Spring 2024

Ribbon Synapses' Role in Synaptic Identification

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Review of Current Research on Early Detection of Alzheimer's Disease

Honors Research Project - Biology
The University of Akron
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2023-2024

Introduction:

Alzheimer's Disease (AD), named for the doctor that discovered it in 1906, is a heavily studied neurodegenerative disease due to the high rates of diagnosis as well as the current lack of treatment. The risk of AD development increases with age, with an estimated 6.9 million American citizens above 65 recorded as having the disease (Rajan et al., 2021). It is difficult to determine the exact death statistics of Alzheimer's due to the fact that it can play an underlying role in the cause of death– for example, if a patient passes due to Pneumonia caused by malnutrition or swallowing troubles associated with AD, it will not be counted amongst the deaths caused by AD (Burns et al., 1990).

Pathologically, AD can be identified in a multitude of ways, with pathology being the standard for AD diagnosis and dementia differentiation (Sengoku, 2019). Most commonly, patients with AD exhibit neuron tangling and twisting at interneuron tau proteins as well as an accumulation of beta-amyloid protein deposits outside of affected neurons (Alzheimers Dement., 2024; Sengoku, 2019). Neurofibrillary tangling, identified in the earliest Alzheimer patients, still stands as one of the most common pathological indicators of AD. These tangles occur when tau protein undergoes hyperphosphorylation and forms paired helixes, causes bundles of neurofibril to form both intracellularly and extracellularly (Figure 1A, 1B), which causes axonal instability as well as progressively impairing normal neuronal functions as such transport of nutrients and cell communication (Moloney et al., 2021). AD is also characterized by the presence of amyloid beta plaque accumulations (Figure 1C, 1D). These deposits are formed when beta-amyloid peptides aggregate into toxic deposits following extracellular secretion that causes synapse dysfunction and cognitive impairment, both of which play roles in the presentation of AD (Takahashi et al., 2017). AD is also characterized early on by a series of visible presentations: most prominently prodromic memory loss– but also including visual deficits caused by posterior

cortical atrophy, progressive aphasia (a condition that weakens a patient's ability to communicate through speech), and atrophy of both parietal lobes (Galton et al., 2000). As the parietal lobes play a significant role in integration and processing of information, as well as arithmetic, language, drawing, and more, biparietal atrophy produces many of the common symptoms of dementia.

Figure 1: *From Sengoku, 2000.* Microscopically illustrates neuron tangles (A-B) and amyloid-protein plaque accumulations (C-D) in brain tissue of AD patients.

Research on early detection of AD relies heavily on studying biomarkers that indicate development. For example, beta-amyloid and tau protein levels can be measured in CSF as a biomarker for AD development. However, plaque build-ups and neurofibrillary tangles are only symptoms of AD, not causes and not paths to a cure– as researchers have discovered (Fymat, 2022). Because AD is such a complex and variable disease, researchers have been attempting to study different pathways by which to detect Alzheimer's early in its development. Among the many clinical studies taking place across AD research, are studies regarding how vision, speech, olfactory systems, and genetic disposition play a role in early detection of Alzheimer's Disease (Turner et al., 2020).

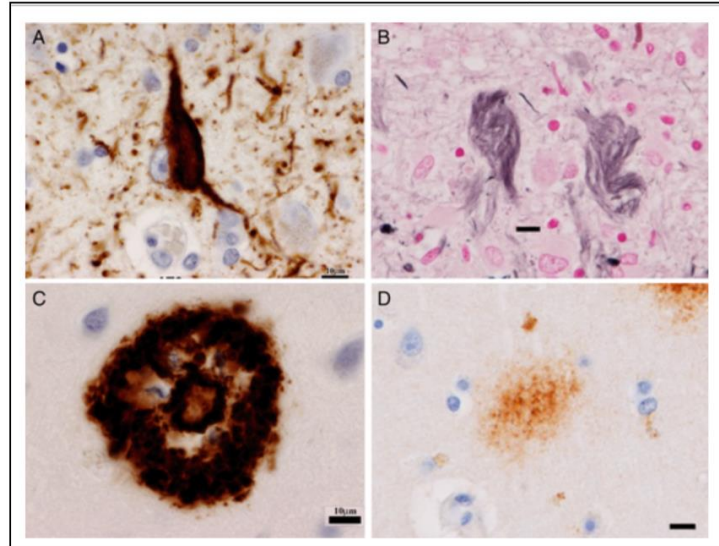**Vision: how does it relate to alzheimer's– anatomically, etc.? Current research? Status of current research? Potential further research? (Five journals, 2-3 pages)**

[Use of ocular biomarkers as a potential tool for early diagn... : Indian Journal of Ophthalmology (lww.com)](#)

[Protein and Imaging Biomarkers in the Eye for Early Detection of Alzheimer's Disease - IOS Press](#)

[Frontiers | Alzheimer's Retinopathy: Seeing Disease in the Eyes (frontiersin.org)](#)

[Ocular biomarkers and their role in the early diagnosis of neurocognitive disorders - Ioannis-Nikolaos Chalkias, Thomas Tegos, Fotis Topouzis, Magda Tsolaki, 2021 (sagepub.com)](#)

[Frontiers | Afferent and Efferent Visual Markers of Alzheimer's Disease: A Review and Update in Early Stage Disease (frontiersin.org)](#)

[Retinal biomarkers for Alzheimer's disease and vascular cognitive impairment and dementia (VCID): implication for early diagnosis and prognosis | GeroScience (springer.com)](#)

Olfactory:how does it relate to alzheimer's– anatomically, etc.? Current research? Status of current research? Potential further research? (Five journals, 2-3 pages)

[Could Early Identification of Changes in Olfactory Function Be an Indicator of Preclinical Neurodegenerative Disease? A Systematic Review | Neurology and Therapy (springer.com)](#)

[Olfaction as an early marker of Parkinson's disease and Alzheimer's disease - ScienceDirect](#)

[Frontiers | Olfactory deficit: a potential functional marker across the Alzheimer's disease continuum (frontiersin.org)](#)

Genetic Biomarkers:how does it relate to alzheimer's– anatomically, etc.? Current research? Status of current research? Potential further research? Genetic predisposition? 23 and me?(Five journals, 2-3 pages)

[Designing the next-generation clinical care pathway for Alzheimer's disease | Nature Aging](#)

[Frontiers | Potential New Approaches for Diagnosis of Alzheimer's Disease and Related Dementias (frontiersin.org)](#)

https://academic.oup.com/brain/article/146/2/690/6564132

[A review on the new age methodologies for early detection of Alzheimer's and Parkinson's disease - Ghosh - 2024 - Basic & Clinical Pharmacology & Toxicology - Wiley Online Library](#)

Speech:how does it relate to alzheimer's– anatomically, etc.? Current research? Status of current research? Potential further research? (Five journals, 2-3 pages)

[systematic literature review of automatic Alzheimer's disease detection from speech and language | Journal of the American Medical Informatics Association | Oxford Academic (oup.com)](#)

[Connected speech assessment in the early detection of Alzheimer's disease and mild cognitive impairment: a scoping review: Aphasiology: Vol 34, No 6 (tandfonline.com)](#)

Conclusion: which research shows the most potential (a scale for potential?) for further research? Any promising new research pathways that are being discovered? Summary of current status of research (1-2 pages)
Andrew Warren, M.D., Adam Rosenblatt, M.D., Alva Baker, M.D., and Constantine G. Lyketsos,

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7. Sengoku, R. (2020). Aging and Alzheimer's disease pathology. *Neuropathology*. 40: 22-29.

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