairment with brain volume changes in older adults. Neuroimage 90:84–92
21. Lin FR, Albert M (2014) Hearing loss and dementia—Who's Listening? Aging Ment Health 18:671–673
22. Cole SW, Hawkley LC, Arevalo JM, Sung CY, Rose RM, Cacioppo JT (2007) Social regulation of gene expression in human leukocytes. Genome Biol 8:R189
23. Cole SW, Hawkley LC, Arevalo JM, Cacioppo JT (2011) Transcript origin analysis identifies antigen-presenting cells as primary targets of socially regulated gene expression in leukocytes. Proc Natl Acad Sci USA 108:3080–3085
24. Lin FR, Yaffe K, Xia J, Xue Q-L, Harris TB, Purchase-Helzner E, Satterfield S, Ayonayon HN, Ferrucci L, Simonsick EM, for the Health ABC Study Group (2013) Hearing loss and cognitive decline in older adults. JAMA Intern Med 173:293–299
25. Australia by the ASPREE clinical trial. http://www.aspree.org
26. Eckert MA, Cute SL, Vaden KI Jr, Kuchinsky SE, Dubno JR (2012) Auditory cortex signs of age-related hearing loss. J Assoc Res Otolaryngol 13:703–713
27. Husain FT, Medina RE, Davis cw, Szymko-Bennett Y, Simonyan K, Pajor NM, Horwitz B (2010) Neuroanatomical changes due to hearing loss and chronic tinnitus: a combined VBM and DTI study. Brain Res 1369:74–88
28. Lin YC, Wang JJ, Wu CM, Wai YY, Yu JF, Ng SH (2008) Diffusion tensor imaging of the auditory pathway in sensorineural hearing loss: changes in radial diffusivity and diffusion anisotropy. J Magn Reson Imaging 28:598–603
29. Groschel M, Gotze R, Ernst A, Basta D (2010) Differential impact of temporary and permanent noise-induced hearing loss on neuronal cell density in the mouse central auditory pathway. J Neurotrauma 27:1499–1507
30. Kakigi A, Hirakawa H, Harel N, Mount RJ, Harrison RV (2010) Tonotopic mapping in auditory cortex of the adult chinchilla with amikacin-induced cochlear lesions. Audiology 39:153–160
31. Schwaber MK, Garraghty PE, Kaas JH (1993) Neuroplasticity of the adult primate auditory cortex following cochlear hearing loss. Am J Otol 14:252–258
32. Peellee JE (2012) The hemispheric lateralization of speech processing depends on what "speech" is: a hierarchical perspective. Front Hum Neurosci 6:1–4
33. Chetelat G, Landeau B, Eustache F, Mezenge F, Viader F, de la Sayette V, Desgranges B, Baron J-C (2005) Using voxel-based morphometry to map the structural changes associated with rapid conversion in MCI: a longitudinal MRI study. Neuroimage 27:934–946
34. Sarampalis A, Kalluri S, Edwards B, Hafter E (2009) Objective measures of listening effort: effects of background noise and noise reduction. J Speech Lang Hear Res 52:1230–1240

35. Mulrow CD, Aguilar C, Endicott JE, Tuley MR, Velez R, Charlip WS, Rhodes MC, Hill JA, DeNino LA (1990) Quality-of-life changes and hearing impairment. A randomized trial. Ann Intern Med 113:188–194
36. Lin FR (2011) Hearing loss and cognition among older adults in the United States. J Gerontol A Biol Sci Med Sci 66:1131–1136
37. Lin FR, Ferrucci L, Metter EJ, An Y, Zonderman AB, Resnick SM (2011) Hearing loss and cognition in the Baltimore Longitudinal Study of Aging. Neuropsychology 25:763–770
38. Van Hoof J, Kort HS, Duijnstee MS, Rutten PG, Hensen JL (2010) The indoor environment and the integrated design of homes for older people with dementia. Build Environ 45:1244–1261