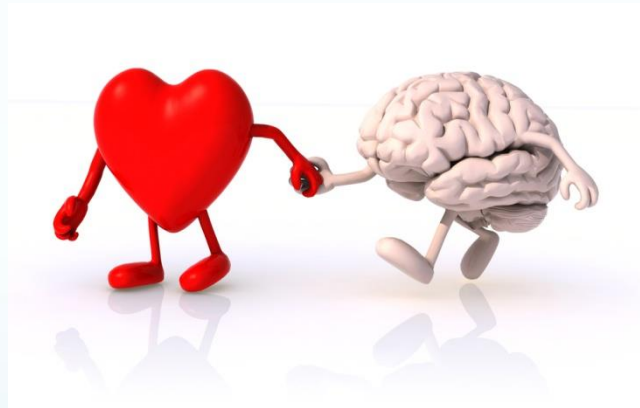


# The Heart and Brain Connection



**Neelum T. Aggarwal, MD**

# Objectives

- Definition of a "Healthy" Heart - Brain Connection
- **Modifiable** Risk Factors for Cognitive Decline ( and AD ) and review the evidence to prevent cognitive decline and AD by controlling risk factors
- Discuss the **Role of Lifestyle Changes** in decreasing the risk of cognitive decline and dementia and improving the quality of health and longevity
- Conclusions

# Brain Aging

- Characteristics include loss of brain volume (white matter > gray matter) especially in the hippocampus and frontal lobes; loss of myelin; synapses and the dendrites
- Increase amount of neurofibrillary tangles and deposition of **amyloid** in brain and blood vessels). Infarcts of various sizes and other evidence of cerebrovascular disease
- Aging is associated with progressive losses in function across multiple systems (sensation, cognition, memory, motor control and affect) and they occur with increasing age

# Healthy Brain Aging

- Maintenance or improvement of cognitive performance
- **Larger brain and hippocampal volumes** were associated with preserved cognitive function
- Ability to make decisions and remain independent
- Avoidance of disease and disability by maintenance of physical, cognitive and sustained social engagement

# Example of Healthy Brain Aging

Madame Jeanne Calment 1875-1997

Lived 122 years!

Guinness Book of Records as the  
“Oldest person Ever”

What was her secret????





# Road to Healthy Brain Aging:

- Preserve cognition (identify modifiable risk factors for AD)
- Improve physical function - get MOVING
- Make lifestyle changes like.....
- Improve social engagements ( ....with people you LIKE!)
- Eat a healthier diet - Heart Diet = Brain Diet
- Reduce Stress and reduce risk factors

# Barriers to Healthy Aging

## Modifiable Risk Factors

- Unhealthy Diet
- Physical Inactivity
- Tobacco Use
- Alcohol Use
- Drug use
- Polypharmacy
- Stress/Sleep

## Intermediate Risk factors

- **Raised blood pressure**
- **Raised Blood glucose**
- **Abnormal lipids**
- **Over weight /obesity**
- **Heart disease**
- Pulmonary disease
- Mental Illness
- Arthritis
- Osteoporosis
- Dental care

# Non-Modifiable Risk Factors

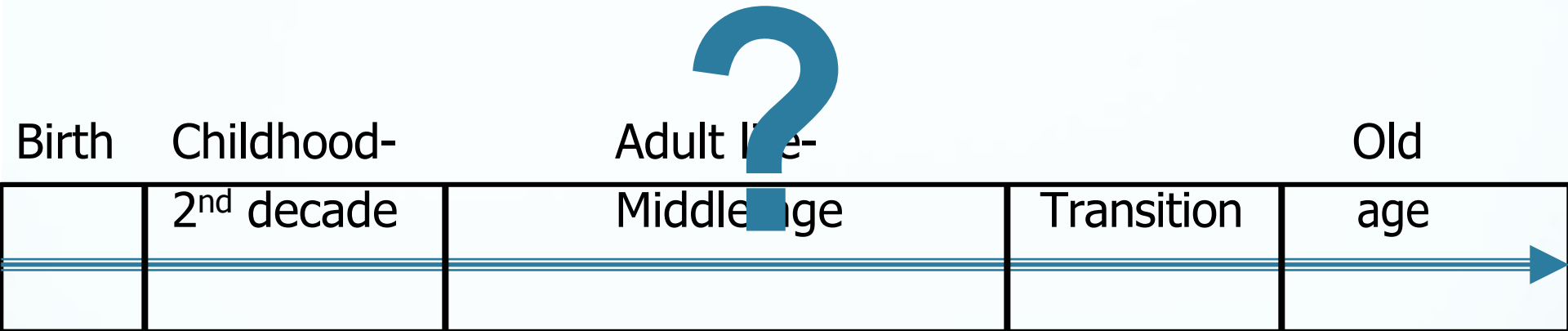
- Age
- Family History
- Genetic Factors
  - For AD Early onset AD mutations: Presenilin-1 (30-70%); APP (10-15%); Presenilin-2 (<5%)
  - Late Onset AD: APOE-4



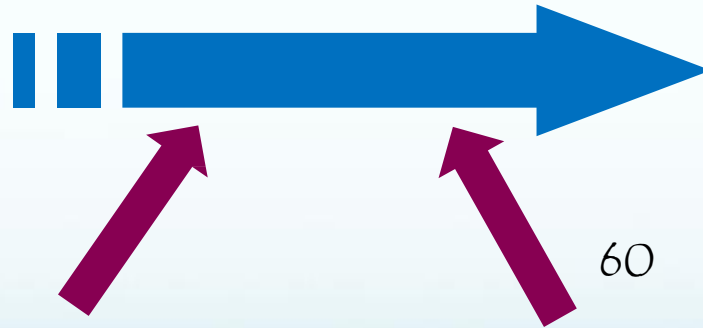
# Alzheimer's Disease

- 5.3 million Americans have AD (Alzheimer's Association 2009). By 2021 the number is expected to increase to 7.5-9 million and by 2051 it could reach 12.6-16 million
- It accounts for 66% of dementias in older adults
- 33-50% of people aged 85 and older have AD
- Women account for 66% of cases
- AD develops over decades and dementia can affect a person over 3-20 years

# Cognitive Continuum



20



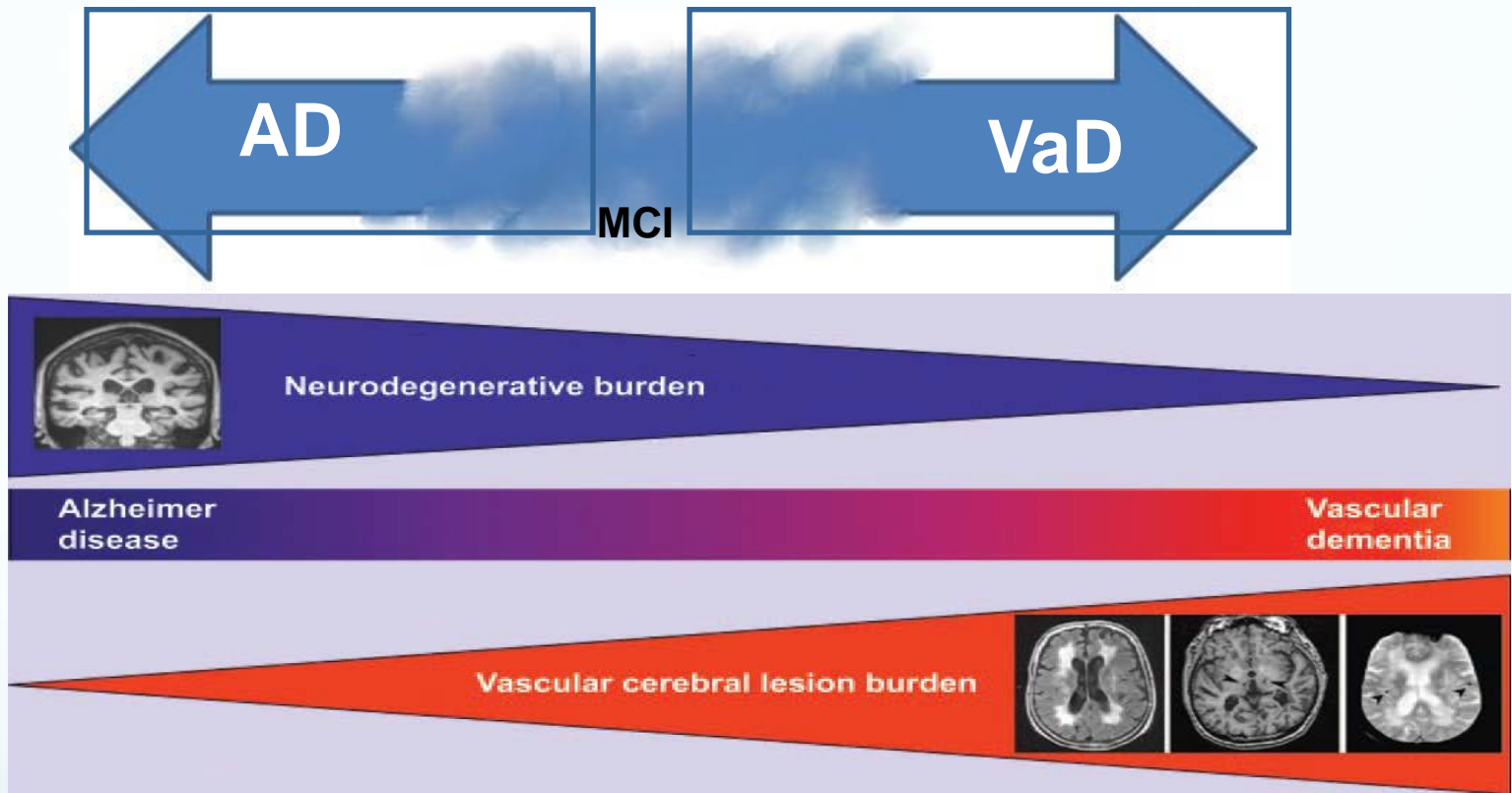
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# Probable Modifiable Risk factors for Cognitive Decline - Top 3 are Cardiovascular Risk Factors

- **Hypertension**
- **Diabetes mellitus**
- **Hyperlipidemia**
- Smoking/Drinking
- Head Trauma
- Depression

# Dementia in advanced age



\*\*\*\***Both** vascular and degenerative mechanisms often contribute to dementia development in older adults\*\*\*



## Heart - Brain (aka- Neurovascular) Coupling in the Normal Brain and in Hypertension, Stroke and Alzheimer's disease

- Regulation of cerebral blood flow (CBF) involves coordinated interaction of neurons, glia, and vascular cells

- Neurons & glia generate signals → vascular change → increased CBF
- Pathological conditions such as **AD, hypertension, atrial fibrillation, ischemic stroke** disrupt neurovascular coupling → CBF not matched to metabolic needs
- Cerebrovascular dysregulation mediated by the enzyme, NADPH oxidase - a major source of cerebral vascular free radicals develop and kill cells



# Diabetes – A Strong Risk Factor for Cognitive Decline and Alzheimer's disease (AD)

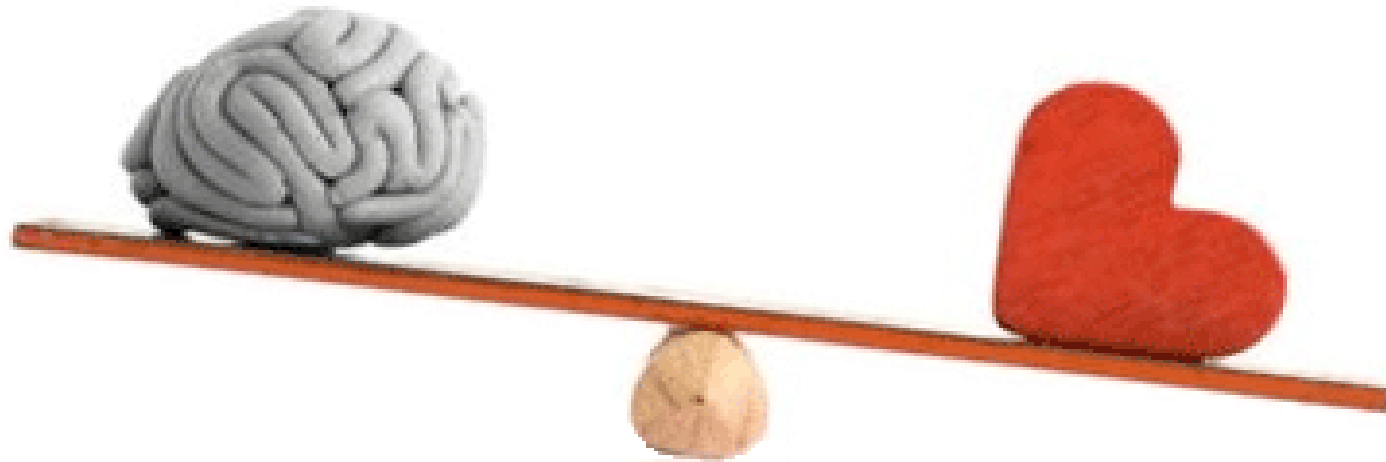
- Type I and Type II diabetes can → heart disease, stroke, renal failure, cognitive decline and AD
- Duration of diabetes esp. important risk factor for AD
- Hyperinsulinemia and hyperglycemia preceding overt diabetes, also increase risk of cognitive changes and AD
- Metabolic changes associated with diabetes such as: oxidative stress, inflammation are also associated with AD

# Diabetes

- Insulin resistance and hyperinsulinemia both alter insulin signaling in the brain – this may contribute to the impact of type II diabetes on cognition and development of AD
- Using transgenic mouse model of AD → diabetes can accelerate AD – associated changes in the brain.
- **ADCS Clinical Trial will be recruiting soon-** Nasal Insulin to prevent worsening of cognitive decline
- [www.adcs.org](http://www.adcs.org)



# The Heart-Brain Connection



# Serum Lipids are Related to Alzheimer's Pathology in Nursing Home Residents<sup>(1)</sup>

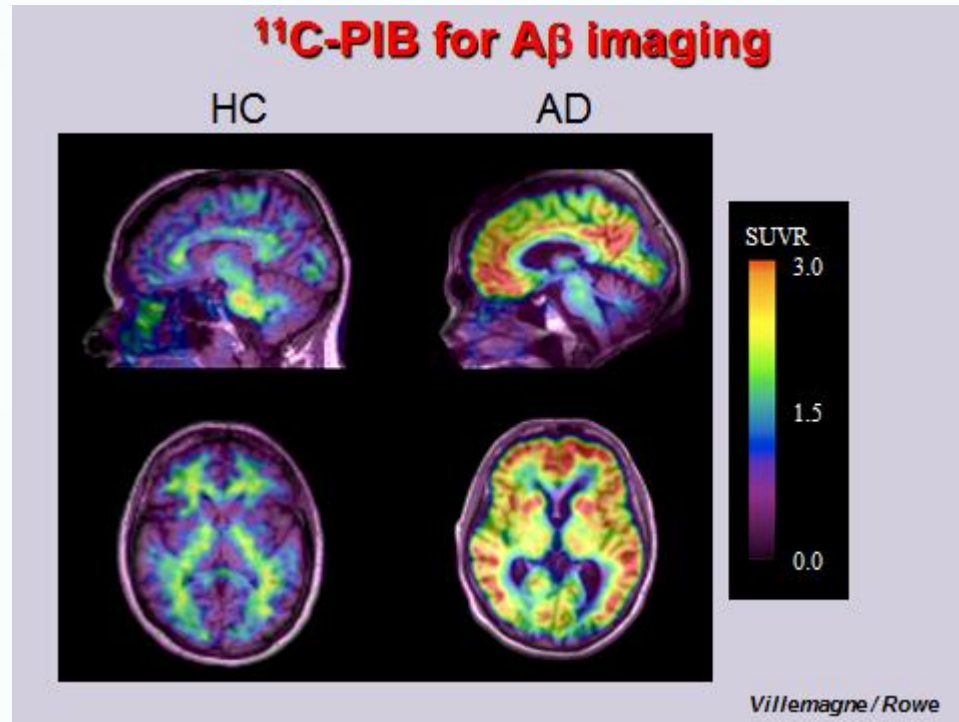
- A study at nursing home in NYC
- Nursing home residents, serum lipids were determined at admission and neuropathologic diagnoses were established at brain autopsy
- Residents with any AD pathology vs. those without AD pathology had higher mean serum total cholesterol and higher mean low-density lipoprotein

Ref: Lesser GT, et al. Dement Geriatr Cogn Disord, 2009;27:42-49

# Moderate Alcohol Intake is Associated with Lower Dementia :Results from the Ginkgo Evaluation of Memory Study (GEMS)

- 3,069 community dwelling adults aged 75 or above without dementia in the GEMS study were followed for 6 years
  - 2,587 were cognitively normal at beginning of study
  - 482 had MCI ( Mild Cognitive Impairment = “The Gap” between normal thinking and dementia)
- Goal: To determine the relationship between alcohol intake and developing dementia
  - intake determined by self-reports as –
    - light = 1-7 drinks/week
    - moderate = 8-14 drinks/week
    - heavy = > 14 drinks/week

- Moderate alcohol intake (1-2 drinks/day) associated with a 37% lower risk of dementia in participants with normal cognition at baseline, but not in MCI patients
- For those with MCI at baseline:
  - any alcohol intake was associated with a faster rate of cognitive decline
  - heavy drinkers (> 14 drinks/week) were nearly twice as likely to develop dementia compared to non-drinkers with MCI
- Recommendations to not exceed one drink/day for women and 2/day for men



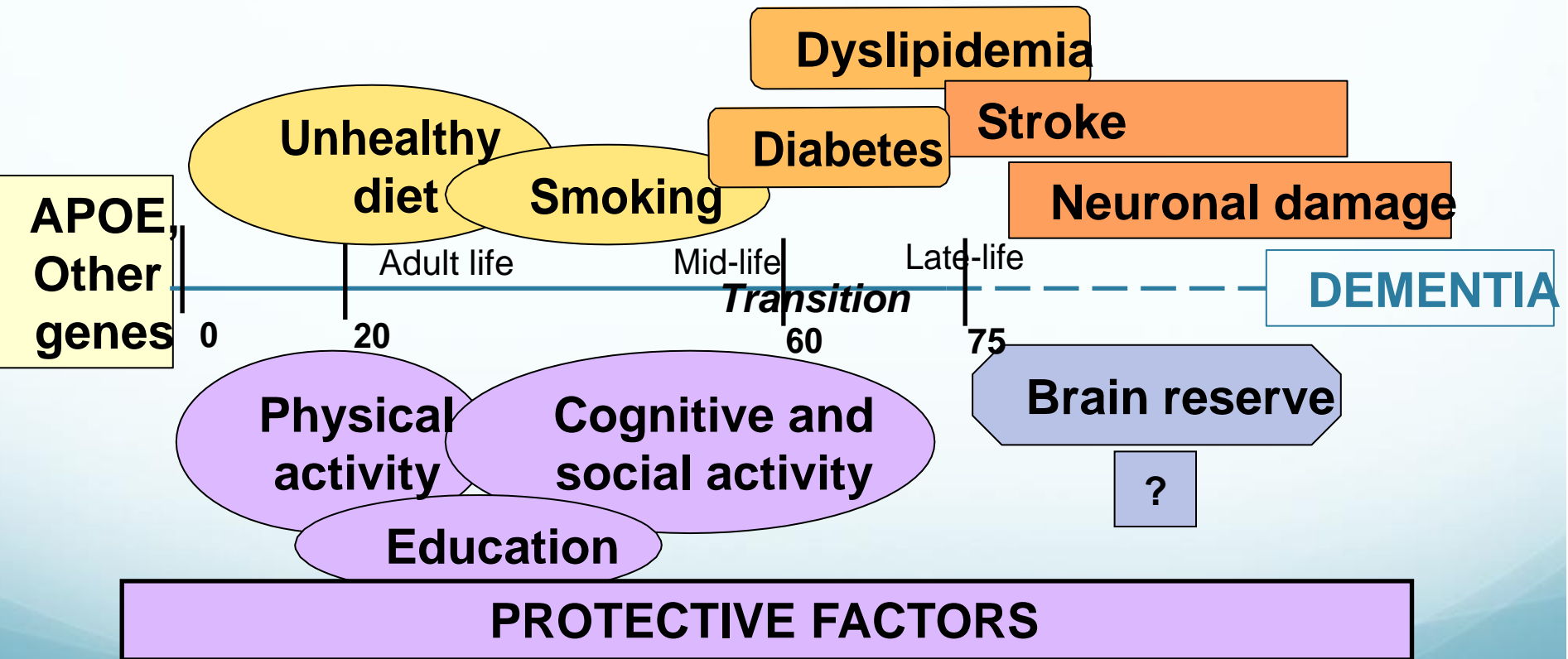
## Amyloid Precursor Protein (APP) and Traumatic Brain Injury (TBI)

- A-Beta peptides accumulate rapidly after TBI in animals and humans

# Change in Depression Symptoms During the Prodromal Phase of Alzheimer's Disease

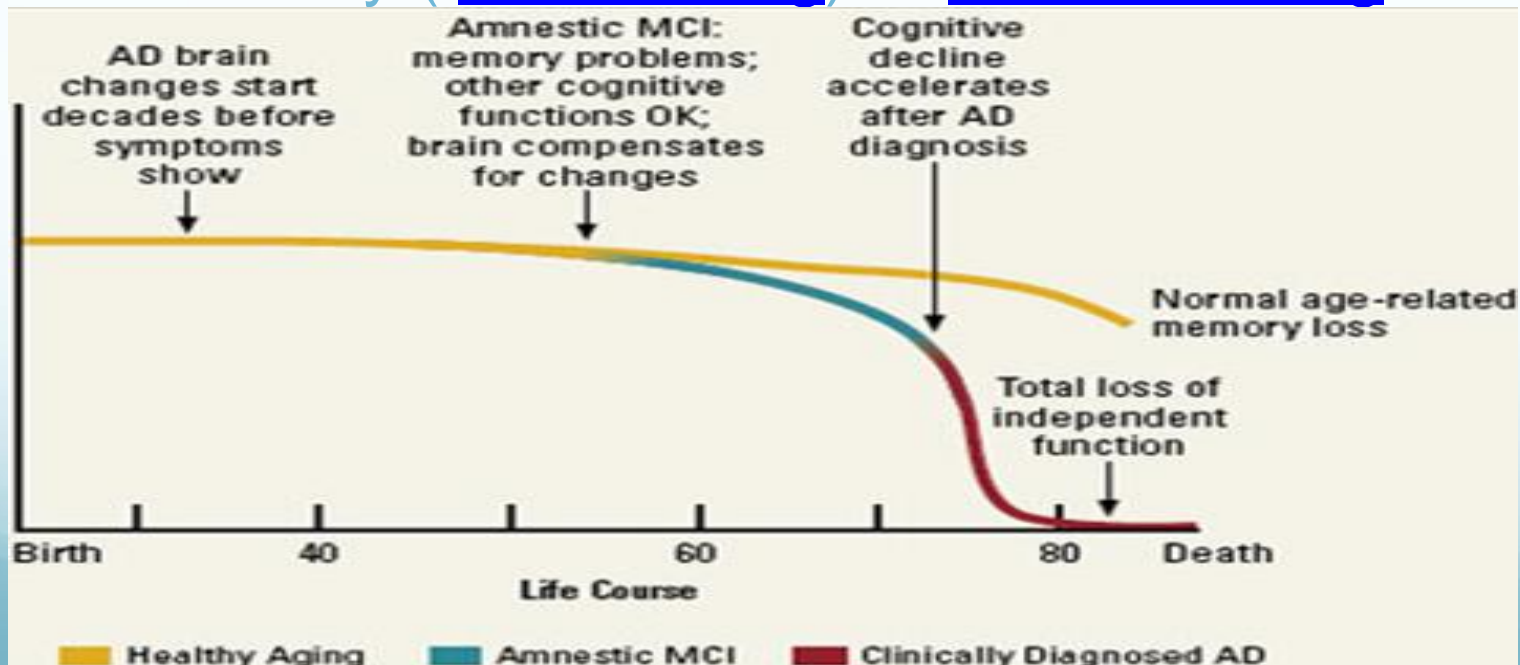
- Rush Religious Orders Study followed 917 older Catholic clergy for 13 years – 190 developed AD
- Having more depressive symptoms at baseline was associated with increased incidence of AD and MCI

# Alzheimer's Disease IS A MULTIFACTORIAL DISEASE



# PREVENTION OF COGNITIVE IMPAIRMENT AND AD

- HOW AND WHEN???
- A4 Study ( [www.a4.org](http://www.a4.org) ) or [www.adcs.org](http://www.adcs.org)





# The Role of Lifestyle changes to Prevent AD and Promote Healthy Brain Aging

- Nutrition/Diet
- Physical Activity
- Social Activity
- Spiritual Activity
- Meditation
- Control of Stress
- Humor/Attitude

# Mediterranean Diet (Mostly Plants)

NEJM June 26, 2003



## High Consumption of:

Fruits (4-6 servings daily)

Berries (flavanoids, phytochemicals)

Vegetables (4-6 servings daily)

Beans (3-6 servings daily)

Nuts (3-5 pieces)

Whole grains (3-6 servings daily)

Olive oil (monounsaturated fatty acids)

Fish – broiled or baked

Alcohol – red

Spices (turmeric, ginger, garlic)

## Low Consumption of:

Saturated fat

Dairy products

Red meat and poultry

# Conclusions: Healthy Nutrition

- Eat fruits, vegetables, whole grains, and fat-free or low-fat milk and milk products
- Include fish, beans, eggs, and nuts
- Water (24-40 ounces daily)
- Spices (turmeric, cinnamon, ginger, garlic)
- Chocolate?- Yes
- Low in saturated fats, *trans* fats, cholesterol, salt, and added sugars
- How healthy is your diet?????



# Mediterranean Diet and Mild Cognitive Impairment

- 1393 community based, cognitively normal elders in New York
- Of those with MCI comparing to subjects in the lowest Med Diet adherence tertile
  - Middle tertile had a 45% less risk of converting to AD (p=0.01)
  - Those in the highest tertile had a 48% lower risk of converting to AD (p=0.02)
    - Ref: Scarmeas N, et al. Arch Neurol, Feb 2009, 66 (2) 215-25



# Physical Activity

Do You Like to Dance?  
Need Some Inspiration ?

Check out Dancing  
Grandma

- [http://www.youtube.com/watch?v=5qMCyyM\\_AtE](http://www.youtube.com/watch?v=5qMCyyM_AtE)

# Physical Activity, Diet and Risk of Alzheimer's Disease

- 1880 community-dwelling elders without dementia in New York City
- Followed from 1992-2006
- Mediterranean-type diet and physical activity profile were measured, relative to correlation with time to develop AD
- Both higher adherence to a Mediterranean-type diet and higher physical activity were independently associated with reduced risk for Alzheimer's Disease

# Physical Activity and Dementia Risk

## Results from a Prospective Italian Study

- A study of 749 subjects 65 years or older who were cognitively normal followed for 3.9 years
- Vascular Dementia risk was significantly lower for the upper levels of walking, moderate and total physical activity (HR=0.24) compared to corresponding lowest level
- Ref: Ravaglia G, et al Neurology, Dec 2007



# Studies that Illuminate the Role of Physical Activity

- Stevens and Killeen (2006) demonstrated that 12 weeks of exercise (3x/week) on demented pts improve their performance on the Clock Drawing Test and Revised Elderly Persons Disability Scale compared to control and social interaction
- Adlard et al (2005) demonstrated that five months of exercise decrease amyloid plaques in frontal cortex and hippocampus. Showed enhanced rate of learning The proposed mechanism: neuronal metabolism change that affects APP processing.
  - J of Neuroscience 25 (17) 4217-4221
  - 
  -

# Exercise Training Increases Size of Hippocampus

- 120 older adults assigned to two groups moderate intensity aerobic exercise 3 days/week pr stretching and toning exercises for one year
- MRI before and after exercise
- Aerobic exercise increased anterior hippocampal volume after one year leading to improve memory
- 
- In summary the one year of aerobic exercise was sufficient to increase the hippocampal volume by 2% - Start moving!
- 
- New Exercise Study on delaying memory loss slated to start late

# Physical, Mental, and Social Activity Stave Off Dementia!

**Study after study has demonstrated that staying physically active is one of the best ways to protect your brain- WALK!!!**

Mental activity is equally important to brain health. So exercise your brain!

Research has also shown that socially connected people are less likely to develop dementia than their isolated peers.



# Road to Successful Aging

- Engage in Social Activity- join groups, discuss topics, travel with friends
- Have a Spiritual Belief System
- Mental Activity – learn something new
  - (language, game, music, instrument, dance, video games, computers..)
- Meditation (Mindfulness, Transcendental)
- Yoga, Tai-chi



# Examining the Association Between Participation in Late-life Leisure Activity and Cognitive Function in Community-dwelling Elderly Chinese in Hong Kong

- 512 participants 60 years or older
- Four categories of leisure time activities
  - physical
  - intellectual
  - social
  - recreational
- Higher levels of leisure-time activity, in particular, intellectual activity, were associated with better cognitive function

# Example of Healthy Heart and Brain Aging

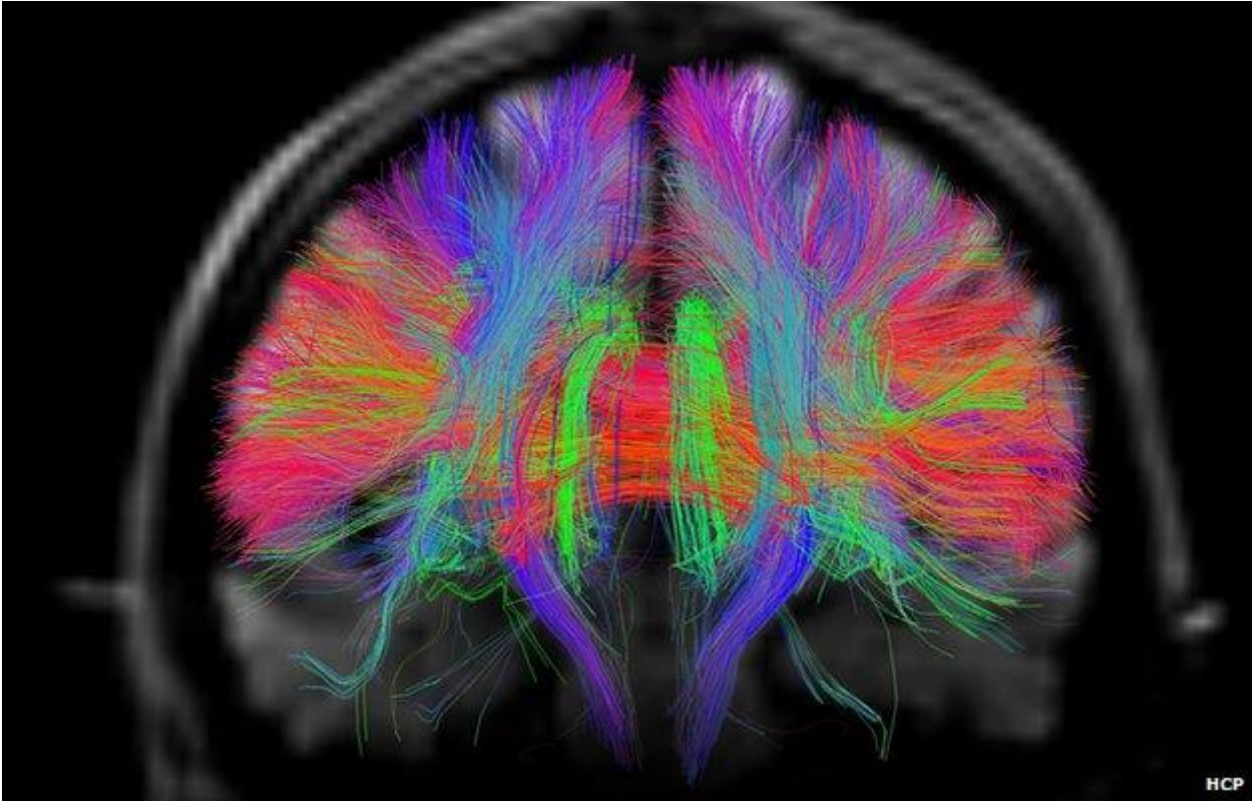
Madame Jeanne Calment 1875-1999

**5 Lifestyle Secrets: Exercise,  
Nutrition, Stress Control,  
Social Activities, Great Sense  
of Humor!**

“If you can’t do anything about it, don’t  
worry”

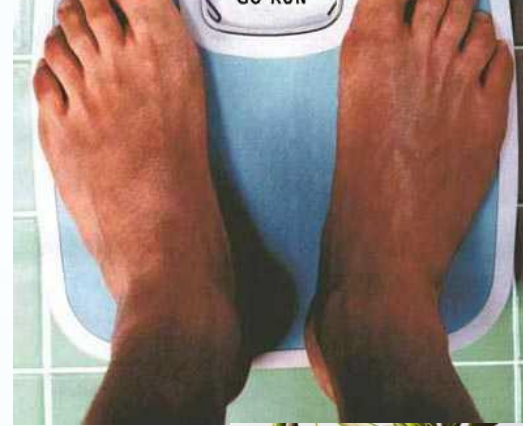
“I’ve never had but one wrinkle and  
I am sitting on it”





HCP





What helps  
your heart



can help  
your brain,  
too.

