

Alzheimer's Disease: Why Is Early Detection Important?

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ABSTRACT

Early detection of Alzheimer's disease (AD) can bring benefits to the patient by giving them time to process and prepare for the development of the disease in the future. To detect the early stages of AD, patients can take brain imaging tests, auto-encoders, genetic tests, mental state tests, and cerebral spinal fluid tests. Through these tests, patients can determine their amyloid build-up levels, tau build-up levels, possible chromosomes related to AD, and mental health illnesses related to AD.

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Alzheimer's disease has many hidden factors; it's possible even people with remarkable memory can end up with Alzheimer's while aging. Alzheimer's disease, a neurodegenerative disease, is one of the leading causes of dementia, one that often begins with symptoms such as memory impairment, difficulty concentrating, visual or space difficulties, and language problems, such as being unable to collect words that make sense together. Understanding the underlying factors of AD is an essential goal in neuroscience. AD is considered caused by a buildup of amyloid plaques that block neurotransmission between neurons and an excessive amount of tau, another protein that forms tangles between neurons.

To lessen the impact of Alzheimer's disease, patients should receive the earliest diagnosis, so that it is possible to understand the disease's severities before it worsens, receive medication, and give family and caregivers time to plan for the future regarding financial issues, the choice between residential and at-home care, and other concerns (Mayo Clinic 2022). Although early detection of AD can cause patients to lose their jobs or driver's licenses, and create a possible economic burden, it can also provide closure for the patients regarding their symptoms and reduce risks associated with the disease (Rasmussen & Langerman 2018). The current possible methods for early detection include brain imaging tests, auto-encoders, genetic tests, mental state tests, and cerebrospinal fluid (CSF) tests.

One of the most common ways to identify Alzheimer's disease is by using brain-imaging, or neuroimaging, tests such as magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), positron emission tomography (PET), magnetic resonance spectroscopy (MRS) scans, diffusion tensor imaging (DTI), and brain quantitative susceptibility mapping (QSM). MRI scans are used to observe the structure of the brain regarding the shape, position, or volume of the brain tissue. Regarding Alzheimer's disease, the CA lateral zone, CA2-4 superior zone, dentate gyrus regions, and subiculum inferior medial zone of the hippocampus are examined. Through this test, neurologists look for loss of grey matter volume in the hippocampus, specifically in the CA1, dental gyrus regions, para-hippocampus, amygdala, and posterior cingulate cortex. Along with the loss of grey matter volume, neurologists also look for structural brain changes with stages of neurofibrillary temple deposition, which is a significant detector of AD. MRI scans can also see cerebral blood flow in the posterior cingulate cortex and precuneus and the thinning of the entorhinal cortex. This thinning is one of the

earliest detections of Alzheimer's, considering how it's also the earliest sight of atrophy before the hippocampus, amygdala, and para-hippocampus (Mandal and Sharma 2022).

fMRI scans are used for "measuring and mapping the activity of the brain in response to stimuli or actions" (Mandal and Sharma 2022). fMRI scans can be used for pre-surgical planning, obtaining medication, therapy, pre-symptomatic diagnosis, and understanding functional brain disorders, such as Alzheimer's. With these tests, neurologists can see the decreasing and increasing levels of hippocampal activity in mild cognitive impairment (MCI) and AD patients. However, this method is too dependent on the blood-oxygenated level, which is also dependent on the magnetic properties of oxygenated and deoxygenated blood. In certain cases where the patient does not have the blood-oxygenated level needed, they may not be able to use this method. Regardless of the necessities, fMRI scans can detect white and grey matter density and fractional anisotropy in the para-hippocampus.

Another common way to diagnose AD at its early stages is PET scans, which are used to measure the concentration of specific molecules in the brain. For AD, clinicians use Amyloid-PET scans to measure the build-up of abnormal amyloid proteins around the neurons (Columbia 2018). These scans are often carried out with an MRS scan, which is used to determine the changes in physical properties and concentration of biochemicals called metabolites, very similar to the PET scan. In the case of AD, MRS scans can determine a fall in levels of glutathione, which causes oxidative stress that leads to the development of AD.

A lesser-known test is the DTI scan, which looks at the microstructure of brain tissue and neural activity. Through this scan, neurologists can examine the microscopic changes in brain tissue by estimating the rate of water diffusion from different locations of the tissue. This can also "finds the loss of coherency between water molecules that come into existence when some move freely and some move in a restricted manner" (Mandal and Sharma 2022). This test is mainly performed on the hippocampus and the parahippocampus to predict the progression of mild cognitive impairment to Alzheimer's disease, which can help with the diagnosis of early AD.

As early detection tests develop, there are always even more emerging tests that can identify the early stages of AD, such as the new QSM scan, which determines the extent of magnetization when placed in an external magnetic field. With a similar technique to MRI scans, QSM scans monitor and measure iron levels in the regions of interest. Iron levels are studied because they are used in biological processes like the formation of a neural network, DNA synthesis, neurotransmitter synthesis, oxygen transportation, and cellular metabolism with enzymatic processes. Disruption of iron homeostasis will lead to brain function impairments that can then lead to neurodegeneration. With the QRS scan, neurologists found that the caudate nucleus, putamen, red nucleus, precuneus, and allocortex are used to diagnose mild and moderate AD (Mandal and Sharma 2022).

In more recent studies, scientists have discovered that autoencoders can also diagnose AD in its early stages. An autoencoder, a neural network, consists of at least three layers (an input, a hidden layer, and an output layer). The inputs send features from MRI, PET, and CSF data to hidden layers that show a high-level representation of the input layer; the output layers are a specific representation of the input layer with the same dimensionality as the input. In other words, they modify the number of neurons at each hidden layer, performing dimensionality reduction. Auto-encoders have been used in algorithms such as SVM, a classification algorithm in neuroimaging data. This algorithm has been applied to voice activity detection, pattern recognition, classification, and regression analysis, also been used to differentiate AD and MCI patients. This introduces a possible new method for diagnosing AD by recovering data imputation and feature reduction using autoencoders, brain imaging scans such as MRIs and PET, MMSE scores, personal information, and the SVM classifier. By using data normalization, this method was tested to have the highest accuracy of 95.57% and an average accuracy of around 90%. Overall, autoencoders can help recover missing data from brain imaging scans and increase AUC values.

Recent studies have suggested that genetics are related to the possible diagnosis of AD. Certain variations of genes are shown in people with Alzheimer's and they are now starting to be used in early diagnosis of

the disease. These chromosome pair variations include the Presenilin-1 (PS-1), Presenilin- 2 (PS-2), Apolipoprotein E e-4 (APOE4), and β -amyloid. The amyloid precursor protein is used for neural repair and growth. It breaks down and should be chopped off by the enzymes α -secretase and γ -secretase, leading it to dissolve. However, if β -secretase chops off part of the amyloid precursor protein, called β -amyloid, is insoluble. β -amyloid then groups with more β -amyloid to create a beta-amyloid plaque and hangs out in between neurons, interrupting the synapses transmission by blocking the neurotransmitters from traveling from the presynaptic cell to the postsynaptic cell and also causing inflammation which can destroy neurons. An increasing level of amyloid is critical to the development of AD in a person and early detection of amyloid can possibly slow down the spreading of the plaque. Regarding the presenilin genes, PS-1 interferes with γ -secretase (Medline 2021) while PS-2 can alter neurotransmission between neurons (NIH 2015), both causing the creation of β -amyloid and the destruction of neurons. From recent studies, it is known that the mutations of APP and presenilin genes are biomarkers of AD. However, the implication of the APOE gene is only a theory. Mutations of the APOE gene interfere with carrying cholesterol and fat through the bloodstream which neuroscientists believe plays an important role in AD and similar diseases (Bryant 2021).

Finishing in 2022, a study located in France and the UK determined some of the common mental health issues that can also cause Alzheimer's disease throughout the 20th century (Nedelec et al. 2022). The scientists took two-thousand volunteers from France who represented the French population in terms of age, sex, and living area, and four-hundred practitioners from the UK, representing 6% of the UK population to find trends in the volunteers ten years before their possible diagnosis with AD. Resulting of this study, the scientists found that major depressive disorder, anxiety, reaction to severe stress and adjustment disorders, hearing loss, constipation, spondylosis, memory loss symptoms, malaise and fatigue, syncope, and collapse, abnormal weight loss all increased from less than 0.00001 P-values to around 1.0 P-values and correct CI decreased. From these results, the impact of mental health (and related symptoms) are all determinants of AD and can be prevented years before a person is clinically diagnosed with the disease. Taking mental state tests can help prevent the worsening of mental health issues such as depression or anxiety, thus decreasing the chance of being diagnosed with Alzheimer's disease. (Nedelec et al. 2022)

Another method to determine AD at its earlier stages is a cerebral spinal fluid (CSF) test. CSF, being an important fluid that flows around the brain and spinal cord, can determine the diagnosis of AD through the amyloid and tau levels in it along with the levels of neurofilament light. Knowing that amyloid and tau are major indicators of Alzheimer's, the CSF test can help determine how many of the amyloid and tau live in the spinal fluid. This method has been shown to correctly identify 90% of those who were clinically diagnosed with Alzheimer's and 70%-80% of patients with mild cognitive impairment (Columbia 2018). However, this test cannot identify what type of dementia those patients had. To do this, scientists take samples of the patient's spinal fluid through a lumbar puncture and study them to only provide a yes or no answer (Penn Medicine 2021). Although this test does provide the specifics needed for different types of dementia, its accuracy in testing Alzheimer's makes it a possible option for diagnosing the disease.

Brain imaging tests, autoencoders, genetic tests, mental state tests, and CSF tests are all methods that scientists have developed to create better and more accurate technology for diagnosing Alzheimer's disease. With these methods, scientists make it more possible for patients to achieve the earliest diagnosis possible for AD and allow them to have more time to process their illness. The commonality and spread of Alzheimer's are inevitable. Currently, there are 6 million people diagnosed with Alzheimer's and that number is expected to double by 2050 (Alzheimer's Association 2022). While this disease affects the patient, it also affects the people around them including their family members and caregivers. With no cure, AD is separating families and saddling them with unexplainable costs. To prevent this spread, further research in the early detection of Alzheimer's disease can reduce the risk of the disease and hopefully develop a cure for it.

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