Dementia research update

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What’s new in epidemiology?
Projections of a tripling of world’s dementia population by 2050

World Alzheimer Report, ADI, 2009
Quadrupling in Australia

Access Economics for Alzheimer’s Australia, 2009

Translating dementia research into practice

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Cost of dementia

Cost of aged care (HACC, community care, RACF)

Number of RACF places

Epidemiology: Rates in Aboriginal people in Kimberley

Dementia prevalence all ages = 12.4%

Environment and AD

• Up to 50% 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

Barnes D & Yaffe K, 2011
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
Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL)

• Prospective longitudinal study of ageing
• Aims: to improve understanding of causes & diagnosis of Alzheimer’s disease & prevention of AD
• Sample: N = 1112, 60+ yo
• Includes patients with AD, MCI and healthy volunteers
Sydney Memory & Ageing Study (MAS)

• Aims: to examine clinical characteristics of MCI
  – ...rate of change in cognitive function over time
• Longitudinal, population based study
  – Non-demented, community dwelling
  – N = 1037, 70-90 yrs, eastern Sydney

Brodaty H, Sachdev P et al.
Older Australian Twins Study

- Longitudinal study on healthy brain ageing in elderly twins
- Aims: what influences memory and thinking as we age
  - Environmental (lifetime physical & mental activity, socioeconomic status)
  - Biological (hypertension, genes)

Sydney Centenarian Study

• Fastest growing age group world wide
  – Models of ‘successful ageing’
• Aims: better understand physical & mental health of this group
  – Which factors contribute to longevity?
• Over 250 people aged 95+ recruited

Sachdev P et al.
What’s new in prevention?
Physical activity = protective

- Several studies show physical activity protective against cognitive decline, dementia, Alzheimer’s, vascular dementia
- More is better – puffed, weights
- At least 3x per week; > 150 mins/wk
- Check with your doctor

Effect of Physical Activity on Cognitive Function in Older Adults at Risk for Alzheimer Disease: A Randomized Trial

Nicola T. Lautenschlager; Kay L. Cox; Leon Flicker; et al.

*N = 138 memory complainers

Lautenschlager et al (2008) JAMA; 300(9):1027-1037
Study of Mental & Regular Training (SMART)

- **Aim:** Does increased mental activity lead to decreased dementia risk?
- **Intervention:** 3 days/wk for 6 months
  - Memory series + stretching/callisthenics
  - Memory series + strength exercise
  - Memory & thinking exercises + stretching/callisthenics
  - Memory & thinking exercises + strength
- **Follow up after 1 year to test for lasting benefits**
The power of physical activity

Erickson et al., 2011
Mind your brain: Accumulating evidence for mental exercise/cognitive training
Mental Activity & Dementia \textsuperscript{1,2}

- Meta-analysis of 22 studies, 29,000 people
- \textit{Lifetime}: Education, occupation, IQ, leisure each reduce risk by about half
- \textit{Late life}: $\uparrow$ complex mental activity $\downarrow$ risk of dementia by half
- Dose - response relationship evident
- Complex patterns of mental activity in early, mid- and late-life associated with $\downarrow$ dementia

Mind your diet

- Mediterranean diet
- Antioxidants
Nutrition / Supplements

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

• Current smoking
  – increase risk for AD
• Previous smoking
  – Risk not significantly increased

Anstey K. Am J Epidem 2008
Mind your health checks

- Blood pressure
- Sugar
- Cholesterol
Metabolic syndrome & dementia risk

- Diabetes/ raised fasting sugar
- Abdominal obesity
- High cholesterol
- High blood pressure

- 23% increased dementia risk for each component of metabolic syndrome

BrainyApp: developed by Alzheimer’s Australia to raise awareness of AD/dementia risk factors
What’s new in cause of Alzheimer’s disease
AD: a progressive CNS disorder with a characteristic pathology

Katzman, 1986
Cummings and Khachaturian, 1996
Amyloid plaque
Proteolytic Processing of APP Gives Rise to Aβ

sAPPβ

sAPPβ

sAPPα

Aβ

AICD

C83

Courtesy of Ron Petersen
Tangles – tau protein
What’s new in diagnosis?
Advances in biomarkers

- Cerebrospinal fluid
  - Amyloid β Protein (Aβ42) ↓
  - Tau Protein (τt and τp) ↑
- MRI scans – serial, fMRI
- SPECT scans + dopamine label
- PET Scans + amyloid ligands

From the - online newspaper of Prof Yasser Metwally
PiB-PET Scans: AD vs MCI vs control

From the online newspaper of Prof Yasser Metwally
New diagnostic criteria

1. Preclinical AD: Earliest signs of disease, before symptoms are noticed
   – Measurable changes in biomarkers

2. MCI due to AD: Mild changes to memory & thinking abilities
   – Measurable but do not affect everyday activities

3. Dementia due to AD: Memory & thinking changes that impact daily life

The GPCOG website: A web-based assessment of cognitive impairment in the primary care setting

www.gpcog.com.au
Welcome to the official website of the GPCOG (The General Practitioner assessment of Cognition). The GPCOG is a screening tool for cognitive impairment. It has been designed for the primary care setting (i.e. general practitioners, primary care physicians, family doctors, etc.). This website is available in different languages. To select your language please use the drop down menu at the top of the start page.

Start Test
Learn more about the test
Read national guidelines for dementia and standard investigations

Disclaimer: Every attempt is made to ensure that all information is correct. However responsibility for investigations and further management remains in the clinician’s responsibility.
GP diagnosis & management

- 4-site NHMRC-funded study
- Newcastle (Dimity Pond
- Sydney, Melbourne, Bendigo
- Can training GPs improve practice?
- Against nurse 1-hour standard GPs miss up to 50% and over diagnose ≤ 20%
Drug Trials
Current medications approved have modest benefits and are symptomatic:

- Aricept (donepezil)
- Exelon (rivastigmine)
- Reminyl (galantamine)
- Ebixa (memantine)

(Others under trial)
Disease modification

- 953 drug trials listed
- 294 trials recruiting participants
  [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (16.08.11)
- All promising at some stage
Cures for AD?

Potential
- $\beta$ & $\gamma$ secretase inhibitors
- Vaccines
  - Active
  - Passive (antibodies)
- Metals
- Stem cells

Failed trials
- Trimiprosate (Alzhemed)
- Flurbiprofen (tarenflurbil)
- Anti-inflammatory
- Rosiglitazone
- Statins
- Leuprolide
- Semagacestat ($\gamma$-secretase inhibitor)
Reducing BPSD & Improving QoL in RACFs
Caring for the Aged Dementia Residents Study - CADRES

- Prospective RCT comparing
  - DCM
  - Person-centred care (PCC)
  - Usual care (UC)
- Primary outcome = Cohen-Mansfield Agitation Inventory
Effects of DCM and PPC on CMAI

Chenoweth et al.
Lancet Neurology
2009
Costs per CMAI point averted...

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<tr>
<th></th>
<th>After intervention</th>
<th>At Follow-up</th>
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<tbody>
<tr>
<td>PCC</td>
<td>$ 8.01</td>
<td>$ 6.43</td>
</tr>
<tr>
<td>DCM</td>
<td>$ 48.95</td>
<td>$ 46.89</td>
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Chenoweth et al. Lancet Neurology 2009
ElderClowns -> Humour therapists
The Sydney Multisite Intervention of LaughterBosses and ElderClowns (SMILE) study

- Primary aim: To evaluate the effects of humour therapy on the mood, quality of life, agitation & behavioural disturbance of residents in aged care facilities
- Assessments:
  - Before intervention (baseline)
  - After 12 week intervention (post) – did it work?
  - At 26 wks (follow-up) – were results sustained?
Results

- No significant differences between groups over time in
  - depression
  - quality of life (self or proxy rated)
  - social engagement
  - neuropsychiatric symptoms

- Significant *decrease* in agitation in humour group compared to controls at post and follow-up
Clinically significant?

- 20% reduction in agitation symptoms in SMILE
- The same effect size as is achieved by antipsychotic medications used to treat agitation
The Three Country Study (3CS)

Prof M Mittelman, New York

Prof A Burns, Manchester

Prof H Brodaty, Sydney

Investigator initiated study
Sponsored by Pfizer International Inc
Results on CG depression

Mittelman, Brodaty, Burns (2008) AJGP
Survival at Home by Country

Cum survival

USA   HR: 0.23 (0.11-0.46)

UK     HR: 0.34 (0.17-0.68)

Australia

Brodaty et al, Am J Ger Psych 2010
PWD still at home in AUS, UK & USA (≤ 5y)

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<tr>
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<th>AUS</th>
<th>UK</th>
<th>USA</th>
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<tr>
<td>At Home</td>
<td></td>
<td></td>
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<tr>
<td>treatment</td>
<td>13 (50%)</td>
<td>12 (44%)</td>
<td>19 (73%)</td>
</tr>
<tr>
<td>control</td>
<td>6 (23%)</td>
<td>14 (58%)</td>
<td>20 (77%)</td>
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χ²: df=1, p=0.044

χ²: df=1, n.s.
Some other studies ‘at’ DCRC

- Younger onset dementia (BD)
- Alcohol dementia (BD, AW)
- Dementia in hospitals (BD, AIHW)
- Aborigines and dementia (TB, RC, BD)
- CALD communities and dementia (LFL)
- Consumer Directed Care (LFL)
- Quality indicators in community care (LFL, MG)

Brian Draper, Lee-Fay Low, Adrienne Withall, Tony Broe, Robert Cumming, Australian Institute of Health and Welfare, Meredith Graham

Translating dementia research into practice

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Research on dementia in Australia

- Broad canvas
- Exciting developments
- Research funding lags behind diabetes, cancer, heart disease
- Alzheimer’s Australia Dementia Research Ltd → >$1m 2011
Thank you

- Took up fencing, aged 85
- Rode bicycle till 100
- Lived alone till 110
- Poured olive oil on food and rubbed onto her skin
- Port wine, 2 cigs/day, 1Kg chocolate every week
- Died 122 without dementia

Jeanne Calment
1875-1997

www.dementiaresearch.org.au

Ritchie. BJP 1997, 171:501