



**Is it Possible to Reduce My Risk for Alzheimer's Disease ? An Overview of Current Risk Reduction Strategies**

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Core Leader: Outreach, Recruitment and Education Core, Minority Recruitment Core  
University of Wisconsin Madison

**Wisconsin Alzheimer's Disease Research Center**  
UNIVERSITY OF WISCONSIN  
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## Acknowledgements

- Nathaniel Chin MD, Assistant Professor of Geriatrics
- Cynthia Carlson MD, Professor of Geriatrics



## Risk factors for Alzheimer's disease

- Age
- Family history of AD
- Apolipoprotein E4 (APOE4) – genetic risk
- Low educational level
- Head trauma with loss of consciousness
- Vascular risk factors
- Inflammation
- Insulin resistance & metabolic risk factors
- Depression




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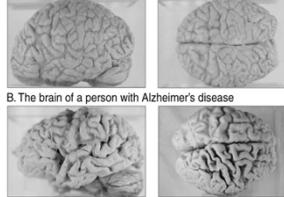
## Vascular Risk Factors Associated with Alzheimer's Disease

- Elevated blood pressure in midlife
- Obesity
- Diabetes
- Obstructive sleep apnea
- Physical inactivity

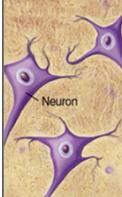


## AD Brain Changes

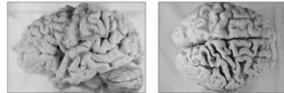
A. The brain of a normal elderly person



Normal

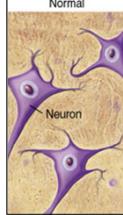
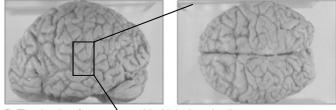


B. The brain of a person with Alzheimer's disease

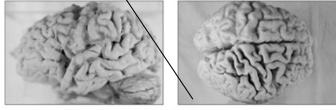


## AD Brain Changes

A. The brain of a normal elderly person



B. The brain of a person with Alzheimer's disease



<https://www.brightfocus.org/alzheimers/infographic/amyloid-plaques-and-neurofibrillary-tangles>

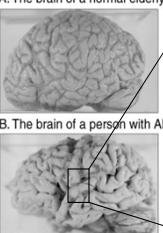
Mandel S et al. Predictive Diagnostics and Personalized Treatment, 2009.



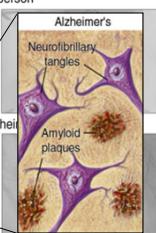
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## AD Brain Changes

A. The brain of a normal elderly person



B. The brain of a person with Alzheimer's



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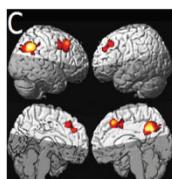
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## Brain Blood Flow Is Reduced in AD & MCI

C



20 patients with AD  
20 people without AD

Blood flow is reduced in areas of the brain related to memory & learning in persons with AD compared to older adult controls

Johnson NA et al. Radiology 2005;234:851-859.

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## Addressing modifiable risk factors may impact disease course

- Physical activity
- Diet
- Stress reduction
- Sleep
- Cognitive activity
- Social activity
- Hearing



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## Can Exercise Prevent Memory Loss and Improve Cognition ?

- Possibly- the data suggests that exercise affects brain structure and function:
- The known benefits of exercise include:
  - Reduced risk of cardiovascular disease and diabetes
  - Strengthening bones and muscles
  - Reduced stress.

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## Regular Exercise Benefits the Brain

- Studies show that people who are physically active are less likely to experience a decline in their mental function,
- Physical activity is associated a lowered risk of developing Alzheimer's disease
- Some evidence suggests that aerobic exercise is associated with improved performance on tests of memory and thinking among people with vascular cognitive impairment.
- Physical activity also tends to counter some of the natural reduction in brain connections that occurs with aging.

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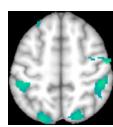
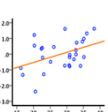
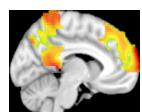
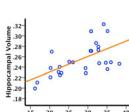
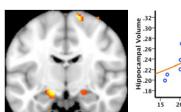


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## Cardiorespiratory fitness strengthens our brain



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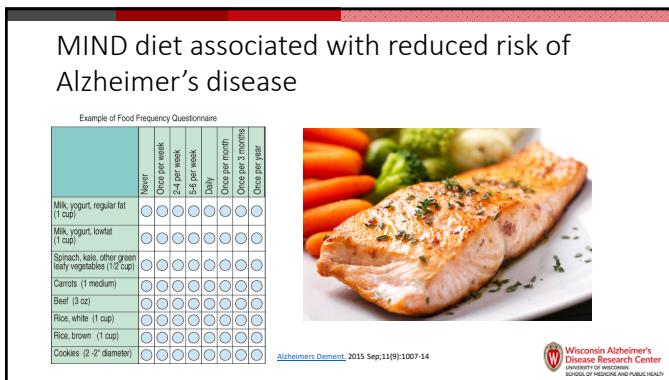
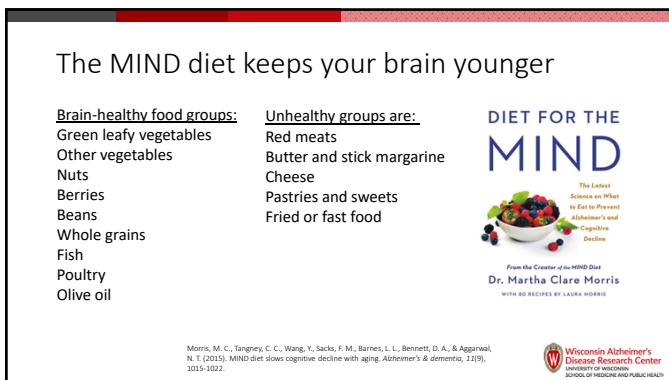
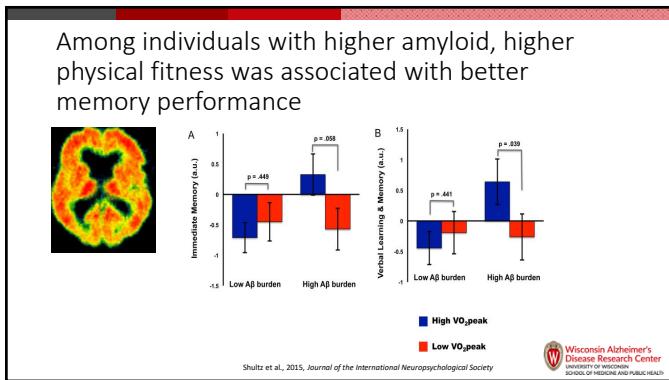
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## Benefits of the MIND Diet

- A 2015 study called the Chicago Health and Retirement Study of 6,000 seniors, discovered that study participants who followed the Mediterranean diet (and the MIND diet) were associated with a 35% lower risk of cognitive impairment.*

## MIND diet associated with reduced risk of Alzheimer's disease

Example of Food Frequency Questionnaire

	Never	Once per week	2-4 per week	5-6 per week	Daily	Once per month	Once per 3 months	Once per year
Milk, yogurt, regular fat (1 cup)	<input type="radio"/>							
Milk, yogurt, lowfat (1 cup)	<input type="radio"/>							
Spinach, kale, other green leafy vegetables (1/2 cup)	<input type="radio"/>							
Carrots (1 medium)	<input type="radio"/>							
Beef (3 oz)	<input type="radio"/>							
Rice, white (1 cup)	<input type="radio"/>							
Rice, brown (1 cup)	<input type="radio"/>							
Cookies (2-2' diameter)	<input type="radio"/>							

Alzheimer's Dement. 2015 Sep;11(9):1007-14

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Alzheimer's Dement. 2015 Sep;11(9):1007-14

Social Engagement and Brain Health

- Studies indicate that maintaining strong social connections and keeping mentally active as we age lowers the risk of cognitive decline.
  - It may be due to direct mechanisms through which social and mental stimulation strengthen connections between nerve cells in the brain
  - Social support also associated with reduced stress



Stress can affect our brain and its function

ARTICLE

## Circulating cortisol and cognitive and structural brain measures

The Framingham Heart Study

Justin B. Echouffo-Tcheugui, MD, PhD, Sarah C. Conner, MPH, Jayandra J. Himali, PhD, Pauline Maillard, Charles S. DeCarli, MD, Alexa S. Beiser, PhD, Ramachandran S. Vasan, MD, and Sudha Seshadri, MD  
Neurology® 2018;00:1-10. doi:10.1212/WNL.0000000000006549

- **High cortisol associated with...**
    - Worse memory and visual perception
    - Lower total brain volume, occipital and frontal gray matter volume
    - Microstructural change in areas connecting parts of the brain
    - More evident in women
    - No relationship to APOE4



Perceived stress can affect our brain function

## Perceived Stress and Change in Cognitive Function Among Adults 65 Years and Older

NEELUM T. AGGARWAL, MD, ROBERT S. WILSON, PhD, TODD L. BECK, MS, KUMAR B. RAJAN, PhD, CARLOS F. MENDES DE LEON, PhD, DENIS A. EVANS, MD, AND SUSAN A. EVERSON-ROSE, PhD  
**Psychosomatic Medicine** 76:80–85 (2014)

- **Increasing levels of perceived stress associated with...**
  - Lower initial cognitive testing scores
  - Faster rate of cognitive decline
  - Present in both black and white adults 65+
- 30% greater risk of MCI [Alzheimer Dis Assoc Disc.](#), 2016 Apr-

### What is the Link between Sleep and Alzheimer's Disease ?

- Several studies of cognitively normal people and one study in mice have shown a connection between chronic sleep disruption and the development of amyloid plaques.
- The research in mice was particularly interesting because it showed that mice who slept well reduced their levels of beta amyloid, effectively clearing the toxin from their brains.

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### Sleep Quality and AD Risk

- A UW study looked at the relationship between sleep quality and levels of various proteins and inflammatory markers in the cerebrospinal fluid of 101 cognitively healthy adults with an average age of 63.
- All participants had known risk factors for Alzheimer's, such as family history or evidence of the APOE gene, which is associated with a greater chance of developing the disease.
- Sleep quality was rated on a standard scale that measured amount, quality and trouble sleeping, along with daytime drowsiness and naps.
- Participants had brain imaging and lumbar puncture

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### Sleep Quality and AD Risk

- By comparing the spinal fluid against self-reported sleep problems, found the researchers found that at the participants with sleep issues were more likely to show evidence of tau pathology, brain cell damage and inflammation, even when other factors like depression, body mass, cardiovascular disease and sleep medications were taken into account.
- Worse sleep may contribute to the accumulation of Alzheimer's-related proteins in the brain
- The fact that these effects were found in cognitively healthy and people suggests that these relationships appear early, perhaps providing a window of opportunity for intervention

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**Finnish Geriatric (FINGER) study to Prevent Cognitive Impairment**

- 2-year study
- 1260 adults ages 60–77 yrs
- Multi-domain intervention:
  - Diet
  - Exercise
  - Cognitive training
  - Vascular risk monitoring

Ngandu et al. *Lancet* 2015; 385: 2255–63



Improved cognitive performance

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**"What Do You Think About \_\_\_\_\_?"**

- Jelly fish extract
- Statins
- Luminosity
- Coconut oil
- Curcumin
- Crossword puzzles
- Etc.....

 \$15 per month or \$300 lifetime access

 \$35 per month

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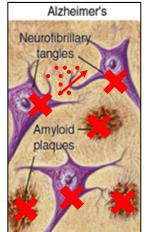
**FDA-approved Medications for Alzheimer's Dementia Treat Symptoms and Not the Disease**

Cholinesterase inhibitors
 

- Donepezil (Aricept)
- Rivastigmine (Exelon)
- Galantamine (Razadyne)

N-methyl-D-aspartate (NMDA) Receptor Antagonists
 

- Memantine (Namenda)



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## Medications Being Studied for Treatment/Prevention of Dementia Due to AD

- Immune therapies to clear  $\beta$ -amyloid from the brain  
Examples: solanezumab, crenezumab, BAN2401, aducanumab (BIIIB037)
- Medications that reduce amyloid production and/or clumping  
Examples: BACE inhibitors, carvedilol
- Therapies to prevent abnormal tau changes  
Examples: exenatide, liraglutide



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Alzheimer's Association International Conference July 2018  
<https://www.alzforum.org/therapeutics/aducanumab>  
<https://www.alzforum.org/therapeutics/ban2401>

## Medications Being Studied for Treatment/Prevention of Dementia Due to AD

- Medications to improve brain chemical signaling
- Therapies that reduce inflammation and protect brain cells
- Medications to improve glucose balance in the brain  
Example: intranasal insulin
- Therapies to improve brain blood flow  
Example: nilvadipine



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Alzheimer's Association International Conference July 2018  
<https://www.alzforum.org/therapeutics/aducanumab>  
<https://www.alzforum.org/therapeutics/ban2401>

## SPRINT-MIND STUDY: Preliminary Results

(Systolic Blood Pressure Intervention Trial - Memory and Cognition in Decreased Hypertension)

- 2800 people (640 in MRI study) with avg systolic blood pressure **130 mm Hg**
- Tested whether treating to a goal blood pressure **<120 mm Hg compared to <140 mm Hg** reduced risk of dementia, MCI, and/or both
- Given 2-3 blood pressure medications
  - thiazide diuretic pill and/or ACE-inhibitor (or ARB) and/or calcium channel blocker



Alzheimer's Association International Conference 2018.  
 Kjeldsen SE et al. Blood Pressure 2018, VOL. 27, NO. 5, 247–248

## SPRINT-MIND STUDY: Preliminary Results

(Systolic Blood Pressure Intervention Trial - Memory and Cognition in Decreased Hypertension)

- New cases of MCI were reduced by 19%; combined outcome of MCI and dementia was reduced by 15%
- On MRI scans, vascular changes in the brain were reduced in the intensive treatment group, but brain shrinkage (atrophy) rates were about the same



Alzheimer's Association International Conference 2018.  
Kjeldsen SE et al. Blood Pressure 2018, VOL. 27, NO. 5, 247-248

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**BRAVE**  
EPA STUDY  
  
BRAIN AMYLOID AND VASCULAR EFFECTS  
OF EICOSAPENTAENOIC ACID STUDY

## Brain Amyloid and Vascular Effects of Eicosapentaenoic Acid (BRAVE-EPA)

- 150 VA-eligible Veterans, ages 50-75 years old
- Normal memory and thinking abilities
- Parental history of Alzheimer's disease
- 18-month clinical trial of Vascepa (a prescription fish oil) vs. placebo
- Monitoring effects on brain blood flow, spinal fluid levels of amyloid, and cognitive tests



John Hart, Wisconsin State Journal, Dec. 9, 2017

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## Supplements and Vitamins Being Studied for Treatment/Prevention of Dementia Due to AD

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## Supplements and Vitamins Being Studied for Treatment/Prevention of Dementia Due to AD

- Supplement combinations
  - Example: **Souvenaid** is a multinutrient combination (Fortasyn Connect: DHA; EPA; uridine monophosphate; choline; vitamins B12, B6, C, E, and folic acid; phospholipids; and selenium)
- **LipiDiet** studied the effects of Souvenaid in a randomized, controlled, double-blind, multicenter, international trial
- **No significant difference was found between groups in cognitive performance or conversion to dementia**

Soininen H et al. Lancet Neurol 2017; 16: 965–75  
van Wyk N et al. J Alzheimers Dis. 2014;38(3):459–79. doi: 10.3233/JAD-130998.

## Finnish Geriatric (FINGER) study to Prevent Cognitive Impairment

- 2-year study
- 1260 adults ages 60–77 yrs
- Multi-domain intervention:
  - Diet
  - Exercise
  - Cognitive training
  - Vascular risk monitoring



Improved cognitive performance

Ngandu et al. Lancet 2015; 385: 2255–63

## What Can I Do Now to Reduce My Chances of Getting Dementia Due to AD?

- GET SYSTOLIC BLOOD PRESSURE <120 MM Hg Part of SPRINT-MIND Study
- Diet
- Exercise
- Cognitive training
- Vascular risk monitoring
- Social engagement
- Cognitively-stimulating activities
- Good sleep
- Treat sleep apnea

Part of FINGER Study

**Not yet proven!**

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## What Else Can I Do?

### Join a clinical trial!

- Wisconsin Alzheimer's Research Center (ADRC)
  - <http://www.adrc.wisc.edu/>
- Clinical Trials in Alzheimer's disease
  - <http://clinicaltrials.gov/>
- Alzheimer's Association TrialMatch
  - [http://www.alz.org/research/clinical\\_trials/find\\_clinical\\_trials\\_trialmatch.asp](http://www.alz.org/research/clinical_trials/find_clinical_trials_trialmatch.asp)




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## How Can You Keep Up to Date with the Latest Alzheimer's Study Results?

- AlzForum
  - <https://www.alzforum.org/>
- Alzheimer's & Dementia Alliance
  - <http://www.alzwisc.org/>
- Alzheimer's Association
  - <http://www.alz.org/>
- Clinical Trials in Alzheimer's disease
  - <http://clinicaltrials.gov/>
- Wisconsin Alzheimer's Institute
  - <http://www.wai.wisc.edu/>




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*Thank you!*




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