

Elderly Tinnitus and Neuropsychological Dysfunction

Subjects: **Biology**

Contributor: Anna Rita Fetoni

Tinnitus is a common and disabling symptom often associated with hearing loss. While clinical practice frequently shows that a certain degree of psychological discomfort often characterizes tinnitus sufferers, it has been recently suggested in adults as a determining factor for cognitive decline affecting attention and memory domains.

tinnitus

cognition

psychological aspects

auditory pathways

elderly

1. Introduction

Tinnitus consisting of the perception of sounds in the absence of external stimuli is a very common and disabling condition with pervasive effects on health and wellbeing. In 95% of cases, tinnitus is subjective and described as a buzz, click, hiss, ring, roar, hum, or pulsatile. The prevalence increases with age, affecting 24–45% of the elderly ^[1], where tinnitus is frequently associated to hearing impairment. Noise exposure, which is the greater risk factor for the development of both hearing loss and tinnitus ^{[2][3]}, contributes to the increase in prevalence among the elderly. Tinnitus can occur as an isolated idiopathic symptom or in association with otologic disease, such as otosclerosis ^[4] and Meniere disease ^[5], drug ototoxicity ^[6], cerebrovascular diseases, hypertension, dyslipidemia, metabolic diseases ^[7], chronic kidney disease, and diabetes mellitus ^[8]. On the other hand, it could be associated with any type of deafness as well as with a normal hearing threshold as in the case of ototoxicity from aspirin and quinine ^[9] or migraine ^[10]. Cochlear mechanism and involvement of central auditory and non-auditory pathways thought to underlie tinnitus with or without hearing loss are still controversial. Major evidence suggests that tinnitus is related to a failure of the central auditory pathway to adapt to the loss of afferent peripheral fibers due to peripheral damage ^{[11][12]}, leading to plastic neuronal changes in the tonotopic map of the auditory cortex, as a “maladaptive plasticity”, which concurs in maintaining tinnitus in a sort of “vicious circle” ^{[13][14][15][16][17]}. All these changes in the central auditory pathway, together with the neuroplastic reorganization within the thalamus and the structures of the limbic and paralimbic circuits ^[18], induced us to speculate about a possible relationship between tinnitus, psychological distress, and cognitive impairment, with a positive correlation to tinnitus severity ^{[19][20]}.

2. Possible Links between Tinnitus and Neuropsychological Dysfunction in the Elderly

2.1. Psychological Distress

It is largely demonstrated that psychiatric discomfort is present in a large number of tinnitus sufferers, with a higher prevalence of anxiety rather than depression [21][22] (Table 1). Tinnitus may directly determine a psychiatric condition; even if sleep disorders and insomnia evoked by tinnitus could induce emotional distress or unmask a pre-existing but compensated disorder. Aazh H et al. [23] retrospectively verified a strong association between tinnitus annoyance, depression level, and insomnia score in the elderly.

Table 1. Evidence linking chronic tinnitus to psychological disorders in the elderly.

Author, Year [Ref]	Inclusion Criteria	Exclusion Criteria	N° of Cases, Age	Type of Study	Objective	Methods (Outcome Evaluation)	Results	Level of Evidence	Evidence of Association
Fetoni AR, 2021 [24]	-Chronic tinnitus -Age ≥ 55 y -With or without HL	-History of neurological diseases -Psychiatric disorders -Otologic diseases -Antipsychotic drugs use	102 patients ≥55 y; 70.4 ± 9.6 y (range 55–94 y)	Prospective cross-sectional study	To assess the value of self-administered screening tests in comparing severity of tinnitus perception with emotional disorders and cognitive status	THI, HADS, MMSE (questionnaires)	THI score related to HADS-A score, HADS-D score, there was no relationship between tinnitus severity and MMSE	II	Yes
Aazh H, 2017 [23]	-Age ≥ 60 y -Tinnitus sufferers with/without hyperacusis -With/without HL	History of neurologic and psychiatric diseases, or sleep disorders	184 patients ≥60 y; mean age of 69 y	Retrospective cross-sectional study	To assess issues associated with tinnitus and hyperacusis handicap	HADS, HQ, ISI, THI, VAS (questionnaires)	THI was significant in predicting tinnitus annoyance. Hyperacusis handicap and insomnia were both predicted by level of depression	III	Yes
Park SY, 2017 [25]	-Age < and ≥ 65 y -With/without HL	History of psychiatric or neurologic diseases	76 patients ≥65 y	Retrospective cohort study	To assess differences between tinnitus-related features and psychological aspects between younger and	THI, BDI, and BEPSI (questionnaires)	No differences in tinnitus severity, depression, and stress between younger and older subjects	III	Yes/No

Author, Year [Ref]	Inclusion Criteria	Exclusion Criteria	N° of Cases, Age	Type of Study	Objective	Methods (Outcome Evaluation)	Results	Level of Evidence	Evidence of Association
					older tinnitus sufferers				
Gopinath B, 2010 [26]	-Age ≥ 50 y - With/without tinnitus - With/without HL	History of psychiatric diseases	1214 participants (602 with tinnitus) ≥50 y	Longitudinal cohort study	To evaluate the risk factors and effects of tinnitus (depression)	SF-36; MHI for depression and/or CES-D (questionnaires)	Lessened quality of life and wellbeing in patients with tinnitus	II	Yes
Lasisi AO, 2010 [27]	-Age ≥ 65 y - With/without tinnitus; - With/without HL	History of neuropsychologic diseases	184 patients ≥65 y; mean age of 77.3 y	Longitudinal cohort study	To establish the prevalence of tinnitus in the elderly and its influence on their life quality	WHOQOL (questionnaire)	Tinnitus sufferers had a lower perception of their overall health and a worse life quality; twofold likelihood to suffer activities impairment in daily living	II	Yes
Loprinzi PD, 2013 [28]	-Age ≥ 70 y - With/without tinnitus - With/without HL	Age < 70 years old	696 patients 76 ± 0.2 y (range 70–85 y)	Prospective cross-sectional study	To evaluate the association between tinnitus and depression	Patient Health Questionnaire-9 (questionnaire)	Positive association between tinnitus (at least a moderate) and depression; patients bothered by tinnitus before going to bed were nearly 3 times more likely to be depressed	II	Yes, in moderate/severe tinnitus
Beukes EW, 2018 [29]	-Age < and > 60 y - Chronic tinnitus -	History of neuropsychiatric diseases	146 patients stratified for age (> 60 y)	A randomized, delayed intervention efficacy trial	To establish if an internet-based cognitive behavioral	ISI, Generalized Anxiety Disorder-7, Patient Health Questionnaire-	Significant reduction in tinnitus and comorbidities (insomnia,	I	Yes

Author, Year [Ref]	Inclusion Criteria	Exclusion Criteria	N° of Cases, Age	Type of Study	Objective	Methods (Outcome Evaluation)	Results	Level of Evidence	Evidence of Association
	With/without HL who completed therapy				therapy is useful in reducing tinnitus severity and associated comorbidities	9, Hearing Handicap Inventory for adults, HQ, Cognitive Failures Questionnaire, Satisfaction with Life Scales (questionnaires)	depression, hyperacusis, cognitive failures) and improving of life quality		
Park HM, 2020 [30]	-Age ≥ 60 y - With/without tinnitus - With/without HL	History of neurologic or psychiatric diseases	5129 patients ≥60 y (range 60–79 y)	Retrospective cross-sectional study	To find a possible association of tinnitus, mental health, and health-related quality of life	Stress was tested asking: "How much stress do you usually feel in your daily life?"; depression was tested using CIDI-SF; suicide ideation with the question: "Have you ever thought about committing suicide within 12 months?" (questionnaires)	The annoying tinnitus patients had more depression, psychological stress, and suicidal ideation if compared to control group	III	Yes

y = years; HL = hearing loss; THI = Tinnitus Handicap Inventory; HADS = Hospital Anxiety and Depression Scale; MMSE = Mini Mental State Examination; HQ = Hyperacusis Questionnaires; ISI = Insomnia Severity Index; BDI = Beck’s Depression Inventory; BEPSI = Brief Encounter Psychosocial Instrument; SF-36 = Short Form 36-item Health Survey; MHI = Mental Health Index; CES-D = Centre for Epidemiologic Studies Depression Scale; WHOQOL = World Health Organization Quality of Life; CIDI-SF = World Health Organization’s Composite International Diagnostic Interview-Short Form.

2.2. Cognitive Impairment

Based on behavioral evidence, psychological markers of attention switching (i.e., cognitive and emotional control) are impaired in chronic tinnitus suggesting that the reduced cognitive control may be pivotal in maintaining the awareness of tinnitus. According to the literature (Table 2), tinnitus patients have poor cognitive performance, but it is still unclear whether cognitive impairment is a response to tinnitus manifestations or a feature of it, especially in the elderly. By using MMSE as a screening tool for cognitive impairment hearing threshold and anxious–depressive traits measured with hospital anxiety depression scale (HADS) questionnaire, scores for cognitive dysfunction were

slightly increased by age and gender ^[24] (Table 1). Few other reports suggest the relationship between neurocognitive abilities and tinnitus severity ^{[31][32]}, even if its mechanism remains controversial ^[5]. Thus, a key point in the elderly population is whether cognitive impairment is related to age-related hearing loss (ARHL) or to tinnitus per se.

Table 2. Evidence linking chronic tinnitus to cognitive decline in the elderly.

Author, Year [Ref]	Inclusion Criteria	Exclusion Criteria	N° of Cases, Age	Type of Study	Objective	Methods (Outcome Evaluation)	Results	Level of Evidence	Association
Lee SY, 2020 ^[33]	-Age > 60 y -Diagnosed for MCI - With/without tinnitus	-Moderate or severe hearing loss -Otologic diseases -History of psychiatric or neurologic disorders	23 patients (12 with tinnitus) 74.0 ± 6.1 y (range 63–83 y)	Retrospective cohort study	To examine the glucose metabolism and gray matter volume in patients with MCI and tinnitus	MCI with or without tinnitus: FDG-PET and magnetic resonance imaging were performed (imaging)	Specific brain regions are associated with cognitive decline and increased tinnitus severity	III	Yes
Lee SY, 2020 ^[34]	-Age ≥ 65 y - With/without HL	History of psychiatric or neurologic disorders	58 patients 68.1 ± 5.1 y (range 65–82 y)	Prospective cohort study	To examine the cognitive domains and the association between tinnitus severity and cognitive functions	K-PHQ-9, K-IADL, MoCA-K (questionnaires)	THI score in the MCI group was higher than in the non-MCI	II	Yes
Yun Y, 2020 ^[35]	-Age > 50 y -Chronic tinnitus	-History of Alzheimer's disease or neurologic diseases -Hearing loss or otologic diseases	55 patients > 50 y	Cross-sectional study	To examine plasma c-proteasome activity in association with cognitive functions in chronic tinnitus patients	Plasma c-proteasome activity was achieved with fluorogenic reporter substrate; MoCA (cut-off score of 22/23) to assess MCI (markers and questionnaires)	Circulating proteasomes were lower in patients with chronic tinnitus and MCI	III	Yes
Fetoni AR, 2021 ^[24]	-Chronic tinnitus -Age ≥ 55 y -	-History of neurological diseases -Psychiatric disorders	102 patients ≥ 55 y	Prospective cross-sectional study	To evaluate the use of self-administered screening	THI, HADS, MMSE (questionnaires)	THI score was directly related to HADS score, there was no	II	No

Author, Year [Ref]	Inclusion Criteria	Exclusion Criteria	N° of Cases, Age	Type of Study	Objective	Methods (Outcome Evaluation)	Results	Level of Evidence	Evidence of Association
	With/without HL	-Otologic diseases- Antipsychotic drugs use			tests to correlate the severity of tinnitus with emotional disorders and the overall cognitive status		relationship between tinnitus severity and MMSE		
Beukes EW, 2018 [29]	-Age < and > 60 y -Chronic tinnitus- With/without HL -Who completed therapy	History of neuropsychiatric diseases	146 patients stratified for age (>60 y)	Randomized delayed intervention efficacy trial	To establish if an internet-based cognitive behavioral therapy is useful to lessen tinnitus severity and associated comorbidities	ISI, Generalized Anxiety Disorder, Patient Health Questionnaire, Hearing Handicap Inventory for Adults Screening version, HQ, Cognitive Failures Questionnaire, Satisfaction with Life Scales (questionnaires)	Significant reduction in tinnitus and comorbidities (insomnia, depression, hyperacusis, cognitive failures) and a significant rise in life quality	I	Yes
Ruan Q, 2021 [36]	-Age ≥ 58 y - With/without frailty - With/without HL - With/without tinnitus	No history of disability, cophosis, and vision loss	429 patients ≥58 y	Longitudinal cohort study	To study whether cognitive frailty is associated with HL and tinnitus	To assess MCI: with executive and attention domain (TMT A and B); language domain (BNT and animal list generation); memory domain (HVLT-R) (questionnaires)	Cognitive frailty patients had higher risks of severe HL and tinnitus. Cognitive impairment in tinnitus patients involved executive, memory, and attention domains; altered processing speed	II	Yes/No

y = years, HL = hearing loss; MCI = mild cognitive impairment; K-PHQ-9 = Korean version of the Patient Health Questionnaire-9; K-IADL = Korean version of the Lawton instrumental activities of daily living scale; MoCA-K = Korean version of the Montreal Cognitive Assessment; THI = Tinnitus Handicap Inventory; HADS = Hospital Anxiety and Depression Scale; MMSE = Mini Mental State Examination; HL = Hearing Loss; TMT A and B = Trail Making Test; BNT = Boston Naming Test; HVLT-R = Hopkins Verbal Learning Test, Revised.

How chronic tinnitus causes cognitive deficits might be found in functional and structural brain alterations that were studied by Lee et al. [33]. Patients with MCI were divided in two groups (tinnitus and non-tinnitus groups) and were tested through FDG-PET to evaluate glucose metabolic connectivity. The tinnitus–MCI group showed a lower metabolism in the right superior temporal pole (which comprises the auditory cortex and is associated with the cognitive social processes interacting with limbic areas) and in the fusiform gyrus (which is altered in semantic dementia), if compared with non-tinnitus group. Furthermore, they exhibited significantly lower gray matter volume in the right insula (which is involved in the emotional reaction to tinnitus), and the THI was inversely correlated with it. Thus, the evidence for a causal link between tinnitus and MCI might be found in the pathophysiology of tinnitus and in the central neural changes that it determines. Surely, future studies in this direction could help to establish the causal link.

3. Summary

The association between tinnitus and psychological distress has been demonstrated, although only a few studies addressed this topic to the elderly. More difficult is the task of proving the association between cognitive dysfunction and tinnitus. Patients with chronic tinnitus (with or without hearing impairment) refer attention and memory failures, which reflects the dropped ability to shift attention away from phantom sounds in order to achieve proper cognitive performances [32].

A current key point is to evaluate if tinnitus-related comorbidities effectively depend on tinnitus or the hearing loss that is often associated. Limitations of this systematic review are that there are no reports on the effect of tinnitus on specific cognitive domains and its impact in older patients with good hearing.

Another limit is that, even if some studies (i.e., those of Lee and Yun) evaluated the relationship with MCI, which is a common dysfunction in older patients [37], results are hardly comparable, as they use different methods to validate cognitive impairment. Therefore, it is hard to understand if tinnitus matters as an independent risk factor.

Tinnitus is a common and disabling symptom especially in adults, and it is often associated with hearing loss in older people. Elderly patients affected by chronic tinnitus have dysfunctional traits, such as anxiety and depression, and demonstrate reduced cognitive functions. In older patients affected by hearing loss, tinnitus seems to worsen cognitive dysfunction. However, further studies are required to improve the evidence supporting the relationship between cognitive dysfunction and tinnitus.

References

1. Sindhusake, D.; Mitchell, P.; Newall, P.; Golding, M.; Rochtchina, E.; Rubin, G. Prevalence and characteristics of tinnitus in older adults: The Blue Mountains Hearing Study: Prevalencia y características del acúfeno en adultos mayores: El Estudio de Audición Blue Mountains. *Int. J. Audiol.* 2003, 42, 289–294.
2. Ralli, M.; Balla, M.P.; Greco, A.; Altissimi, G.; Ricci, P.; Turchetta, R.; De Virgilio, A.; De Vincentiis, M.; Ricci, S.; Cianfrone, G. Work-Related Noise Exposure in a Cohort of Patients with Chronic Tinnitus: Analysis of Demographic and Audiological Characteristics. *Int. J. Environ. Res. Public Health* 2017, 14, 1035.
3. Paciello, F.; Podda, M.V.; Rolesi, R.; Cocco, S.; Petrosini, L.; Troiani, D.; Fetoni, A.R.; Paludetti, G.; Grassi, C. Anodal transcranial direct current stimulation affects auditory cortex plasticity in normal-hearing and noise-exposed rats. *Brain Stimul.* 2018, 11, 1008–1023.
4. Skarzynski, P.H.; Dziendziel, B.; Gos, E.; Włodarczyk, E.; Miaskiewicz, B.; Rajchel, J.J.; Skarzynski, H. Prevalence and Severity of Tinnitus in Otosclerosis: Preliminary Findings from Validated Questionnaires. *J. Int. Adv. Otol.* 2019, 15, 277–282.
5. Nakashima, T.; Pykkö, I.; Arroll, M.A.; Casselbrant, M.L.; Foster, C.A.; Manzoor, N.F.; Megerian, C.A.; Naganawa, S.; Young, Y.-H. Meniere's disease. *Nat. Rev. Dis. Prim.* 2016, 2, 16028.
6. Cascella, V.; Giordano, P.; Hatzopoulos, S.; Petruccelli, J.; Prosser, S.; Simoni, E.; Astolfi, L.; Fetoni, A.R.; Skarżyński, H.; Martini, A. A new oral otoprotective agent. Part 1: Electrophysiology data from protection against noise-induced hearing loss. *Med. Sci. Monit.* 2012, 18, BR1–BR8.
7. Huang, Y.-S.; Koo, M.; Chen, J.-C.; Hwang, J.-H. The association between tinnitus and the risk of ischemic cerebrovascular disease in young and middle-aged patients: A secondary case-control analysis of a nationwide, population-based health claims database. *PLoS ONE* 2017, 12, e0187474.
8. Shih, C.-P.; Lin, H.-C.; Chung, C.-H.; Hsiao, P.-J.; Wang, C.-H.; Lee, J.-C.; Chien, W.-C. Increased risk of tinnitus in patients with chronic kidney disease: A nationwide, population-based cohort study. *PLoS ONE* 2017, 12, e0183192.
9. Ralli, M.; Lobarinas, E.; Fetoni, A.R.; Stolzberg, D.; Paludetti, G.; Salvi, R. Comparison of Salicylate- and Quinine-Induced Tinnitus in Rats. *Otol. Neurotol.* 2010, 31, 823–831.
10. Hwang, J.-H.; Tsai, S.-J.; Liu, T.-C.; Chen, Y.-C.; Lai, J.-T. Association of Tinnitus and Other Cochlear Disorders with a History of Migraines. *JAMA Otolaryngol. Neck Surg.* 2018, 144, 712–717.
11. Knipper, M.; Van Dijk, P.; Nunes, I.; Rüttiger, L.; Zimmermann, U. Advances in the neurobiology of hearing disorders: Recent developments regarding the basis of tinnitus and hyperacusis. *Prog.*

- Neurobiol. 2013, 111, 17–33.
12. Fetoni, A.R.; Etroiani, D.; Epetrosini, L.; Epaludetti, G. Cochlear Injury and Adaptive Plasticity of the Auditory Cortex. *Front. Aging Neurosci.* 2015, 7, 8.
 13. Stolzberg, D.; Chen, G.-D.; Allman, B.; Salvi, R. Salicylate-induced peripheral auditory changes and tonotopic reorganization of auditory cortex. *Neuroscience* 2011, 180, 157–164.
 14. Salvi, R.J.; Wang, J.; Ding, D. Auditory plasticity and hyperactivity following cochlear damage. *Hear. Res.* 2000, 147, 261–274.
 15. Diesch, E.; Andermann, M.; Flor, H.; Rupp, A. Interaction among the components of multiple auditory steady-state responses: Enhancement in tinnitus patients, inhibition in controls. *Neuroscience* 2010, 167, 540–553.
 16. Vanneste, S.; De Ridder, D. The auditory and non-auditory brain areas involved in tinnitus. An emergent property of multiple parallel overlapping subnetworks. *Front. Syst. Neurosci.* 2012, 6, 31.
 17. Hébert, S.; Fournier, P.; Noreña, A. The Auditory Sensitivity is Increased in Tinnitus Ears. *J. Neurosci.* 2013, 33, 2356–2364.
 18. Rauschecker, J.P.; Leaver, A.M.; Mühlau, M. Tuning Out the Noise: Limbic-Auditory Interactions in Tinnitus. *Neuron* 2010, 66, 819–826.
 19. Araneda, R.; De Volder, A.G.; Deggouj, N.; Philippot, P.; Heeren, A.; Lacroix, E.; Decat, M.; Rombaux, P.; Renier, L. Altered top-down cognitive control and auditory processing in tinnitus: Evidences from auditory and visual spatial stroop. *Restor. Neurol. Neurosci.* 2015, 33, 67–80.
 20. Wang, Y.; Zhang, J.-N.; Hu, W.; Li, J.-J.; Zhou, J.-X.; Shi, G.-F.; He, P.; Li, Z.-W.; Li, M. The characteristics of cognitive impairment in subjective chronic tinnitus. *Brain Behav.* 2018, 8, e00918.
 21. Fetoni, A.R.; Lucidi, D.; De Corso, E.; Fiorita, A.; Conti, G.; Paludetti, G. Relationship between Subjective Tinnitus Perception and Psychiatric Discomfort. *Int. Tinnitus J.* 2016, 20, 76–82.
 22. Panza, F.; Solfrizzi, V.; Logroscino, G. Age-related hearing impairment—A risk factor and frailty marker for dementia and AD. *Nat. Rev. Neurol.* 2015, 11, 166–175.
 23. Aazh, H.; Lammaing, K.; Moore, B.C.J. Factors related to tinnitus and hyperacusis handicap in older people. *Int. J. Audiol.* 2017, 56, 677–684.
 24. Fetoni, A.R.; Di Cesare, T.; Settimi, S.; Sergi, B.; Rossi, G.; Malesci, R.; Marra, C.; Paludetti, G.; De Corso, E. The evaluation of global cognitive and emotional status of older patients with chronic tinnitus. *Brain Behav.* 2021, in press.

25. Park, S.Y.; Han, J.J.; Hwang, J.H.; Whang, E.S.; Yeo, S.W.; Park, S.N. Comparison of tinnitus and psychological aspects between the younger and older adult patients with tinnitus. *Auris Nasus Larynx* 2017, 44, 147–151.
26. Gopinath, B.; McMahon, C.M.; Rochtchina, E.; Karpa, M.J.; Mitchell, P. Risk factors and impacts of incident tinnitus in older adults. *Ann. Epidemiol.* 2010, 20, 129–135.
27. Lasisi, A.O.; Abiona, T.; Gureje, O. Tinnitus in the elderly: Profile, correlates, and impact in the Nigerian study of ageing. *Otolaryngol. Head Neck Surg.* 2010, 143, 510–515.
28. Loprinzi, P.D.; Maskalick, S.; Brown, K.; Gilham, B. Association between depression and tinnitus in a nationally representative sample of US older adults. *Aging Ment. Health* 2013, 17, 714–717.
29. Beukes, E.W.; Baguley, D.M.; Allen, P.M.; Manchaiah, V.; Andersson, G. Audiologist-Guided Internet-Based Cognitive Behavior Therapy for Adults With Tinnitus in the United Kingdom: A Randomized Controlled Trial. *Ear Hear.* 2018, 39, 423–433.
30. Park, H.-M.; Jung, J.; Kim, J.-K.; Lee, Y.-J. Tinnitus and Its Association with Mental Health and Health-Related Quality of Life in an Older Population: A Nationwide Cross-Sectional Study. *J. Appl. Gerontol.* 2020, 733464820966512.
31. Taljaard, D.S.; Olaithe, M.; Brennan-Jones, C.G.; Eikelboom, R.H.; Bucks, R.S. The relationship between hearing impairment and cognitive function: A meta-analysis in adults. *Clin. Otolaryngol.* 2016, 41, 718–729.
32. Trevis, K.J.; McLachlan, N.M.; Wilson, S.J. Cognitive Mechanisms in Chronic Tinnitus: Psychological Markers of a Failure to Switch Attention. *Front. Psychol.* 2016, 7, 1262.
33. Lee, S.-Y.; Kim, H.; Lee, J.Y.; Kim, J.H.; Lee, D.Y.; Mook-Jung, I.; Kim, Y.H.; Kim, Y.K. Effects of Chronic Tinnitus on Metabolic and Structural Changes in Subjects With Mild Cognitive Impairment. *Front. Aging Neurosci.* 2020, 12, 594282.
34. Lee, S.-Y.; Lee, J.Y.; Han, S.-Y.; Seo, Y.; Shim, Y.J.; Kim, Y.H. Neurocognition of Aged Patients with Chronic Tinnitus: Focus on Mild Cognitive Impairment. *Clin. Exp. Otorhinolaryngol.* 2020, 13, 8–14.
35. Yun, Y.; Lee, S.-Y.; Choi, W.H.; Park, J.-C.; Lee, D.H.; Kim, Y.K.; Lee, J.H.; Lee, J.-Y.; Lee, M.J.; Kim, Y.H. Proteasome Activity in the Plasma as a Novel Biomarker in Mild Cognitive Impairment with Chronic Tinnitus. *J. Alzheimer's Dis.* 2020, 78, 1–11.
36. Ruan, Q.; Chen, J.; Zhang, R.; Zhang, W.; Ruan, J.; Zhang, M.; Han, C.; Yu, Z. Heterogeneous Influence of Frailty Phenotypes in Age-Related Hearing Loss and Tinnitus in Chinese Older Adults: An Explorative Study. *Front. Psychol.* 2021, 11, 617610.
37. Tangalos, E.G.; Petersen, R.C. Mild Cognitive Impairment in Geriatrics. *Clin. Geriatr. Med.* 2018, 34, 563–589.

Retrieved from <https://encyclopedia.pub/entry/history/show/26095>