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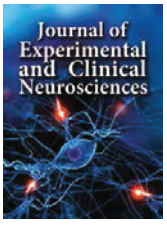


*Letter to Editor*

# Early Detection and Current Therapies for Alzheimer's Disease

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With life expectancy increasing across the world, the number of elderly people at risk of developing dementia is growing rapidly. The prevalence of dementia rises steeply with age which remains the number one risk factor, doubling every five years from the age of 60. Therefore, more than one-third of individuals over the age of 80 years are likely to develop dementia.

Alzheimer's disease (AD) remains the most common cause of dementia in all age groups. AD is a slowly progressive neurodegenerative brain disorder that, according to several imaging and neuropsychological studies, has the prodromal stage that can be traced back to 15-20 years prior to symptom presentation. AD is characterized by the presence of amyloid plaques and neurofibrillary tangles together with the loss of cortical neurons and synapses. Post mortem studies suggest that temporal lobes are the first brain regions that are affected.

The cognitive deficits that are associated with AD become evident and gradually worsen in later years. The combination of aging population and the promise of possible modifications in therapies in the near future has made the characterization of the early stages of AD a topic of major research interest.

The transitional stage between normal memory and dementia is called Mild Cognitive Impairment (MCI). Although it has been difficult to develop robust and applicable criteria for MCI, it is generally agreed that it is a pre-dementia state that in the majority of cases evolves into a full-blown dementia within five years from diagnosis. In this stage, there are also persistent memory lapses observed. Research has suggested that early detection and treatment of AD provides symptomatic improvement and better quality of life, though it does not address the underlying pathology or prolonged survival. For many patients, the quality of life is important since the disease progresses slowly.

For several years, the brain PET imaging has been used to diagnose AD by demonstrating decreased metabolism in the temporal and parietal regions. Given the importance of early detection, several tracers, such as Pittsburgh compound B (PIB), Florbetapir, and Flutemetamol have been developed to detect the amyloid deposits in the brain, and along with the CSF studies of measuring the concentration of beta amyloid, have significantly improved the accuracy of AD diagnosis. The majority of the above-mentioned measures are mainly utilized in research centers. Other measures include genetic testing with APO E, PS1, PS2, and APP genes. Given the lack of effective treatments for AD, routine genetic testing is not recommended.

The current standard of care in clinical evaluation of patients with cognitive disorders includes a comprehensive interview with the family and the patient, a full neuropsychological evaluation, brain MRI, and blood tests including thyroid function, B12, folic acid, vitamin D, and rapid plasma reagin (RPR) to rule out other reversible causes of dementia.

Currently, there are two classes of drugs that are used in clinical practice; one class is the cholinesterase inhibitors donepezil, rivastigmine, and galantamine with some minor differences, but similar effects. The mechanism of action of these drugs is by inhibiting the enzyme cholinesterase; they increase the availability of acetylcholine in the synapse. The other class of drug is the N-Methyl D-Aspartate (NMDA) receptor antagonist memantine. The mechanism of action of this drug is thought to be inhibiting calcium influx and hyper-excitability and reducing cell death.

In the present state of research, we are testing several classes of promising drugs that are in various stages of development. These include beta-site APP Cleaving Enzyme (BACE) inhibitors, passive anti-amyloid antibody infusion, nicotinic and muscarinic agonists and several serotonin agonists and antagonists that can be offered with and without the current marketed drugs.

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Considerable progress has been made in recent years in both the characterization of the cognitive profile of early AD and its neural basis. Much more work is still required, however, to clarify with accuracy and precision the transitional zone between healthy aging and the first manifestation of AD. With earlier detection and development of disease-modifying drugs, we are hoping to influence the underlying pathology of the disease, and halt or significantly slow the progression of this devastating disease.