14 essentials in the practice & art of diagnosis & management of dementia

Henry Brodaty
Multiple conflicts of interest

- All drug companies interested in dementia
- Advisory Board, investigator, consultant, sponsored speaker
1. Do not dismiss as "old age"

- Prevalence of subjective cognitive complaints (SCC) in older people
  - Review of SCC prevalence, rate of 25-30%¹
  - In Sydney Memory and Ageing Study
    95.5% of participants (70+ yrs) or informants endorsed SCC if asked ²

¹Jonker et al. 2000 *Int J Geriatr Psychiatry*, 15, 983-991
²Slavin et al. (2010). *Am J Geriatr Psychiatry*, 18:8, 701-710
2. Be alert to cognition in older pts

- Especially those aged 75+; routinely ask about difficulties
- Cognitive complaints x-sectionally correlate w.
  - Neurotic personality, depression, anxiety
  - Poor QoL, Poor physical health
- Cognitive complaints longitudinally correlate w.
  - Cognitive decline and dementia

What is dementia?

• An umbrella term to describe a syndrome
• Usually progressive and irreversible
• Over 100 causes

1. Alzheimer’s disease = most common
2. Vascular dementia (multi-infarct dementia; cerebrovascular disease)
3. Lewy body dementia
4. Fronto-temporal dementias
What is dementia - definition

• Decline in at least one cognitive function:
  • Memory
  • Language
  • Executive abilities - planning, abstract thinking, organisation, conceptual shift
  • Visuo-spatial abilities
• Represents a decline
• Impairs daily function: occupational or social
Prevalence of dementia

• > 5% of population ≥ 65 years old
• 20% of persons ≥ 80 years
• 30% of ≥ 90 years old
• In Australia ≅ 330,000 people w dementia
• In 1000 GP practice, ≅ 200>65 → 10+ with dementia & ≅ 24-36 pre-dementia (MCI)
  – Approx. 2 new dementia cases per year
World prevalence of dementia

- Low and middle income countries:
  - 2013: 44 million
  - 2030: 76 million
  - 2050: 136 million

- High income countries:
  - 2013: 44 million
  - 2030: 76 million
  - 2050: 136 million

Dementia in NZ \textsuperscript{1,2}

- 2011 \approx 48,000
- 2050 \approx 147,000
- Maori, Pacific Island, Asian over-represented.
- NZ$955m cost to NZ

\textsuperscript{1} Dementia Economic Impact Report 2011
\textsuperscript{2} Alzheimers NZ 23.08.14
What is Mild Cognitive Impairment?

- Petersen criteria revised \(^1,^2\)
  - Not normal, not dementia
  - Self and/or informant report
  - Impairment on objective cognitive tasks and/or
  - Evidence of decline over time on objective cognitive tasks
  - Preserved basic ADLs and minimal impairment of complex function
  - Generally intact global cognition

\(^1\) Petersen et al, Arch Neurol 1999;56:303–308
Mild Cognitive Impairment (MCI)
Normal > MCI > AD

On all measures, MCI is intermediate between normal controls and AD:

• Neuropsychology
• Neuroimaging
• Neuropsychiatry
• Neuropathology
MCI – why the fuss?

• Prevalence rate 3-25%\(^1\)
• Progression to dementia 2.6% to 15%\(^1\) p.a.
  – Higher than age matched population of 1.8%\(^2\)
• Early diagnosis may identify those who would benefit from earlier treatment

\(^1\)Petersen et al. (2009). *Arch Neurol*, 66(12), 1447-1455.
3. Take history regarding cognition & function from informant

- Clinical history
- Interview informant, assess carer needs
  - See informant separately if possible
- Activities of daily living – dress, wash, toilet, teeth, shave
- Instrumental ADLs – cooking, shopping, meds, finance, transport, telephone, driving, safety
- More complex activities – bridge, languages
4. Assess cognition if any indication or suspicion of impairment

- www.dementia-assessment.com.au
- MMSE *and* Clock Drawing Test
- GPCOG  www.gpcog.com.au
- If uncertain repeat over time
GP diagnosis of dementia

- 74% of people consult a GP first after noticing symptoms of cognitive decline, and …
- 79% consider GPs to be easily accessible¹
- GPs are best placed to identify dementia early
- But, GPs do not diagnose about 50% (< 91%) of mild cases²,³

¹Wilkinson et al (2004); ²Valcour et al *Archives Int Med* 2000;160:2964-8
³Boustani et al *J Ger Int Med* 2005;20:572-7
GP Screening for cognitive impairment

- GPs screen for high blood pressure, cholesterol, diabetes, cancer
- Prevalence of dementia >10% in 75+
- Why not screen for dementia?
  - Because it takes too long, not sure how?
  - Because there is no treatment if diagnosed?
  - Because not sure of next steps?
  - Complicated rules for ChEIs
  - Low Positive Predictive Value (PPV)
Why don’t GPs diagnose dementia?

- Time
- No point
- Nihilism; “Terrible” Dx
- Unsure of skill
- Not sure of next step
- Lack of knowledge about guidelines

Brodaty et al, MJA, 1994; Williams JS, Byrne J, Pond D (2009) Gaps between practice and literature
Why don’t GPs diagnose dementia?

- Poor remuneration
- Patients/families not presenting full picture
- Skill in breaking bad news
- Worry about effect on patient
- Worry about effect on family carer

Brodaty et al, MJA, 1994
GPCOG

Cognition (/9)

- Learn name, address (5 items)
- Date = 1 (exact)
- Clock numbers = 1
- Hands of a clock for 11.10 = 1
- Current event (detail) = 1
- Recall name and address = 5

\[
\begin{align*}
9/9 & \rightarrow \text{OK} \\
<5 & \rightarrow \text{impaired} \\
5-8 & \rightarrow \text{informant interview...}
\end{align*}
\]
GPCOG: 6 informant questions

Compared to 5 years ago

More difficulty:
- Memory
- Word finding
- Recalling conversations

Less able to:
- Manage finances
- Manage transport
- Manage medications

If > 3 ‘Yes’ → impaired
Translating dementia research into practice

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

www.gpcog.com.au
The General Practitioner assessment of COGNition

Downloads:
- Recommended standard investigations
- Printable versions of GPCOG
- Papers about GPCOG

Available languages:
- English, French, German, Greek, Spanish, Italian, Mandarin, Cantonese, Russian, Polish, Thai, Hebrew, Portuguese

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.
...and realises that the 12 is missing
Draw in the hands to show 10 past 11 o’clock or 11.10
Other frontal tasks

- Tapping
  - When I tap once, I want you to tap twice
  - When I tap twice, I want you to tap once
- Explain proverbs – culture bias
- Verbal fluency: FAS, animals
- History – can’t follow movies, lack of anticipation, change in sense of humour, disinhibition, change in personality
- Interview – trouble understanding
5. Conduct mental state and physical examination

• Look for specific conditions that mimic dementia (depression, delirium, drugs) or that can compromise cognition (eg cardiac failure, use of anti-cholinergic drugs)

• Check nutrition, hygiene, vision, hearing
6. Investigate causes of cognitive decline

- Rule out rare, but reversible causes eg. Abnormal thyroid, calcium or Vit B12, tumour
- See guidelines
Investigations: Routine/ minimum

- FBC, ESR or CRP
- Clinical chemistry *including calcium*
- Thyroid function tests
- B12, folate
- CT scan of brain (*without contrast*)
Investigations if indicated

- ECG
- CXR
- EEG
- micro-urine
- Fasting glucose, lipids, HCy
- Serology for HIV, syphilis
- Neuropsychological Ax*
- MRI*
- PET scan* Amyloid scan*
- SPECT (?)*  

* = specialist referral
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
7. Diagnose cause

- Exclude depression and delirium
- Diagnose type of dementia
  - Type of dementia
    - 90% AD, vascular or mixed, then Lewy body and frontotemporal
    - Most older pts. have mixed dementia
    - Outline of clinical features of different dementias
Clinical features: Alzheimer’s disease

- Prototype of dementia
- Insidious onset with gradual decline
- Death usually within 10 yrs (1-20+yrs)
- Some familial clustering
- Four stages: MCI, mild, moderate and severe
Symptom Progression in AD

BADL = basic activities of daily living.
Vascular dementia types

- Single strategic stroke
- Multiple small strokes
- Thickening of walls of arterioles
- Haemorrhage
Plumbing and arteries
VaD clinical features

- Sudden onset, step-wise deterioration, uneven steps, varying plateau
- Vascular risk factors
- Focal neurological symptoms and signs
- Impairment reflects damage deep in brain
- Abnormal brain scans
VaD clinical features

- Many vascular dementias have slow gradual progression
- More slowing of mentation
- Difficulty with retrieval rather than learning
- Evidence of cardiovascular risk factors
- Gait $\Delta$, depression
- MRI scan – DWMH++, lacunes, strokes, hippocampi not especially atrophic
Vascular dementia with preserved hippocampi
Dementia with Lewy Bodies

- 3rd most common dementia
- M > F; usually >65 yo
- Survival shorter than AD, mean 7yrs
Lewy body disease

Cortical Lewy bodies

Synuclein stain

Cortical Lewy bodies in diffuse Lewy body dementia
Dementia with Lewy Bodies

- Progressive cognitive decline that interferes ...
- ... with normal social and occupational function
- Fluctuating cognition (looks like delirium)
- Recurrent visual hallucinations (40-75%)
- Spontaneous features of parkinsonism
- Impaired attention, visuo-spatial, frontal-subcortical abilities
- Memory decline usually evident with time
LBD supportive features

- Repeated falls
- Syncope, transient loss of consciousness
- Neuroleptic sensitivity
- Systematised delusions
- Hallucinations in other modalities
- REM Sleep behaviour disorder
- Depression
Fronto-temporal dementias (Pick syndrome/complex)

- 2-5% of all dementing diseases
- In people aged <65 yrs, as common as AD
- Different presentation and issues
- Two main variants
  - Behavioural
  - Language

Arnold Pick
Fronto-temporal dementias

- Atrophy only frontal and temporal areas (until late disease)
- Often asymmetrical
- Two different protein forms accumulate
  - Tau
  - Progranulin (Ubiquitin, TDP 43)
Fronto-temporal dementias

- Onset usually 50-60y.o. (20-80 y. range)
- Positive Family History in ≈15-30%
- Cases with autosomal dominant inheritance
- Death occurs within 2-15 years (6-12 yrs)
- Rare types
  - MND
  - CBD
  - C-17 mutation → tauopathy → FTD and parkinsonian Sx
Frontotemporal Dementia

FTD

- Behavioural form
- Language form (Primary progressive aphasia)
  - Progressive Nonfluent aphasia (PNFA)
  - Semantic dementia

MND

Slide from John Hodges
Fronto-temporal dementias

• Preservation of memory until late
• Early, prominent personality changes
• Apathy
• Irritability
• Jocularity and euphoria
• Loss of tact and concern
• Impaired judgement and insight
• Word finding difficulties; repetitive
FTD – clinical features

- Compulsive behaviours
  - Repetitive acts, verbal or motor stereotypies
  - Collecting, hoarding
  - Rituals, superstitious acts

- Hyperorality, hypersexuality
8. Refer to specialist if...

- Unsure of diagnosis
- Patient is young or atypical
- Symptoms and signs are atypical
- Psychotic or severe behavioural disturbance
- Multiple, complex comorbidities exist; or
- Considering cholinesterase inhibitor Rx
Drugs for AD

4 drugs approved - all symptomatic:

- **Aricept** (donepezil) - cholinesterase inhibitor
- **Exelon** (rivastigmine) - cholinesterase inhibitor
- **Reminyl** (galantamine) - cholinesterase inhibitor
- **Ebixa** (memantine) - NMDA receptor antagonist

Snowdrop bulb, an original source of reminyl
Benefits of ChEIs

- Period of modest cognitive enhancement
- Symptomatic treatments not cures
- 2 in 3 maintain baseline or improve
- Functional and behavioural benefits
- Mean 38 to 52 weeks before patients cross baseline of cognitive decline

![Diagram showing cognition over time with a peak at 9-12 months.](chart.png)
Contraindications

- Active peptic ulcer
- Bradyarrhythmias eg sick sinus syndrome
- Asthma?
- Previous adverse response
ChE Inhibitors: AEs

- Nausea
- Anorexia
- Vomiting
- Insomnia
- Dizziness
- Muscle cramps
- Nightmares
Brain AChEIs - what differences?

- Acetyl cholinesterase inhibition - all
- Butyryl cholinesterase - rivastigmine
- Nicotinic receptors - galantamine
- Efficacy ? No difference
- Side effects, may be differences
- Duration of action - about same
What dose do you start → titrate to?

**Aricept**
- 5mg → 10mg

**Reminyl**
- 8mg PRC → 16mg PRC

**Exelon**
- Patch 5 → Patch 10

All once per day – after breakfast
9. Inform patient and family of diagnosis, management plan and prognosis

• How to break the news
• Truth telling

• What is your practice?
The art of truth telling in dementia

- Therapeutic privilege – withholding information justified if likely to injure the patient
- Depends on person’s understanding
- Psychiatric symptoms influence decision
Should family always be told?

- Most clinicians do, but…
- Should Drs ask patients for permission to tell family and/or other health professionals?
- Do patients retain equal status?
Fears expressed by families

- **Disclosing a diagnosis of dementia can lead to**
  - Depression; anxiety
  - Stigma
  - “Leprosy syndrome”
  - Giving up; decompensationng
  - Family members acknowledging own vulnerability
  - Risk of suicide
Family conflict and those who refuse to accept diagnosis

- *Fighter or frightened?* Family member refuses to accept diagnosis

- *Families at war:* One side accepts and the other rejects diagnosis

- *Families:*  
  - sibling rivalry (especially if estate or $$)  
  - where will mum live?
Breaking bad news

**Recommended strategies**¹

- prepare patient for possible diagnosis
- include others that pt would like present
- assess patient’s perceptions; correct misinformation²
- *And this requires real clinical skill:*
  - give pt as much info as desired
  - let patient set pace of disclosure

²Mueller P, Postgraduate Medicine 2002 112(3):15-6, 18
Breaking bad news ctd

- Present information clearly
- Be reassuring and empathetic
- Encourage involvement in treatment decisions
- Discuss patients’ questions on the same day
- Beware of overload and strong emotion
- Provide written information/ summary

²Mueller P, Postgraduate Medicine 2002 112(3):15-6, 18
Breaking bad news ctd

- Acknowledge and discuss pt’s feelings
- Provide realistic and honest hope
- Assure patient of doctor’s availability
- Summarise areas discussed
- Offer second appointment shortly after

1Schofield P et al Annals of Oncology 2003; 14:48-56
2Mueller P, Postgraduate Medicine 2002 112(3):15-6, 18
My own practice

- For assessment always see patient and informant separately
- Tell patient and family together but offer to see separately, or....
- Patient first and then family & then together
- Allow time
Breaking the news by degrees

• Memory problems confirmed; test results
  – Age related degeneration
  – Disease that causes this….?
  – Alzheimer’s
• Strategies to compensate, practical issues
• Drug treatments, research
• Arrange follow-up for family and patient
Compassionate honesty is the best policy

- Most people want to know their diagnosis
- Attitudes over time are changing (cf cancer)
- Families often protective
- Formulae do not work
- Need to tailor information to person
- Follow-up visits/ contacts
10. Discuss key issues with patient and family

- Legal issues
- Medication for AD if appropriate
- Lifestyle – regular exercise, mental stimulation, establish routine
- General health – blood pressure, other health conditions
Legal Issues

• Enduring Power of Attorney
• Enduring Guardianship
• Advance Directives
• Informed consent for medical treatment
• Capacity to drive
• Capacity to work
Enduring Power of Attorney

- PoA relates to money and estate, *not* health, etc
- Recommend for all persons diagnosed with dementia (and for all persons >50)
- Tests for capacity?
- EPoA applications vary by jurisdiction
- May come into effect immediately or when triggered
Enduring Guardianship

- Proxy decision maker for services, accommodation, health
- Triggered by loss of decision making capacity
- Flexible: 1 or more guardians, severally or jointly, different guardians different powers
- Prudent to arrange early in dementia
- Prudent for us all to consider this now
Advance Directives

- Treatment
- Withholding treatment
- Participation in research
- Disposal of body, tissue donation at death, funeral arrangements
Informed Consent for Medical Treatment

• Person must understand
  – the nature of the treatment
  – the possible effects
  – the potential side effects
  – the alternatives

• Understanding varies with complexity

• Person must be able to communicate understanding and wishes
Informed Consent for Medical Treatment

• Dementia will affect understanding; holding information in head while weighing up pros & cons; and communication
• Loss of capacity is a point on a sliding slope
• If unable to give consent, then proxy consent
• Who can give proxy consent varies by jurisdiction. In NSW = person responsible
• If no proxy, Guardianship Tribunal may appoint Public Guardian or similar
Capacity to Drive

- Mentally incompetent can be danger to self and others
- Level of cognitive impairment poor correlation with capacity to drive
- Best test is on road
- “Co-pilot”, familiar routes only, day time only – help but not sufficient
- Better for specialist to bear blame
Capacity to Drive

- No person with dementia can have unconditional licence
- All persons with dementia will lose ability time
- If person already obviously incompetent cancel licence immediately
- Approach 1: cancel licence immediately
- Approach 2: graded restrictions and warning about cessation “later”
- Approach 3: send for *On-road Assessment*

**Note:** Poor correlation between cognitive testing and driving performance
Capacity to Work

• Capacity vs Competency
• Capacity vs Safety
• Decision for employer usually
• May become legal matter
  – doctor, lawyer, architect
  – judge, politician
11. Develop Care Plan

- Include legal/financial matters
- Make follow-up appointments
12. Refer patient and family for further information & support

- Alzheimer’s NZ
- Alzheimer’s NZ Auckland
- Community services
Comorbidities

- Falls/ gait disorder
- Delirium
- Weight loss
- Frailty
- Oral health
- Epilepsy
- Vision
- Sleep disorders
- BPSD

Behavoural & psychological Sx

- Citalopram may help agitation, delusions, hallucinations
- Antipsychotics have a place
  - for aggression
  - For psychosis
  - but ↑CVA & Mortality Rate
- Antidepressants - disappointing
- Informed consent from pt. or proxy in writing
- Review regularly, ≥ 3rd monthly
14. Regularly review care plan

• Medications
• Physical health
• Carer health and stress levels 3 – 6 monthly
• Cognitive testing at least 12 monthly
• Behavioural symptoms – assess and manage
Novel treatments

• Many trials have failed
  – Semagecestat
  – IV Ig
• For AD
  – β-secretase inhibitors
    • Merck
    – Antibodies to Aβ
    • Roche
    • Lilly
  – Intranasal insulin
• For MCI
  – Many of same Rxx
  – Computer cognitive training programs eg Lumosity, Posit Science
  – CCT + tDCS
  – Exercise programs
Role for GPs in prevention

- Physical Exercise 30'/day, \( \geq \) 5 days per week
  - More may be better, aerobic + resistance
- Mentally active
- Socially engaged
- Diet - Mediterranean; antioxidants
- Alcohol – moderate
- Blood pressure, cholesterol, weight – mid-life
- Depression
Alzheimer’s Australia

- [http://yourbrainmatters.org.au](http://yourbrainmatters.org.au)
• Brodaty H et al.
Conclusions

• You will have more patients presenting with memory problems
• Assessment is good medicine
• Case for screening the very old is debatable
• Assessment is manageable...
• ... and there is good business model
• 14-step model presented
• www.dementiaresearch.org.au
• www.cheba.unsw.edu.au
• www.fightdementia.org.au