Healthy Cognitive Ageing
Hunter’s Hill (11.04.18)
*Henry Brodaty*
My grandpa started walking five kilometres a day when he was 65

Now he's 97 years old
My grandpa started walking five miles a day when he was 60

Now he's 97 years old

And we have no idea where he is
HOLD ON... IF I'VE GOT A SUPPOSITORY IN MY EAR - WHERE THE HELL IS MY HEARING-AID?
Dementia: quick facts

• Umbrella term, >100 causes
  – Alzheimer’s 50% of dementias
  – Vascular 15-20%
  – Mixed 15-20%
  – Lewy body; Fronto-temporal dementia

• Global: 46.8m worldwide → 136m by 2050

• Australia: 425,000 → 1.1m by 2056

• Costs: Global USD818b; 1.09% GDP
  – Australia AU$14b+ (2/3 direct costs); ≈1% GDP
AD: a progressive CNS disorder with a characteristic pathology

Katzman, 1986
Cummings and Khachaturian, 1996
AMYLOID plaques in the brain of an Alzheimer patient are visible as a black globular mass in this stained image. The plaque is surrounded by a halo of abnormal neurites (axons and dendrites) and degenerating neural cell bodies that appear darker than the normal neurons.
PET amyloid imaging: normal vs AD

• 1 in 3 persons over 60 have amyloid+

• Amyloid+ → ↑ risk clinical progression

• Will all amyloid+ develop AD?

• When??

Hotter colours = more amyloid
Vascular dementia types

- Single strategic stroke
- Multiple small strokes
- Thickening of walls of arterioles
- Haemorrhage
Plumbing

Arteries

Clogged artery

Clot totally blocking channel

Cross Section

Longitudinal Section

Healthy Brain - Positive Ageing

UNSW
Strokes on brain scan
Can we prevent dementia?
Can we prevent Alzheimer’s disease?
Can we prevent any other type of dementia?
Can we prevent dementia?

- The adult brain weighs about 1.3 kg
- Dementia shrinks it to 1/2 its usual size
Elimination vs Postponement

• Disease elimination
  – eg smallpox vaccination
  – best prospect is AD vaccine
• Disease postponement\(^1\): delay AD onset by…
  – 2 years, \(\downarrow\) prevalence by 20%
  – 5 years, \(\downarrow\) prevalence by 50%

\(^1\)Brookmeyer et al. (1998)
When to prevent?

Risk factors

- Genetic risk factors
- SES-related factors

Life habits (eg, smoking)
- Vascular risk factors
- Vascular diseases
- Depression
- Head trauma
- HRT(?)

Occupational exposure

Years: 0, 20, 40, 60, 80

Protective factors

- High education
- Antihypertensive drugs
- Rich social network
- Mental activities
- Physical activities
- Diet: fish, vegetables
- Moderate alcohol
- Antihypertensive drugs, statins, NSAID, HRT(?)
Is early life the most important target?

• 70% of world dementia in developing countries
  – Low foetal birth weight
  – Poor or no education
  – Poor socio-economic environment

• 12.4% West Australia’s Kimberley Aboriginal people have dementia = 5.2x non-indigenous

Smith K et al, Neurology, 2008;71: 1470-1473
• Look after your heart
• Be physically active
• Mentally challenge your brain
• Follow a healthy diet
• Enjoy social activity

yourbrainmatters.org.au
Blood Pressure (BP) and Dementia

- Mid-life hypertension associated with late-life dementia
- BP ↓ before dementia onset
- Hypertension Rx may → risk ↓
- Each year of Rx → dementia risk ↓
- 5 RCTs conflicting results
- Can harm if lower BP too much in older old
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
Statins to prevent AD

Mixed evidence
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 up e.g. brain volume
- Animal studies – growth factors up, BDNF up, neurogenesis up, inflammation down, AD path. down

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

Erickson et al., 2011
Cognitive training

- Sudoku, crossword puzzles, reading, bridge??
- New language, musical instrument?
- Computer cognitive training
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 Randomised Controlled Trials with follow-up (more than 3mths) in healthy elderly¹
  – 7 RCTs met inclusion criteria, low quality
  – Strong effect size for cognitive exercise intervention versus wait-and-see controls
  – Longer follow-up effect remained
• Review of cog. training or rehabn in dementia²
  – 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)
Bahar-Fuchs, Clare, Woods – Cochrane Database Syst Rev. 2013 Jun
Mind your diet

- Mediterranean diet
- Antioxidants
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
Mediterranean Diet

Daily Physical Activity

Drink water

Monthly

Wine in moderation

Weekly

MEAT

Monthly

SWEETS

Weekly

EGGS

Daily

POULTRY

Daily

FISH & SEAFOOD

Daily

CHEESE & YOGURT

Daily

OLIVE OIL

Daily

FRUITS

Daily

LEGUMES & NUTS

Daily

VEGETABLES

Daily

WHOLEGRAIN BREAD, PASTA, RICE, COUSCOUS, POLENTA, QUINOA, OTHER GRAINS & POTATOES

Daily

Daily
Nutrition / Supplements

- Alcohol ? moderate
- Fish/Seafood/ω3 ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C x

Food sources better than supplements
B Vits and homocysteine

- **OPTIMA**: Folic acid 0.8mg + Vit B12 0.5mg + B6 20mg $^{1,2}$
  - Reduce brain atrophy and improve cognition
  - Principally in people with high homocysteine
- Two systematic reviews and one trial did not find homocysteine lowering treatments beneficial $^{3,4,5}$

2. Douaud et al. PNAS 2013;110:9523-9528
5. van der Zwaluw 2yr RCT,B vits in 2919 Ps w HCy↑ Neurology;2014:83:1–9
Okinawa: Reasons for Longevity

- A lean diet with fewer calories:
  - Vegetables
  - Tofu
  - Miso soup
  - A little fish or meat
- Confucian-inspired adage:
  - "hara hachi bu" = until your stomach is 80% full
Power 9 Principles of the Blue Zones

1. Moderate, regular physical activity
2. Life purpose
3. Stress reduction
4. Moderate calories intake
5. Plant-based diet
6. Moderate alcohol, esp wine
7. Engage in family life
8. Engage spiritually/religion
9. Engage in social life
Nutrition / Supplements

- Fish $\sqrt{\omega 3}$ ?
- Vitamin D ?
- Caffeine ?
- Vitamin E ?
- Vitamin C $\times$

*Food sources better than supplements*
Vit D, NSAIDs, fish, curcumin

- Vit D – low levels of Vit D are common and associated with development of dementia
  - No evidence that taking Vit D lowers risk
- Anti-inflammatories – mixed epidemi. evidence
- Fish oil – some evidence, natural source ie fish (epidemiological)
- Curcumin – some evidence (laboratory)
Smoking and AD

- Current smoking
  - Increase risk for AD
- Previous smoking
  - Risk not significantly increased

Anstey K. Am J Epidem 2008
Alcohol

- Some evidence benefit with moderate alcohol
  - i.e. abstinent → higher risk, j-shaped curve
- Not all studies confirm
- Heavy alcohol is risk factor
- Which alcohol – (red) wine?
  - Evidence not strong
- What is moderate?
Natural therapies

- Ginkgo biloba
- Turmeric, circumin
- DHA, omega 3
- Fo-ti root
- Soy isoflavone
- Vitamin E, Selenium
- Folate, B6, B12
- Saffron
- Brahmi
- Huperzine A
Unproven but popular

- Ketogenic diet
- Grain Brain
- Coconut oil
- Many others??

Promising?

- Resveratrol
- Next generation anti-ageing compounds
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
• Prevention trial, NHMRC funded, 5 years
  – Internet based, largest trial in world
  – 18,000 Australians 55-75 years old
  – Exercise, cognitive training, diet, blood pressure, cholesterol, glucose, depression
  – Tailored to individual risk factors

www.cheba.unsw.edu.au
HEALTHY AGEING FORUM
10am – 1pm Wed 31 October 2018
The Juniors
558A Anzac Pde
Kingsford
Free to attend and enjoy morning tea
You must book
Phone: 9382 3753
Email: ACPforum@health.nsw.gov.au
Thank you

- Eat half
- Exercise double
- Love without limit

Centre for Healthy Brain Ageing (CHeBA)
www.cheba@unsw.edu.au

Dementia Collaborative Research Centre
www.dementiaresearch.org.au