Henry Brodaty
Scientia Professor, UNSW
Montefiore Chair of Healthy Brain Ageing

Maintain Your Brain

Dementia Collaborative Research Centres
Healthy Brains Positive Ageing

Never Stand Still

UNSW
What does it mean to be “old”? 

At 65 years of age

- In 1800, you were dead 27 yrs ago
- In 1900, you were dead 12 yrs ago
- In 2000, you had 12-15 yrs to go
- In 2100, you may be two-thirds through your life

In 2030, Australia’s population will be approx 28.48 million

Approx 1 in 5 will be 65 years or older
There will be almost 3 times as many centenarians as there are today.

2013: 6,364 centenarians
2030: 18,923 centenarians
A girl born today has a 40% chance of reaching 100
Adding years to life or adding life to years
Successful ageing?
Successful ageing?
I went to the doctor with fluid on the knee and he said "You're not aiming straight"
You've heard of the three ages of man?

- Youth
- Age
- You are looking wonderful
The secret of staying young is

• Live honestly .......... 
• Eat slowly, and ..... 
• Lie about your age
Getting Older

I'm at an age when my back goes out more than I do
Lifestyle

Seven protective factors
• Not being a smoker or stopping young
• Adaptive coping style
• Absence of alcohol abuse
• Healthy weight
• Stable marriage
• Some exercise
• Years of education

Centre for Healthy Brain Ageing

https://cheba.unsw.edu.au/

Our vision is to achieve, through research, healthier brain ageing and better clinical care of age-related brain diseases
Our brains

• The adult brain weighs about 1.3 kg
• Dementia shrinks it to ½ its usual size
Who is worried about their memory?
NOW... AM I GOING UPSTAIRS FOR SOMETHING OR HAVE I JUST COME DOWN?
Remember this shopping list

- Milk
- Sausages
- Peas
- Flour
- Oranges

- Steak
- Cheese
- Apple
- Yoghurt
- Sugar
Hold on... If I've got a suppository in my ear - where the hell is my hearing-aid?
Can Alzheimer’s disease (AD) and other dementias be prevented?
Can AD and other dementias be prevented?

Not yet but ... 
..may be delayed
Can AD be prevented? Not yet but ...
..may be delayed

yourbrainmatters.org.au

- Look after your heart
- Be physically active
- Mentally challenge your brain
- Follow a healthy diet
- Enjoy social activity
Elimination vs Postponement

- **Disease elimination**
  - eg smallpox vaccination
  - best prospect is AD vaccine

- **Disease postponement**: delay AD onset by…
  - 2 years, ↓ prevalence by 20%
  - 5 years, ↓ prevalence by 50%

Brookmeyer et al. (1998)
Dosage effect

As CVD risk factors accumulate, AD dementia risk increases

If we count risk factors...

- Hypertension
- Smoking
- Hypercholesterolemia
- Obesity
- Diabetes
- Physical inactivity

Luchsinger et al 2005

Slide adapted from Michael Valenzuela
How much exercise do you do?

<table>
<thead>
<tr>
<th>Each week</th>
<th>Each day</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Less than 1 hour</td>
<td></td>
</tr>
<tr>
<td>• 1 hour</td>
<td>about 8.5 minutes</td>
</tr>
<tr>
<td>• 2 hours</td>
<td>17 minutes</td>
</tr>
<tr>
<td>• 3 hours</td>
<td>26 minutes</td>
</tr>
<tr>
<td>• 4 hours</td>
<td>34 minutes</td>
</tr>
<tr>
<td>• 5 hours</td>
<td>43 minutes</td>
</tr>
<tr>
<td>• 6 or more hours</td>
<td>approaching 1 hr</td>
</tr>
</tbody>
</table>
Exercise addresses risk factors for cognitive decline and dementia.
Physical activity = protective

• Several studies show physical activity protective against cognitive decline, dementia, Alzheimer’s, vascular dementia
• More is better – puffed, weights
• > 3x per week; >150 min/wk, e.g. Perth Study
• Check with your doctor

Can aerobic exercise protect against dementia?

- Preserve cognition and slow cognitive decline
- Decreased incident dementia
- 8/11 RCTs in healthy older persons: cognitive & fitness improved
  - especially cognitive speed and attention
- Biomarkers ↑ e.g. brain volume
- Animal studies – growth factors ↑, BDNF ↑, neurogenesis ↑, inflammation ↓, AD path. ↓

Graff-Radford NR, Alzheimer’s Research and Therapy 2011, 3:6
The power of physical activity

Erickson et al., 2011
Physical activity benefits

- Improved fitness
- Improved physical health - ↓ heart disease, Hi BP, diabetes, some types of cancer, osteoporosis, sarcopenia
- Reduced morbidity & mortality
- Improved mental health
- Improved confidence, quality of life

http://www.mednwh.unimelb.edu.au/research/health_promotion.htm
Physical activity

- Physical activity benefits older adults to prevent dementia: Never too late to start
- Moderate intensity (brisk walking) 30 min 5d/wk
- Evidence for specific exercise not clear; more than one type and more exercise may be better
- Resistance training better in SMART Trial\(^2\)
- Combine with social and mental activity better?

Fiatarone Singh MA et al *JAMDA* 2014;15:873-80
To get back my youth I would do anything in the world, except take exercise, get up early or be respectable.

Oscar Wilde
1854-1900
Physical activity:
Recommendations for older adults
From National Ageing Research Institute

• Think of movement as an opportunity, not an inconvenience
• Be active every day in as many ways as you can
• At least 30 minutes of moderate intensity physical activity on most, preferably all, days
• If you can, also enjoy some regular, vigorous activity for extra health and fitness

http://www.mednwh.unimelb.edu.au/research/health_promotion.htm
What about mental exercise?

- Education
- What mental exercise??
- At what age?
Computer cognitive training

- Lumosity
- Happy Neuron
- Posit Science
- Many others
Mental Activity & Dementia

- Meta-analysis of 22 studies, 29,000 individuals
- ↑ complex mental activity in late life = ↓ risk of dementia by half; OR = 0.54 (0.49-0.59) \(^1\)
- Dose - response relationship evident\(^1\)
- Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence\(^1\)
- Results held when covariates in source studies were controlled for\(^2\)

Cognitive interventions healthy older adults & people with MCI

- 20 RCTs with healthy adults
  - Memory improvements in 17/20
- 6 RCTs with MCI
  - Memory improvements in 4/6
- Unclear whether these improvements generalise to everyday activities

Cognitive training

- Systematic review of RCTs with longitudinal follow-up (> 3mths) in healthy elderly
  - 7 RCTs met inclusion criteria, low quality
  - Strong effect size for cognitive exercise intervention vs wait-and-see controls
  - Longer follow-up (>2yrs) → effect no lower

- Review of cog. training or rehab in dementia
  - 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)
Eating for brain health

Mediterranean Diet Pyramid

Red meat - a few times per month in very small amounts
A few times per week
Daily

Olive Oil

Vegetables

Beans, Legumes, Nuts

Fruits

Bread, pasta, rice, couscous, polenta, bulgar, other grains, and potatoes

* Adapted from Consumer Reports, Nov94
What is Mediterranean diet?

- Abundant plant foods
- Fresh fruit as typical daily dessert
- Olive oil as principal source of fat
- Dairy products (cheese and yogurt)
- Fish and poultry - low to moderate
- 0-4 eggs week
- Red meat - low amounts
- Wine - low to moderate amounts
- Total fat = 25% to 35% of calories
- Saturated fat ≤ 8% of calories
Socialising
Social ties linked to cognitive health

- Marital status
- Frequency of contact with family, neighbours
- Volunteering
- 6 yr Harvard study: the least socially integrated memory declined 2x more than the most
- At any age, 35-85, people with more social contacts did better on tests of memory and executive function
Drugs to preserve memory
Do elixirs of youth exist?
# Patriarchs

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Name</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoch</td>
<td>365 yrs</td>
<td>Seth</td>
<td>912 yrs</td>
</tr>
<tr>
<td>Lamech</td>
<td>777 yrs</td>
<td>Adam</td>
<td>930 yrs</td>
</tr>
<tr>
<td>Mahalalel</td>
<td>895 yrs</td>
<td>Noah</td>
<td>950 yrs</td>
</tr>
<tr>
<td>Enosh</td>
<td>905 yrs</td>
<td>Jared</td>
<td>962 yrs</td>
</tr>
<tr>
<td>Kenan</td>
<td>910 yrs</td>
<td>Methuselah</td>
<td>969 yrs</td>
</tr>
</tbody>
</table>

10 oldest people on record (according to modern standards) have an age range from 115 to 122 years.

Jeanne Calment
1875-1997
Ancient Greek myth

— Sorceress Medea injected King Aeson with a mixture of ram’s blood, snake’s skin, roots, herbs & other ingredients which gave him energy and youthful vitality
Quest for eternal life

– Pope Innocent VIII (1432-1492)
– Requested injection of blood of young men
– He died almost immediately
Quest for eternal life

19th century Dr. Charles Edouard Brown-Sequard claimed old men could be made young by the injections of mashed up dog testicles.
Quest for eternal life

20th century John Romulus Brinkley advocated transplanting goat testicles into men

Goat testicles at Beijing market
Health & Tonics, Elixirs and Potions for the Look and Feel of Youth

by Carlson Wade

Foreword by Amil J. Johnson, M.D.

Here are scores of easy-to-make, easy-to-use tonics, potions and elixirs which may help you look and feel years younger than your actual age!

GURU SHOTS

High Vibration Life Elixirs.
Eternal life?

• “What do the ancient purveyors of physical immortality all have in common?
• They are all dead.”
Natural therapies

• Ginkgo biloba
• Turmeric, curcumin
• DHA, omega 3
• Fo-ti root
• Soy isoflavone
• Vitamin E, Selenium
• Folate, B6, B12
• Saffron
• Brahmi
• Huperzine A

Ginkgo leaves

Member of ginger family
A “cure” for ageing?

- Anti-ageing medicine
- Antioxidants, hormones
- Nutrition, Caloric restriction
- Resveratrol
- Exercise
- Telomerase
- Embryonic stem cells
- Replacing body parts
- Lifestyle modification
Environmental factors

- 30% of population attributable risk of AD cases from 7 environmental factors
- If 25% lower prevalence of these risk factors → 3 million fewer AD cases worldwide
- Highest estimated Pop$^u$ Attributable Risk for AD
  - Global: low education (19.1%, 95% CI 12.3–25.6)
  - USA: physical inactivity (21.0%, 95% CI 5.8–36.6)
  - Europe, UK, US similar (20.3%, 95% CI 5.6–35.6)

Barnes & Yaffe, 2011; Norton et al, 2014
How much AD can be attributed to environmental factors?

- 2% diabetes mellitus (type 2)
- 2% midlife obesity*
- 5% midlife hypertension
- 10% depression
- 13% physical inactivity*
- 14% smoking
- 19% cognitive inactivity/education#

Barnes & Yaffe, 2011
Is incidence of dementia/ cognitive impairment declining?
Is number of people with dementia↓?

- **UK: Cohorts 1: c 1990 & 2: c. 2010**
  - Based on 1990 Cohort, estimated dementia prevalence in 2010 was 8.3%
  - Actual prevalence 6.5%
- **Sweden: Cohorts 1: c 1990 & 2: c. 2005**
  - Fewer new cases
- **Denmark: Cohorts 1 born 1905 (assessed at 93y) and 2, born 1915 (assessed at 95 yrs)**
  - 1915 performed better in cognitive measures

Implications of reduced prevalence

• Environmental factors
  – Better education?
  – Better attention to lifestyle factors?
    o Cardiovascular?
    o Diet?
    o Perinatal and early childhood?
SMART Trial

• 65yo+ with mild cognitive impairment
  – Resistance training
  – Computer cognitive training
  – Both
  – Neither

• Best results on cognition were with resistance training

• Too much not as good

Fiatarone-Singh M, Valenzuela M et al JAMDA 2014
FINGER study

• Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)
• First large, long term RCT of multi-domain interventions aimed at improving cognition
• Eligibility: 60-77 yrs, CAIDE dementia risk score ≥6; cognition at or slightly below mean for Finnish norms (eg, ≤ 26 MMSE)

Ngandu et al. The Lancet. 2015;
http://dx.doi.org/10.1016/S0140-6736(15)60461-5
Finger intervention

- Diet
- Cognitive training
- Exercise – PMR and aerobic
- Manage metabolic and vascular risk factors
- Social activities
Mean change in cognition over 2 years

NTB Total Score

- Control
- Intervention

p = 0.03

Executive Function

- Control
- Intervention

p = 0.04

Ngandu et al. The Lancet. 2015;
http://dx.doi.org/10.1016/S0140-6736(15)60461-5
• NHMRC funded Dementia Research Team Grant
• $6.5m over 5 years, team of 20 CIs and AIs
• Patron Ita Buttrose
• 18,000 55-75 yos randomised to information or active intervention – internet based, GP liaison
• Tailored modules according to risk factor profile – Exercise, Diet, Cognitive Training, Depression – Weight, blood pressure, cholesterol
Centre for Healthy Brain Ageing

https://cheba.unsw.edu.au/

Our vision is to achieve, through research, healthier brain ageing and better clinical care of age-related brain diseases
Conclusions

• About 30% of Alzheimer’s is preventable
• Exercise is most important
• Mental stimulation, diet, health (BP, cholesterol, diabetes, obesity)
• No smoking
• Cannot prevent but can delay cognitive decline and dementia
Fauja Singh, at 100 yrs old became the oldest person ever to complete a marathon (18/10/11)