Henry Brodaty

**Depression, Dementia, Pseudodementia, Pseudodepression.**

- Centre for Healthy Brain Ageing
  [www.cheba.unsw.edu.au](http://www.cheba.unsw.edu.au)
- Dementia Centre for Research Collaboration
  [www.dementiaresearch.org.au](http://www.dementiaresearch.org.au)

University of New South Wales (UNSW Australia)
Depression, apathy & cognition

- Depression
- Cognitive impairment
- Apathy
Depression & cognition

Depression

Cognitive impairment
Cognition during episode of depression

- Deficits = core feature at all ages
  - Memory, executive function, processing speed
- More in older people, if depression more severe

Airaksinen E Psycholog Medicine 2010; 34, 83–91
Cognitive deficits persist after recovery from depression

- Related to underlying neurobiological changes (atrophy, DWMH)
- More in elderly, late onset depression

1 Kohler S et al Psychological Medicine 2010;40:591-602
Older person with cognitive impairment and depression

- Is cognitive impairment secondary to depression?
- Is depression secondary to underlying brain pathology such as dementia?
Depression: risk factor for dementia

• Is it prodrome?
  – 30 year build up of AD pathology
• Is it secondary to depression?
  – Depⁿ → cortisol↑ → temporal lobe atrophy
• Is it secondary to treatment of depression?
  – Unlikely
• Mid-life depression associated with (?↑) risk
• Late-life depression associated with ↑↑ risk
25-year follow-up of depression

- 71 depressed in-pats (10 deceased) and 50 surgical controls assessed 25 years later
- No signif. differences between depressed pts and controls on any neuropsychological test
- 10 depressed patients but no controls had dementia at follow-up $P<0.01$
- Dementia predicted by older age at baseline
- Vascular dementia was most common type

Dementia: risk factor for depression

- Dementia associated with depression
  - $\approx 20\text{-}50\%$ people with dementia have dep$^n$
- Not associated with recency of diagnosis
  - Suggesting unlikely to be reaction
- Associated with type of dementia
  - More in subcortical dementia (PDD, VaD)
  - Suggesting likely linked to brain pathology
Risk factors common to both Depression, Dementia, Brain pathology eg CVD
Vascular depression

- CVD predisposes, precipitates or perpetuates depressive syndrome
- MRI: > WMHs esp frontal-subcortical
- Cognitive ↓, psychomotor retardation/slowing, apathy, executive dysfunction
- Poorer response to treatment
- Worse prognosis: depression, dementia, death

Krishnan 1988, 1997; Coffey 1990; Alexopoulos 1997; Hickie 1997
Apo E\(\varepsilon4\) & depression

- Late onset depression 43% vs EO 8% (Krishnan, 1996)
- HAAS - ApoE\(\varepsilon4\) modulates effect of depression on dementia risk in men (Irie F, 2006)
  - Non-depressed w ApoE\(\varepsilon4\) ns
  - Depressed w/out ApoE\(\varepsilon4\), 1.6x risk (0.8-3.0)
  - Depressed men w ApoE\(\varepsilon4\), 7.1x risk (3.0-16.7)
- Cache County – no effect of ApoE\(\varepsilon4\) on LO depression, except those >80 (Steffens DC, 2003)
Depression & dementia

Clinical features overlap

Depression

Cognitive impairment
Symptoms common to both

- Hamilton Depression Rating Scale-21 in dementia
  - total possible score of 64
  - Sleep disturbance, agitation, retardation, loss of interest, loss of weight/ appetite, loss of libido, loss of energy, lack of insight, paranoid delusions, hallucinations → ≤ 34
<table>
<thead>
<tr>
<th>Depression</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset recent, course &gt; rapid</td>
<td>Longer duration, &gt;gradual</td>
</tr>
<tr>
<td>Family always aware</td>
<td>Family often not aware</td>
</tr>
<tr>
<td>PPH, FH of dep &gt;likely to be +ve</td>
<td>FH of dementia may exist</td>
</tr>
<tr>
<td>&gt; cognitive Sx, &gt; specific</td>
<td>Pt. complains less</td>
</tr>
<tr>
<td>Pt highlights failures</td>
<td>Pt. highlights success</td>
</tr>
<tr>
<td>Affect pervasive</td>
<td>Affect labile, shallow</td>
</tr>
<tr>
<td>Behaviour incongruent with cognitive Sx eg social skills ↓</td>
<td>Behaviour compatible with cognitive Sx</td>
</tr>
<tr>
<td>O/E – “don’t know” answers, memory loss, past = recent; memory gaps often</td>
<td>O/E recent memory&lt;&lt;past, memory gaps unusual</td>
</tr>
</tbody>
</table>

Wells CE, Am J Psychiatry, 1979 (n = 10, 33-69yo, 9 in-pts, 1 out-pt)
Depression* (n = 14)
- DMV: worse in morning
- >EMW, > anxiety, > libido↓

Dementia (n = 28)
- DMV: Worse in evening
- > disorientation to time
- > difficulty finding their way
- > impairment with dressing

*Pts in larger research on sleep and ageing, 35/42 in-pts.
Pseudodementia the debate
First episode:

- 78yo man with 1st onset depression resistant to TCA Rx; MMSE 19/30
- Depression treated as inpatient with MAOI
- Recovery from depression; MMSE 30/30
- A case of pseudodementia

One year later, recurrence:

- cognitive impairment, longer time to recover, ECT; cognition did not fully recover
Pseudo-dementia case ctd

Two years later
- Third episode – only partially responsive to ECT, cognitive deficits more pronounced
- MRI reveals multiple DWMH

Three years later
- Dementia, now needs help with ADLs
Pseudodementia

- Wernicke (1934) chronic hysterical state mimicking mental weakness\(^1\)
- Madden (JAMA, 1952): 10% of 300 cases

\(^1\) Snowdon J, Australasian Psychiatry, 2011
Kiloh put term “on the map”¹

- Dementia very closely mimicked by psychiatric condition
- Many patients misdiagnosed with depression which was untreated
- Cures with ECT and antidepressants

¹ Kiloh L, 1961 Acta Psych Scandanavica
Pseudodementia

- Defn: Dx confirmed if cognition recovers when psychiatric condition resolves
- Psychiatric conditions → Pseudodementia¹
  - Depression
  - Schizophrenia, paraphrenia
  - Mania and bipolar ∆
  - Hysteria
  - Malingering, Ganser syndrome

¹Kiloh LG, Acta Psych Scandanavica 1961
Pseudodementia

• Intellectual impairment in patients with primary psychiatric disorder in which the features of intellectual abnormality resemble … those of a neuropathologically induced cognitive deficit.

• This neuropsychological impairment is reversible and there is no apparent primary neuropathological process

Caine ED. Arch Gen Psych 1981; 38:1359-1364
Publications with “pseudodementia” as keyword

PubMed (retrieved on 8 January 2018)
The myth of pseudodementia

- Single case, 85yo ♂
- Lifelong history of unipolar depression
- With Rx his verbal IQ 86 → 99, tho’ deficits
- Stressed importance of treating pts with potential reversible depression even if cognitive impairment
- Used term pseudo-pseudodementia

Pseudo-pseudodementia

- Cognitive deficits do not completely recover
- Persistent executive dysfunction, visuo-spatial and amnestic deficits
- Neurological Sg → > progression to dementia
- Longer follow-up many of pseudodementia pts. → true dementia

Kral 1983; Kral & Emery 1989; Reding 1985; Copeland 1992; Alexopoulos 1993
Depression + ‘reversible dementia’

- Shraberg (1978) ‘Pseudo-pseudodementia’, single case whose deficits continued after Rx
- Alexopoulos (1993) followed up 23 in-pts with depression and criteria for dementia vs 34 with depression and no dementia
  - Age ≈74 ± 6.7; follow-up ≈33 months
  - HRSD on admission 36.6 vs 27.3 **
  - MMSE on admission 18.6 vs 27.3 ***
  - MMSE at discharge 26.4 vs 27.6 (p<0.09)
  - Dementia follow-up 43% vs 12% **; OR 4.69

Alexopoulos GS et al Am J Psychiatry 1993; 150: 1693-9
Kiloh’s pseudodementia patients

• Sachdev (1990) followed up 19/21 Kiloh’s PD pts 2-14 yrs later; two did not meet PD criteria
• Pts 26-63 yo at baseline; 6 Sz, 13 Affective △
• All those alive followed for ≥ 12 yrs.
• 1 pt’s Dx changed to dementia; 1 pt possible dementia
• Conclusion: study validates clinical utility of pseudodementia
Pseudodementia: a term for its time

- 50th Anniversary of Kiloh’s paper
- Written when dementia defined as irreversible. Research since...
- .... cognitive deficits in depression often not fully reversed
- ...depression can herald underlying progressive dementing disorder
- Pseudodementia still useful in fostering discussion of potentially treatable psychiatric symptoms, even in progressive dementia

Snowdon J. Australasian Psychiatry, 2011; 19: 391-7
Lit. review – longitudinal outcome

- 40,277 articles identified
- 22,941 individual articles (duplicates removed)
- 50 eligible articles
- Total number of patients = 237
  - 194 depressive pseudodementia
  - 18 conversion disorder
  - 12 psychosis
  - 10 bipolar disorder
  - 2 personality disorders
  - 1 post-traumatic neurosis

Connors M et al, in preparation
Lit. review – longitudinal outcome$^1$

- Total number of patients = 237
  - 77 (33%) progressed to dementia
  - 63 (27%) remained stable
  - 62 (26%) improved
  - 28 (12%) died
  - 7 (3%) lost to follow up

Connors M et al, in preparation
### Follow-up studies of pts with depressive pseudodementia

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age at baseline Mean (SD)</th>
<th>Follow-Up (yrs)</th>
<th>Proportion with frank dementia at follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsiouris et al. (1997)</td>
<td>4</td>
<td>44.0 (4.2)</td>
<td>0.5-3</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sachdev et al. (1990)</td>
<td>8</td>
<td>57.8 (6.1)</td>
<td>7.9</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Reynolds III et al. (1987)</td>
<td>8</td>
<td>71.8 (7.7)</td>
<td>0.2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pearlson et al. (1989)</td>
<td>15</td>
<td>71.9 (1.5)</td>
<td>2.0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Rapinesi et al. (2013)</td>
<td>20</td>
<td>72.7 (5.3)</td>
<td>0.2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Alexopoulos et al. (1993)</td>
<td>23</td>
<td>73.7 (6.8)</td>
<td>2.7</td>
<td>10 (44%)</td>
</tr>
<tr>
<td>Bulbena &amp; Berrios (1986)</td>
<td>10</td>
<td>75.4 (6.9)</td>
<td>1.3-3.9</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>McNeil (1999)</td>
<td>13</td>
<td>76.2 (7.1)</td>
<td>3.0</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Kral &amp; Emery (1989)</td>
<td>44</td>
<td>76.5 (N/R)</td>
<td>4.0-18.0</td>
<td>39 (89%)</td>
</tr>
<tr>
<td>Sáez-Fonseca et al. (2007)</td>
<td>21</td>
<td>77.6 (N/R)</td>
<td>5.0-7.0</td>
<td>15 (71%)</td>
</tr>
<tr>
<td>Rabins et al. (1984)</td>
<td>18</td>
<td>N/R</td>
<td>2.0</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Copeland et al. (1992)</td>
<td>4</td>
<td>N/R</td>
<td>3.0</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Wells (1979)</td>
<td>6</td>
<td>N/R</td>
<td>&lt;1.0</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
### Follow-up studies of pts with depressive pseudodementia

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age at baseline Mean (SD)</th>
<th>Follow-Up (yrs)</th>
<th>Proportion with frank dementia at follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsiouris et al. (1997)⁵⁶</td>
<td>4</td>
<td>44.0 (4.2)</td>
<td>0.5-3</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sachdev et al. (1990)⁵²</td>
<td>8</td>
<td>57.8 (6.1)</td>
<td>7.9</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Reynolds III et al. (1987)⁵⁷</td>
<td>8</td>
<td>71.8 (7.7)</td>
<td>0.2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pearlson et al. (1989)⁵⁵</td>
<td>15</td>
<td>71.9 (1.5)</td>
<td>2.0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Rapinesi et al. (2013)³¹</td>
<td>20</td>
<td>72.7 (5.3)</td>
<td>0.2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Alexopoulos et al. (1993)⁵⁰</td>
<td>23</td>
<td>73.7 (6.8)</td>
<td>2.7</td>
<td>10 (44%)</td>
</tr>
<tr>
<td>Bulbena &amp; Berrios (1986)</td>
<td>10</td>
<td>75.4 (6.9)</td>
<td>1.3-3.9</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>McNeil (1999)⁶</td>
<td>13</td>
<td>76.2 (7.1)</td>
<td>3.0</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Kral &amp; Emery (1989)⁵¹</td>
<td>44</td>
<td>76.5 (N/R)</td>
<td>4.0-18.0</td>
<td>39 (89%)</td>
</tr>
<tr>
<td>Sáez-Fonseca et al. (2007)⁵³</td>
<td>21</td>
<td>77.6 (N/R)</td>
<td>5.0-7.0</td>
<td>15 (71%)</td>
</tr>
<tr>
<td>Rabins et al. (1984)⁵⁴</td>
<td>18</td>
<td>N/R</td>
<td>2.0</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Copeland et al. (1992)¹²</td>
<td>4</td>
<td>N/R</td>
<td>3.0</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Wells (1979)¹⁵</td>
<td>6</td>
<td>N/R</td>
<td>&lt;1.0</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
## Longitudinal outcomes: depression

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Sex female</th>
<th>Follow-Up (yrs)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dementia</td>
</tr>
<tr>
<td>Tsiouris et al. (1997)</td>
<td>4</td>
<td>44.0 (4.2)</td>
<td>3 (75%)</td>
<td>0.5-3.0</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sachdev et al. (1990)</td>
<td>8</td>
<td>57.8 (6.1)</td>
<td>7 (88%)</td>
<td>7.9</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Reynolds III et al. (1987)</td>
<td>8</td>
<td>71.8 (7.7)</td>
<td>7 (88%)</td>
<td>0.1</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pearlson et al. (1989)</td>
<td>15</td>
<td>71.9 (1.5)</td>
<td>4 (27%)</td>
<td>2.0</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Rapinesi et al. (2013)</td>
<td>20</td>
<td>72.7 (5.3)</td>
<td>13 (65%)</td>
<td>0.2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Alexopoulous et al. (1993)</td>
<td>23</td>
<td>73.7 (6.8)</td>
<td>N/R</td>
<td>2.7</td>
<td>10 (43%)</td>
</tr>
</tbody>
</table>
## Longitudinal outcomes: depression

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Sex</th>
<th>Follow-Up (yrs)</th>
<th>Dementia</th>
<th>Stable</th>
<th>Outcome</th>
<th>Dead</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulbena &amp; Berrios (1986)</td>
<td>10</td>
<td>75.4 (7.9)</td>
<td>7 (70%)</td>
<td>1.3-3.9</td>
<td>3 (30%)</td>
<td>5 (50%)</td>
<td>0 (0%)</td>
<td>2 (20%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>McNeil (1999)</td>
<td>13</td>
<td>76.2 (7.1)</td>
<td>9 (69%)</td>
<td>3.0</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>7 (54%)</td>
<td>5 (38%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Kral &amp; Emery (1989)</td>
<td>44</td>
<td>76.5 (N/R)</td>
<td>N/R</td>
<td>4.0-18.0</td>
<td>39 (89%)</td>
<td>5 (11%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Sáez-Fonseca et al. (2007)</td>
<td>21</td>
<td>77.6 (N/R)</td>
<td>17 (81%)</td>
<td>5.0-7.0</td>
<td>15 (71%)</td>
<td>6 (29%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Copeland et al. (1992)</td>
<td>4</td>
<td>N/R</td>
<td>N/R</td>
<td>3.0</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Rabins et al. (1984)</td>
<td>18</td>
<td>N/R</td>
<td>N/R</td>
<td>2.0</td>
<td>2 (11%)</td>
<td>0 (0%)</td>
<td>15 (83%)</td>
<td>1 (6%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
## Longitudinal outcomes: depression

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Dementia</th>
<th>Stable</th>
<th>Improved</th>
<th>Dead</th>
<th>Attrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>188</td>
<td>72 (38%)</td>
<td>35 (19%)</td>
<td>54 (29%)</td>
<td>22 (12%)</td>
<td>5 (3%)</td>
</tr>
</tbody>
</table>

48%
Follow-up studies of pts with depressive pseudodementia x age

- 55 pts <73yo: only one (1.8%) → dementia
- 111 pts >73: 67 (60.4%) → dementia
- 28 pts age not reported 4/28 (14.3%) → dementia
Pseudo- vs pseudo-pseudodementia

- Older age
- Poorer memory performance on delayed word list recall
- Imaging - cortical atrophy, ↑ VBR, ↓ pre-frontal cerebral blood flow, DWMH, CVD

Visser 2000
## Longitudinal outcomes: conversion disorder

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Sex female</th>
<th>Follow-Up (yrs)</th>
<th>Dementia</th>
<th>Stable</th>
<th>Improve</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepple (2004)</td>
<td>10</td>
<td>66.6</td>
<td>7 (70%)</td>
<td>13.4</td>
<td>0 (0%)</td>
<td>10 (100%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Liberini et al. (1993)</td>
<td>6</td>
<td>N/R</td>
<td>3 (50%)</td>
<td>2.0</td>
<td>1 (17%)</td>
<td>5 (83%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Overall</td>
<td>16</td>
<td></td>
<td></td>
<td>1.6</td>
<td>1 (6%)</td>
<td>15 (94%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

94% pts stable ≤ 13 yrs follow-up
## Longitudinal outcomes: psychosis

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Dementia</th>
<th>Stable</th>
<th>Improve</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>11</td>
<td>2 (18%)</td>
<td>5 (46%)</td>
<td>0 (0%)</td>
<td>4 (36%)</td>
</tr>
</tbody>
</table>
# Follow-up of pts with non-depressive pseudo-dementia

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnoses</th>
<th>n</th>
<th>Age Mean (SD)</th>
<th>Follow-Up (yrs)</th>
<th>Proportion with dementia at follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sachdev et al. (1990)⁵²</td>
<td>Psychosis, bipolar</td>
<td>11</td>
<td>52·5 (10·6)</td>
<td>11·8 (2·1)</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Hepple (2004)⁷⁴</td>
<td>Conversion disorder</td>
<td>10</td>
<td>66·6 (N/R)</td>
<td>13·4</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bulbena &amp; Berrios (1986)⁶</td>
<td>Psychosis, bipolar, personality disorder*</td>
<td>12</td>
<td>71.6 (12·2)</td>
<td>1·25-3·9</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Liberini et al. (1993)⁷⁵</td>
<td>Conversion disorder</td>
<td>6</td>
<td>N/R</td>
<td>2·0</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Wells (1979)¹⁵</td>
<td>Conversion disorder, psychosis, post-traumatic neurosis</td>
<td>4</td>
<td>N/R</td>
<td>&lt;1·0</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
## Longitudinal outcomes: psychosis

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Sex</th>
<th>Follow-Up (yrs)</th>
<th>Dementia</th>
<th>Stable</th>
<th>Improve</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sachdev et al. (1990)</td>
<td>6</td>
<td>52.3 (13.7)</td>
<td>4 (67%)</td>
<td>11.8</td>
<td>1 (17%)*</td>
<td>5 (83%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bulbena &amp; Berrios (1986)</td>
<td>5</td>
<td>82.2 (7.4)</td>
<td>4 (80%)</td>
<td>1·3-3·9</td>
<td>1 (20%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>Overall</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td>2 (18%)</td>
<td>5 (46%)</td>
<td>0 (0%)</td>
<td>4 (36%)</td>
</tr>
</tbody>
</table>
## Longitudinal outcomes: Bipolar AD

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Sex (female)</th>
<th>Follow-Up (yrs)</th>
<th>Dementia</th>
<th>Stable</th>
<th>Improve</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sachdev et al. (1990)</td>
<td>5</td>
<td>52.6</td>
<td>4 (80%)</td>
<td>11.8</td>
<td>0 (0%)</td>
<td>4 (80%)</td>
<td>0 (0%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Bulbena &amp; Berrios (1986)</td>
<td>5</td>
<td>63.0</td>
<td>4 (80%)</td>
<td>1·3-3·9</td>
<td>2 (40%)</td>
<td>3 (60%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Overall</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td>2 (20%)</td>
<td>7 (70%)</td>
<td>0 (0%)</td>
<td>1 (10%)</td>
</tr>
</tbody>
</table>
Methodological weaknesses

- Small sample sizes
- Lack of blinding in follow-up assessment
- Lack of exclusion of underlying dementia
  - No brain scans
  - Few did neuropsychological assessments
- Lack of basic demographic data (age, sex)
- Fail to specify criteria for pseudodementia
Conclusions 1

- Pseudodementia ≠ diagnosis but is a clinical Px
- Age and past psychiatric history important
- Misdiagnosing a person with pseudodementia as true dementia when underlying condition is treatable is the tragedy that Kiloh highlighted
- Late onset depression and other psychiatric conditions may be harbinger of organic brain
- Dementia & psychiatric disorders may co-exist
Pseudodementia: a term for its time

- ... depression can herald underlying progressive dementing disorder
- Pseudodementia still useful in fostering discussion of potentially treatable psychiatric symptoms, even in progressive dementia

Snowdon J. Australasian Psychiatry, 2011; 19: 391-7
Pseudodepression and apathy?

(Psychiatry ward 1946)
What is apathy?

• A form of executive cognitive dysfunction
• Overlaps with other psychological & behavioural aspects such as mood, personality & cognitive functioning
• An internal state of lack of interest or a state of behavioural inaction
• Synonyms - passivity, abulia, amotivation

What is apathy?

The apathy spectrum includes reduced:

- initiative
- interest
- motivation
- spontaneity
- affection
- energy
- enthusiasm
- emotion
- persistence

+ blunted affect

Apathy components

- Behavioural: ↓ motivation, initiative
- Cognitive: ↓ drive, ↓ interest
- Affect: ↓ emotional responsiveness
I wouldn’t say I’m apathetic.
I just don’t give a hoot
WORLD RECORD ATTEMPT AT APATHY.
Frequency of apathy

- Apathy associated with neurological, psychiatric, medical, drug-induced & socioenvironmental conditions\(^1\)
- Frequency in neurological disease \(\leq 92\%\)\(^2\)
- Dementia & schizophrenia commonest \(^2\)

\(^1\text{Marin Seminars of Clinical Neuropsychiatry 1996;1:304-314}\)
\(^2\text{Pluck & Brown Journal of Neurol Neurosurg Psychiatry 2002;73:636-642}\)
Frequency of apathy

- Highest prevalences of apathy in
  - Progressive supranuclear palsy\(^1\)
  - Fronto-temporal dementia\(^2\)
  - Severe AD\(^3\)
- Apathy following stroke $\sim 25\%$\(^4\)

\(^1\)Litvan et al *J Neurol Neurosur Psychiatry* 1998;65:717-721
\(^2\)Hodges *Neurology* 2001; 56:S6-S10
\(^3\)Mega et al *Neurology* 1996;46:130-135
\(^4\)Brodaty et al *Psychol Med* 2005;35:1707-1716
Apathy & cognition

Cognitive impairment

Apathy
Apathy is the most common behavioural or psychological symptom in dementia
BPSD prevalence (%) Robert S et al, 2005
Frequency of apathy in dementia

• One of the most challenging, prevalent & persistent behavioural symptoms of dementia
• Occurs in up to 70% of those with AD
• A major clinical feature of dementia with subcortical & frontal pathology
  – Dementia with Lewy bodies
  – Huntington’s disease
  – Vascular dementia
  – Binswanger’s disease

1Starkstein et al European Journal of Psychiatry 2006;20:96-106
2Galvin et al Alzheimer Dis Assoc Disord 2010;24:177-181
3Baudic et al Dementia & Geriatric Cognitive Disorders 2006; 21:316-321
4Staekenborg et al J Neurol Neurosurg Psychiatry 2010;81:547-551
5Caplan Neurology 1995;45:626-633
Apathy in MCI

- In 11.1-39.8% of cases\(^1\)
- Intermediate between older normal controls & AD\(^2\)
- Predicts a higher rate of conversion to AD\(^3\)

\(^1\)Lyketsos et al *JAMA* 2002;288:1475-83
\(^2\)Crocco & Lowenstein *Current Psychiatry Reports* 2005;7:32-36
\(^3\)Robert et al *Clin Neurol Neurosurg* 2006;108:733-736
Apathy increases with severity and duration of dementia

Diagnosis

- Lack of standardised diagnostic criteria\(^1\)
- Difficult for family caregivers to identify & quantify \(\Rightarrow\) under-reporting\(^2\)
- Differentiate lack of motivation rather than cognitive impairment \(^3\)

\(^1\) Starkstein et al European J Psychiatry 2006;20:96-106
\(^3\) Marin Am J Psychiatry 1990; 147:22-30
How do we diagnosis apathy?

- History
- Clinical impression
- Apathy rating tools
  - Apathy Evaluation Scale\(^1\)
  - Apathy Index\(^2\)
  - Apathy Inventory\(^3\)
  - Apathy Scale\(^4\)

- Apathy items in behavioural scales
  - NPI\(^5\)
  - Behaviour and Mood disturbance Scale\(^6\)
  - Clifton Assessment Procedures for the Elderly\(^7\)

\(^1\)Marin RS et al Psychiatry Res 1991;38:143-162
\(^2\)Mayo et al Stroke 2009;40:3299-3307
\(^3\)Robert et al IJGP 2002;17:1099-1105
\(^4\)Starkstein et al Euro J Psych 2006;20:96-106
\(^5\)Cummings et al Neurology 1994;44:2308-14
\(^6\)Neville & Byrne Collegian: J Royal College of Nursing, Aust 2001;20:166-172
\(^7\)Pattie Br J Clin Psychol 1981;20:173-178
Depression & apathy & cognition

- Related to but distinct from depression & dysphoria\(^1\)
- Symptoms overlap

\(^1\)Marin et al J Nerv Ment Dis 1994;182:235-39
Depression → apathy?

• Apathy common in depression
• 3 items in GDS:
  – Have you dropped many of your activities or interests?
  – Do you prefer to stay at home, rather than go out and do things?
  – Do you feel full of energy?
Depression → apathy?

• 2 items in Hamilton
  – Loss of interest, lack of activity in work or hobbies
  – Decreased energy
• When depression lifts apathy improves

BUT …

• apathy can occur independently of depression
• Depression can occur without apathy
Depression & apathy & cognition

• Apathy > associated with right frontal subcortical circuits

Depression with left

After stroke as > CVD

– overlap between apathy & depression increases

– overlap between apathy & cognition increases

Withall A, Brodaty H... Sachdev P Int Psychoger, 2011;23:264-273,
Distinct from depression

• Related to but distinct from depression & dysphoria¹
• Symptoms overlap

• Association between apathy & cognitive impairment (esp. executive function) stronger in apathy than depression²

¹Marin et al J Nerv Ment Dis 1994;182:235-239
Apathy vs depression

**Apathy**
- Lack emotion
- Don’t care
- Not suicidal
- Not usually anxious
- Vegetative Sx absent usually except lose interest in food/ sex
- No sadness ‘transmits’
- AD Rx: Poor response

**Depression**
- Sad, tearful
- No point to life
- May be suicidal/ “rather be dead”
- May be anxious
- Vegetative symptoms
  - Sleep, appetite, weight, libido
- Clinician ‘feels’ sadness
- Rx: Moderate response
Symptoms in common

- Lack interest
- Lack initiative
- Lack motivation
- Decreased libido
- Decreased concentration
- Less energy
Secondary apathy

- Quiet delirium
- Medical $\Delta$ - infection
- Medication side effects can initiate, maintain or imitate apathy$^{1,2}$
  - antipsychotics
  - antidepressants
  - neuroleptics

$^1$Colling J Gerontol Nurs 1999;25:27-32
APOE ε4 & apathy

- In pts with probable AD, apathy has been associated with APOE ε4 independent of age, sex, cognitive ability and disease duration (1,2)
- Other cross-sectional studies no association 3-6

2. D’Onofrio G. IJGP 2011;26:1062–70.
Pseudodepression

- Apathy misdiagnosed as depression
- Wife: *My husband is depressed, doctor*
- Dr: “How do you know he is depressed?”
- Wife: “*He just sits all day and does nothing*”
- Dr: “Is he sad, does he cry, does he say life has no meaning?”
- Wife: “*No he does not say anything unless I ask him. He just sits!*”
Pseudodepression

- Apathy often misdiagnosed as depression
- Apathy is common in depression
- Apathy is unresponsive to antidepressants\(^1\)
- Apathy may respond to ChE inhibitors\(^1\)
- Apathy and depression may be comorbid

Depression ↔ Apathy

Frontal – subcortical pathology

\(^1\)Brodaty and Burns
Am J Ger Psychiatry
2012; 20(7):549–564
Pseudo-depression case

- 67 yo man hit by a car → closed head injury
- “Dep<sup>d</sup>” → Multiple antidepressants, group and individual therapy, ECT – no better
- Five years later, referred w Treatment Resistant Depression
- His P/Sx: I’ve lost the need to talk
- CT brain scan normal, MMSE 29/30
- MRI – frontal pathology
- Neuropsych – frontal executive dysfunction
Conclusions

• Overlapping syndromes
• Overlapping symptoms
• Common pathologies
• Underlying brain chemistry, pathology differ
• Treatments/ management strategies differ
• Careful diagnosis is important
Thank you

www.cheba.unsw.edu.au

www.dementiaresearch.org.au

h.brodaty@unsw.edu.au

Thanks to Michael Connors for lit review