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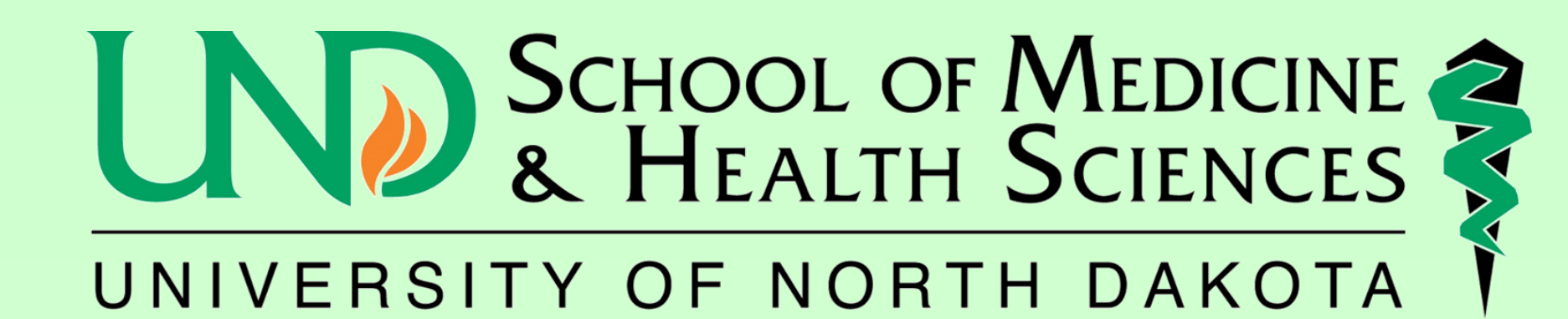
# A Multimodal Approach to Preventing and Treating Alzheimer's Disease

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## Abstract

As of 2015 over 47 million people worldwide are diagnosed with Alzheimer's disease (AD). The incidence of AD increases with age, and affects males and females equally. Current pharmacologic treatment includes two classes of drugs. The purpose of this study was to determine if a multimodal approach (i.e. diet, exercise, cognitive stimulation) towards the prevention and treatment of AD would be more beneficial than pharmacologic therapy alone. Research methods included reviewing peer reviewed journal articles published within the past five years obtained from PubMed, Dynamed, Cochrane, CINAHL, and Clinical Key. Ehret and Chamberlin (2015) found donepezil (Aricept) increased MMSE scores (95% CI, 1.3 to 2.5; P< 0.001); whereas memantine (Namenda) increased MMSE scores (95% CI, 0.6 to 1.8; P< 0.001). Combination therapy of donepezil and memantine revealed no significant improvement of MMSE scores (95% CI, -0.1 to 1.6; P= 0.07). The MIND diet and FINGER studies evaluated multimodal approaches to preventing and treating AD. Morris et al. (2015) found that participants who adhered to the MIND diet significantly reduced the rate of developing AD over an average of 4.5 years by 53% (HR= 0.47; 95% CI: 0.29, 0.76; P= 0.002) compared to those who were the least adherent to the diet. The FINGER study compared four factors between an intervention and control group. Ngandu et al. (2015) found NTB scores revealed a mean difference between groups of 0.022 (95% CI: 0.002 to 0.042; P = 0.030) per year with the intervention group scoring 25% higher at 24 months. The intervention group revealed differences in executive functioning (P = 0.039) 83% higher, and processing speed (P = 0.029) 150% higher than the control group. Memory scores analysis revealed a mean difference in memory decline between the intervention and control groups 1.31 (95% CI: 1.01 to 1.71; P = 0.036) after 24 months. Drug therapy alone provides nominal and short term improvement in cognitive functioning. A multimodal approach can improve or maintain cognitive functioning in those who are at risk for or who already have AD. Primary care providers should consider a multimodal approach to treating patients who have AD or early cognitive decline. Utilizing a multidisciplinary healthcare team by employing the expertise of other health professionals who are trained in working with older adults may be beneficial in the treatment of individuals who are at risk for, or who have AD.

## Introduction

- Alzheimer's dementia is the leading cause of dementia worldwide (Sindi, Mangialasche, & Kivipelto, 2015).
- It is estimated that 47 million people throughout the world have been diagnosed with AD as of 2015 with the prevalence expected to triple by 2050 if no effective intervention is instituted (Baumgart et al., 2015).
- Recent studies have revealed that employing a multimodal approach may delay the onset of AD.
- Studies have also revealed that a multimodal approach may slow the rate of cognitive decline or even improve cognitive functioning in those who are at risk for developing AD.

## Statement of the Problem

- As the population ages, AD will continue to increase in prevalence.
- This will impart significant emotional and financial stress on those affected, family members, and the healthcare system.
- There are currently no disease modifying treatments, or cure for AD.
- AD.

## Research Question

- In patients who are at risk for, or who have been diagnosed with AD; could modifiable risk factors such as diet, exercise, and cognitive stimulation be more effective in preventing and treating AD than current pharmacological treatment or no treatment at all?
- Can lifestyle modification create a significant improvement in cognition and quality of life?

## Literature Review

### The Pathophysiology and Clinical Manifestations of AD

AD accounts for approximately 60-70% of all cases of dementia (Sindi, Mangialasche, & Kivipelto, 2015).

- AD is clinically diagnosed after other sources of dementia have been ruled out. Currently, it can only be definitively diagnosed post mortem following autopsy (McCance & Heuther, 2014).
- AD is classified as nonhereditary/late onset (sporadic) accounting for 90% of all cases. Hereditary/early onset AD (familial) is responsible for the remaining 10% of cases (McCance & Heuther, 2014).
- The exact pathophysiology of AD is unknown, however high concentrations of beta-amyloid plaques and neurofibrillary tangles are found in the affected brain (McCance & Heuther, 2014).
- Beta-amyloid plaques and neurofibrillary tangles result in disruption of neuronal impulses and eventual death of the neuron (McCance & Heuther, 2014) (Figure 1 and 2).
- The clinical manifestations of AD tend to appear after several years to decades of pathophysiologic changes and neuronal damage occurring (McCance & Heuther, 2014).
- In the end stages of the disease, all cognitive function and ability to speak is lost, as well as the ability to ambulate and feed oneself (McCance & Heuther, 2014).

### Current Pharmacologic Therapy used to Treat AD

- There are four medications approved by the FDA for the treatment of AD. These are donepezil, rivastigmine, and galantamine- acetylcholinesterase inhibitors (ACEI's), and memantine- a N-methyl-D-aspartate (NMDA) receptor antagonist (Ehret & Chamberlin, 2015).
- The American Academy of Neurology and the National Institute for Health and Care Excellence recommend the use of 1 of 3 ACEI's for treating mild to moderate AD (Ehret & Chamberlin, 2015).
- Ehret and Chamberlin (2015) performed a systematic review on the current therapy recommendations of the four above mentioned drugs.
  - All three of the ACEI's improve cognitive functioning when used at approved dosing recommendations, although high rates of adverse events such as nausea, vomiting, and diarrhea are common (Hogan, 2014).
  - The combination of memantine and donepezil revealed no significant improvement in MMSE or BADLS scores (95% CI, -0.1 to 1.6; P = 0.07) and (95% CI, -2.2 to 1.2; P = 0.57) respectively (Ehret & Chamberlin, 2015).
  - Memantine is used for those in which ACEI's cannot be tolerated, are contraindicated, or for severe AD (Ehret & Chamberlin, 2015).
  - Studies have not indicated that ACEI's can prevent normal cognition to progressing to mild cognitive impairment (Ehret & Chamberlin, 2015).

### A Multimodal Approach- The MIND diet study

- The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet incorporates natural plant-based foods and small amounts of animal and saturated fats. The diet emphasizes the consumption of high amounts of green leafy vegetables and berries. Olive oil is the main fat component (Morris et al., 2015).
- Morris et al. (2015) found that participants who adhered to the MIND diet significantly reduced the rate of developing AD over an average of 4.5 years by 53% (HR= 0.47; 95% CI: 0.29, 0.76; P= 0.002) compared to those who were the least adherent to the diet.

### The FINGER Study

- The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) was a two-year, double-blind, RCT that investigated a multimodal approach preventing cognitive decline in at-risk elderly people compared to the general population (Ngandu et al., 2015).
  - Ngandu et al. (2015) found NTB scores revealed a mean difference between groups of 0.022 (95% CI: 0.002 to 0.042; P = 0.030) per year with the intervention group scoring 25% higher at 24 months. The intervention group revealed differences in executive functioning (P = 0.039) 83% higher, and processing speed (P = 0.029) 150% higher than the control group.
  - Memory scores analysis revealed a mean difference in memory decline between the intervention and control groups 1.31 (95% CI: 1.01 to 1.71; P = 0.036) after 24 months (Ngandu et al., 2015).

### Developing a Unified Clinical Trial Database for AD

- The Coalition Against Major Diseases (CAMD) was developed to help improve progress in preventing and treating neurodegenerative diseases such as AD by combining the knowledge of several organizations (Neville et al., 2015).
- CAMD developed a data repository called C-Path Online Data Repository-Alzheimer's Disease (CODR-AD) which gathers worldwide data on randomized controlled clinical trials focused on the treatment and prevention of AD (Neville et al., 2015).
- CODR-AD is an evolving, standardized database which can help develop a more comprehensive understanding of AD (Neville et al., 2015).

## Figures

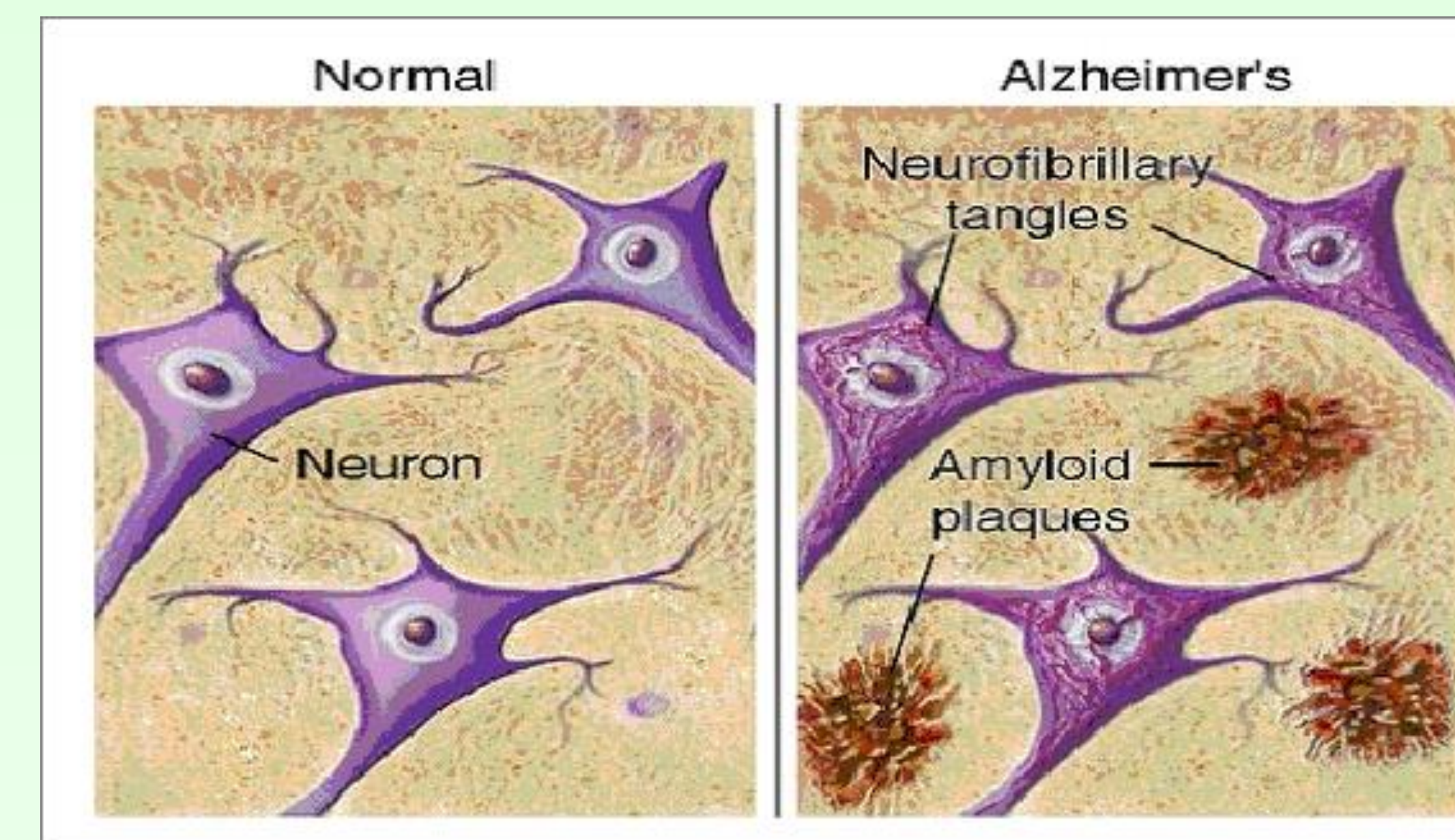


Figure 1. Neuronal damage from amyloid plaques and neurofibrillary tangles. <http://www.brightfocus.org/alzheimers/infographic/amyloid-plaques-and-neurofibrillary-tangles>

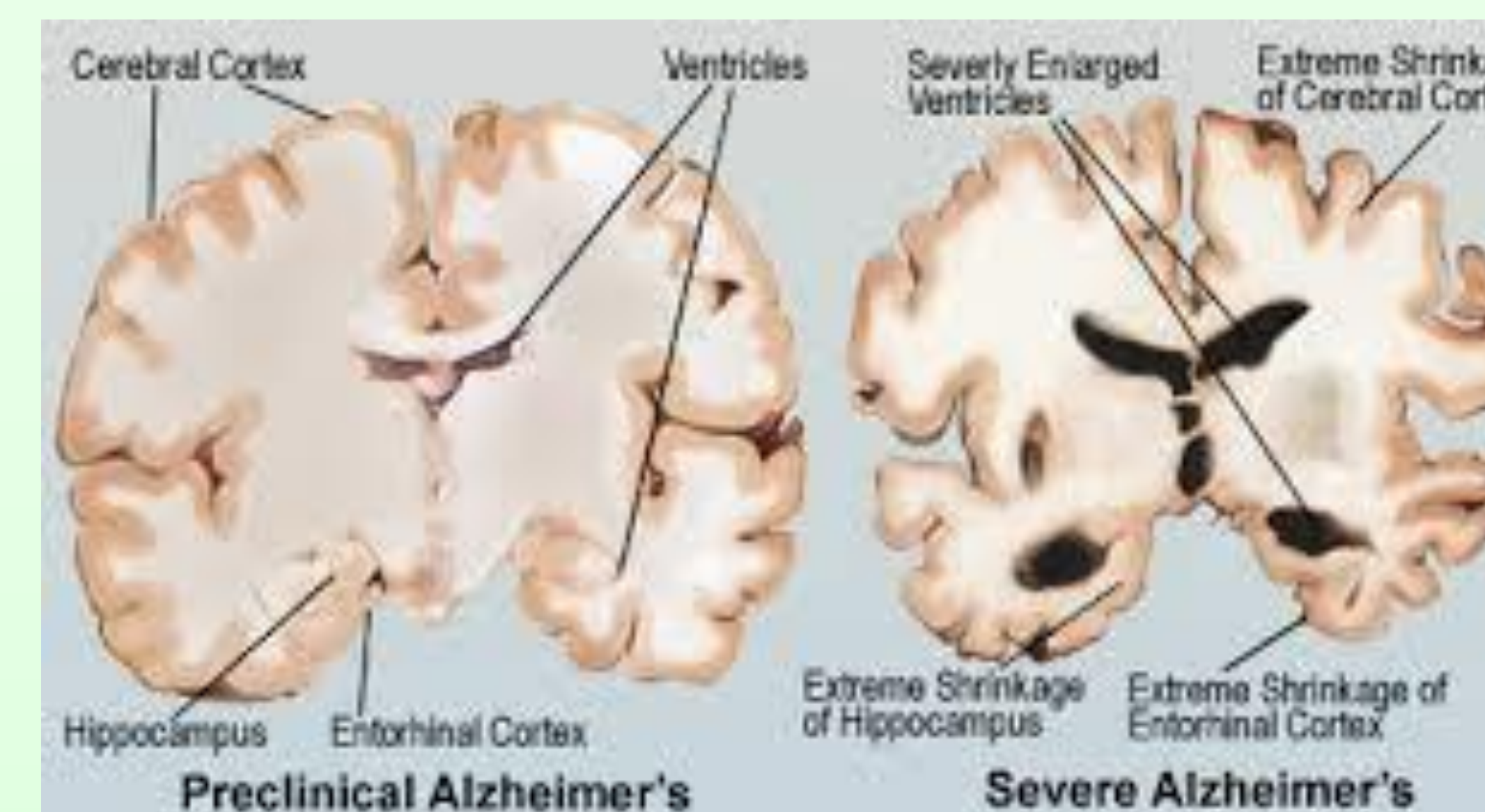


Figure 2. The preclinical and Alzheimer's brain. Image courtesy of the National Institute on Aging/National Institutes of Health. <http://memory.ucsf.edu/education/diseases/alzheimer>

## Discussion

- Current pharmacologic treatments are aimed at enhancing memory performance which provides only nominal symptomatic efficacy (Ehret & Chamberlin, 2015).
- Hogan (2014) suggests both ACEI's and NMDA antagonists have a relatively high adverse effect profile especially in causing gastrointestinal problems and urinary frequency.
- The results of the MIND diet study were promising, although there were limitations to the study. The observational study design may imply cause and effect, and there were several components involved in which the study cannot specify which component or combination may be the most beneficial (Morris et al., 2015).
- Yannakoulia et al. (2015) suggest that a healthy lifestyle including diet, exercise, and social/cognitive engagement may be a larger indicator of improved cognition and prevention of AD than simply diet alone.
- The FINGER study was the first large scale RCT to support a multimodal approach to preventing and treating AD (Ngandu et al., 2015). However, the study was performed in Finland and the Finnish population may not accurately represent the general population.

## Applicability to Clinical Practice

- PCP's have a deep knowledge of their patient's medical and family history. This knowledge puts them in a unique position to understand which patients are at a high risk for developing AD (Vellas & Oustric, 2014).
- Many older individuals have memory complaints, and some decline in memory is considered to be normal with aging (Vellas & Oustric, 2014).
- The PCP must be vigilant in determining whether a patient's memory complaint is normal, or an indicator of impending AD related dementia (Vellas & Oustric, 2014).
- The PCP should take the opportunity to counsel the patient presenting with memory complaints about making adjustments to modifiable factors such as quitting smoking, treating depression, losing excess weight, controlling type II diabetes, eating a healthy diet, beginning an exercise regimen, and engaging in cognitively stimulating activities (Vellas & Oustric, 2014).
- The PCP can utilize the expertise of other healthcare professionals such as dietitians, social workers, addiction counselors, and psychologists to provide resources to the patient (Vellas & Oustric, 2014).
- Research has determined that assisting patients at risk for, or who have AD with changing modifiable risk factors can slow or arrest the progression of cognitive decline.

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