

Is age-related hearing loss a potentially modifiable risk factor for dementia?



The public health burden of dementia is of increasing concern as older adults represent an increasing percentage of the human population in the 21st century. Alzheimer's disease, the most common form of dementia, is a leading cause of mortality worldwide. Clinical trials aimed toward developing a disease-modifying pharmacological treatment for Alzheimer's disease are ongoing but progress has been slow because the cause of this disease remains unclear due to its complex and multifactorial pathogenesis.¹ In a *Lancet* Commission published in 2020, it was reported that modification of 12 risk factors across the lifespan could substantially help reduce the global impact of dementia.² The most consequential of these risk factors was age-related hearing loss,² which is predicted to affect nearly 2.5 billion people globally by 2050.³ Similarly, a meta-analysis has also reported an association of age-related hearing loss with accelerated cognitive decline and an increased risk of developing cognitive impairment along with dementia.⁴ However, a limitation of this research is the small number of cohort studies of dementia, since only three met the inclusion criteria including the use of pure-tone audiometry, an objective measure of peripheral hearing loss.^{2,4}

In a study by John Marinelli and colleagues,⁵ reported *The Lancet Healthy Longevity*, the association between age-related hearing loss and dementia was examined using data from 1200 participants. These individuals were a subsample from the Mayo Clinic Study of Aging (MCSA), a population-based study of risk factors for mild cognitive impairment and dementia. Hearing function was assessed objectively by an audiologist using pure-tone audiometry and word recognition scores. It was also assessed using an informant-based measure. Over a mean follow-up of 7 years, 207 (17%) participants developed dementia. The association of the hearing measures with dementia was evaluated using Cox proportional hazards regression models adjusted for demographic and health-related factors including APOE $\epsilon 4$ carriership and hearing rehabilitation. By contrast with previous research, neither of the objective measures of hearing loss were significantly associated with an increased risk of dementia, whereas informant-based

hearing difficulties did show a significant association with the development of dementia. However, both objective measures were significantly associated with poorer scores in assessment of global cognition and four cognitive domains (memory, attention/executive function, language, and visuospatial skills) whereas informant-based hearing difficulty was associated with poorer scores in language only.

A possible explanation for the discrepancy of these findings with those of previous studies^{2,4} is how this subsample of the MCSA was selected. It was based on participants who had undergone audiometric evaluation due to hearing concerns or a health assessment.⁵ Additionally, a higher percentage of those included reported having undergone hearing rehabilitation than the other MCSA participants. However, the pure-tone audiometric outcomes of the sample were well distributed and previous studies have reported a dose-response relationship between this measure and the risk of developing dementia. These interesting findings require further exploration, particularly because age-related hearing loss and dementia are complex disorders and the mechanistic basis underlying their potential association has not yet been clarified.⁶ In the pathophysiology of age-related hearing loss, there can be a deterioration in peripheral and central auditory processes,^{6,7} which have been linked to dementia in separate cohort studies.⁶ The findings of this study highlight the importance of a more comprehensive assessment of these processes, and therefore age-related hearing loss, when examining how their impairment could relate to the risk of developing dementia.

The relationship of measures of age-related hearing loss such as pure-tone audiometry might not be as consistently associated with risk of dementia as previous studies have suggested. Peripheral age-related hearing loss has been posited as a midlife risk factor for dementia² and the strength of this association might alter with severity or with years lived with age-related hearing loss. Other epidemiological research has reported that the initial stages of age-related hearing loss (assessed with pure-tone audiometry) might be associated with a higher rate of cognitive decline than later stages,⁸ and

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greater severity of hearing loss may be increasingly less predictive of further decline.⁴ In later age-related hearing loss, measures of impairment in central auditory processing might become more sensitive to risk of dementia than peripheral auditory function.⁵ Future clinical trials must clarify this and also ascertain whether there is a window after onset of age-related hearing loss during which its treatment could significantly reduce future risk of dementia. Additionally, research that further examines the association of age-related hearing loss with biomarkers of dementias including Alzheimer's disease would also help assess its clinical relevance as a potentially modifiable risk factor.⁹ Further examination of this association in more diverse populations is required to estimate its potential impact worldwide, especially because around two-thirds of people with dementia live in low-income and middle-income countries.¹⁰

I declare no competing interests.

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