What you can do to prevent dementia

Jewish Centre on Ageing  (06.03.18)

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TWO CERTAINTIES OF LIFE

100,000BC - 2017AD

NO NEW TAXES!

HERE LIES
EVERYONE
A THIRD CERTAINTY
Who is worried about their memory?
Who is worried about their memory?
My memory really sucks Mildred, so I changed my password to “incorrect”
That way when I log in with the wrong password, the computer will tell me ...

“Your password is incorrect”

***
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?
Can we prevent dementia?
Can we prevent Alzheimer’s disease?
Can we prevent any other type of dementia?
Non Sequitur by Wiley

Science vs. everything else

Answers

Simple but wrong
Complex but right
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
PLAQUE OF AMYLOID BETA-PROTEIN in the brain of an Alzheimer patient is 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

Hotter colours = more amyloid
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
Strokes on brain scan
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)
WHAT are we aiming to prevent: Dementia, AD, VaD, Mixed dementia?

- With ↑age, mixed dementia > common
- At post mortem, over 80% of older people with dementia have vascular disease

1 MRC CFAS Study (2003)
When to prevent?

Risk factors
- Genetic risk factors
- SES-related factors
  - Life habits (e.g., smoking)
  - Vascular risk factors
  - Vascular diseases
  - Depression
  - Head trauma
  - HRT(?)

Protective factors
- High education
- Antihypertensive drugs
- Rich social network
  - Mental activities
  - Physical activities
- Diet: fish, vegetables
- Moderate alcohol
- Antihypertensive drugs, statins, NSAID, HRT(?)

Years: 0, 20, 40, 60, 80
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
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 ↓
• Each year of Rx → dementia risk ↓
• 60% ↓ risk of all dementia and AD
• 5 RCTs conflicting results
• Can harm if lower BP too much in older old
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
Questions

• 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
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

How older guys stay in shape
Advice for an old guy...

I was working out at the gym when I spotted a sweet young thing walking in...
Advice for an old guy...

I asked the trainer standing next to me, "What machine should I use to impress that lady over there?"
Advice for an old guy...

The trainer looked me over and said; "I would recommend the ATM in the lobby."
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 increased e.g. brain volume
- Animal studies – growth factors increased, BDNF increased, neurogenesis increased, inflammation decreased, AD path decreased

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
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 elderly¹
  – 7 RCTs met inclusion criteria, low quality
  – Strong effect size for cognitive exercise intervention vs wait-and-see controls
  – Longer FU duration (>2yrs) → ES no lower

• Review of cog. training or rehab in dementia²
  – 11 RCTs, no benefit

Valenzuela & Sachdev (2009) Am J Geriatr Psychiatry 17(3)
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
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
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
Centenarian Hotspots Blue Zones

1. Lomo Linda, CALIFORNIA
2. Sardinia, ITALY
3. Okinawa, JAPAN
4. Nicoya, COSTA RICA
5. Ikaria, GREECE
Blue Zone: Okinawa, Japan

- General female life expectancy = 87yrs
- Increase in centenarians:
  - 30 (1975) ↑ 1000 (2016)
- ~35% function independently
- Factors influencing longevity:
  - Diet?
  - Genetics?
  - Physical activity?

Willcox et al. (2016), Mechanisms of Ageing & Development
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 epidem. evidence
- Fish oil – some evidence, natural source ie fish (epidemiological)
- Curcumin – some evidence (laboratory)
HRT for prevention

• Lab studies & epidemiology → protective
• WHIMS – HRT doubles risk of AD/ cog. decline
• Later studies of HRT indicate window of positive effects after menopause (≈ 50 yo)
  – signif. ↓ risk of mortality, heart failure, or myocardial infarction, without increase in risk of cancer, DVT or CVA (Schierbeck LL et al *BMJ* 2012; 345 doi: [http://dx.doi.org/10.1136/bmj.e6409](http://dx.doi.org/10.1136/bmj.e6409))
• Women who had ovaries removed pre-menopause had better cognition if HRT Rx
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
Unproven but popular

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

Promising?

- Resveratrol
- Next generation anti-ageing compounds
REMEMBER THE TWENTY EXTRA YEARS YOU ADDED TO YOUR LIFE THROUGH CLEAN, HEALTHY LIVING? - WELL, THESE ARE THEM.
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 and UK similar  (20.3%, 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?

• Numbers of new cases per 1000 in each age group may be declining
• Evidence from studies done 10-20 years apart from Netherlands, Spain, UK, USA
• But more people growing older is much greater
• Also people with dementia living longer
Implications of reduced prevalence

• Environmental factors
  – Better education?
  – Better attention to lifestyle factors?
    o Cardiovascular?
    o Diet?
    o Perinatal and early childhood?
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
Can AD be prevented? Not yet but … ..may be delayed

yourbrainmatters.org.au

• Look after your heart
• Be physically active
• Mentally challenge your brain
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• Enjoy social activity
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
CHeBA research

• Cohort studies
  – Sydney Memory and Ageing Study
  – Sydney Centenarian Study
  – Older Australian Twin Study
• Neuroimaging, genetics, inflammaging, proteomics, metabolomics
• Interventions
  – SMART trial (Fiatarone Singh)
  – Dance therapy in nursing homes
  – Transcranial Direct Current Stimulation plus computer cognitive training
• 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)
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Dementia Collaborative Research Centre
www.dementiaresearch.org.au