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Review Article

An Overview of Auditory and Vestibular Disorders in Alzheimer's Disease: A Narrative Review

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ABSTRACT

Alzheimer's disease (AD) is the most common cause of dementia which, in addition to affecting memory, cognition, language, and other functions, also appears to be associated with hearing loss and vestibular function. In this paper, the neural pathology of AD, relation to neuroplasticity, and associations between AD and auditory and vestibular dysfunction have been reviewed. In this narrative study, articles published between 2000 and 2021 were reviewed. Fifty articles, related mostly to hearing and vestibular disorders in AD, were selected from a review of 200 English articles. The keywords Alzheimer's disease, neuroplasticity, auditory and vestibular rehabilitation, auditory and vestibular disorders were searched in PubMed, ScienceDirect, Scopus, ProQuest and Google Scholar databases. Recent studies have shown an association between AD and auditory and vestibular function. Hearing loss can cause dementia and reduced communication skills in patients with AD. It has also been observed that some patients with AD lose their vestibular function, leading to an imbalance in the body and an increased risk of falling. It seems neuroplasticity of the brain is a good treatment for degenerative diseases such as AD, which is possible through auditory and vestibular rehabilitation. Hearing and vestibular evaluation in people with AD can be effective in identifying related problems, so that in cases where the disorder is observed, through the phenomenon of neuroplasticity and the use of auditory and vestibular rehabilitation, therapists can take effective steps in improving the performance and quality of life of these patients.

Background

Based on the World Alzheimer Report 2021, dementia is currently the 7th cause of mortality universally. Not only among those with the highest cost to society as previously noted, but also from 55 million people now living with dementia, maybe less than a quarter of them around the world are correctly diagnosed [1].

In elderly people, dementia can occur as one of the most prevalent brain disorders. Alzheimer's disease (AD) is the most common cause of dementia. AD mostly appears as progressive memory decline along with other cognitive

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impairments, such as visuospatial abnormalities, navigation difficulties, and language disturbance. These cognitive dysfunctions and dementia affect the life quality and daily activities, global functioning, physical health, and many behavioral psychological symptoms of dementia [2, 3]. It is helpful to identify possibly modifiable risk factors for the management of patients with AD and to slow the progressive process [4].

One of the risk factors for dementia is hearing loss. Age related hearing loss or presbycusis is the most frequent sensory deficit in elderly people which is defined as progressive, symmetrical, bilateral hearing loss caused by aging effects on the auditory system [5, 6]. The factors related to dementia and age-related hearing impairment include age, environment, genetics, lifestyle, drugs, and other factors [7]. The prevalence of AD or other dementias and hearing disability will be highly increased as the number of elderly people is increasing steadily [8].

In addition to hearing loss, aging can adversely affect the vestibular system including a reduction in number of vestibular hair cells, the size and number of neurons of the vestibular nucleus, and the number of vestibular nerve fibers [9]. Factors such as changes of somatosensory function due to aging, cognitive decline, and decreased strength may also impact balance-related sensory integration in the elderly population with vestibular pathology [10, 11].

Many studies have explored the relationship between AD and auditory-vestibular disorders [12–14]. The inner ear is part of the peripheral auditory system which includes the cochlea and vestibular organs, i.e. the utricle, saccule, and three semicircular canals. The peripheral vestibular organ sends widespread projections, the neural basis for the association between vestibular and cognitive function, to cortical areas involved in memory and spatial orientation, especially the hippocampus [10]. Harun et al. revealed that the vestibular function in patients with cognitive impairment is poorer compared with age-matched controls, and they observed a significantly higher prevalence of vestibular loss among individuals with dementia. In addition, it has been found that patients with dementia compared to controls have greater impairments of both saccular and utricular function, although there was no semicircular canal dysfunction. Finally, vestibular disorder is more likely to occur in individuals with AD than in age-matched controls [15].

Auditory sensory organs are triggered by related stimuli and send neural impulses along the cochlear nerve to the central auditory nervous system, terminating at the temporal lobe. The central auditory system begins at the cochlear nucleus in the brainstem and its neural pathways which conduct to the auditory cortex [16]. According to anatomy and physiology, it is rational that hearing loss occurs due to any auditory organ damage or central auditory processing dysfunction [7]. In exploring the relationship between hearing loss and AD, researchers suggested that either peripheral or central auditory system changes can be found in early stages of AD, so they can be an early probable manifestation of AD. Hence, it is effective to assess peripheral and central auditory system in at-risk subjects for early diagnosis of AD and planning of rehabilitation interventions to ameliorate their quality of life [17].

In this review, the current evidence on the neural pathology of AD, association between AD and auditory dysfunctions, association between AD and vestibular dysfunctions, clinical management of patients with AD and auditory and vestibular dysfunction, and the association between neuroplasticity and AD will be discussed.

Methods

This narrative review included articles from April 2006 to November 2021. From the 200 English-written texts primarily identified, 49 papers, most of which were related to auditory and vestibular disorders in AD, were selected and reviewed. Papers were found by a search for the keywords AD, neuroplasticity, aural and vestibular rehabilitation, auditory and vestibular disorders in search engines such as PubMed, ScienceDirect, Scopus, ProQuest, and Google Scholar. Papers which were not full text and those presented in a congress were excluded.

Results

Neural Pathology of AD

AD is a neurodegenerative disorder, the main cause of which is not yet clear, but factors like beta-amyloid (βA) plaque, hyperphosphorylated tau, apolipoprotein E (APOE) gene, and autoimmune disorders have been introduced as potential reasons for this disorder. Among these factors, βA may have the greatest effect [18, 19]. It may play a role in neurodegeneration by disrupting synapses and increasing tau [20]. Tau is one of the microtubule-associated proteins found in significant amounts in neurons in the distal parts of axons. In its normal condition, tau contributes to diverse cellular processes by binding to different proteins [21, 22]. One study indicated that βA and tau caused dysfunction in different stages. It was demonstrated that synaptic dysfunction was one of the reasons of dementia and cognitive decline in AD [23]. Hearing loss is also associated with AD, as it affects hippocampal and memory damage, and its suggested mechanism can be related to pathological tau [24]. Several common enzymes and proteins may have a role in the pathogenesis of both presbycusis and AD. An abnormal expression of these structures such as vascular endothelial growth factor (VEGF) may cause both AD and dysfunction of cochlear hair cells. Furthermore, it is hypothesized that their common pathological pathways may also impact the progression of each other [7, 25].

Other factors like physical activity can decrease toxic tau and βA. As mentioned above, tau is one of the microtubule-associated proteins found significantly in neurons in distal parts of axons. The normal form of tau plays an operational role in cell structure, but when it aggregates and hyper-phosphorylates, it abnormally produces neurofibrillary tangles (NFTs). NFTs can affect neuroplasticity in two ways: a) preserve nodes of the brain network by reducing degeneration; b) damage axon activity and deactivate synapses. Therefore, it reduces the connections between neural networks. The abnormal form of tau may cause

mislocalization to dendritic spines and thereby change the ratio of AMPA receptors to N-methyl-D-aspartate receptors (some of the main components of synaptic plasticity) and cause a defect in neuroplasticity [21, 22]. Because toxic tau and βA can negatively affect neuroplasticity, these factors will preserve synaptic activity, increase neural plasticity, and finally regress AD condition [26]. It has been demonstrated that treatments which target synaptic plasticity can affect memory positively and reduce AD symptoms, thus improving hippocampal long-term potentiation, which is a process in synaptic plasticity and involved in restoring the brain's networks [27].

Aassociations between AD and Auditory Dysfunction

Evidence suggests that characteristic pathological changes including senile plaques, and NFTs have also been observed in the major thalamic relay station for the auditory system known as the ventral nucleus of the medial geniculate body, which has a relationship with the inferior colliculus by neural fibers, the central nucleus of the inferior colliculus, and primary auditory and the auditory association cortices. Thus, it is not surprising that there is an association between hearing loss and cognitive decline [28]. A biological study using animal models showed that damage to the central auditory system causes damage to hippocampal synapses or increases the vulnerability of these synapses to damage, resulting in hearing loss being a risk factor for AD [29]. In addition, hearing loss in older people may lead to perceptual effort, partly because the auditory signal is poor and degraded by peripheral hearing loss, and due in part to atrophy of the auditory cortex. Age, therefore, potentially disrupts auditory processing. In such situations, more cognitive resources will be needed, even in quiet conditions, to achieve auditory perception. As a result, elderly people will have difficulty hearing and understanding the meaning of words in background noise and may ultimately withdraw from conversations. This induces perceptual effort, and reduced cognitive spare capacity could be what accelerates cognitive decline in elderly, hearing impaired people, and isolationism may be a result [30, 31]. Among all hypotheses, the most accepted one to explain the correlation between AD and hearing loss is that hearing impairment may result in sensory deprivation and social isolation which leads to dementia [32]. Central auditory impairment, which is suggested to possibly be the main auditory impairment related to AD, may lead to both dementia and deterioration of peripheral hearing [33]. A study that explored the molecular pathway that may be involved in the pathogenesis of hearing loss and AD concluded that peripheral hearing loss may play a more direct role in dementia. Moreover, hearing loss is associated with a reduction in the volume of tissue in the auditory cortex, temporal lobe, and the entire brain [34]. All in all, AD and hearing loss in older adults can highly manifest together. However, it does not clearly determine that their relationship is surely unidirectional or bidirectional or that they are both just the clinical manifestations of aging [7].

Aassociations between AD and Vestibular Dysfunction

Recent research has shown that patients with AD have vestibular function loss [14, 15]. It should be noted that the first target of AD is atrophy of the hippocampus which is associated with memory and may cause memory impairment [12]. The hippocampus plays a very important role in aspects of memory, such as retrieval, encoding, consolidation, and spatial memory functions. Scientists emphasize that there is a direct relationship between spatial memory, hippocampal size, and navigation. Head direction cells of the thalamus and place cells of the hippocampus become active after vestibular stimulation, and fMRI also shows that in caloric stimulation, hippocampal formation is active. The pedunculopontine tegmental nucleus and the dorsal tegmental nucleus are the anatomical connections which join the hippocampus to the vestibular nuclei via the thalamus. Following chronic bilateral vestibular loss (BVL) or spatial memory disturbance, navigational deficits and hippocampal atrophy will appear [35]. It is suggested that reduced vestibular function may appear at the onset of AD [36]. The risk factors for AD implicated in vestibular dysfunction are age, diabetes, cardiovascular insufficiency, and traumatic brain injury [32]. Vestibular dysfunction is known to lead to vertigo and postural instability. The risk of falling is increased, and patients will have difficulty performing daily living activities [16, 20]. From the point of correlation between vestibular function and AD, it is demonstrated that the vestibular system has an important role in cognition and emotion [36]. Vestibular impairment may cause reduced saccular functions and reduced spatial cognition. In one study, EEG showed that an increase in vestibular cortical area activity occurred with saccular stimulation. In this experiment, AD patients had poorer saccular and lost spatial cognitive function [14]. So, the neural system is destroyed in AD, and vestibular dysfunction (especially if it is reciprocal) is a result of atrophy of this system. Damage to sensory organs induces apoptotic cell death with synapses removed from the end-organ, and eventually anterograde degeneration occurs [36].

These studies indicated that because of the role of the vestibular system in spatial memory, vestibular loss could be not only a risk factor for dementia, but also a contributing factor to the development of AD. It has been proposed that age related vestibulolimbic/cortical pathways degeneration could be relevant to the development of AD [36].

Clinical Management of Patients with AD and Auditory Dysfunction

Currently, there is no certain treatment for dementia. However, management of risk factors for cognitive loss may be significantly effective [4]. Many studies have suggested that the evaluation of brain and central auditory function as well as peripheral auditory system in cases of age-related hearing loss is necessary for the early diagnosis of and intervention in possible AD occurrence. Elderly people with severe central auditory dysfunction need special interventions including not only hearing assessment, but also auditory rehabilitation, cognitive psychology, and neurologic evaluation [13, 37, 38].

Hearing aids (HAs) are a helpful tool in aural

rehabilitation to either delaying dementia or improve auditory skills [39, 40]. In a study investigating the efficacy of HAs as an auditory rehabilitation strategy, audiometric promotion and better speech recognition threshold approved by positive changes of functional magnetic resonance imaging (fMRI) activity and cortical thickness after one year of HA use were shown. These physiological and anatomical changes in auditory, language, and multimodal cortices suggest hearing aid efficacy for the management of hearing-impaired patients [41]. Among studies on HA efficacy in AD patients, speech perception in quiet, self-reported listening disability, and quality of life improvement as well as improvement in both speech recognition in a monaural task and dichotic listening in a binaural integration task after HA use were concluded [40, 42]. It is further indicated that HA use as an early intervention for the hearing impaired elderly might delay or stop cognitive loss [40].

Severe to profound hearing loss with insufficient benefit from hearing aids or cochlear implantation (CI) using electrodes to stimulate the auditory nerve directly has proven successful in increasing quality of life in older adults [43]. It is indicated that CI should also be considered for those who may have a specific subtype of mild cognitive impairment in addition to profound hearing loss. The possible positive effects of cochlear implementation on limiting age-related cognitive loss are suggested by the relationship between hearing restoration and cognitive function preservation in older adults [43].

Although hearing loss leads to central auditory changes and consequently speech processing disorders, there is strong evidence suggesting relevant brain plasticity along with aural rehabilitation [13, 44]. In older people with hearing loss, the evidence of cross-modal re-organization accompanied by compensatory cortical neuroplasticity was found (by more recruitment of auditory, frontal, and pre-frontal cortices during a visual motion processing task). Following great degrees of hearing loss, the more the extensive cross-modal recruitment of the right auditory cortex is, greater difficulty in speech recognition in noise and worse cognitive function will occur. After clinical rehabilitation including HAs, a reversal in cross-modal re-organization of the auditory cortex by vision along with improvement in speech perception and cognitive performance was found. As a result, auditory training with well-fit amplification may provide cognitive benefits as well as positive improvements in terms of social isolation and depression [45]. Along with the proper amplification for elderly people, auditory training would both accelerate the secondary brain plasticity and increase the learning capacity and level of listening performance [31].

Overall, a multidisciplinary team including audiologists, speech and language therapists, and neurologists is required to manage patients with AD and hearing loss [4].

Clinical Management of Patients with AD and Vestibular Dysfunction

Vestibular rehabilitation is a therapeutic approach for vestibular impairments. Neuroplasticity (known as adaptation, habituation, and substitution) occurs in vestibular rehabilitation, increases static and dynamic postural stability, and improves vestibule-ocular reflex when there is conflicting sensory information [46]. Improved balance and gait, reduced symptoms of dizziness along with anxiety, and increased self-confidence and quality of life can be the results of vestibular rehabilitation. A study on amnestic mild cognitive impairment (MCI) showed that in patients who have a more prominent Alzheimer's prognosis, oVEMP (ocular vestibular evoked myogenic potential) occurrence was lower, although cVEMP (cervical vestibular evoked myogenic potential) was not. It is suggested that the higher brainstem is the first side of lesion, which then extends to other areas and the cortex [47]. Although there is no specific vestibular rehabilitation for AD patients in audiology practice, physical exercise improves physical and executive function and spatial memory of AD patients in the scope of physical therapy including a set of exercises involving head movements that stimulate the vestibular system and, over time, fosters adaptation and compensation for vestibular loss [48].

As one of the effects of aging is an increased risk of falling the most important risk factor of which is loss of balance, vestibular rehabilitation (VR) through reducing vertigo, physical activity, and improving a patient's balance can increase improvement in quality of life (QOL) and reduce falling in elderly people.

A randomized study on 60 women (equal number of subjects in control and experimental groups) ranging in age from 60 to 74 with a history of falling showed that interventions including strengthening exercises for the sensory-motor system and balance exercise training according to the Cawthorne-Cooksey (CC) protocol are effective in improving balance affected by vertigo, increasing restitution of the central nervous system, and reducing FES-I (Fall Efficacy Scale-International). In addition, using a multidimensional fall prevention program for these patients can ameliorate the QOL [49].

A new, useful tool t development for screening cognitive performance in vestibular loss patients is called the Internet-based Neuropsychological Vertigo Inventory (NVI; French). It is proposed to assess attention, memory, emotion, space perception, time perception, vision, and motor abilities. Because no effect of hearing difficulties, an inverse age effect for attention and emotion subscales, and reduced problems with increased age in vertigo participants are demonstrated, the NVI provides a helpful questionnaire for evaluating cognitive and emotional neuropsychological problems related to vertigo [50].

Conclusion

In this study, articles related to the current evidence on the association between AD and auditory and vestibular dysfunctions and the management of patients with AD and auditory and vestibular dysfunction were reviewed. Recent studies have shown that hearing loss is a risk factor for AD. Furthermore, it has been shown that hearing loss can cause dementia and decrease the communication abilities of AD patients. Another problem of AD patients is vestibular dysfunction. Disorder in the

vestibular system may cause an imbalance in the body and increase the risk of falls in affected patients. It has also been demonstrated that neuroplasticity of brain is a good solution for degenerative diseases such as AD. Auditory and vestibular rehabilitation can further reduce the problems associated with AD.

Conflict of Interest: None declared.

References

1. Gauthier S, Rosa-Neto P, Morais JA, & Webster C. 2021. World Alzheimer Report 2021: Journey through the diagnosis of dementia. London, England: Alzheimer's Disease International.
2. World Health Organization. (2008). WHO global report on falls prevention in older age. World Health Organization. https://apps.who.int/iris/handle/10665/43811
3. Huang LK, Chao SP, Hu CJ. Clinical trials of new drugs for Alzheimer disease. J Biomed Sci. 2020 Jan 6;27(1):18.
4. Ralli M, Gilardi A, Stadio AD, Severini C, Salzano FA, Greco A, Vincentiis M. Hearing loss and Alzheimer's disease: A Review. Int Tinnitus J. 2019 Sep 4;23(2):79-85.
5. Martini A, Castiglione A, Bovo R, Vallesi A, Gabelli C. Aging, cognitive load, dementia and hearing loss. Audiol Neurotol. 2014;19(Suppl. 1):2–5.
6. Phillips SL, Gordon-Salant S, Fitzgibbons PJ, Yeni-Komshian G. Frequency and temporal resolution in elderly listeners with good and poor word recognition. J Speech, Lang Hear Res. 2000;43(1):217–28.
7. Shen Y, Ye B, Chen P, Wang Q, Fan C, Shu Y, Xiang M. Cognitive Decline, Dementia, Alzheimer's Disease and Presbycusis: Examination of the Possible Molecular Mechanism. Front Neurosci. 2018 Jun 8;12:394.
8. Leirer VM, Glöckner F, Elbert T, Kolassa IT. An auditory computer-based training for mild cognitive impairment and mild Alzheimer's disease -German prototype of the brain fitness program. ACM Int Conf Proceeding Ser. 2009 Jun 9;1-4.
9. Anson E, Jeka J. Perspectives on aging vestibular function. Front Neurol. 2016;6:269.
10. Redfern MS, Jennings JR, Martin C, Furman JM. Attention influences sensory integration for postural control in older adults. Gait Posture. 2001;14(3):211–6.
11. Deveze A, Bernard-Demanze L, Xavier F, Lavieille J-P, Elziere M. Vestibular compensation and vestibular rehabilitation. Current concepts and new trends. Neurophysiol Clin Neurophysiol. 2014;44(1):49–57.
12. Wei EX, Oh ES, Harun A, Ehrenburg M, Xue QL, Simonsick E, Agrawal Y. Increased Prevalence of Vestibular Loss in Mild Cognitive Impairment and Alzheimer's Disease. Curr Alzheimer Res. 2019;16(12):1143-1150.
13. Parham K, Lin FR, Coelho DH, Sataloff RT, Gates GA. Comprehensive management of presbycusis: central and peripheral. Otolaryngol Head Neck Surg. 2013 Apr;148(4):537-9.
14. Lee JY. Relationship between vestibular dysfunction and dementia in elderly patients: Peripheral vertigo or central vertigo: Human neuropathology/clinico-pathologic correlations. Alzheimer's Dement. 2020 Dec;16:e040102.
15. Harun A, Oh ES, Bigelow RT, Studenski S, Agrawal Y. Vestibular Impairment in Dementia. Otol Neurotol. 2016 Sep;37(8):1137-42.
16. Benoudiba F, Toulgoat F, Sarrazin JL. The vestibulocochlear nerve (VIII). Diagn Interv Imaging. 2013 Oct;94(10):1043-50. doi: 10.1016/j.diii.2013.08.015. Epub 2013 Oct 1. PMID: 24095603.
17. Swords GM, Nguyen LT, Mudar RA, Llano DA. Auditory system dysfunction in Alzheimer disease and its prodromal states: A review. Ageing Res Rev. 2018 Jul;44:49-59.
18. Long JM, Holtzman DM. Alzheimer Disease: An Update on Pathobiology and Treatment Strategies. Cell. 2019 Oct 3;179(2):312-339.
19. Arshavsky YI. Alzheimer's Disease: From Amyloid to Autoimmune Hypothesis. Neuroscientist. 2020 Oct-Dec;26(5-6):455-470.
20. Hanseeuw BJ, Betensky RA, Jacobs HIL, Schultz AP, Sepulcre J, Becker JA, et al. Association of Amyloid and Tau With Cognition in Preclinical Alzheimer Disease: A Longitudinal Study. JAMA Neurol. 2019 Aug 1;76(8):915-924.
21. Binder LI, Frankfurter A, Rebhun LI. The distribution of tau in the mammalian central nervous system. J Cell Biol. 1985 Oct;101(4):1371-8.
22. Avila J, Lucas JJ, Perez M, Hernandez F. Role of tau protein in both physiological and pathological conditions. Physiol Rev. 2004 Apr;84(2):361-84.
23. Spires-Jones TL, Hyman BT. The intersection of amyloid beta and tau at synapses in Alzheimer's disease. Neuron. 2014 May 21;82(4):756-71.
24. Park SY, Kim MJ, Kim HL, Kim DK, Yeo SW, Park SN. Cognitive decline and increased hippocampal p-tau expression in mice with hearing loss. Behav Brain Res. 2018 Apr 16;342:19-26.
25. Picciotti PM, Fetoni AR, Paludetti G, Wolf FI, Torsello A, Troiani D, et al. Vascular endothelial growth factor (VEGF) expression in noise-induced hearing loss. Hear Res. 2006 Apr;214(1-2):76-83.
26. Klatt BN, Ries JD, Dunlap PM, Whitney SL, Agrawal Y. Vestibular Physical Therapy in Individuals with Cognitive Impairment: A Theoretical Framework. J Neurol Phys Ther. 2019 Apr;43 Suppl 2(Suppl 2 Spec International Conference on Vestibular Rehabilitation):S14-S19.
27. Jang SS, Chung HJ. Emerging Link between Alzheimer's Disease and Homeostatic Synaptic Plasticity. Neural Plast.2016:7969272:1-19.
28. Sinha UK, Hollen KM, Rodriguez R, Miller CA. Auditory system degeneration in Alzheimer's disease. Neurology. 1993 Apr;43(4):779-85.
29. Chang M, Kim HJ, Mook-Jung I, Oh SH. Hearing loss as a risk factor for cognitive impairment and loss of synapses in the hippocampus. Behav Brain Res. 2019 Oct 17;372:112069.
30. Cardin V. Effects of Aging and Adult-Onset Hearing Loss on Cortical Auditory Regions. Front Neurosci. 2016 May 11;10:199.
31. Tye-Murray N. Foundations of aural rehabilitation: Children, adults, and their family members. Plural Publishing; 2020.5th ed.pp.105.
32. Shankar A, Hamer M, McMunn A, Steptoe A. Social isolation and loneliness: relationships with cognitive function during 4 years of follow-up in the English Longitudinal Study of Ageing. Psychosom Med. 2013 Feb;75(2):161-70.
33. Johnson JCS, Marshall CR, Weil RS, Bamiou DE, Hardy CJD, Warren JD. Hearing and dementia: from ears to brain. Brain. 2021 Mar 3;144(2):391-401.
34. Lin FR, Ferrucci L, An Y, Goh JO, Doshi J, Metter EJ, Davatzikos C, Kraut MA, Resnick SM. Association of hearing impairment with brain volume changes in older adults. Neuroimage. 2014 Apr 15;90:84-92.
35. Lee YW, Lee H, Chung IS, Yi HA. Relationship between postural instability and subcortical volume loss in Alzheimer's disease. Medicine (Baltimore). 2017 Jun;96(25):e7286.
36. Previc FH. Vestibular loss as a contributor to Alzheimer's disease. Med Hypotheses. 2013 Apr;80(4):360-7.
37. Gates GA. Central presbycusis: an emerging view. Otolaryngol Head Neck Surg. 2012 Jul;147(1):1-2.
38. Gates GA, Anderson ML, McCurry SM, Feeney MP, Larson EB. Central auditory dysfunction as a harbinger of Alzheimer dementia. Arch Otolaryngol Head Neck Surg. 2011 Apr;137(4):390-5.
39. Wei EX, Oh ES, Harun A, Ehrenburg M, Xue QL, Simonsick E, Agrawal Y. Increased Prevalence of Vestibular Loss in Mild Cognitive Impairment and Alzheimer's Disease. Curr Alzheimer Res. 2019;16(12):1143-1150.
40. Sarant J, Harris D, Busby P, Maruff P, Schembri A, Lemke U, Launer S. The Effect of Hearing Aid Use on Cognition in Older Adults: Can We Delay Decline or Even Improve Cognitive Function? J Clin Med. 2020 Jan 17;9(1):254.
41. Pereira-Jorge MR, Andrade KC, Palhano-Fontes FX, Diniz PRB, Sturzbecher M, Santos AC, Araujo DB. Anatomical and Functional MRI Changes after One Year of Auditory Rehabilitation with Hearing Aids. Neural Plast. 2018 Sep 10;2018:9303674.
42. Pinheiro MM, Iório MC, Miranda EC, Dias KZ, Pereira LD. The influence of cognitive aspects and auditory processes on the hearing aid acclimatization in the elderly. J Soc Bras Fonoaudiol. 2012;24(4):309-15. English, Portuguese.
43. Mosnier I, Vanier A, Bonnard D, Lina-Granade G, Truy E, Bordure P, Godey B, Marx M, Lescanne E, Venail F, Poncet C, Sterkers O, Belmin J. Long-Term Cognitive Prognosis of Profoundly Deaf Older Adults After Hearing Rehabilitation Using Cochlear Implants. J Am Geriatr Soc. 2018 Aug;66(8):1553-1561.
44. Parada JC, Hillyer J, Parbery-Clark A. Performance on the standard and hearing-impaired Montreal Cognitive Assessment in cochlear implant users. Int J Geriatr Psychiatry. 2020 Apr;35(4):338-347.
45. Glick HA, Sharma A. Cortical Neuroplasticity and Cognitive Function in Early-Stage, Mild-Moderate Hearing Loss: Evidence of Neurocognitive Benefit From Hearing Aid Use. Front Neurosci. 2020 Feb 18;14:93.

46. Samartsev IN, Zhivolupov SA. The significance of neuroplastic mechanisms in compensation of statodynamic impairments during vestibular disorders. Zhurnal Nevrologii i Psikhiatrii Imeni SS Korsakova. 2021 Jan 1;121(5):165-72.
47. Shamsi N, Ghahraman MA, Hoseinabadi R, Aghamollaii V, Jalaie S. Vestibular evoked myogenic potentials: early predictors of Alzheimer's disease? Audit Vestib Res. 2018 Mar 7;27(2):80-5.
48. Lacour M, Bernard-Demanze L. Interaction between vestibular compensation mechanisms and vestibular rehabilitation therapy: 10 recommendations for optimal functional recovery. Front Neurol. 2015 Jan 6;5:285.
49. Kaveh MH, Bahadori F, Doosti A, Asadollahi A. The Effect of Balance Exercise Training on Balance Status, and Quality of Life in Elderly Women: A Randomized Controlled Trial. Malaysian Journal of Medicine and Health Science. 2021; 17. 2636-9346.
50. Lacroix E, Deggouj N, Salvaggio S, Wiener V, Debue M, Edwards MG. The development of a new questionnaire for cognitive complaints in vertigo: the Neuropsychological Vertigo Inventory (NVI). Eur Arch Otorhinolaryngol. 2016 Dec;273(12):4241-49.