

# Can Alzheimer's disease (AD) be prevented?

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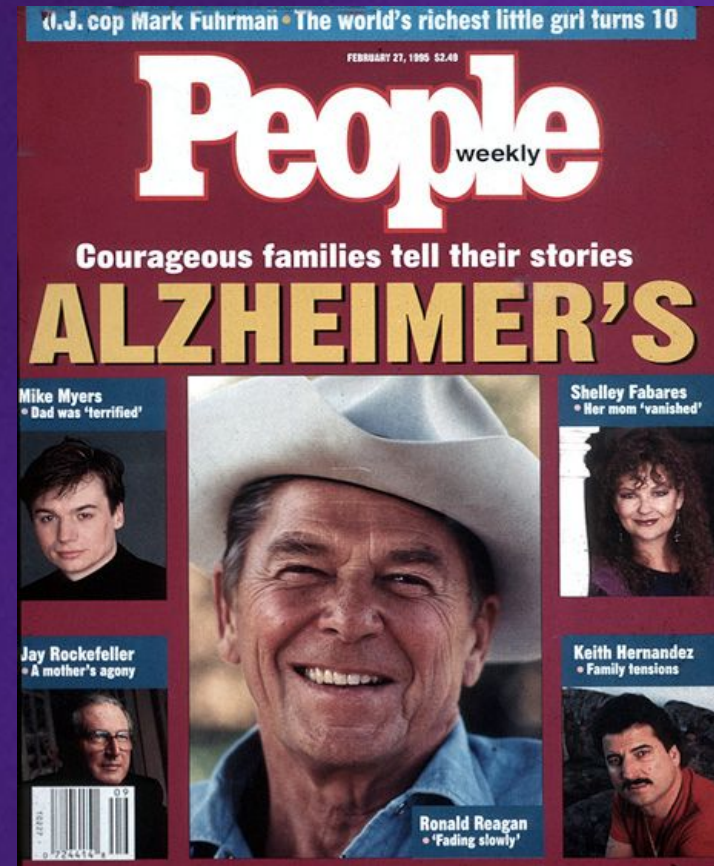
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# **Mental Activity and Dementia: A Case of Use it or Lose it?**

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# Mental activity and dementia

## Overview

- ❑ Is mental activity really important?
- ❑ How can mental activity change the biology of Alzheimer's Disease?
- ❑ What kind of mental activity is effective?

# Is mental activity really important?

## Mental activity and dementia

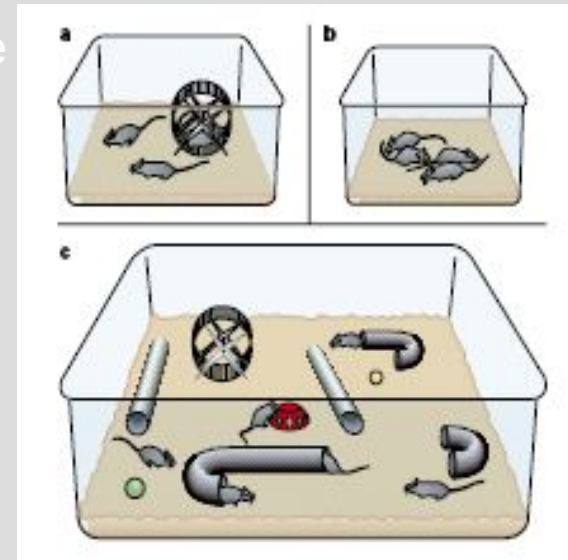
- ❑ 22 international studies, > 21,000 persons
- ❑ those with high levels of mental activity had  $\leq \frac{1}{2}$  risk for developing dementia
- ❑ Mental activity was measured by level of education, occupational complexity or cognitive lifestyle activities
- ❑ *Complex mental activity reduces risk for dementia*



# How could this work?

## Mental Activity in Mice

- ❑ Effects of mental activity on the brain have been studied using 'environmental enrichment'
- ❑ Enrichment involves comparing standard housing to housing with more littermates, more toys, more exercise devices
- ❑ Dozens of studies have now shown that mice reared in enriched environments perform much better on tests of memory, problem solving, reaction time etc
- ❑ Enrichment also has a number of effects on the mouse brain



# How could this work?

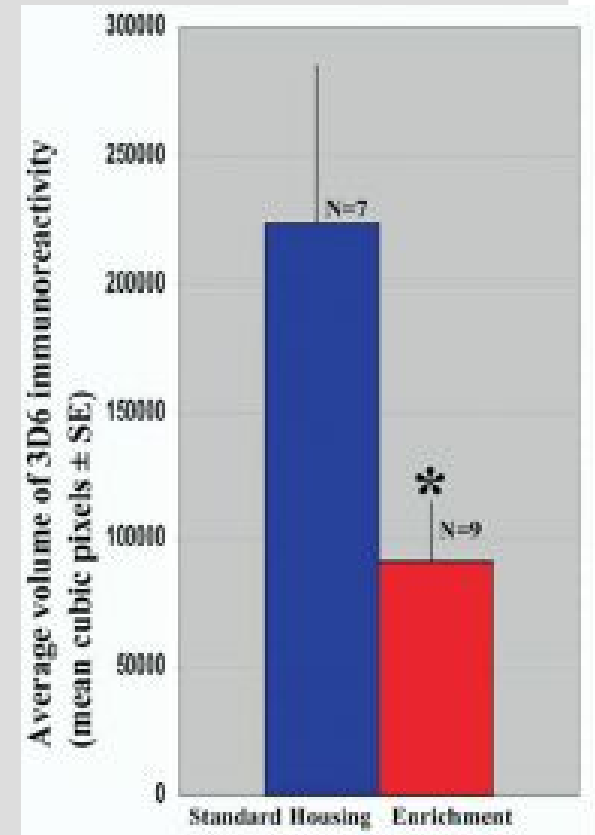
- ❑ Neurogenesis refs to the process of producing new brain cells (neurons)
- ❑ Is common in adult mammals, even older mammals!
- ❑ Hippocampus is important for memory and loss of neurons in this area is critical to first clinical expression of Alzheimer's Disease

# How could this work?

- ❑ Increased mental activity (via environmental enrichment) increases number and survival of newly created neurons *in hippocampus*
- ❑ Generating more neurons in hippocampus may counteract expression of AD

# How could this work?

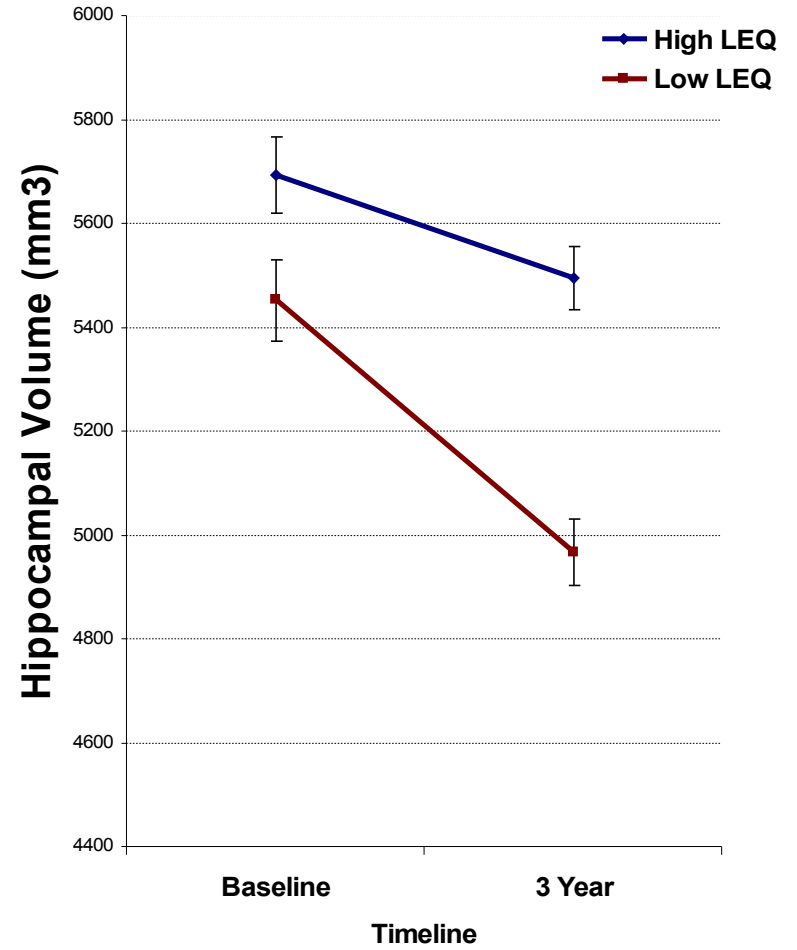
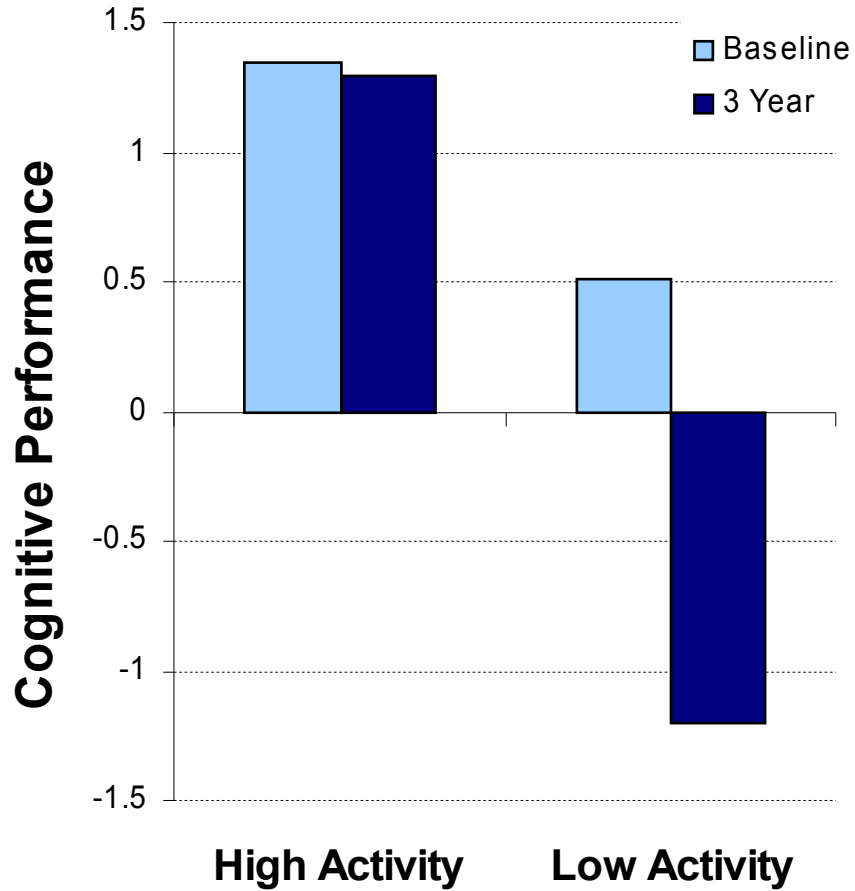
- Genetically modified mice simulate some of biological and cognitive effects of AD
  - Amyloid plaques occur in brains in AD
  - 5 months environmental enrichment → 50% ↓ no. & size of plaques vs standard housing



Lazarov et al (2005)

# How could this work? Hippocampus Shrinkage

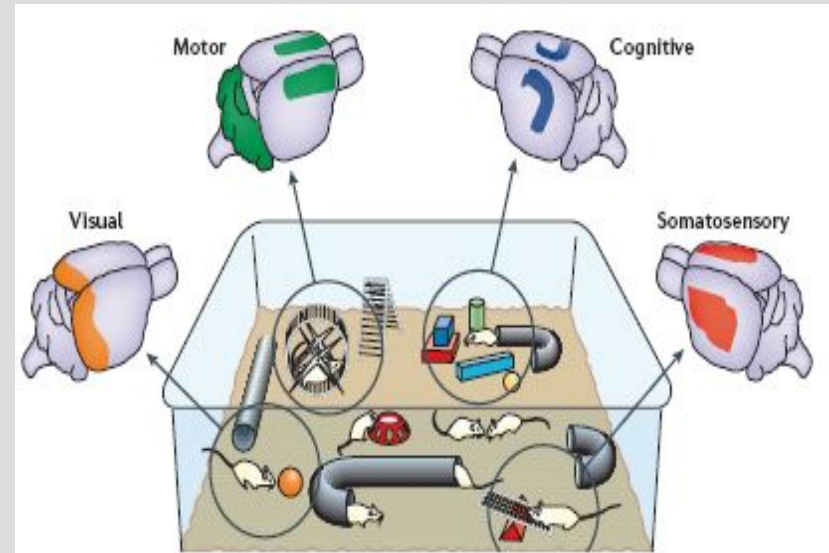
- ❑ **Sydney Stroke Study**
- ❑ **81 healthy elderly followed for > 3 years**
- ❑ **At start of study, *Lifetime of Experiences Questionnaire* (LEQ) assessed complex mental activity across lifespan -> LEQ score**
- ❑ **High LEQ people had much less cognitive decline over three years**
- ❑ **High LEQ people had 50% less shrinkage of hippocampus over three years**



# What kind of mental activity?

## Lessons from Mice

- ❑ Analysis of enriched environment many cognitive processes involved and different parts of the brain used
- ❑ No one component is sufficient
- ❑



- ❑ **Mice need social, cognitive + physical activity to → benefit to brain**

# What kind of mental activity?

## Three Key Ingredients

Human studies support  
mice findings:

3. Cognitive: activity should involve an aspect of learning something new, problem solving, remembering or strategy



# Three key ingredients

- 2. Social: activity should occur with other people. Proper socialisation demands good cognitive and physical activity as well!**
- 3. Physical: activity should involve some type of physical exercise or skill**

# What activity? Suggestions...

*Has to be fun!* A new passion or hobby that you will continue to practice and learn for the rest of your life is going to be the most effective...

Learn to Dance

Practice Tai Chi

Take up Sailing



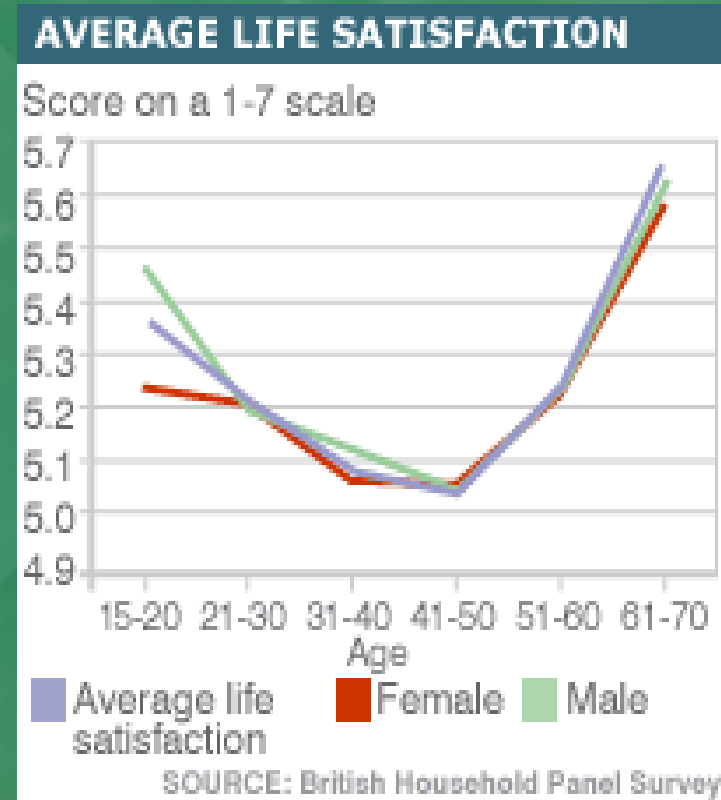
**Modify your own past-time if a key ingredient is missing**

# **Happiness in Ageing and its Effect on Memory**

**Dr Adrienne Withall**

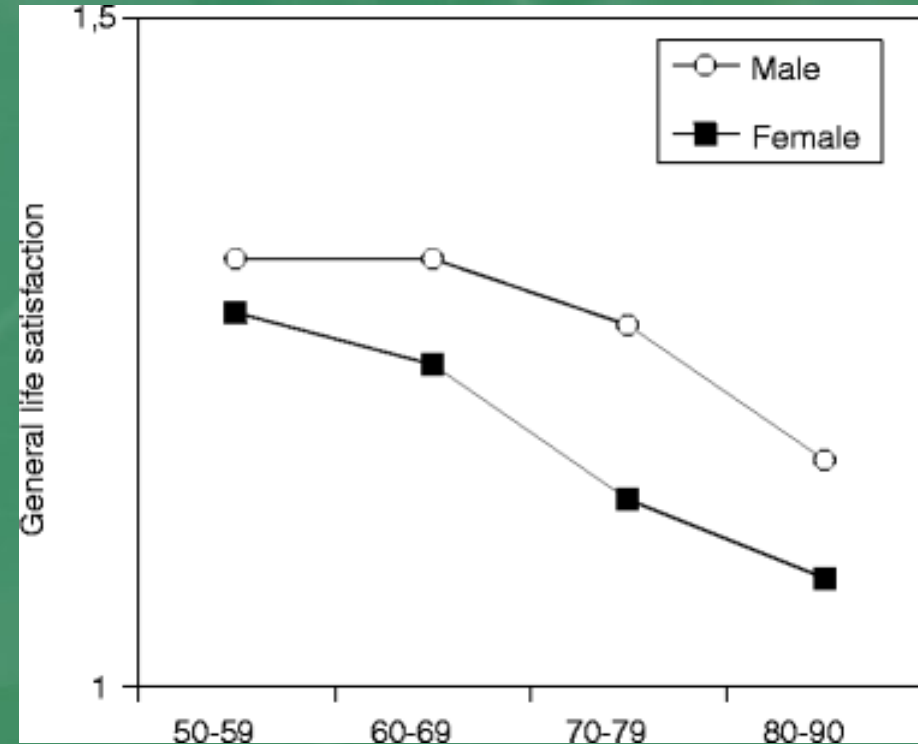
# Happiness and Ageing

- Little difference between younger and older age groups with respect to life satisfaction (smile-shaped)
- “Satisfaction paradox” → older people are better at regulating their happiness eg, they settle for a good result rather than striving for the best one



# How Happy Are Older People?

- **European Study on Adult Wellbeing**
- **6 countries; 12478 people; 50-90 yrs.**
- **Shows life satisfaction falls over time within older groups**



# Happy People....

- Have more quantity & quality of contacts with friends rather than contact with family members
- Are more likely to participate in a variety of social & physical activities



# Happiness and Memory

- Happier people have higher current cognitive function, such as memory, but not intelligence
- Well-established link between mood and memory, i.e., as mood goes down, so does memory



# Happiness Not Just Good for Memory

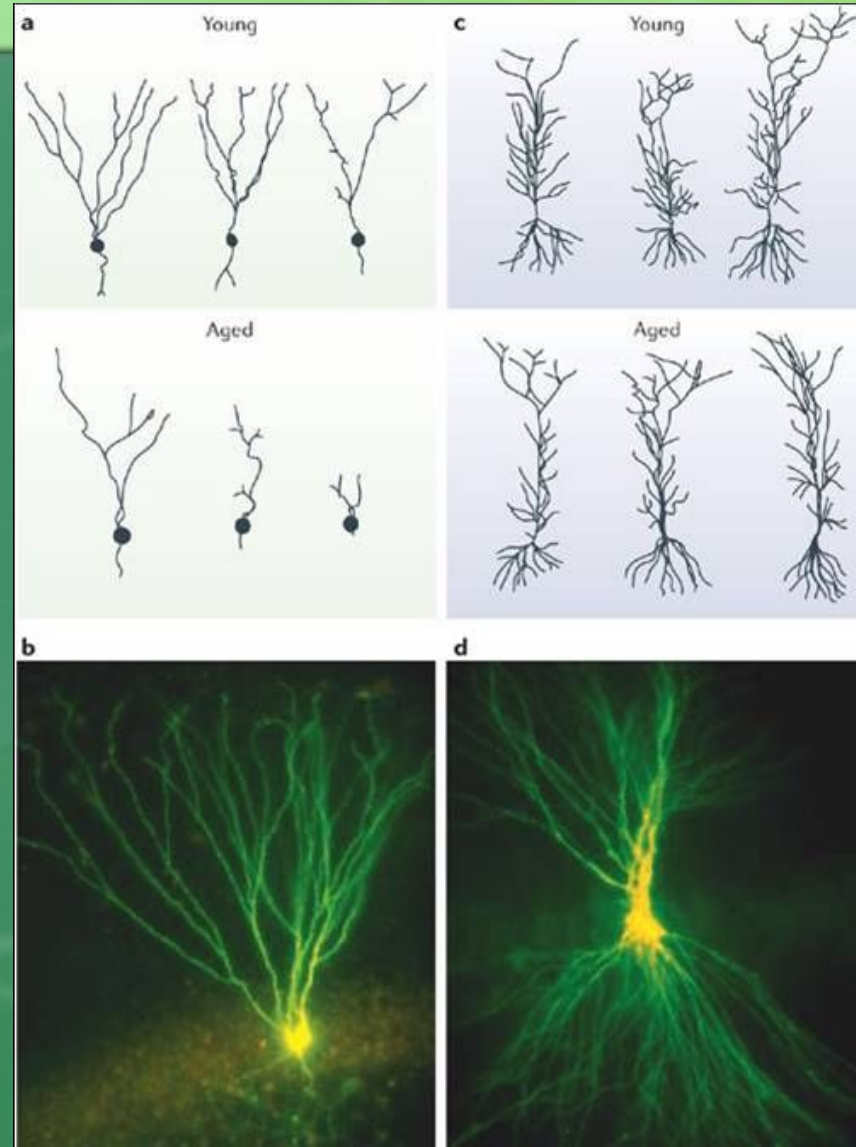
- **Laughter and positive mood boosts:**
  - Immune function
  - Cardiovascular function e.g., lowers blood pressure
  - The body's ability to cope with stress

# Get Active - Older People are Doers!

- Claude Monet was 80 when he painted his famous series of water lilies
- Giuseppe Verdi was 80 when he composed the opera Falstaff
- Sigmund Freud made seminal contributions to psychoanalysis in his 80s
- George Bernard Shaw was 91 when he penned the play "Buoyant Billions." Shaw lamented: "... if only I could live longer to properly benefit from life's experience. Youth is wasted on the young!"

# The Myth of Brain Ageing

- Previously thought that older people couldn't build new brain connections
- Now we know that the brain can regenerate at all ages!
- Changing your habits now can affect your memory.



# Things You Can Do to Increase Your Happiness Levels

- Absence of role identity in later life: volunteering can improve mood
- “Three Good Things” exercise - write down 3 things daily that went well & why each happened
- Get active! Exercise can improve both memory AND your mood

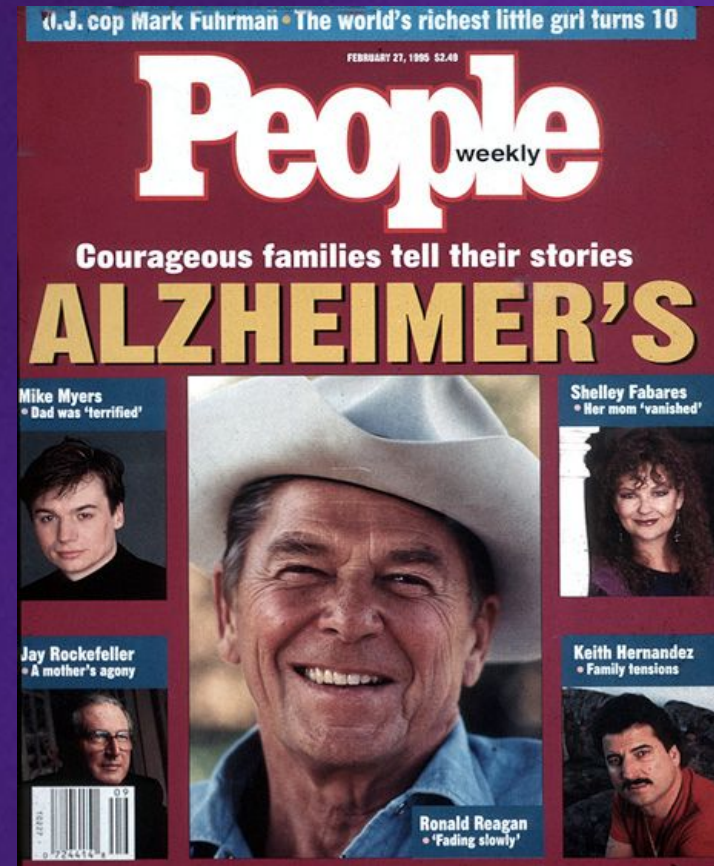


Courtesy of Getty and ARA Content

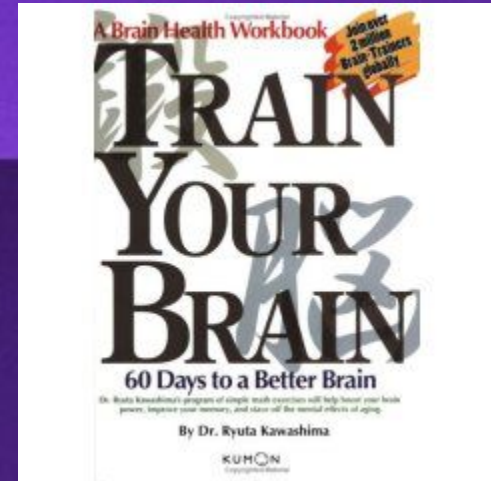
# Can vitamins, supplements or medications prevent Alzheimer's?

Professor Henry Brodaty  
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& University of  
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Sydney, Australia

[www.med.unsw.edu.au/adfoap](http://www.med.unsw.edu.au/adfoap)



# Train the Brain 4990 hits on Google!!



# How often do you drink alcohol?

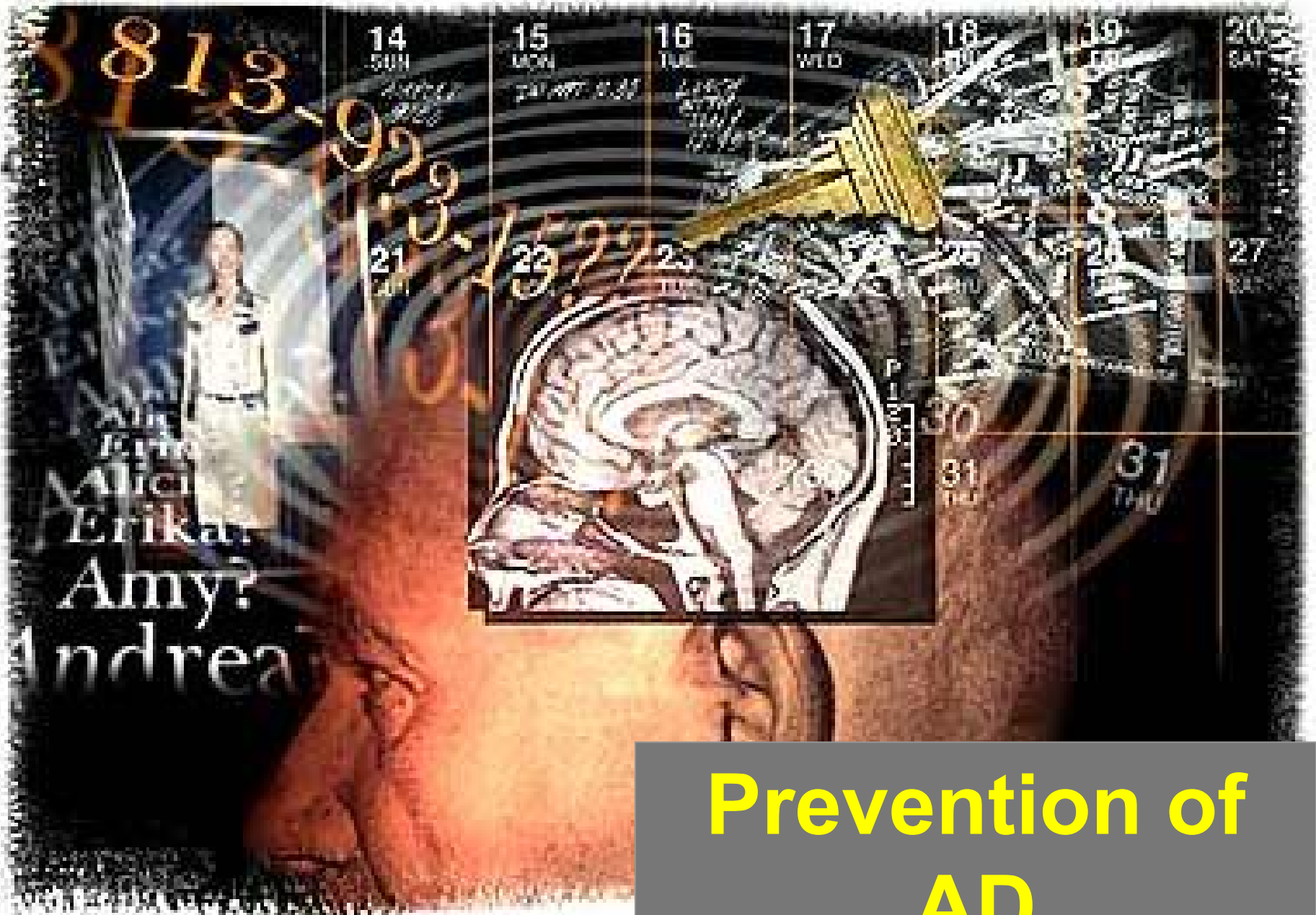
- 1. Never or hardly ever**
- 2. Less than once a week**
- 3. 1 - 3 times a week**
- 4. 4 or more times a week**

# How often do you eat fish?

- 1. As infrequently as possible**
- 2. Less than once a week**
- 3. 1 - 3 times a week**
- 4. 4 or more times a week**

# Who takes vitamin supplements?

- **Vitamin E**
- **Vitamin C**
- **Folic Acid**
- **Ginkgo biloba**
- **Others**



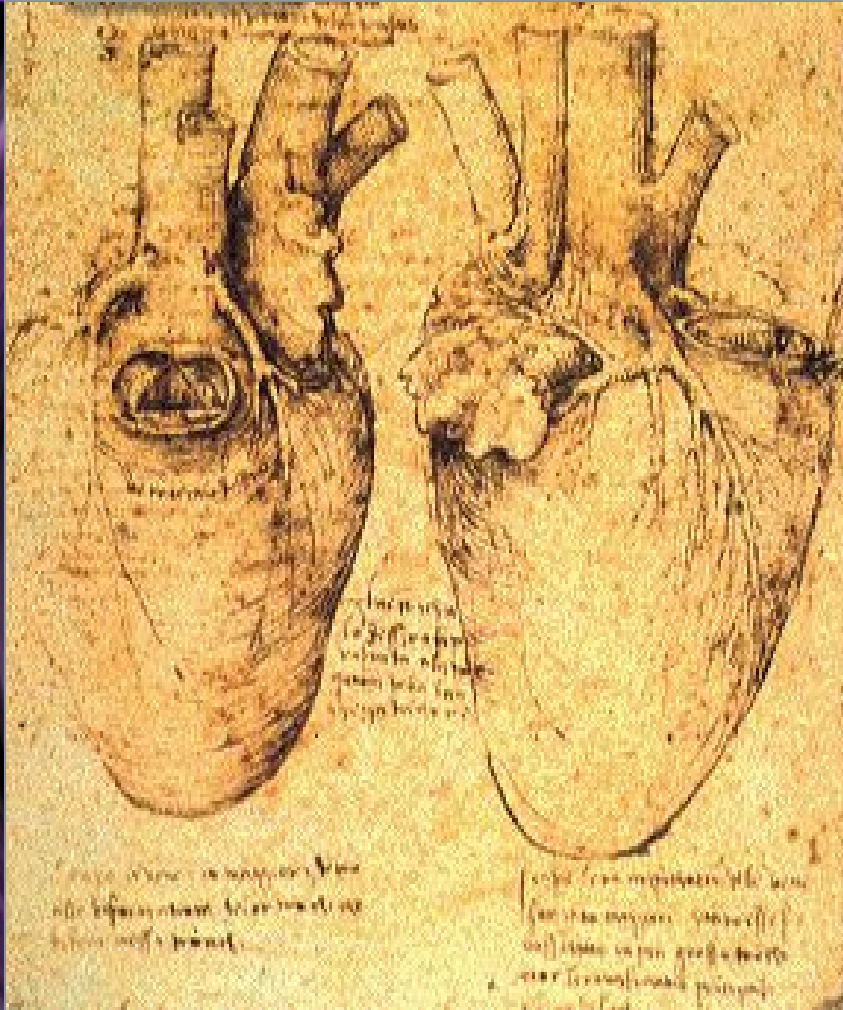
Erika  
Alice  
Erika  
Amy?  
Andrea

# Prevention of AD

# Elimination vs Postponement

- **Disease elimination**
  - eg smallpox vaccination
  - best prospect is AD vaccine
- **Disease postponement**
  - delay AD onset by 2 yrs, ↓ prevalence by >20%
  - delay AD onset by 5 yrs, ↓ prevalence by 50%

# Cardiovascular factors



- Hypertension
- High cholesterol
- Homocysteine

The human heart, Leonardo Da Vinci

# High blood pressure

- **Increases risk of heart disease, cardiac failure, stroke and.....**
- **..... Alzheimer's disease**
- **Reducing high blood pressure reduces risk of all of these factors**
- **European study showed lower rate of dementia after 5 years in group whose blood pressure had been treated**

# High cholesterol

- **Associated with heart disease, stroke and vascular dementia**
- **Different fats in blood - some good for you, some bad**
- **Statins, drugs used to lower cholesterol may help prevent AD but this effect appears independent of lower cholesterol**
- **No evidence (?yet) that lowering cholesterol is beneficial in reducing risk of AD**

# Homocysteine

- Homocysteine is an amino acid which is a building block to make proteins
- High levels have been associated with heart disease, stroke, vascular dementia and AD
- Homocysteine = the new cholesterol?
- HCy be readily lowered with folic acid
- Dose? (folate) 0.5 or 1 or 5mg per day
- Even more ↓ if take with Vit B12 (and B6)

# Medications



- **Statins**
- **HRT**
- **NSAIDs**
- **Anti-diabetes**

# Statins

- **Statins are drugs to lower cholesterol**
- **Examples: Lipex, Lipitor, Lopid, Pravachol, Vastin, Zocor**
- **Statin users less likely to develop Alzheimer's disease than non-users**
- **No evidence yet from randomised controlled trials**
- **Statins generally well tolerated but can have side effects.**

# HRT and AD

- Up until May 2003 epidemiological evidence was convincing that HRT was protective against AD in post-menopausal women
- Then came an RCT
- **Women's Health Initiative Memory Study**
- Women 65+, six years on HRT or placebo
- Combined oestrogen and progestin (Prempro) had double risk of developing of dementia (AD or vascular dementia) vs placebo

# Non-steroidal anti-inflammatory drugs (NSAIDs)

- **Examples: Voltaren, Naprosyn, Indocid, Celebrex, Feldene, Brufen, Vioxx**
- **Epidemiological studies - associated with lower rate of Alzheimer's disease**
- **Risks now well recognised: heart disease, high blood pressure, stomach ulcers**
- **No randomised controlled trial of effect**
- **Not recommended for prevention**

# Non-steroidal anti-inflammatory drugs (NSAIDs)

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# Diabetic medication

- Link between obesity and diabetes
- Link between diabetes and AD
- Prevention of obesity reduces risk of type 2 diabetes and possibly of AD
- Drugs to lower blood sugar eg Metformin, Avandia - no evidence
- Trial of Avandia (rosiglitazone) now at Sydney Centre for Clinical Cognitive Research, POW Hospital
- Call 9382 3733

# Nutrition/ Supplements



- Alcohol
- Fish/Seafood
- Caffeine
- Vitamin E
- Vitamin C
- Ginkgo biloba

# Alcohol & dementia



- Light to moderate alcohol consumption associated with lower risk of dementia *and* AD
- Example - Rotterdam study<sup>1</sup>  
45% less risk of any dementia in those who drink 1-3 drinks per day vs non drinkers

***Recommendation - no need to cease (or begin!) Moderate alcohol use***

# Fish



- Higher intake of omega-3 fatty acids possibly also protective<sup>2</sup>
- Fish oil is high in omega-3

1. Arch Neurol 2003; 60:194-200

2. BMJ 2002; 325:932-933

# Antioxidants

- **Some evidence that antioxidants may delay or reduce risk of AD**
- **Vitamins E and C, Ginkgo biloba, green tea, alcohol (red wine), polyphenols (fruits/ juice, vegetables/ juice)**
- **Circumin, ginger**
- **DHA (docosahexaenoic acid)**

# Natural therapies



## Curry spice curcumin<sup>1,2</sup>

- active ingredient in turmeric, member of ginger family)
- metal chelator
- antioxidant
- anti-inflammatory agent & COX inhibitor

8. Ringman JM et al, Current Alz Research

9. Zhang H-Y, Science Direct 2005

Zingiberaceae ginger family

# Vitamin E & C

- **Mixed evidence whether vitamin E has protective effects on dementia including AD**
- **Theoretically appealing - antioxidant**
- **Dietary Vit E ? more effective v. supplements**
- **Vit C enhances antioxidant effect of Vit E**
- **One review : 0.4% increased mortality rate when several studies of people taking Vit E for chronic medical conditions were pooled**
- **Negative trial of Vit E for MCI (Mild Cognitive Impairment)**

# **Vitamin E & C supplements & AD: Honolulu-Asia Aging Study<sup>1</sup>**

- **N = 3385 Japanese-US males aged 71-93**
- **Over 10 yrs, 132 developed dementia (47 AD)**
- **Mail survey on # of pills of multivitamins, Vitamin E or C in past year**
- **No benefit for Vits E or C or E+C for AD**
- **But both protective for VaD or mixed/other dementia**

<sup>1</sup>Masaki et al *Neurology* 2000;54:1265-1272

# Foods naturally rich in vitamin E



- Nuts, such as almonds
- Vegetable oils
- Seeds
- Wheat germ

- Spinach
- Other dark, green leafy vegetables



# Other possibilities

- **Brahmi**
- **KH3**
- **Selenium**
- **Lecithin**

.....no evidence either way

# Looking forward

- **AD Vaccine**
- ▽  **$\beta$ - and  $\delta$ - secretase inhibitors**
- **Nerve growth factor**
- **Gene therapy**
- **Stem cells**
- **New pharmaceuticals**

# Prevention: the bottom line



**The bottom line**

- Active leisure, physical and intellectual life
- Vigorous blood pressure, cholesterol control
- Avoid harm
- Balance diet rich in Vit E, folic acid, antioxidants
- 1-2 glasses of red wine
- Perhaps supplements with Vit E, Vit C, Folic acid, B12 + B6 ???

# Who intends to change their level of alcohol intake?

1. Increase
2. No change
3. Decrease

# Who intends to change their fish intake?

1. Increase
2. No change
3. Decrease

# Who intends to or will continue to take vitamin supplements?

- **Vitamin E**
- **Vitamin C**
- **Folic Acid**
- **Ginkgo biloba**
- **Others**

**Thank you**

**The end**

**[www.med.unsw.edu.au/adfoap](http://www.med.unsw.edu.au/adfoap)**