Dementia, diagnosis and treatment recommendations

Susan Kurrle

Geriatrician

Hornsby Ku-ring-gai and Eurobodalla Health Services
Curran Professor in Health Care of Older People,
Faculty of Medicine, University of Sydney

susan.kurrle@sydney.edu.au

COGNITIVE DECLINE PARTNERSHIP CENTRE

Jan 28th 2016

Disclosures

- Susan Kurrle has provided consultation or advice to, or has been involved in drug trials with: Astra-Zeneca, Buck, Forum, Glaxo Smith Kline, Johnson & Johnson, Lilly, Lundbeck, Medivation, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, Servier, Tau Therapeutics, Wyeth

- She is partly funded by NHMRC Partnership Centre Program ID 9100000

Dementia

- “de mens” – without mind

- progressive irreversible syndrome of impaired memory, intellectual function, personality and behaviour, causing significant impairment in function

Types of dementia

- Alzheimer's Disease
- Vascular Dementia
- "Mixed" Dementia (Alzheimer's Disease and Vascular Dementia)
- Dementia with Lewy Bodies
- Frontotemporal Dementia
- Parkinson's Disease with Dementia
- Others – CJD, ARBD

Dementia in Australia

- **2015**: 342,000 people with dementia
- **2050**: 900,000 people with dementia
- approx 1800 new cases per week diagnosed
- at age 65: 1 in 12 people have dementia
- at age 80: 1 in 4 people have dementia
- At age 90: 1 in 2 people have dementia
- approx 25,000 under age 65 with dementia

Is dementia inevitable if we live long enough?

Madame Jeanne Calment

- Took up fencing , aged 85
- Rode bicycle till 100
- Lived alone till 110
- Gave up smoking at 120
- Poured olive oil on food and rubbed onto her skin
- Port wine, 2 cigs/ day, 1kg dark chocolate every week
- Outlived husband, child and grandchildren
- **Died 122 without dementia**

Modifiable risk factors for developing AD

- Up to 1/3 of cases of Alzheimer's disease are related to 7 modifiable risk factors:
  - 4% type II diabetes
  - 7% midlife obesity
  - 7% low cognitive activity
  - 8% midlife hypertension
  - 11% depression
  - 11% smoking
  - 21% physical inactivity
- Combined adjusted risk **31%**

Barnes 2011; Norton 2014

Non-modifiable risk factors for developing AD

- older age: 9% aged over 65 years, 22% aged over 80 years
- Down syndrome (APP)
- family history
- other genetic factors:
  - ApoE4 allele (risk for late onset AD)
  - Mutations – Presenilin 1,2, TREM2 variants

Other possible risk factors for AD

- head injury (chronic traumatic encephalopathy)
- cerebrovascular disease
- ischaemic heart disease
- environmental factors
- excess alcohol intake
- benzodiazepine use
- smaller head size
- low Vit D

Llewelyn 2010; Billioti de Gage 2012; Littlejohns 2014

Prevention: what can we do?

- Exercise
  - Physical
  - mental
- Social interaction
- Diet
- Habits
- Medication and supplements

Prevention: does it work?

- FINGER study (Lancet 2015):

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

- Findings from this study suggest that a multi domain intervention may improve or maintain cognitive functioning in at risk older people

Ngandu 2015

Prevention of dementia: the FINGER study

- 1260 people aged 60 to 77 with a CAIDE score of 6 or more indicating increased risk for developing dementia
- Randomised to control (general health advice) or intervention (nutritional advice, exercise, cognitive training, monitoring of metabolic and vascular risk factors)
- Adherence of between 85% and 100% to the 4 intervention domains
- **At 2 year follow up there was a significant improvement in overall cognition (p=0.030) and also in executive functioning and processing speed**

Risk Score for Predicting Dementia in Later Life

	Risk Score
Age	
<47 years	0
47-53 years	3
>53 years	4
Education	
≥10 years	0
7-9 years	2
0-6 years	3
Sex	
Female	0
Male	1
Systolic Blood Pressure	
≤140 mm Hg	0
>140 mm Hg	2
Body Mass Index	
≤30 kg/m^2	0
>30 kg/m^2	2
Total Cholesterol	
≤6.5 mmol/L	0
>6.5 mmol/L	2
Physical Activity	
Active	0
Inactive	1

Source: Lancet Neurology

Ngandu 2015

Prevention: does it work?

- Evidence from the Rotterdam study (The Netherlands) and the Kungsholmen study (Sweden), and studies in the UK and Denmark all comparing 2 cohorts of older people a decade apart, indicates a stable prevalence of dementia and a decreasing incidence of dementia
- Thought to be due to amelioration of risk factors, and increased education

Schrijvers 2012; Qiu 2013; Christenson 2013

Prevention activity in Australia

- yourbrainmatters.org.au

YOUR BRAIN MATTERS
THE POWER OF PREVENTION

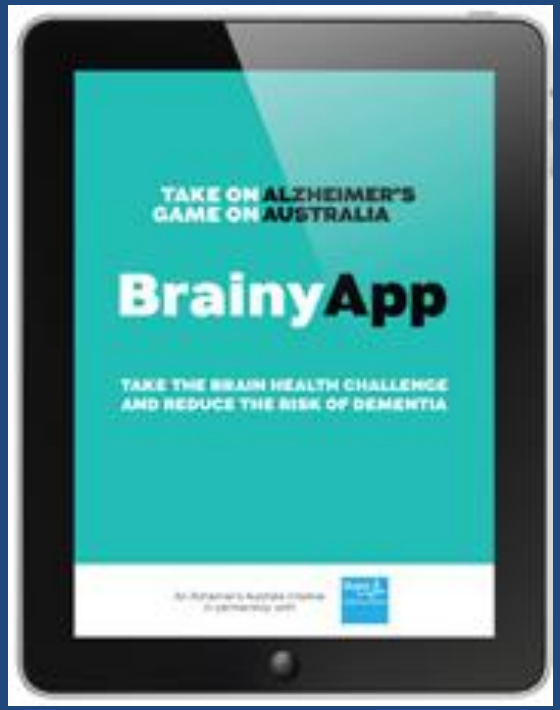
Step One - Look after your heart

Step Two - Be physically active

Step Three - Mentally challenge your brain

Step Four - Follow a healthy diet

Step Five - Enjoy social activity



Prevention

- Physical Exercise
  - Aerobic exercise: at least 30 mins 5X per week, walking, jogging, dancing, swimming, cycling, tennis, golf, walking the dog etc
  - resistance training: weights, therabands
  - balance training: Tai Chi, balance exercises

  - Regular aerobic exercise improves cognitive function, stimulates BDNF, increases brain size, and decreases amyloid in the brain and body

Erickson 2011; Alz Aust 2013

Prevention

- Mental exercise
  - Higher level education
  - Ongoing complex mental activity – new language, musical instrument, chess, computer games
  - Take up a new hobby

ACTIVE 2002

Prevention

- Social activity: increase social interaction
  - Join an activity group – Mens Shed, Stitch & Bitch, U3A
  - Go to concerts, theatres, galleries
  - Become a volunteer
  - (Get married - “living in a couple relationship is one of the most intense forms of social and intellectual stimulation …..”)

Fratiglioni 2000; Hakansson 2009

Prevention

- Habits:
  - Stop smoking
  - Lose weight
  - Moderate alcohol intake

- Diet
  - Mediterranean diet (moderate to good adherence)
  - Curries containing curcumin (turmeric)
  - Concept of “culinotherapy”

Scarmeas 2009: Tsivgoulis 2013

The culinotherapy approach to prevention

- regular fish intake (omega-3 FA)
- regular curries containing curcumin
- alcohol (resveratrols) 2-3 drinks/day
- dark chocolate (resveratrols)
- green tea (polyphenols)
- Mediterranean diet:
    - “avocadoes and olive oil”
    - Fresh fruit and vegetables
    - Legumes, complex carbohydrates, lower red meat intake

Scarmeas 2009: Tsivgoulis 2013; Morris 2015

Prevention

- Hormone replacement therapy
  - Epidemiological and in vitro studies indicate that oestrogen is likely to be protective against Alzheimer's disease
  - WHIMS study showed increased risk of AD (and breast cancer) in older women
  - Later studies indicate HRT from menopause decreases mortality, heart disease (CCF and IHD) with **no** increase in cancer, VTE, stroke
- Nonsteroidal anti inflammatory drugs
- Vitamins and supplements
  - B group vitamins – slow brain atrophy
  - Vit D – deficiency assoc with cognitive impairment

Douaud 2013; Littlejohns 2014; Schierbeck 2012

Drug research

- Cause of AD still unknown
- Most “research breakthrough” headlines relate to mice and rat populations
- Multiple negative trials at Phase 3 levels
- Positive results:
  - Vit E 2000 IU daily slows functional decline in AD
  - Souvenaid – nutraceutical – slight improvement in some cognitive functions in some patients over 1 year
    - Omega-3 fatty acids, selenium, B group vits, choline
    - Yoghurt like drink once daily

Scheltens 2012; Dysken 2014

Drug research in humans

- Most trials targeted at amyloid ("plaques") in established AD have been negative
  - Vaccination
  - Monoclonal antibodies
  - Secretase inhibitors
  - Metal chelators (PBT-2)
- Aducanamab
  - Phase I study in 166 subjects with early AD over 1 year showed reduction in plaques, improved cognitive performance

Drug research in humans

- Trials targeting tau (“tangles”) underway
  - MTX (methylene blue) prevents aggregation of tau within neurones
- Anavex 2-73
  - Blocks tau and amyloid toxicity

COGNITIVE
DECLINE
PARTNERSHIP
CENTRE

CLINICAL PRACTICE GUIDELINES FOR DEMENTIA IN AUSTRALIA

PUBLIC CONSULTATION DRAFT
2015

14 ESSENTIALS FOR GOOD DEMENTIA CARE IN GENERAL PRACTICE

1.	**When patient or family raise concerns about memory/cognition, do not dismiss as "old age"**
2.	**Be alert to cognitive decline in older patients especially those aged 75+ - routinely ask about difficulties**
3.	**Take history regarding cognition and function from informant** a. Clinical history – onset, progression, medications, other illnesses, behavioural & psychological symptoms b. Interview informant, assess carer needs c. Activities of daily living (ADL), instrumental ADLs, mood, driving, safety
4.	**Assess cognition if any indication or suspicion of impairment** a. MMSE^ and Clock Drawing Test, GPCOG* or RUDAS# (for culturally and linguistically diverse groups) b. If uncertain, repeat over time
5.	**Conduct mental state and physical examination** a. Look for specific conditions that mimic dementia (depression, delirium, drugs) or that can aggravate dementia e.g. cardiac failure, use of anti-cholinergic drugs b. Check nutrition, hygiene, visual or hearing impairment
6.	**Investigate for causes of cognitive decline** a. Rule out rare, but reversible causes e.g. abnormal thyroid, calcium or Vit B12; tumour
7.	**Diagnose cause - exclude depression and delirium, diagnose type of dementia** a. Type of dementia – 90% Alzheimer's, vascular or mixed dementia; then Lewy body and frontotemporal dementia
8.	**Refer to specialist if ... unsure of diagnosis; patient is young or atypical; symptoms and signs are atypical; psychotic or severe behavioural disturbance occur; multiple, complex co-morbidities exist; or considering medication**
9.	**Inform patient and family of diagnosis, management plan and prognosis**
10.	**Discuss key issues with patient and family** a. Legal issues – Enduring Power of Attorney, Enduring Guardianship, advance care planning, driving and work - particularly for licensed machinery operators b. Medication for Alzheimer's if appropriate c. Lifestyle – regular exercise, mental stimulation, establish routine d. General health – blood pressure, other health conditions
11.	**Develop care plan (include legal/financial matters) and make follow-up appointments**
12.	**Refer patient and family for further information and support to Alzheimer's Australia (Phone 1800 100 500 National Dementia Help Line) and to community services**
13.	**Manage physical and psychological co-morbidities and maintain optimal health – be alert to delirium**
14.	**Regularly review care plan**

^ Mini Mental State Examination * General Practitioner Assessment of Cognition # Rowland Universal Dementia Assessment Scale

Current treatment recommendations for Alzheimer's disease

- Physical exercise
- Mental exercise
- Vit E
- Symptomatic treatment:
  - Cholinesterase inhibitors – donepezil, rivastigmine, galantamine for mild to moderate Alzheimer's disease
  - Memantine for moderate to moderately severe Alzheimer's disease
  - Risperidone for behavioural and psychological symptoms of dementia for up to 12 weeks
  - Antidepressants for depression eg citalopram, venlafaxine

QUESTIONS?