

What's new in dementia and in prevention

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Centre
for Healthy
Brain Ageing



Dementia statistics in Australia in 2022

- **≈ 487,500 Australians living with dementia**
- **Expected to increase to almost 1.1 million by 2058**
- **≈ 1.6 million people care for someone with dementia**
- **Dementia: 2nd leading cause of death & leading cause for women**

INFOGRAPHIC

The global impact of dementia



Around the world,
there will be one new case
of dementia
**every
3 seconds**

50 million people worldwide are
living with dementia in 2018.
This number will more than

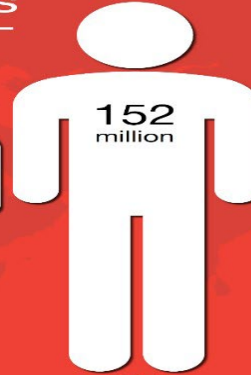
**triple to 152
million by 2050**



2018



2030



2050



2018



2030

The total estimated
worldwide cost of dementia
in 2018 is US\$1 trillion.
This figure will rise to

**US\$ 2 trillion
by 2030**



**Alzheimer's Disease
International**

The global voice on dementia

DEMENTIA

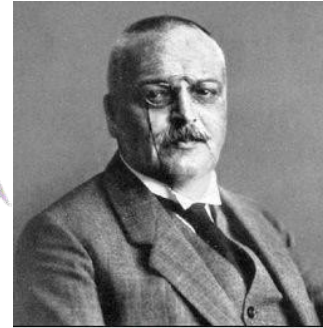
An “umbrella” term used to describe a range of symptoms associated with cognitive impairment.

ALZHEIMER'S
50% - 75%

VASCULAR
20% - 30%

LEWY BODY
10% - 25%

FRONTOTEMPORAL
10% - 15%



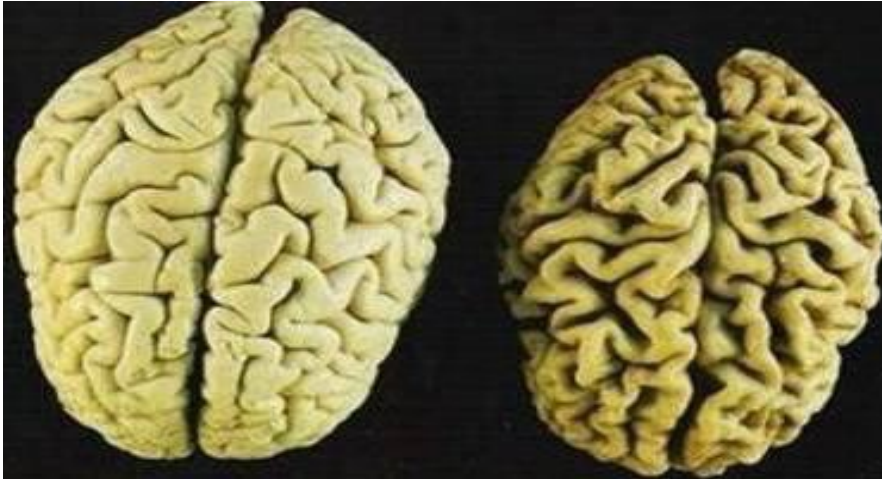
Alois Alzheimer

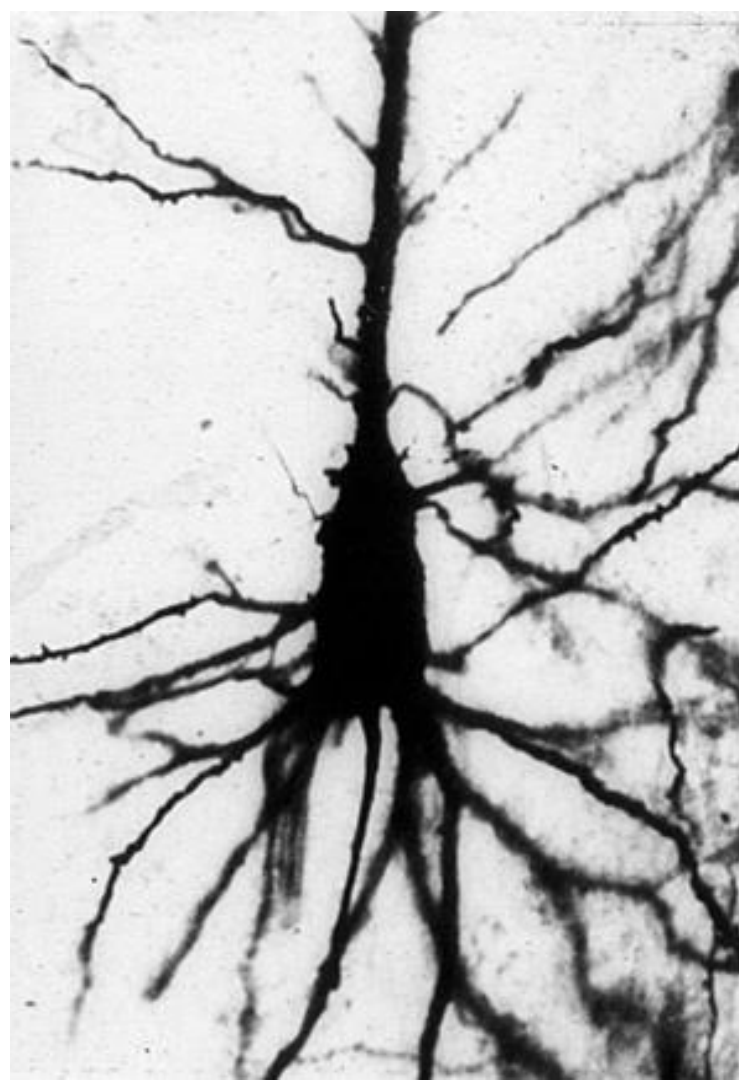


Auguste Deter

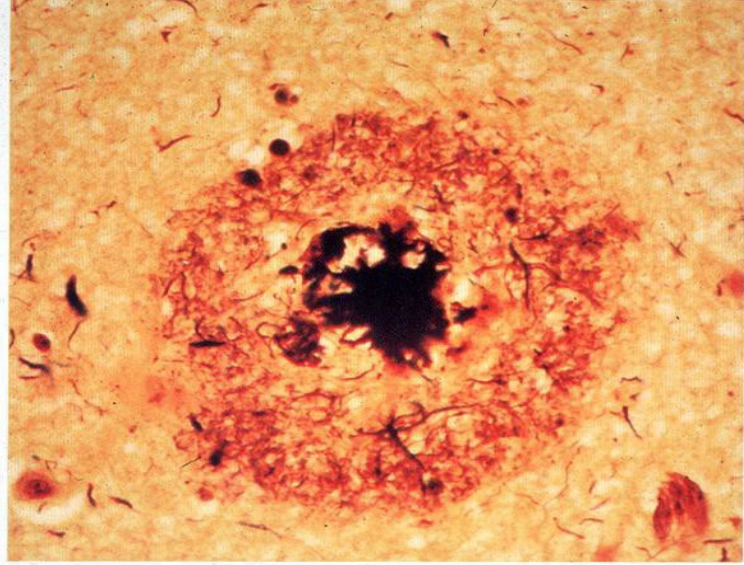
The brain and dementia

- The adult brain weighs about 1.3 kg
- Dementia shrinks it to 1/2 its usual size





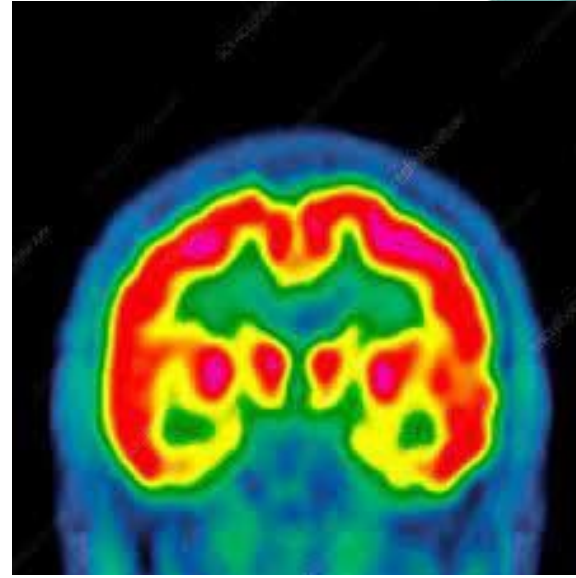
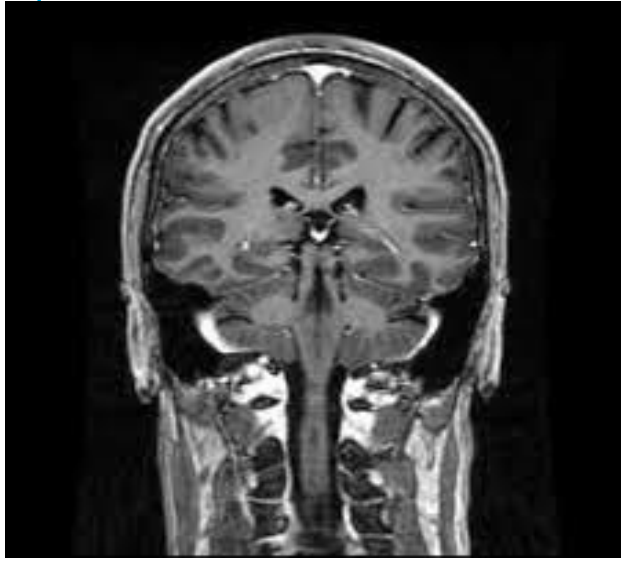
Amyloid plaque



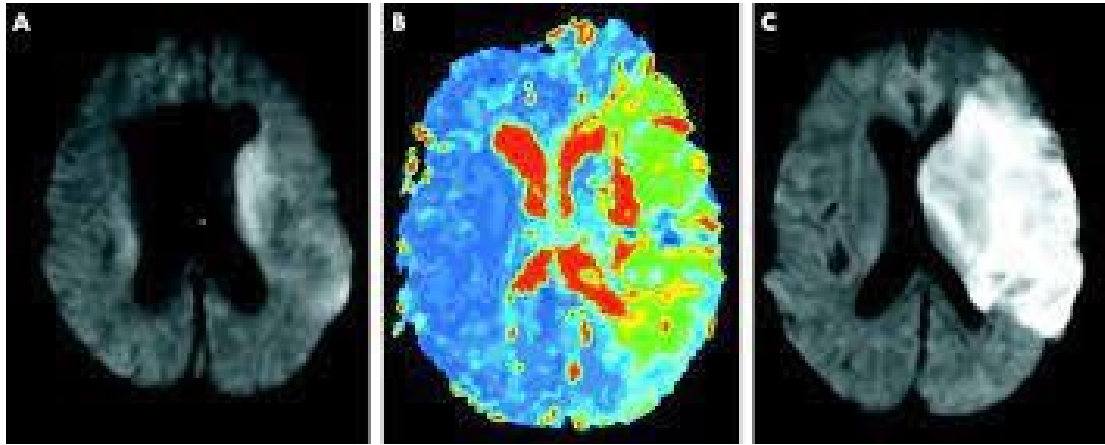
PLAQUE OF AMYLOID BETA-PROTEIN in the brain of an Alzheimer patient is visible as a black globular mass in this stained image. The plaque is surrounded by a halo of abnormal neurites (axons and dendrites) and degenerating neural cell bodies that appear darker than the normal neurons.

Tangles – tau protein

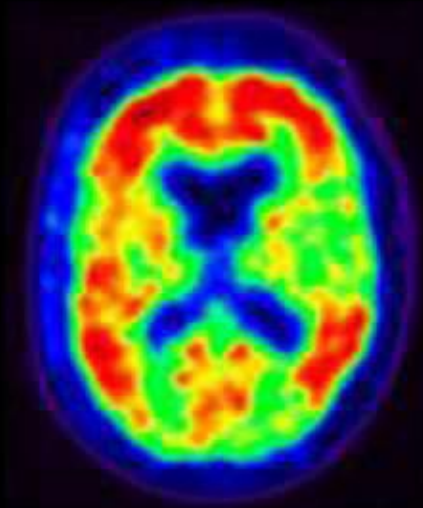




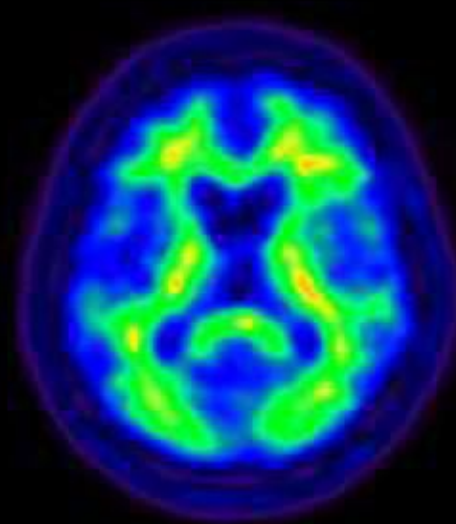
Normal Glucose PET Scan



PET SCAN GLUCOSE in PERSON WITH LARGE STROKE



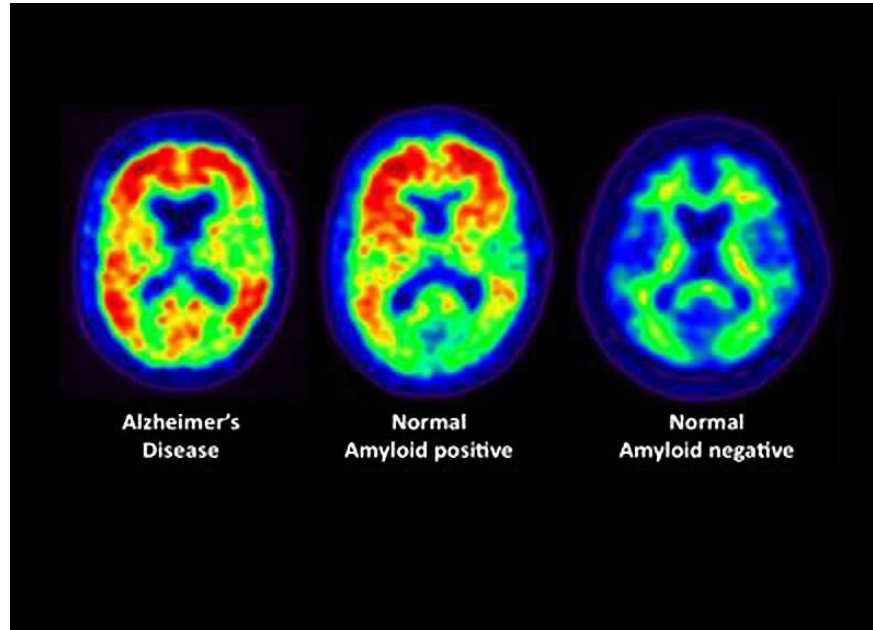
**Alzheimer's
Disease**



**Normal
Amyloid negative**

Hotter colours = more amyloid

PET amyloid imaging: normal vs AD



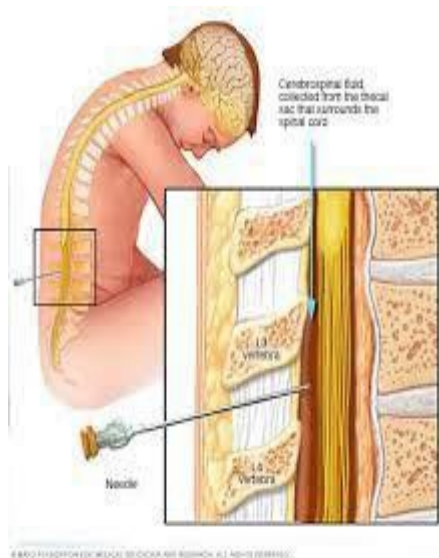
- 35% persons 60+ amyloid+
- Amyloid+ → ↑ risk clinical progression
- Will all amyloid+ develop AD?
- When??

What's new in Dx: lumbar puncture

CSF = cerebrospinal fluid

**Made in ventricles of brain
circulates around brain
and up and down spine**

**Diagnose – meningitis,
haemorrhage, CJD**

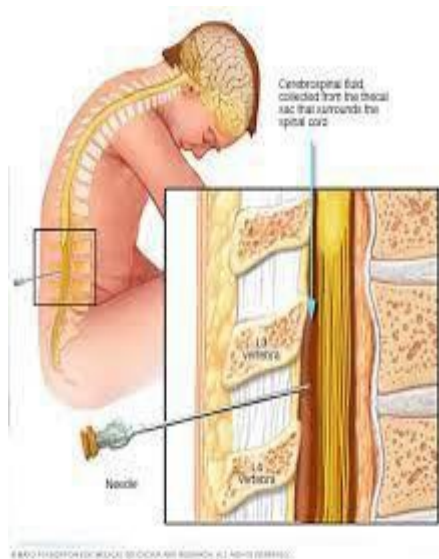


Spinal tap

CSF in Alzheimer's disease

Curious finding in Alzheimer's

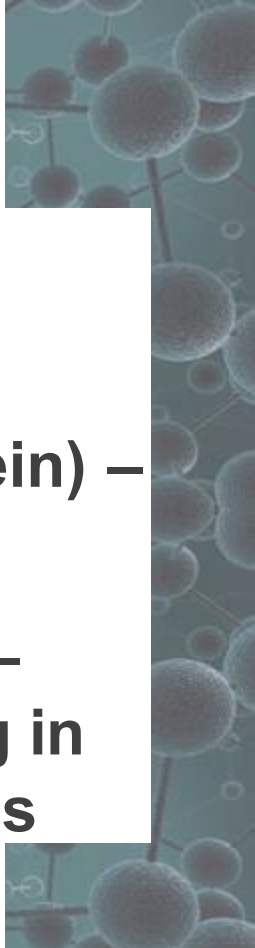
- **Low levels**: amyloid beta protein, especially $A\beta_{42}/A\beta_{40}$ ratio
- High levels of total tau and phospho-tau
- Reasonably good accuracy



Spinal tap

Blood tests for Alzheimer's disease

- $A\beta_{42}/A\beta_{40}$ ratio
- Phospho-tau-181 & 271
- GFAP (Glial fibrillary acidic protein) – marker of astroglia
- NFL (Neurofilament light chain) – marker of neuro-axonal injury eg in MS & other neurological diseases



What's new? New dementias!



LATE (Limbic predominantly Age-related TDP-43 Encephalopathy)

- 50% of dementias that start after age 80
- Often with arteriosclerosis, CAA, A β plaques, tauopathy
- Alzheimer-like memory problems
- Some genes account for small % of cause
- No diagnostic test and no cure

Hippocampal sclerosis

- Initial symptoms and rates of dementia similar to Alzheimer's, scarring of brain, frequently with epilepsy
- Can be caused by multiple fits, infection, trauma, age, vascular disease in brain
- 10% of brains of people aged 85+
- No cure



Other new dementias!

- **PART (Primary Age-Related Tauopathy)**
- **ARTAG (Age-related tau astrogliopathy)**
- **Brain arteriosclerosis**
 - **80% of people aged 80 years or more**

Chronic Traumatic Encephalopathy



What does it all mean?

- Brain is very complex, many parts
- Many different things can go wrong
- Why it matters – if diagnosed with Alzheimer's and it is Hippocampal Sclerosis, any new Alzheimer Rx will not work
- Prognosis may be different too



What's new in dementia: treatment?

- **Antibodies to amyloid beta ($A\beta$) protein**
 - **Aducanumab (Biogen)**
 - **Donanemab (Lily)**
 - **Gantenerumab (Roche)**



Aducanumab = Aduhelm

- **Approved by FDA June 2021**
- **?? If clinical benefit but less amyloid**
- **Furore – rejected by:**
 - **FDA Expert Advisory**
 - **European Medicines Agency**
 - **US Subsidised Medicines committee**



Aducanumab = Aduhelm ®

- **PET Amyloid imaging to confirm**
- **Monthly IV infusions for 12 m ..or more??**
- **Side effects – swelling, microhaemorrhages**
- **Cost AUD\$12,000/month → \$6,000 / month**
- **Recent analysis – not cost effective¹**



So where next?

- There is a signal and hope
- Aduhelm is being prescribed in US
- Biogen & others doing more trials



Other dementias?

- **Vascular dementia**
 - **manage vascular risk factors**
- **Lewy body dementia**
- **Fronto-temporal dementia**



What's new in dementia care

- **Royal Commission into Aged Care Quality and Safety**
- **Non-drug care for changed behaviours in dementia**
- **Better post-diagnostic care**



Survey results

- **Only 30% of PLWD and CPs received a care or support plan**
- **Over 50% of PLWD & 38% of care partners strongly disagreed that they were satisfied with information received**
- **Just 20-25% of PLWD and CPs strongly agreed that they were satisfied**

Left to fend for ourselves – interview results

All people with dementia & care partners (except one) were not satisfied with the post-diagnostic support

People with dementia expressed:

- Left on their own, without support – what happens now?
- Ongoing loss/grief, loss of hope
- Sometimes anger – loss of driver's licence, independence, respect
- Over time – some self-efficacy at figuring things out

Care partners felt:

- All responsibility on them
- Burden
- Blame
- Desperation

Support was something I had to go and find because no one mentioned it to me





Our Goal

1. Re-frame the dementia diagnostic conversation
2. Replace the uncertainty of a dementia diagnosis with clarity
3. Connect people with information and support that is relevant to the first 12 months post-diagnosis

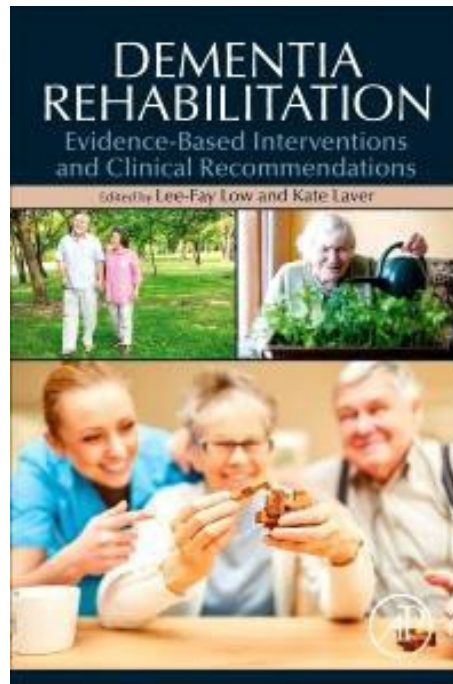


Giving the diagnosis (4 key pillars)



Evidence for post diagnostic interventions*

- Medications
- Behavioural support
- Carer support
- Cognitive focused interventions
- Occupational therapy
- Exercise
- Psychological interventions
- Peer support
- Speech pathology
- Dementia friendly communities



This and next few slides courtesy of Prof Lee-Fay Low

Cognitive-focused interventions



Cognitive training



Cognitive stimulation therapy



Cognitive rehabilitation

Cognitive training

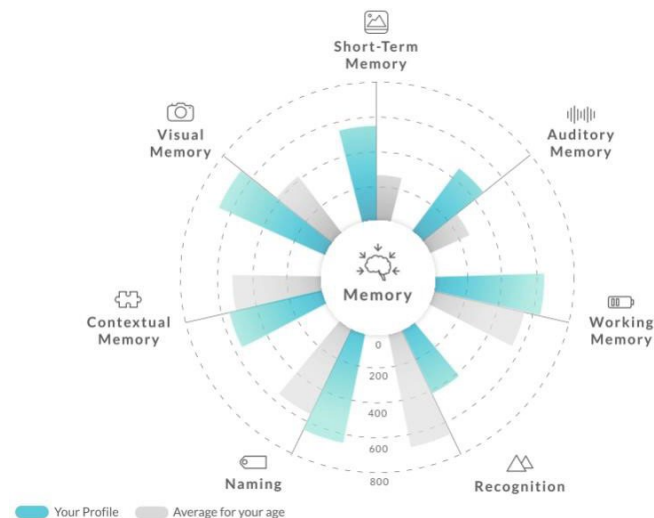
- **Tasks designed to target one or more cognitive processes**
- **Repeated practice**
- **Pen and paper or computerised**
- **Variability in number of sessions, programs**
- **Often tested onsite by trained administrator, sometimes in groups**



Bahar-Fuchs A, et al. Cognitive training for people with mild to moderate dementia. Cochrane Database of Systematic Reviews 2019(3)

Cognitive training evidence

- Systematic review (n = 33, n>2000)
- Small to moderate effect on global cognition immediately after, retained at 3-12 month follow-ups
- Moderate effect on verbal semantic fluency immediately and at follow-up
- Evidence low for clinical disease severity and other outcomes
- Limited training transfer beyond immediate training task



Bahar-Fuchs A, et al. Cognitive training for people with mild to moderate dementia. Cochrane Database of Systematic Reviews 2019(3)

Self-administered brain training programs with evidence

NeuroNation

Brain Training
THAT WORKS



Raising the bar on brain training
There are a lot of “brain games” out there.
BrainHQ is much more.



Forward
with dementia



Cognitive stimulation therapy (CST)

- Targets thinking, concentration and memory and orientation
- Consists of enjoyable activities (usually small group)
- For people with mild-moderate dementia with verbal communication
- Typically 2x week, 7 weeks
- NICE guideline recommends for people with mild to moderate dementia



Woods, B., E. Aguirre, et al. (2012) Cognitive stimulation to improve cognitive functioning in people with dementia. Cochrane Database of Systematic Reviews
<https://www.nice.org.uk/guidance/ng97/chapter/recommendations>

Cognitive stimulation therapy (CST) evidence

- Systematic review (44RCTs, n 2444)
- Medium effect on global cognition immediately after, but not 1-10 months follow-up
- Improved memory, function, depression and dementia ratings



Cafferata, R. M. T., B. Hicks and C. C. von Bastian (2021). "Effectiveness of cognitive stimulation for dementia: A systematic review and meta-analysis." Psychol Bull **147**(5): 455-476

Cognitive rehabilitation

- Principles of rehabilitation flexibly applied to address different types of need at various stages of dementia
- Goal setting in the person's home
- NICE recommends



Clare, L. (2017). "Rehabilitation for people living with dementia: A practical framework of positive support." PLoS Medicine **14**(3): e1002245.

Cognitive rehabilitation

- Learn to use email to keep in contact with friends
- Develop strategies to feel confident enough to go out alone
- Cook meal
- Maintain ability to dress herself
- Participate in enjoyable activities

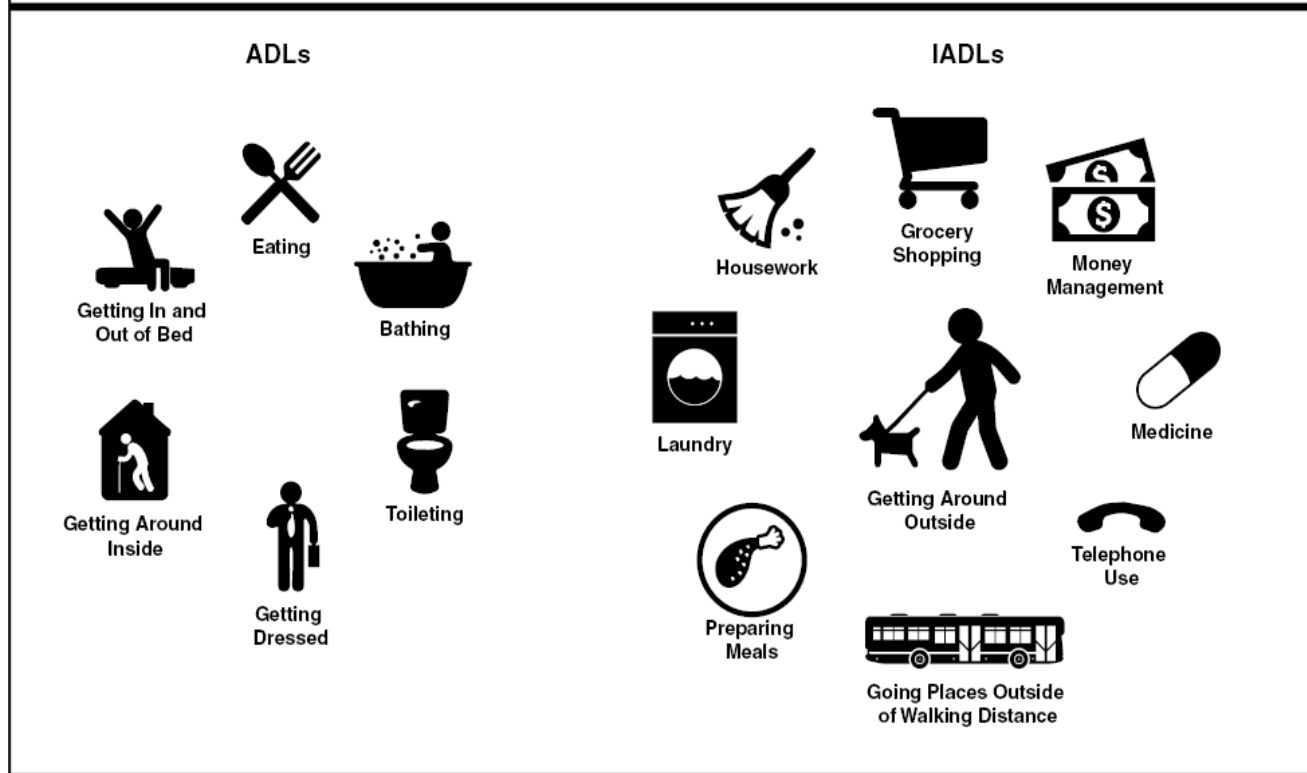


Clare, L. (2017). "Rehabilitation for people living with dementia: A practical framework of positive support." PLoS Medicine **14**(3): e1002245.

Occupational therapy interventions

Figure 1

Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs)



Occupational therapy evidence

- **Systematic review (n = 15, n = 2063)**
- **For person with dementia: Improvements on function, behaviours, Quality of Life after intervention, and at 3-6 months' follow-up**
- **For carers: Less hours spent assisting the person, less distress with behaviours, improved Quality of Life**
- **Effects were small to moderate**
- **Almost always as couples**

Bennett S, et al (2019). "Occupational therapy for people with dementia and their family carers provided at home: a systematic review and meta-analysis." BMJ Open 9(11)

OT for dementia in Australia

Funding:

- GP Chronic Disease Management Plan (5 sessions)
- Transitional care
- Home care package
- Private health insurance
- Community rehabilitation services

Find an OT pages:



Physical activity (exercise)

- Walking
- Aerobic exercise (increases heart rate)
- Resistance training (increases muscle strength)
- High intensity exercise (vigorous, high exertion)



Physical exercise

- Systematic review MCI and dementia (n = 46, n = 5099)
- Exercise reduced decline in global cognition, working memory, changed behaviours, but not other cognitive functions
- Small effects
- Aerobic exercise at moderate intensity or above or total training duration >24 hours - greater effect on global cognition

Law CK et al (2020). J Physiother 66(1): 9-18.



Two separate meta-analyses –
no impact on ADLs or depression

Exercise for dementia in Australia

Few dementia-specific services:

- Local seniors exercise groups, walking clubs, gyms
- GP Chronic Disease Management Plan (if need help to start safe exercising)
- Falls prevention programs (e.g. Stepping On)

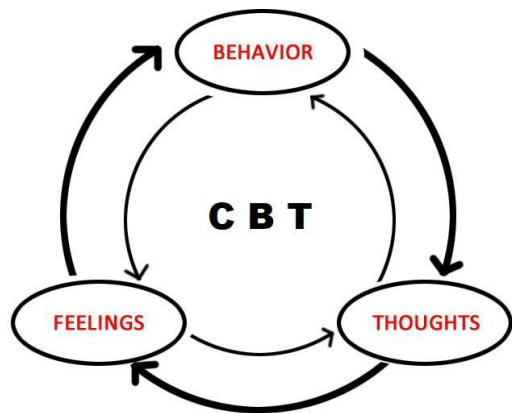
Find a seniors exercise program:

**active &
HEALTHY**

<https://www.activeandhealthy.nsw.gov.au/>

Google

Psychological (talking) therapies



**Cognitive Behaviour
Therapy**



Problem focused therapy



Counselling

Psychotherapeutic services in Australia

Funding

- Mental Health Plan
- Private health insurance



Post-diagnostic support program (counselling)

What's new in prevention?!

- 7 environmental factors accounting for 30% of population attributable risk of dementia
- Now 12 potentially modifiable factors accounting for



What's good for our heart is good for our brain



CHeBA
Healthy Brains Positive Ageing

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Brain Ageing



Prevention vs delay onset



Smallpox vaccine

Never too late, never too early



**Mixed aerobic + anaerobic
better**

CHeBA
Healthy Brains Positive Ageing

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Brain Ageing

CRYPTIC INDM

20-201

ACROSS

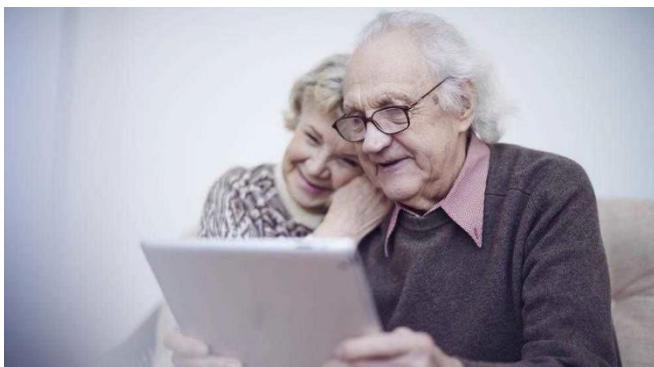
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DOWN

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Obesity in Mid-Life



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Mind your diet

- Mediterranean
- Antioxidants



What is Mediterranean-style diet?

- Abundant plant foods
- Fresh fruit as typical daily dessert
- Olive oil as principal source of fat
- Dairy products (cheese, yogurt)
- Fish and poultry - low to moderate
- 0- 4 eggs week
- Red meat - low amounts
- Wine - low to moderate amounts
- Total fat = 25% to 35% of calories
- Saturated fat $\leq$ 8% of calories



Chronic Traumatic Encephalopathy (CTE)¹

- CTE (aka Dementia Pugilistica, Punch Drunk)
- Mood disorders, neuropsychiatric disturbance & cognitive impairment
- Pathological diagnosis
- NfL (Neurofilament light) = fluid biomarker of axonal damage after mod-severe TBI, peak 10d–6w after injury, predict white matter degeneratⁿ and functional outcomes at 6 & 12m

• ¹ Albayram O et al. *Transl Psychiatry* 2020;**10**:424

• ² Ponsford J et al, *Lancet Neurology* 2022; **21**: 5-6

Anthocyanins – purple diet to protect against dementia



Smoking



Alcohol



**In moderation may
have benefits against
dementia, but.....
...increases risk of
cancer**



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Natural therapies



Tumeric/ curcumin



Omega-3



**Ginkgo
leaves**



Brahmi



Ginger family

Hearing loss



Hearing loss and incident

- Peripheral hearing loss associated with up to 2½ times increased risk for dementia
- 3 studies follow-ups 9-17 years
- 30% increased risk per 10dB worse hearing
- Mid-life hearing loss associated with steeper temporal lobe volume loss
- **Hearing aids ameliorated the risk**

Social isolation



Sleep



Air Pollution



Systematic review, 13 longitudinal studies, 1-15 year follow-up'- exposure to $PM_{2.5}$, NO_2 and CO all associated with dementia risk[↑]
(Peters R, J Alz Dis 2019)

“Air Pollution Robs Us of Our Smarts and Our Lungs”

GIBBENS S, *National Geographic*, 2018

9/10 people breathe in polluted air

Traumatic brain injury



- Increases risk 84%
- for all causes of dementia
- from all severities of TBI
- Fann JR et al, Lancet Psychiatry 2018;5:424-31

Forward
with dementia ●●●

A guide to living with dementia

ForwardwithDementia.org.au
@FWDDementia_AU



Thank you





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