Exercise and Lifestyle Factors
Can cognitive decline & dementia be prevented?

Henry Brodaty
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, ↓ prevalence by 20%
  – 5 years, ↓ prevalence by 50%

\(^1\)Brookmeyer et al. (1998)
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
Cardiovascular Factors

The human heart
Leonardo Da Vinci
Blood Pressure (BP) and Dementia

- Mid-life hypertension associated with late-life dementia
- BP ↓ before dementia onset
- Hypertension Rx → risk ↓
- 5 RCTs conflicting results
- Can harm if lower BP too much in old old
As CVD risk factors accumulate, AD dementia risk increases

- If we count risk factors…
  - Hypertension
  - Smoking
  - Hypercholesterolemia
  - Obesity
  - Diabetes
  - Physical inactivity

Number of risk factors
Statins to prevent AD

Mixed evidence
Not recommended
Physical Exercise

- Does exercise prevent dementia?
- Does exercise improve cognition and brain health?
- How does exercise work?
- What kind of exercise is best?

Slide courtesy of Prof Maria Fiatarone Singh
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/week
- Check with your doctor

Can aerobic exercise protect against dementia?

- 8/11 RCTs in healthy older persons: cognitive & fitness improved
  - especially cognitive speed and attention
- Preserve cognition and slow cognitive ↓
- Decreased incident dementia
- 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
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
The power of physical activity

Erickson et al., 2011
Physical activity

- Physical activity benefits older adults to prevent dementia: *Never too late to start, (never too early)*
- 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
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 evident¹
• Results suggest complex patterns of mental activity in the early, mid- and late-life stages are associated with ↓ dementia incidence¹
• Results held when covariates in source studies were controlled for²

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\(^1\)
  - 7 RCTs met inclusion criteria, low quality
  - Strong effect size for cognitive exercise intervention vs wait-and-see controls
  - Longer FU duration (>2yrs) \(\rightarrow\) ES no lower

- Review of cog. training or rehab in dementia\(^2\)
  - 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)
Supervisory experience at work & low rate of hippocampal atrophy in late life

- 151 cognitively intact persons from Sydney Memory and Ageing Study
- Higher *Lifetime Experiences Questionnaire* scores linked with ↑ grey matter volume in the medial temporal lobe, esp. hippocampus
- Supervisory and managerial experience in midlife was dominant contributor
- Over 2-3 years, those with high level midlife supervisory experience had 5x slower rate of late-life hippocampal atrophy (n 91; p<0.001)
Supervisory experience at work low rate of hippocampal atrophy in late life

- Individual differences in intracranial volume, age, gender, physical activity, depressive symptoms, or ApoE ε4 genetic status could not explain these findings, nor could specific lifestyle patterns in late life.

- Supervisory experience during working life is connected to hippocampal integrity after retirement, some 20-30 years later.

Suo C et al, NeuroImage 2012
Computer-assisted cognitive training (Lampit 2014)

- RCT trial 80 non-demented community-dwelling older adults (mean age ≈72)
- Multiple dementia risk factors
- 65 completed post-training assessment
- 55 followed up one year later
- 36 group-based sessions over 3 months of CCT targeting memory, speed, language, attention, and reasoning tasks, or active control training

Suo C et al, NeuroImage 2012
Computer-assisted cognitive training

- RESULTS: global cognition after 3 weeks (ES = 0.33, P=.04); after 3 months (ES 0.49, P .003) and persisted 3 months after (ES 0.30, P 0.023)
- Significant and durable improvements were noted in memory and processing speed
- Training effects waned gradually but residual gains were noted 12 months post-training.
- No significant effects on ADL

Lampit A 2014
Causality? Reverse causality?

Do leisure, mental or physical activity lower risk of dementia?

Or

Are those with better cognitive function and lower risk of dementia more likely to participate?

Or

Could prodromal dementia (pathology build-up before symptoms apparent) influence activities?
Mind your diet

- Mediterranean diet
- Antioxidants
- B Vits & homocysteine
- Vit D, fish
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
• Interaction with ApoE4 – contradictory results?
• 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
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
Is incidence of dementia/cognitive impairment declining?
Is number of people with dementia down?

- 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

Christensen et al. *The Lancet* 2013. [http://dx.doi.org/10.1016/S0140-6736(13)60777-1](http://dx.doi.org/10.1016/S0140-6736(13)60777-1)
Implications of reduced prevalence

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


Developmental & early life

- Nutrition: Indirect evidence for early life nutrition & development
- Education: Consistently protective, in large number cohort studies & across cultures
- Occupational status: Effects attenuated when controlling for education. ∴ protective effect may not be causal
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)

Finger intervention

- Intervention
  - Diet
  - Cognitive training
  - Exercise – PMR and aerobic
  - Manage metabolic and vascular risk factors
  - Social activities

- Outcomes: ↑ Neuropsychological Test Battery, ↑ Frontal executive function, ↑ Reaction time … not episodic memory
• 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
Thank you

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www.dementiaresearch.org.au

Dementia, Pseudodementia, Pseudodepression Lehar: 5.15pm