Henry Brodaty

UNSW AUSTRALIA

Depression, Dementia, Pseudodementia, Pseudodepression.

Never Stand Still | Medicine

- Centre for Healthy Brain Ageing

www.cheba.unsw.edu.au

- Dementia Centre for Research Collaboration

www.dementiaresearch.org.au

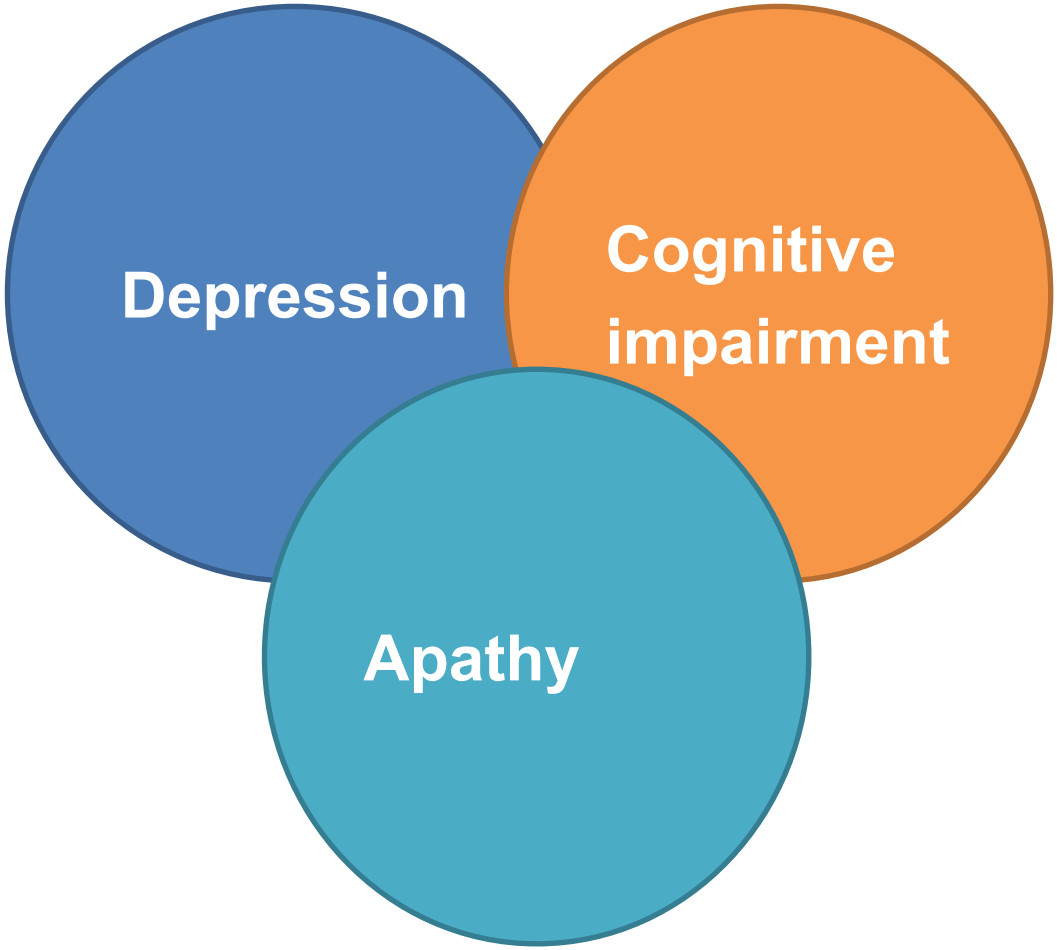
University of New South Wales (UNSW Australia)

DCRC Dementia Collaborative Research Centres

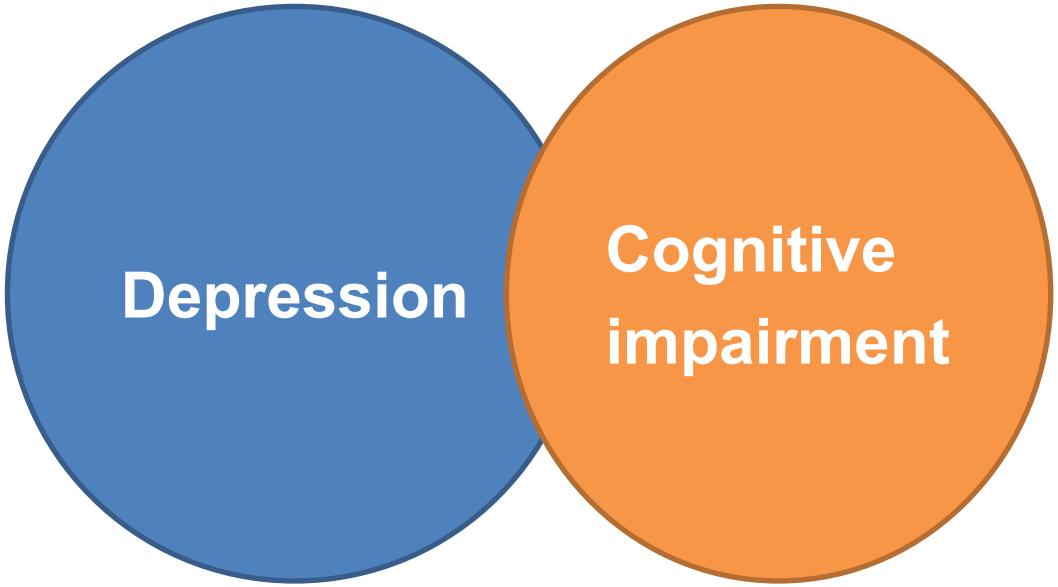
CHeBA Healthy Brains Positive Ageing

UNSW AUSTRALIA

Depression, apathy & cognition



Depression & cognition



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]

[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?
  - Dep^{n} → 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

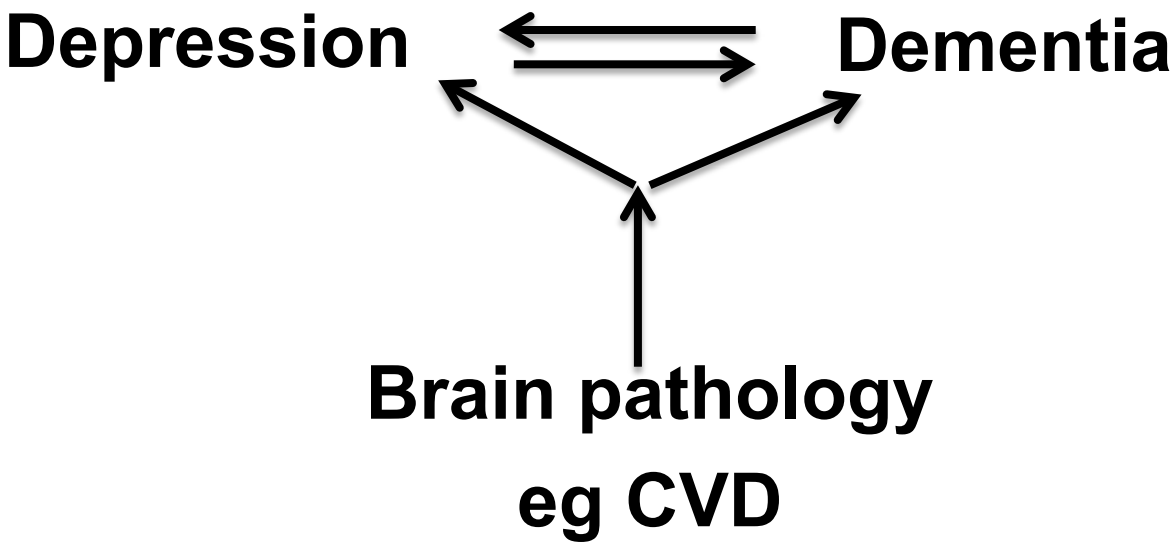
- 71 depressed in-pts (10 deceased) and 50 surgical controls assessed 25 years later
- No signif. differences between depressed pts and controls on any neuropsychological test
- 10 depressed patients but no controls had dementia at follow-up *P*<0·01)
- Dementia predicted by older age at baseline
- Vascular dementia was most common type

Brodaty H et al. *Psychological Medicine* 2003;33(7)1263-1275.

Dementia: risk factor for depression

- Dementia associated with depression
  - ≈ 20-50% 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



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

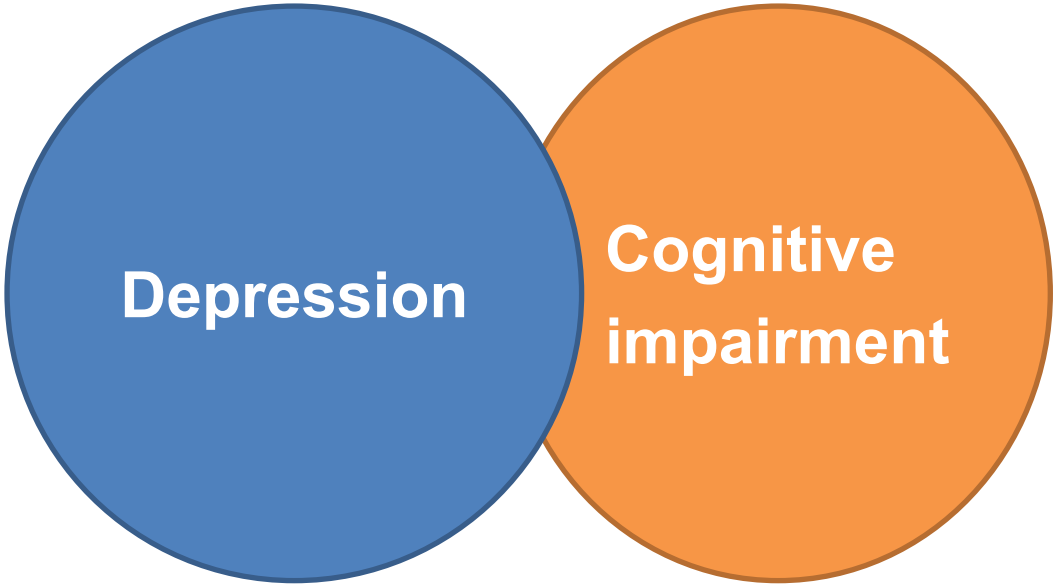
Krishnan 1988, 1997; Coffey 1990; Alexopoulos 1997; Hickie 1997

Apo Eε4 & depression

- Late onset depression 43% vs EO 8% (Krishnan, 1996)
- HAAS - ApoEε4 modulates effect of depression on dementia risk in men (Irie F, 2006)
  - Non-depressed w ApoEε4 ns
  - depressed w/out ApoEε4,1.6x risk (0.8-3.0)
  - depressed men w ApoEε4, 7.1x risk (3.0-16.7)
- Cache County – no effect of ApoEε4 on LO depression, except those >80 (Steffens DC, 2003)

Depression & dementia

Clinical features overlap



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**

Bedside Dx: depⁿ v dementia

Depression

- Onset recent, course > rapid
- Family always aware
- PPH, FH of dep >likely to be +ve
- > cognitive Sx, > specific
- Pt highlights failures
- Affect pervasive
- Behaviour incongruent with cognitive Sx eg social skills ↓
- O/E – "don't know" answers, memory loss, past = recent; memory gaps often

Dementia

- Longer duration, >gradual
- Family often not aware
- FH of dementia may exist
- Pt. complains less
- Pt. highlights success
- Affect labile, shallow
- Behaviour compatible with cognitive Sx
- O/E recent memory<<past, memory gaps unusual

Wells CE, Am J Psychiatry, 1979 (n = 10, 33-69yo, 9 in-pts, 1 out-pt)

Bedside Dx: depⁿ v dementia

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

Reynolds CF et al, Am J Psychiatry 1988; 145:1099-1103

*Pts in larger research on sleep and ageing, 35/42 in-pts.

Pseudodementia the debate

Pseudodementia case

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

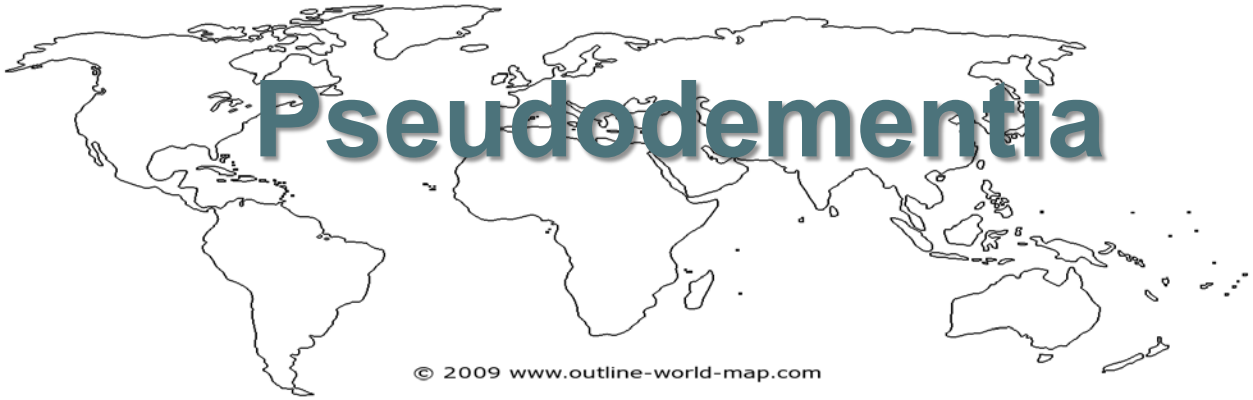
- **Dementia, now needs help with ADLs**

Pseudodementia

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

[1] Snowdon J, Australasian Psychiatry, 2011

Pseudodementia



- 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

- Def^{n}: Dx confirmed if cognition recovers when psychiatric condition resolves
- Psychiatric conditions → Pseudodementia[1]
  - Depression
  - Schizophrenia, paraphrenia
  - Mania and bipolar Δ
  - Hysteria
  - Malingering, Ganser syndrome

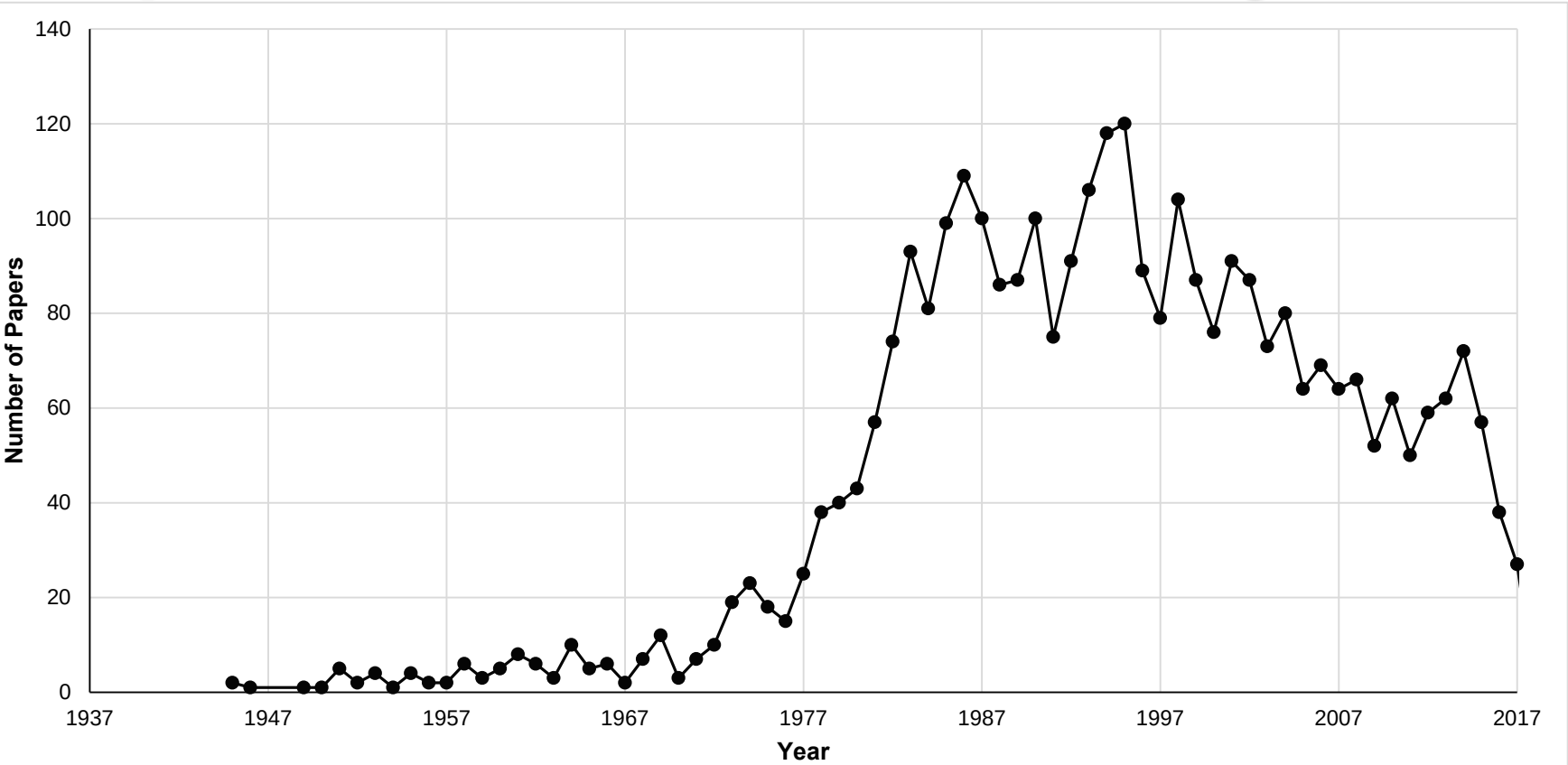
[1]Kiloh LG, Acta Psych Scandanavica 1961

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)
<https://www.ncbi.nlm.nih.gov/pubmed/?term=pseudodementia>

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

Shraberg D, Am J Psychiatry 1978:135:601-2

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*'

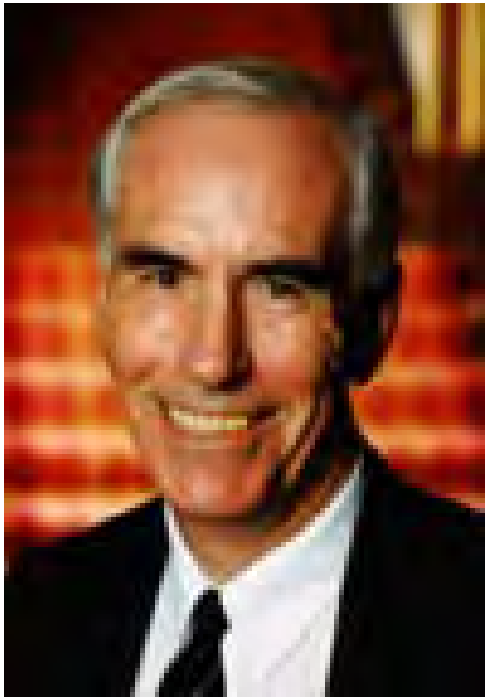
- **Shraberg (1978)** 'Pseudo-pseudodementia', single case whose deficits continued after Rx
- **Alexopoulos (1993)** followed up 23 in-pts with depression and criteria for dementia vs 34 with depression and no dementia
  - Age ≈74 ± 6.7; follow-up ≈33 months
  - HRSD on admission 36.6 vs 27.3 **
  - 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

Shraberg D *Am J Psychiatry* 1978:135:601-2
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 Δ**
- **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



Snowdon J. Australasian Psychiatry, 2011; 19: 391-7

- 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

;

Lit. review – longitudinal outcome[1]

- 40,277 articles identified
- 22941 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

Study	n	Age at baseline Mean (SD)	Follow-Up (yrs)	Proportion with frank dementia at follow up
Tsiouris et al. (1997)[56]	4	44.0 (4.2)	0.5-3	0 (0%)
Sachdev et al. (1990)[52]	8	57.8 (6.1)	7·9	0 (0%)
Reynolds III et al. (1987)[57]	8	71.8 (7.7)	0·2	0 (0%)
Pearlson et al. (1989)[55]	15	71.9 (1.5)	2·0	1 (7%)
Rapinesi et al. (2013)[31]	20	72.7 (5.3)	0·2	0 (0%)
Alexopoulous et al. (1993)[50]	23	73.7 (6.8)	2·7	10 (44%)
Bulbena & Berrios (1986)	10	75.4 (6.9)	1·3-3·9	3 (30%)
McNeil (1999)[6]	13	76.2 (7.1)	3·0	0 (0%)
Kral & Emery (1989)[51]	44	76.5 (N/R)	4·0-18·0	39 (89%)
Sáez-Fonseca et al. (2007)[53]	21	77.6 (N/R)	5·0-7·0	15 (71%)
Rabins et al. (1984)[54]	18	N/R	2·0	2 (11%)
Copeland et al. (1992)[12]	4	N/R	3·0	2 (50%)
Wells (1979)[15]	6	N/R	<1·0	0 (0%)

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Longitudinal outcomes: depression

Study	n	Age	Sex female	Follow-Up (yrs)			Outcome		
					Dementia	Stable	Improve	Dead	Attrition
Tsiouris et al. (1997)	4	44.0 (4.2)	3 (75%)	0.5-3.0	0 (0%)	0 (0%)	4 (100%)	0 (0%)	0 (0%)
Sachdev et al. (1990)	8	57.8 (6.1)	7 (88%)	7.9	0 (0%)	2 (25%)	0 (0%)	6 (75%)	0 (0%)
Reynolds III et al. (1987)	8	71.8 (7.7)	7 (88%)	0.1	0 (0%)	0 (0%)	8 (100%)	0 (0%)	0 (0%)
Pearlson et al. (1989)	15	71.9 (1.5)	4 (27%)	2.0	1 (7%)	10 (67%)	0 (0%)	0 (0%)	4 (27%)
Rapinesi et al. (2013)	20	72.7 (5.3)	13 (65%)	0.2	0 (0%)	0 (0%)	20 (100%)	0 (0%)	0 (0%)
Alexopoulous et al. (1993)	23	73.7 (6.8)	N/R	2.7	10 (43%)	5 (22%)		8 (35%)	0 (0%)

Longitudinal outcomes: depression

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

Longitudinal outcomes: depression

Study	n	Dementia	Stable	Improved	Dead	Attrit^{n}
Overall	188	72 (38%)	35 (19%)	54 (29%)	22 (12%)	5 (3%)

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

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

94% pts stable ≤ 13 yrs follow-up

Longitudinal outcomes: psychosis

Study	n	Dementia	Stable	Improve	Dead
Overall	11	2 (18%)	5 (46%)	0 (0%)	4 (36%)

Follow-up of pts with non-depressive pseudo-dementia

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

Longitudinal outcomes: psychosis

Study	n	Age	Sex female	Follow-Up (yrs)	De-mentia	Stable	Improve	Dead
Sachdev et al. (1990)	6	52.3 (13.7)	4 (67%)	11.8	1 (17%)*	5 (83%)	0 (0%)	0 (0%)
Bulbena & Berrios (1986)	5	82.2 (7.4)	4 (80%)	1·3-3·9	1 (20%)	0 (0%)	0 (0%)	4 (80%)
Overall	11				2 (18%)	5 (46%)	0 (0%)	4 (36%)

Longitudinal outcomes: Bipolar AD

Study	n	Age	Sex (female)	Follow-Up (yrs)	Dementia	Stable	Improve	Dead
Sachdev et al. (1990)	5	52.6 (7.0)	4 (80%)	11.8	0 (0%)	4 (80%)	0 (0%)	1 (20%)
Bulbena & Berrios (1986)	5	63.0 (9.3)	4 (80%)	1·3-3·9	2 (40%)	3 (60%)	0 (0%)	0 (0%)
Overall	10				2 (20%)	7 (70%)	0 (0%)	1 (10%)

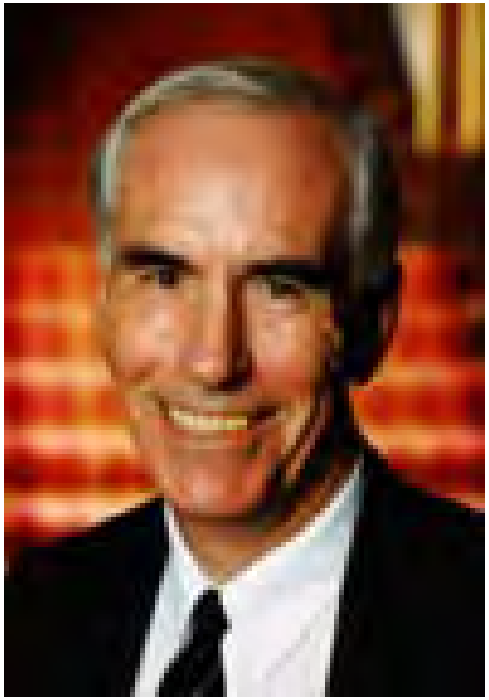
Methodological weaknesses

- 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 Δ
- 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

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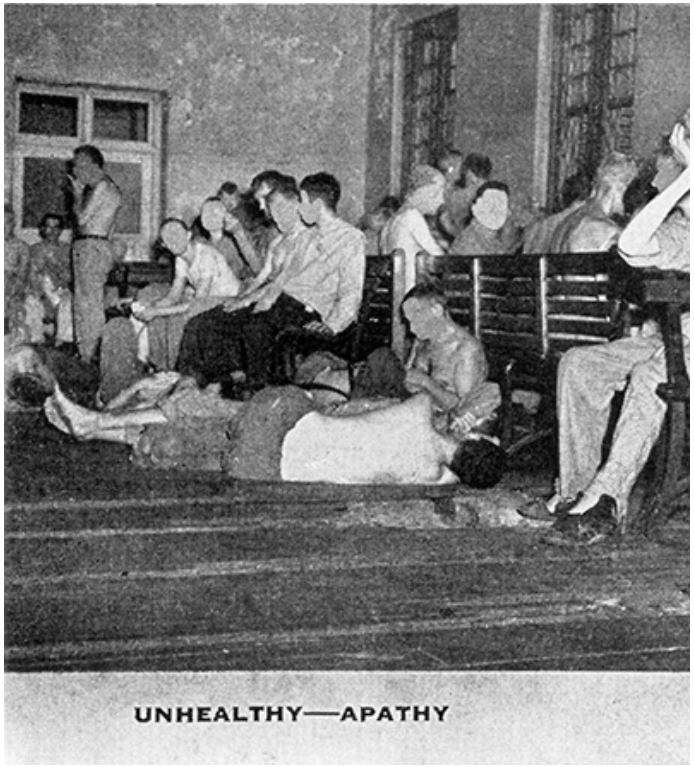
Pseudodepression and apathy?



(Psychiatry ward 1946)

What is apathy?

- A form of executive cognitive dysfunction[1]
- Overlaps with other psychological & behavioural aspects such as mood, personality & cognitive functioning[2]
- An internal state of lack of interest or a state of behavioural inaction[3]
- Synonyms - passivity, abulia, amotivation

[1]Landes et al *JAGS* 2001; 49:1700-07; [2]Pluck & Brown *JNNP* 2002;73:636-642; [3]Burns et al *J Nerv Ment Dis* 1990;178:20-26


LOCAL ELECTIONS
LIB DEM
CON
LAB
APATHY
PUGH

What is apathy?

The apathy spectrum includes reduced:

- initiative
- interest
- motivation
- spontaneity

- affection
- energy
- enthusiasm
- emotion
- persistence

+ blunted affect

Levy et al *J Neuropsychiatry Clin Neurosci* 1998;10:314-9
Overshott et al *Expert Review of Neurotherapeutics* 2004;4:809-821

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 ≤ 92%[2]**
- **Dementia & schizophrenia commonest [2]**

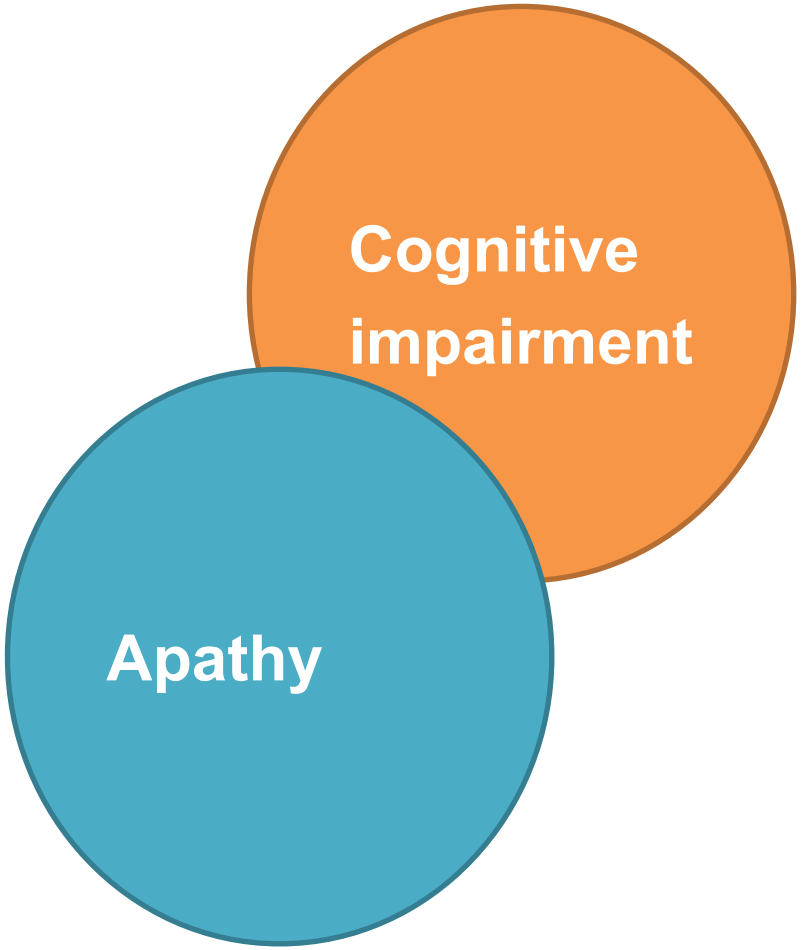
[1]Marin *Seminars of Clinical Neuropsychiatry* 1996;1:304-314
[2]Pluck & Brown *Journal of Neurol Neurosurg Psychiatry* 2002;73:636-642

Frequency of apathy

- Highest prevalences of apathy in
  - Progressive supranuclear palsy[1]
  - Fronto-temporal dementia[2]
  - Severe AD[3]
- Apathy following stroke ~ 25 %[4]

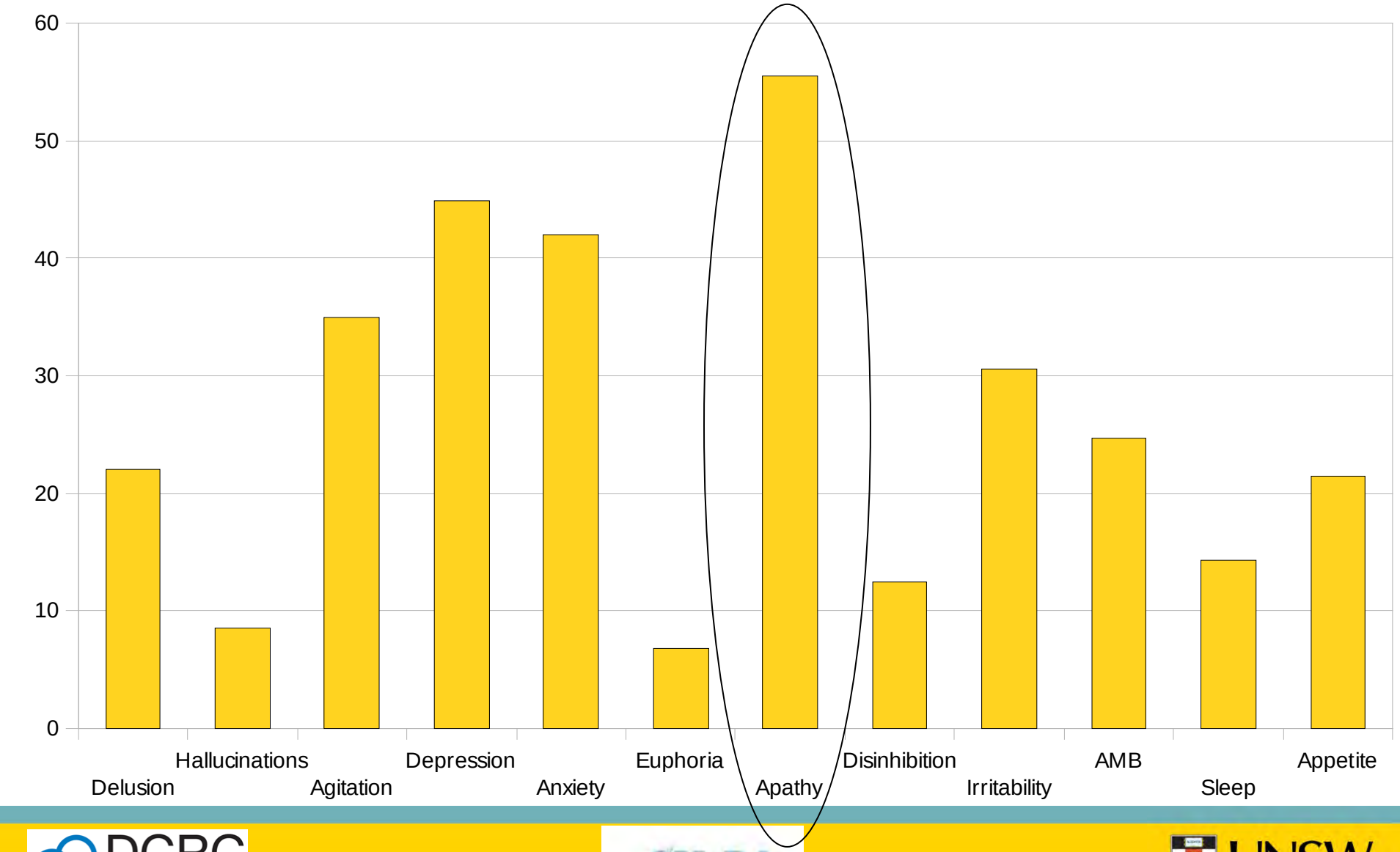
[1]Litvan et al *J Neurol Neurosur Psychiatry* 1998;65:717-721
[2]Hodges *Neurology* 2001; 56:S6-S10
[3]Mega et al *Neurology* 1996;46:130-135
[4]Brodaty et al Psychol Med 2005;35:1707-1716

Apathy & cognition



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[1]
- A major clinical feature of dementia with subcortical & frontal pathology
  - Dementia with Lewy bodies[2]
  - Huntington's disease[3]
  - Vascular dementia[4]
  - Binswanger's disease[5]

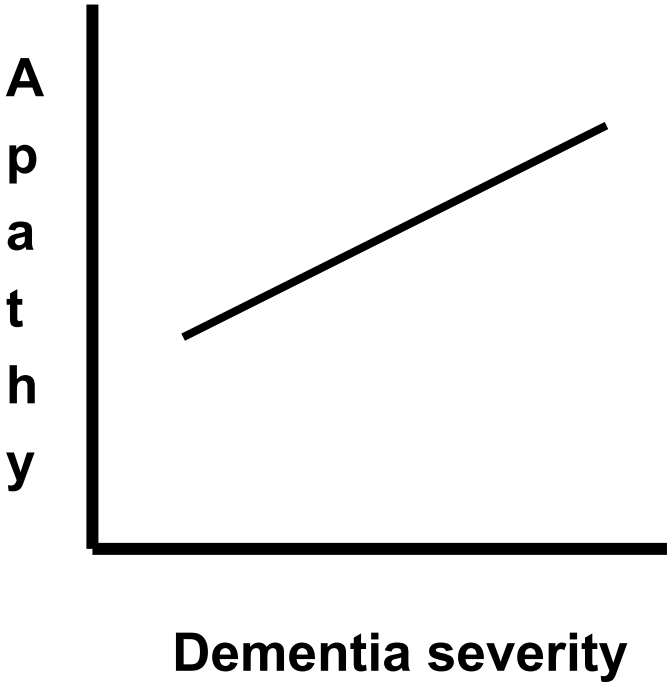
[1]Starkstein et al *European Journal of Psychiatry* 2006;20:96-106
[2]Galvin et al *Alzheimer Dis Assoc Disord* 2010;24:177-181
[3]Baudic et al Dementia & Geriatric Cognitive Disorders 2006; 21:316-321
[4]Staekenborg et al *J Neurol Neurosurg Psychiatry* 2010;81:547-551
[5]Caplan *Neurology* 1995;45:626-633

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 & dementia



Apathy increases with severity and duration of dementia

Wu HZY, et al. *Int Psychogeriatr.* 2009 Jun; 21(3):476-484.

Diagnosis

- Lack of standardised diagnostic criteria[1]
- Difficult for family caregivers to identify & quantify ➔ under-reporting[2]
- Differentiate lack of motivation rather than cognitive impairment [3]

[1]Starkstein et al *European JPsychiatry* 2006;20:96-106
[2]Landes et al *J Am Geriatr Soc* 2001; 49:1700-07
[3]Marin *Am J Psychiatry* 1990; 147:22-30

How do we diagnosis apathy?

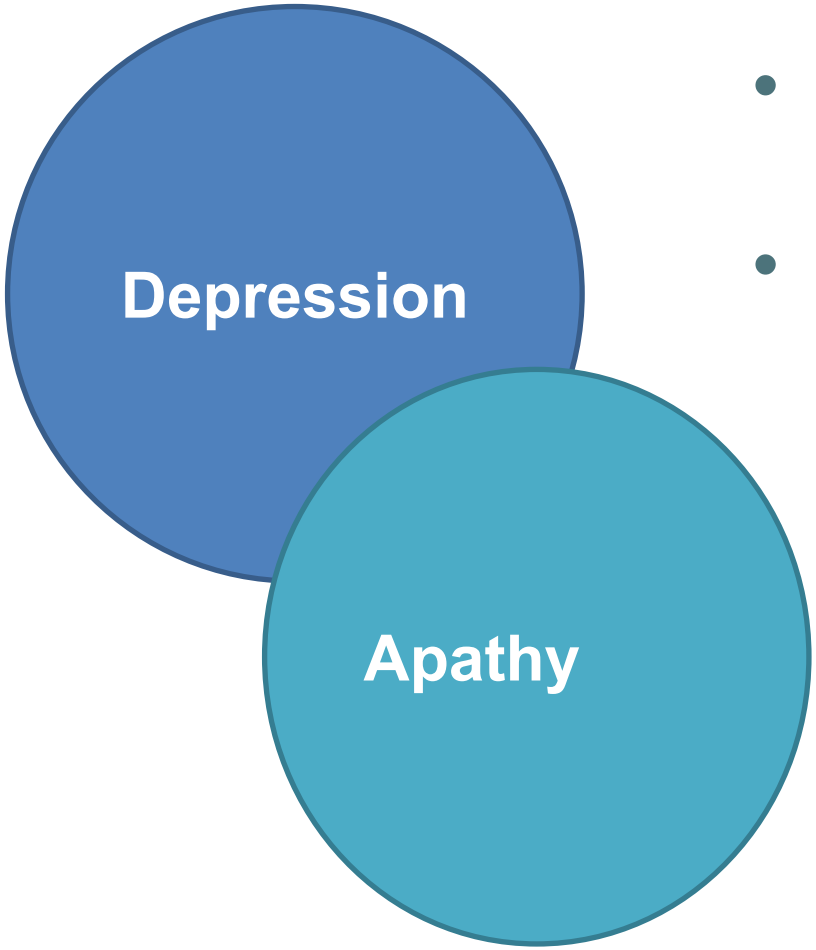
- History
- Clinical impression
- Apathy rating tools
  - Apathy Evaluation Scale[1]
  - Apathy Index[2]
  - Apathy Inventory[3]
  - Apathy Scale[4]

- 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?

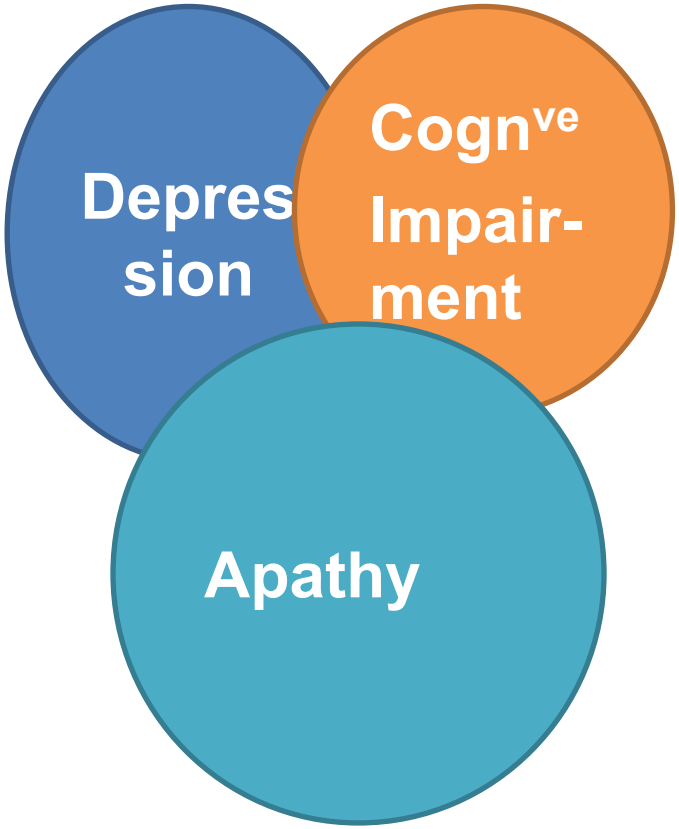
Depression → apathy?

- 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 & dysphoria[1]**
- **Symptoms overlap**

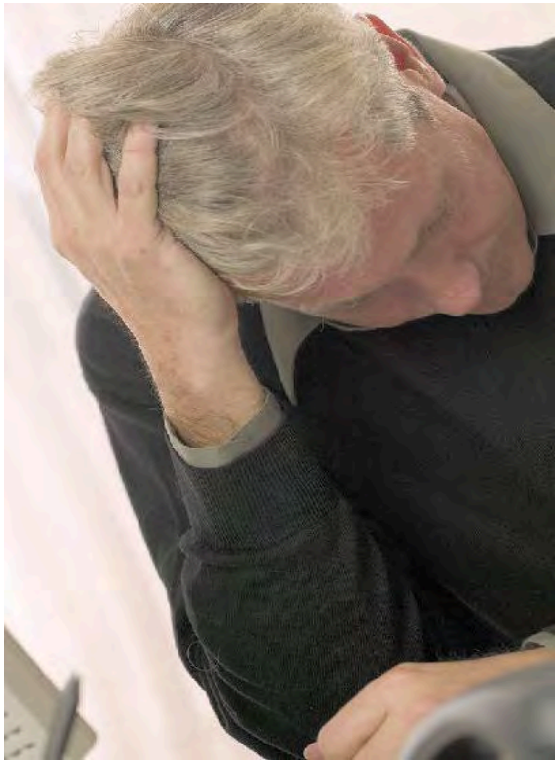
- **Association between apathy & cognitive impairment (esp. executive function) stronger in apathy than depression[2]**

[1]Marin et al *J Nerv Ment Dis* 1994;182:235-239
[2]Brown & Pluck *Trends Neurosci* 2000;23:412-417

Apathy vs depression

Apathy	Depression
• Lack emotion	• Sad, tearful
• Don't care	• No point to life
• Not suicidal	• May be suicidal/ "rather be dead"
• Not usually anxious	• May be anxious
• Vegetative Sx absent usually except lose interest in food/ sex	• Vegetative symptoms – Sleep, appetite, weight, libido
• No sadness 'transmits'	• Clinician 'feels' sadness
• AD Rx: Poor response	• Rx: Moderate response

Symptoms in common



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

Secondary apathy

- **Quiet delirium**
- **Medical Δ - infection**
- **Medication side effects can initiate, maintain or imitate apathy[1,2]**
  - **antipsychotics**
  - **antidepressants**
  - **neuroleptics**

[1]Colling *J Gerontol Nurs* 1999;25:27-32
[2] Barnhart et al *Journal of Psychiatric Practice* 2004;10:196-199

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]**

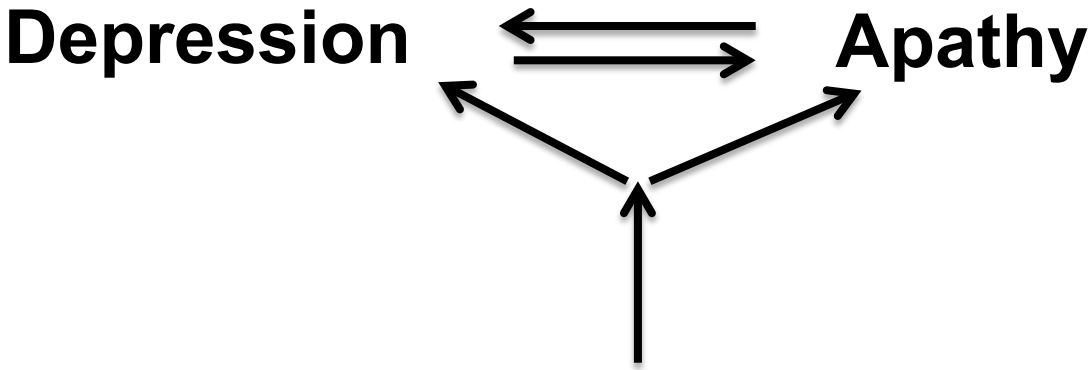
1. Monastero R. Acta Psychiatr Scand. 2006;113:59–63.
2. D'Onofrio G. IJGP 2011;26:1062–70.
3. Del Prete M. Neurol Sci. 2009;30:367–73.
4. Borroni B. Neurobiol Aging. 2006;27:1595–603.
5. van der Flier WM. Dement Geriatr Cogn Disord. 2007;23(1):42–6.
6. Levy ML. Biol Psychiatry. 1999;45(4):422–5.

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

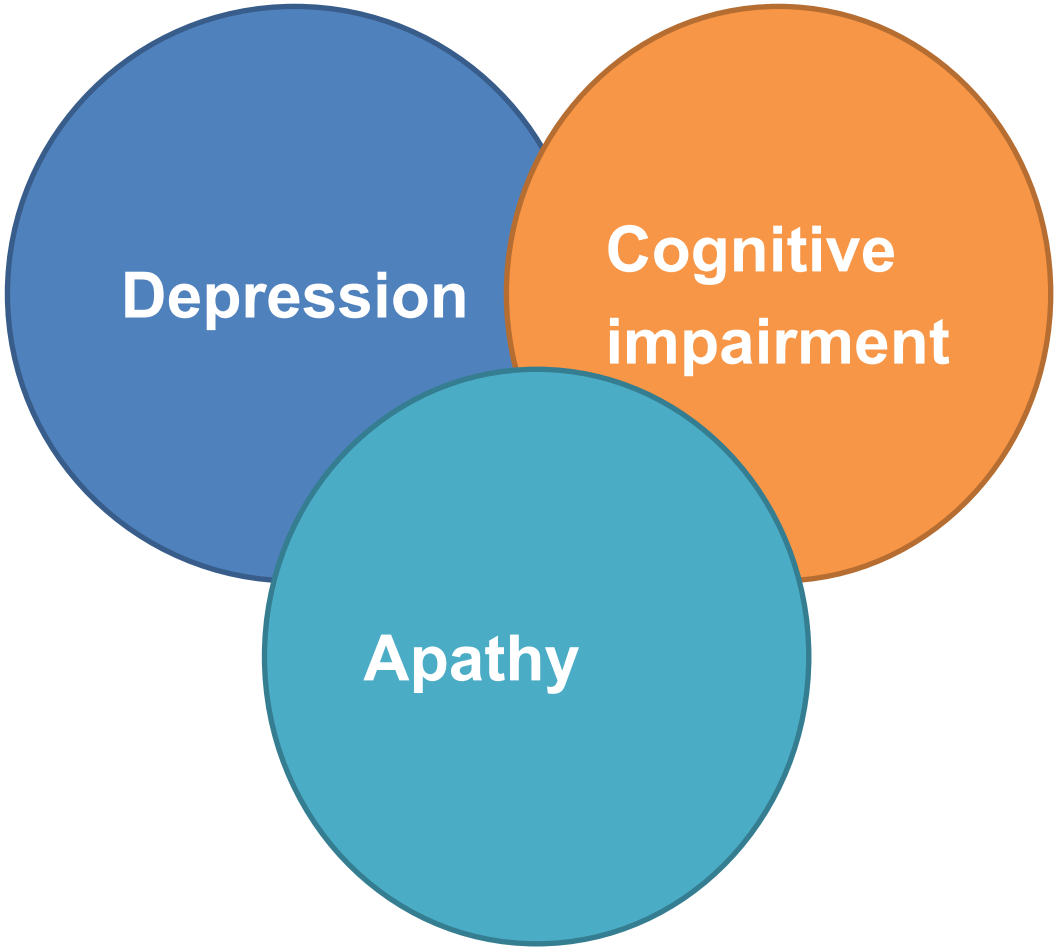


[1]Brodaty and Burns
Am J Ger Psychiatry
2012; 20(7):549–564

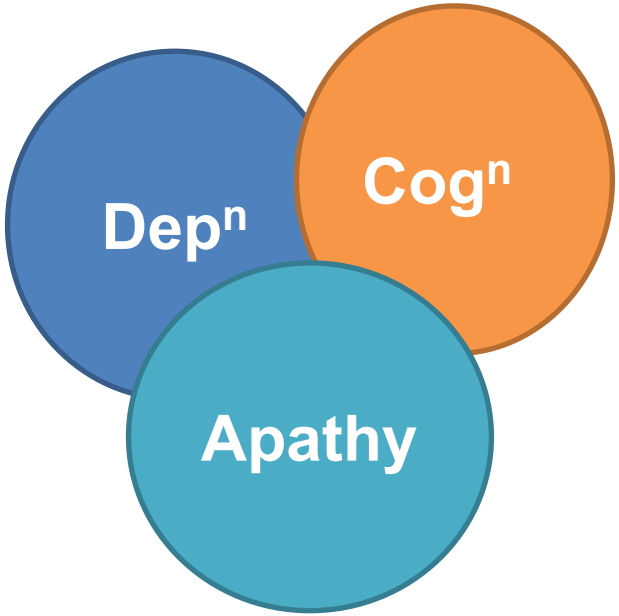
Pseudo-depression case

- 67 yo man hit by a car → closed head injury
- "Dep^{d}" → 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

Depression, apathy & cognition



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

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