

FAQ about Alzheimer's disease
&
Physical Activity and exercise: effects on the
brain and dementia risk

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Alzheimer's disease and dementia: Frequently Asked Questions

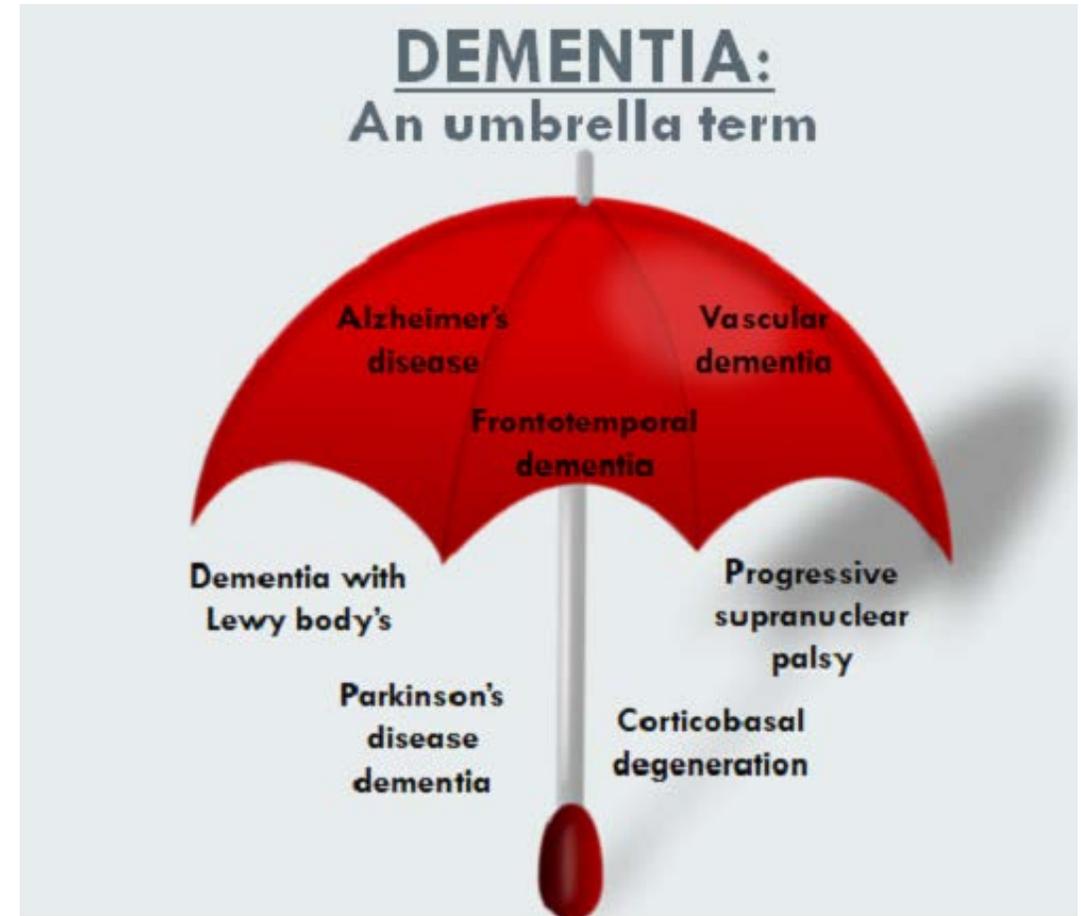
Dr Belinda Brown

FAQ #1

What is the difference between dementia and Alzheimer's disease?

Alzheimer's disease is a form of dementia

- Alzheimer's disease is a form of dementia
- Makes up approximately 60-70% of all dementia cases
- Alzheimer's disease is caused by two proteins, beta-amyloid and tau that cause damage to the brain
- A lot of the time it's actually a mixed dementia (i.e. some vascular changes and Alzheimer's pathology)

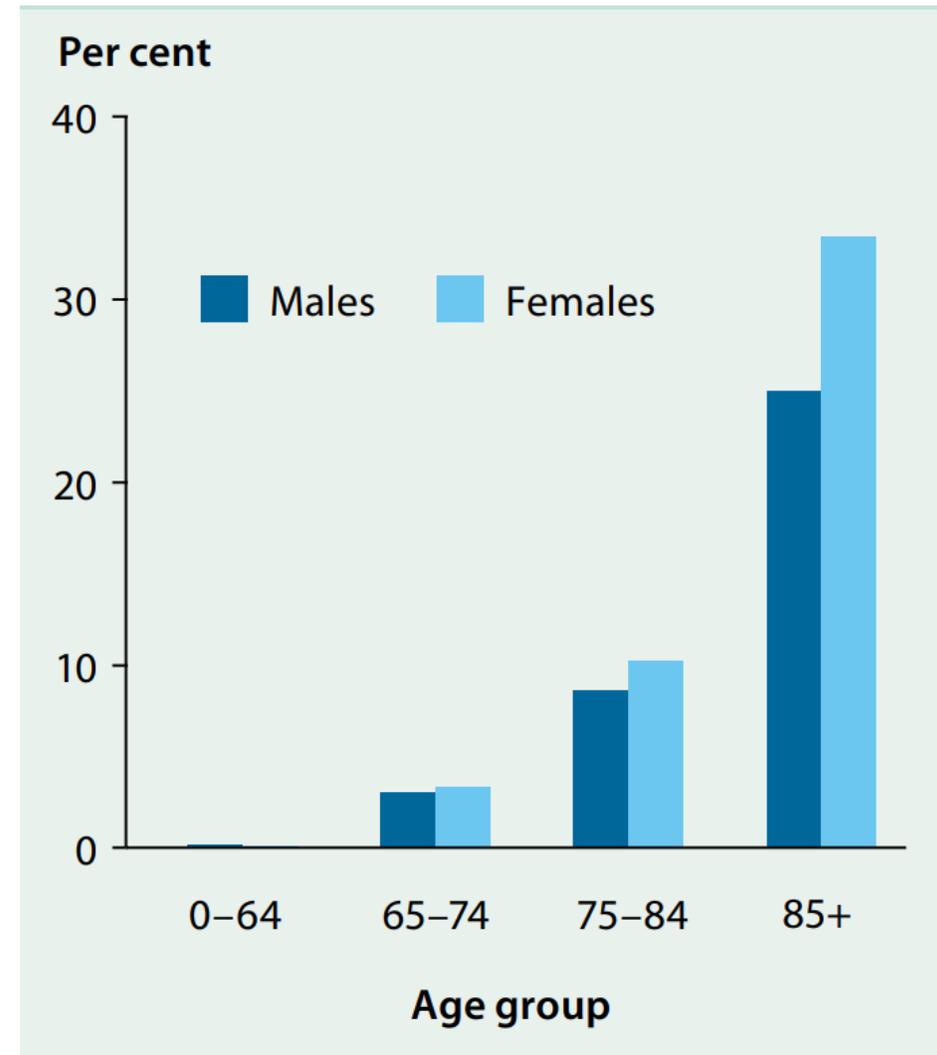


FAQ #2

Is dementia a natural part of getting older?

Dementia is *not* a normal part of ageing

- Age is the greatest risk factor for dementia, but does not *cause* it
- For example, 70% of people aged over 85 are 'dementia-free'



FAQ #3

If someone is experiencing changes in memory, do they have dementia?

Age-related brain changes versus dementia

Age-related changes	Dementia
Not being able to remember the name of an acquaintance	Not recognising or knowing the names of family members
Forgetting details and events occasionally	Forgetting events and details often
Occasionally having difficulty finding the right word	Frequently substituting words and pauses when trying to find the right word
May forget small details of a recent event	May forget part or all of an event
You are worried about your memory, but those around you are not	Your relatives are worried about memory, and have noticed <i>change</i> over time

FAQ #4

My mother/father/sister had Alzheimer's disease/dementia, am I going to develop it as well?

There are two different types of Alzheimer's disease

Dominantly Inherited Alzheimer's disease

- Very rare (less than 3% of all Alzheimer's cases)
- Caused by mutations to one of three genes that accelerates the production of toxic proteins
- Affects people in their 30s to 50s
- 50% chance of passing mutation on to children

There are two different types of Alzheimer's disease

Sporadic Late-Onset Alzheimer's disease

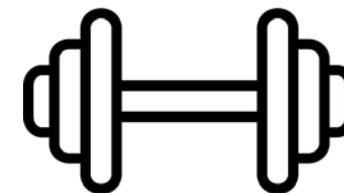
- The common form of Alzheimer's disease that occurs later in life
- Believed to be caused by a combination of genetic and environmental factors
 - *More on this next....*
- There is a known genetic **risk** factor (APOE e4 allele)
 - There is a lot of debate as to whether knowing this information is beneficial

FAQ #5

Can I change my risk of dementia?

The research suggests you **CAN** alter your risk for dementia (evidence strength indicated by WHO)

- Physical activity (*moderate evidence*)
- Management of blood pressure and cholesterol (*moderate to high evidence*)
- Healthy diet
 - Mediterranean diet (*moderate evidence*)
- Alcohol (*moderate evidence for reducing harmful intake*)
- Smoking (*recommendation to cease regardless of evidence*)





Australian Government

NHMRC National Institute for Dementia Research

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Physical activity and exercise: effects on the brain and dementia risk

Opportunity for intervention

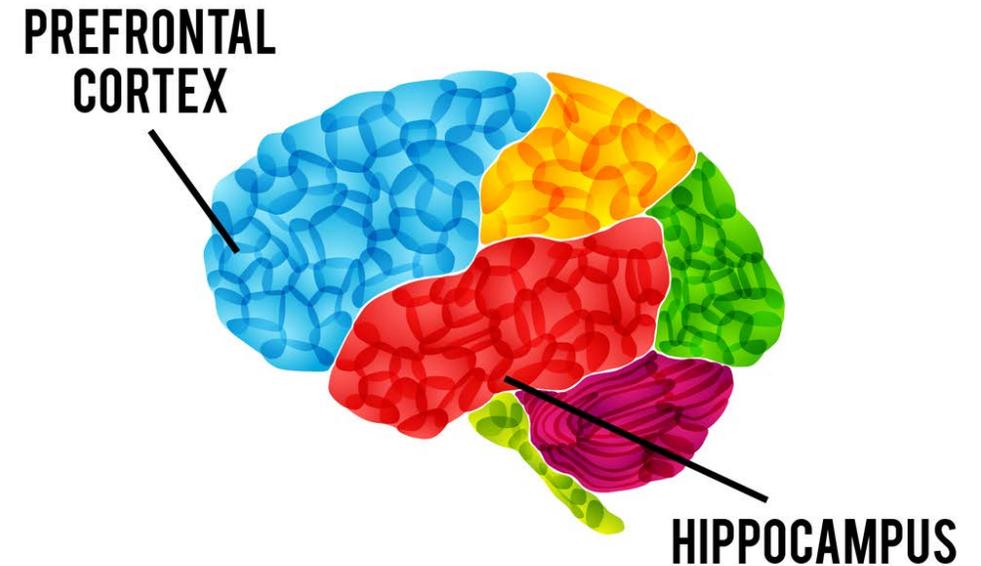
- No cure available
- Costs associated with dementia care set to reach \$80 billion by 2060
- Current Alzheimer's disease treatments alleviate symptoms for a short period (usually 1-2 years) in some patients
- By time of diagnosis, it's believe damage to the brain is too advanced to be reversed
- Growing evidence for modifiable risk factors

Risk factors for AD

Modifiable Factor	Population attributable risk (UK)
<i>Diabetes Mellitus</i>	1.9%
<i>Midlife hypertension</i>	7.0%
<i>Midlife obesity</i>	6.6%
<i>Depression</i>	8.3%
<i>Smoking</i>	10.6%
<i>Low educational attainment</i>	12.2%
<i>Physical inactivity</i>	21.8%

Physical activity and cognition

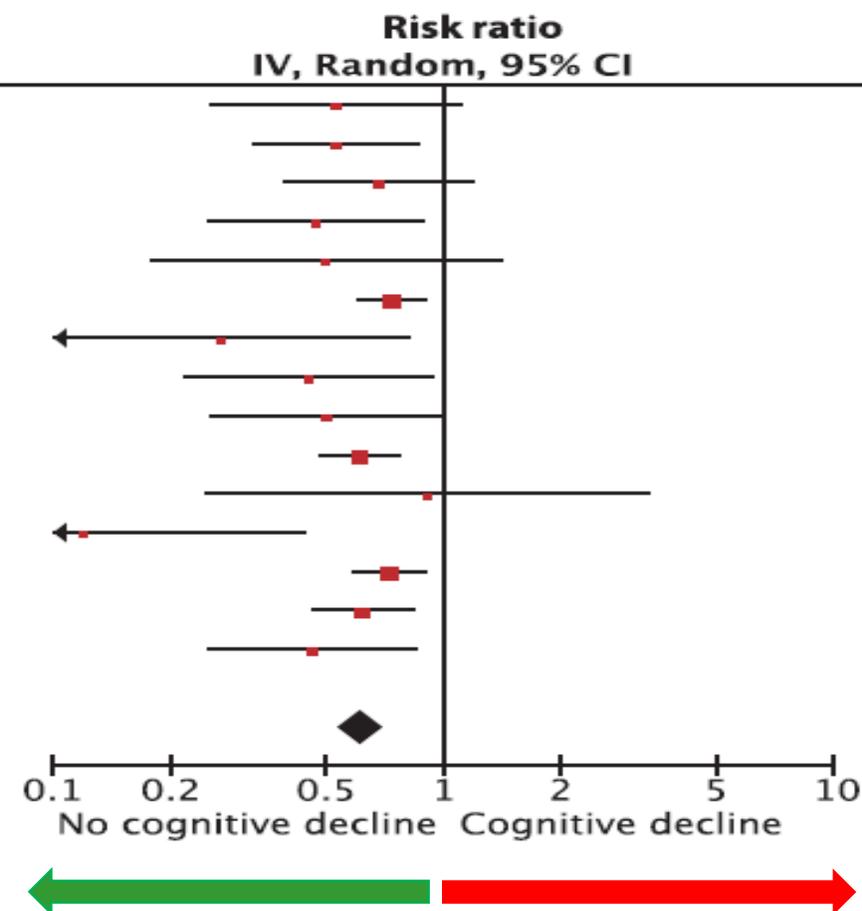
- Higher levels of physical activity are associated with better:
 - Verbal memory (hippocampus)
 - Executive functioning (prefrontal cortex)
- Areas of the brain most affected by disease and ageing appear to be those that gain the most benefit from physical activity



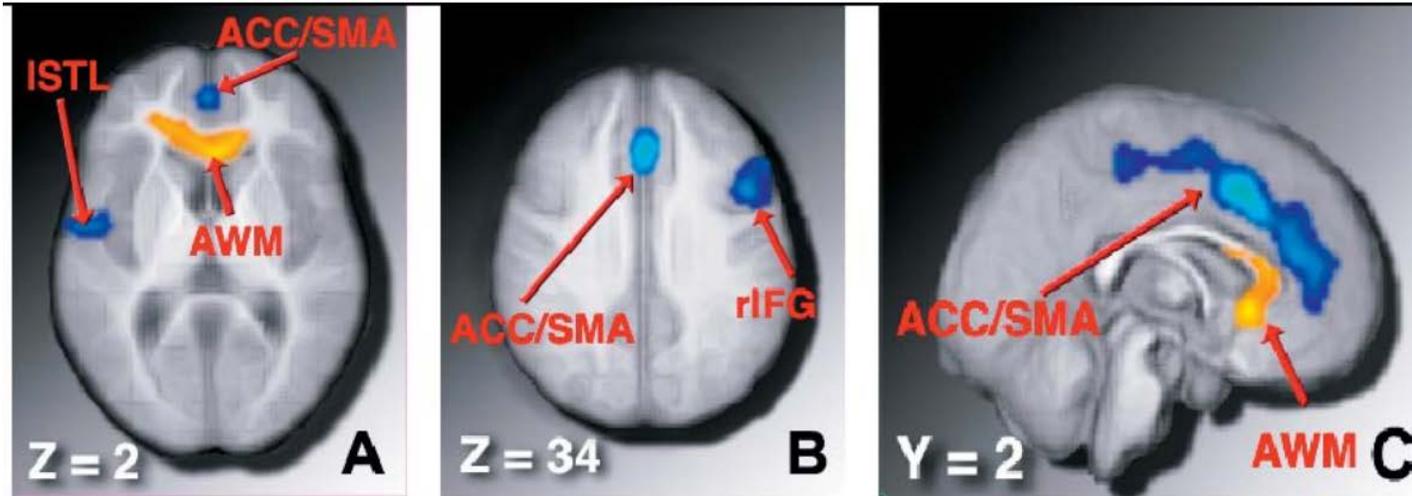
Physical activity and cognitive decline

Study or Subgroup	Weight	Risk ratio	
		IV, Random, 95% CI	
Ho <i>et al.</i> , (M)	2.7%	0.53	[0.25, 1.12]
Ho <i>et al.</i> , (F)	5.8%	0.53	[0.32, 0.87]
Laurin <i>et al.</i> , (M)	4.6%	0.68	[0.39, 1.19]
Laurin <i>et al.</i> , (F)	3.6%	0.47	[0.25, 0.89]
Schuit <i>et al.</i> ,	1.4%	0.50	[0.18, 1.41]
Yaffe <i>et al.</i> ,	20.5%	0.74	[0.60, 0.91]
Pignatti <i>et al.</i> ,	1.3%	0.27	[0.09, 0.82]
Lytle <i>et al.</i> ,	2.8%	0.45	[0.22, 0.94]
Flicker <i>et al.</i> ,	3.2%	0.50	[0.25, 1.00]
Singh-Manoux <i>et al.</i> ,	16.7%	0.61	[0.48, 0.78]
Sumic <i>et al.</i> , (M)	0.9%	0.91	[0.25, 3.36]
Sumic <i>et al.</i> , (F)	0.9%	0.12	[0.03, 0.44]
Middleton <i>et al.</i> ,	19.1%	0.73	[0.59, 0.91]
Niti <i>et al.</i> ,	12.6%	0.62	[0.46, 0.84]
Etgen <i>et al.</i> ,	3.9%	0.46	[0.25, 0.85]
Total (95% CI)	100.0%	0.62	[0.54, 0.70]

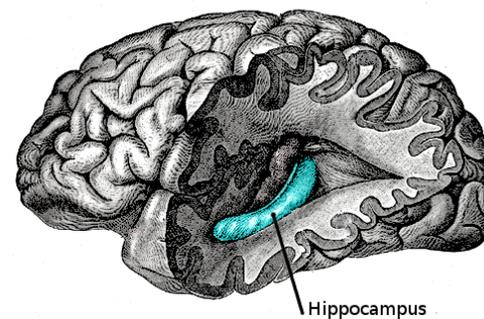
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 16.94$, $df = 14$ ($P = 0.26$); $I^2 = 17\%$
 Test for overall effect: $Z = 7.49$ ($P < 0.00001$)



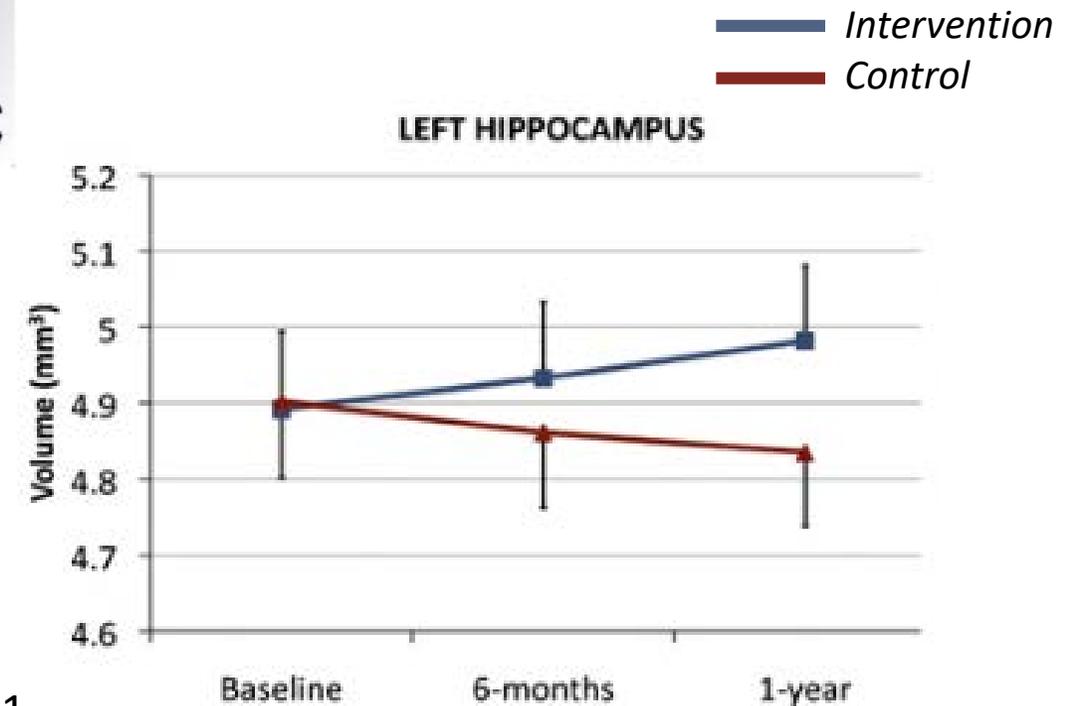
Exercise interventions increases brain volume



Colcombe, 2006



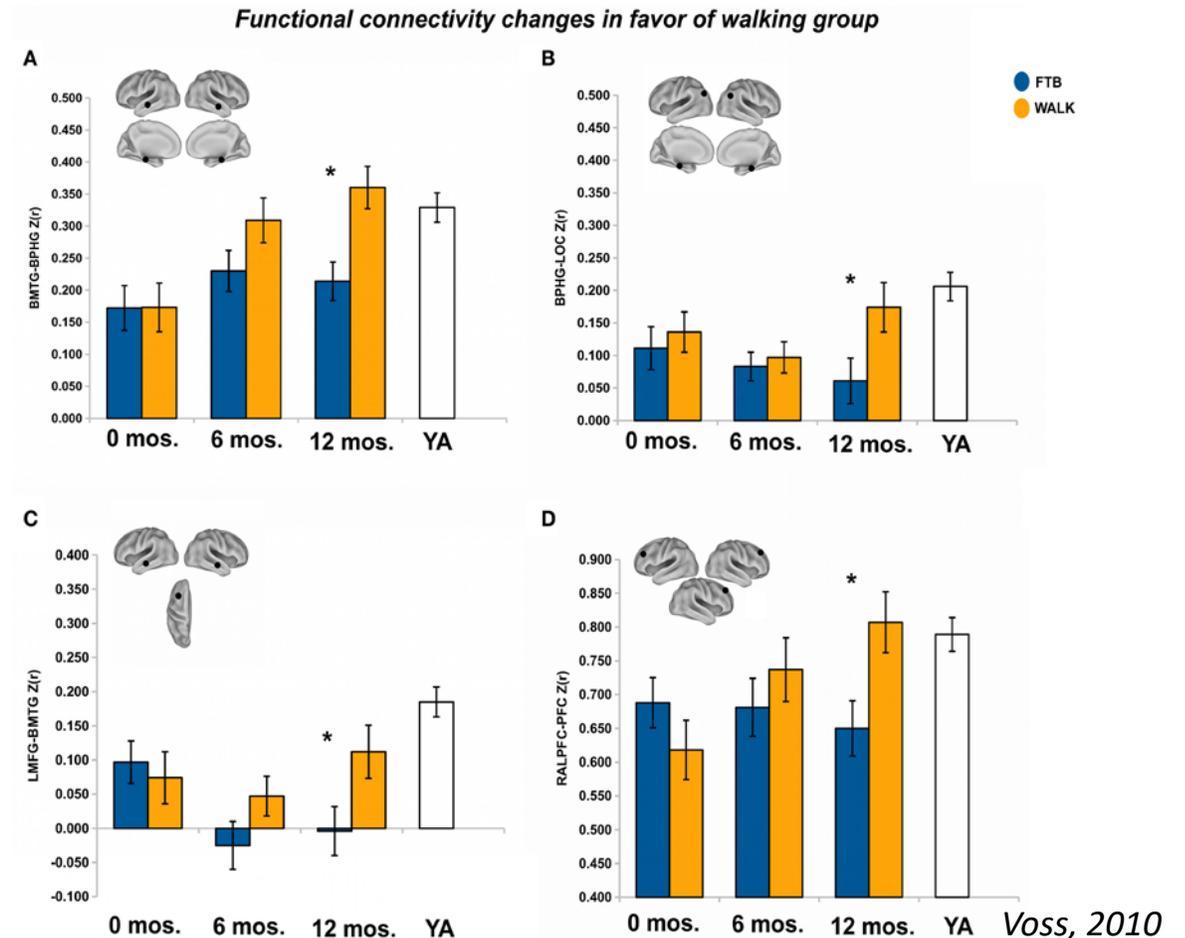
Erickson, 2011



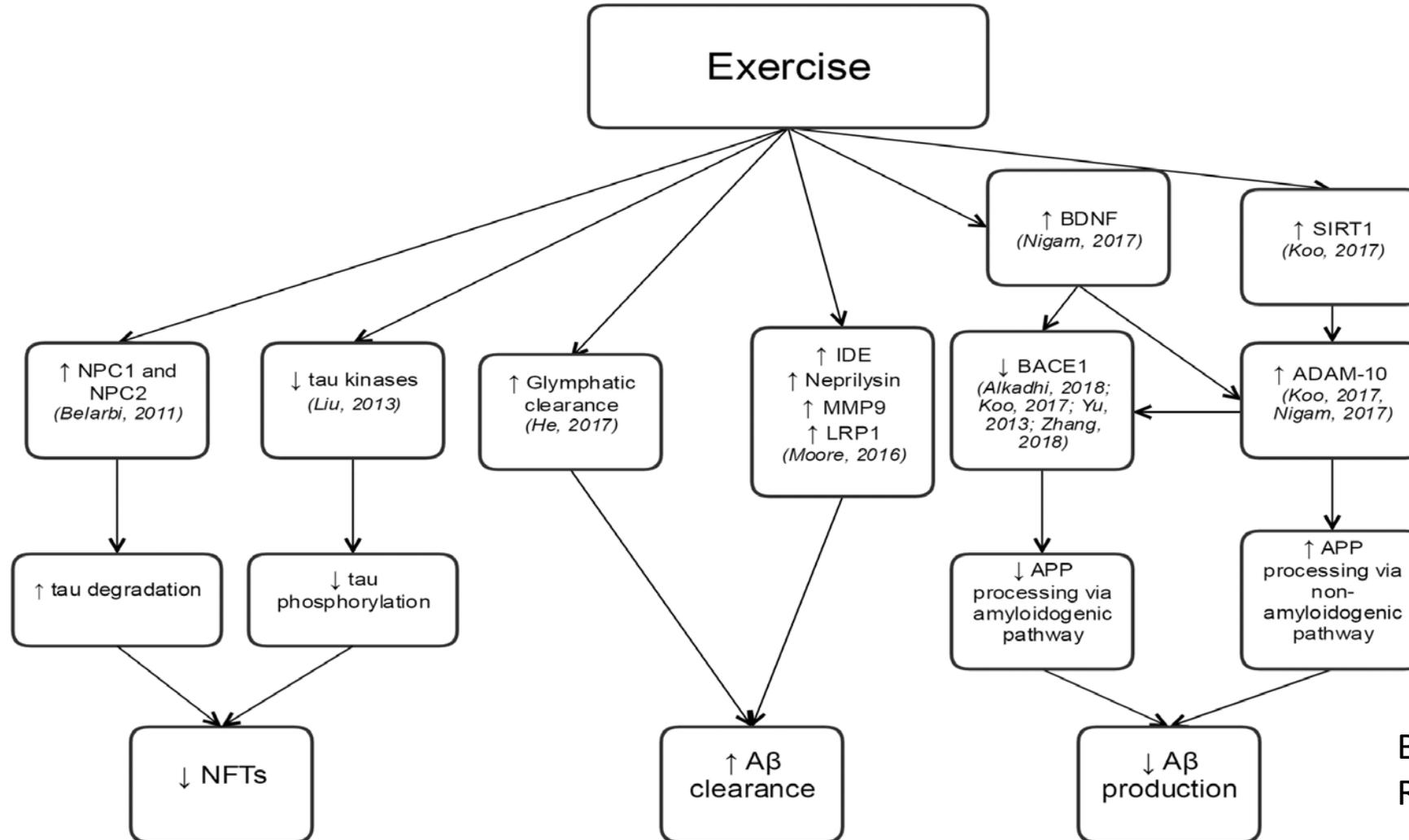


Physical activity and brain connectivity and activation (using

- Higher fitness is associated with enhanced recruitment of important brain regions (including prefrontal cortex)
- A walking intervention was associated with enhanced connectivity of the default mode network (a brain network that is decreased in dementia)

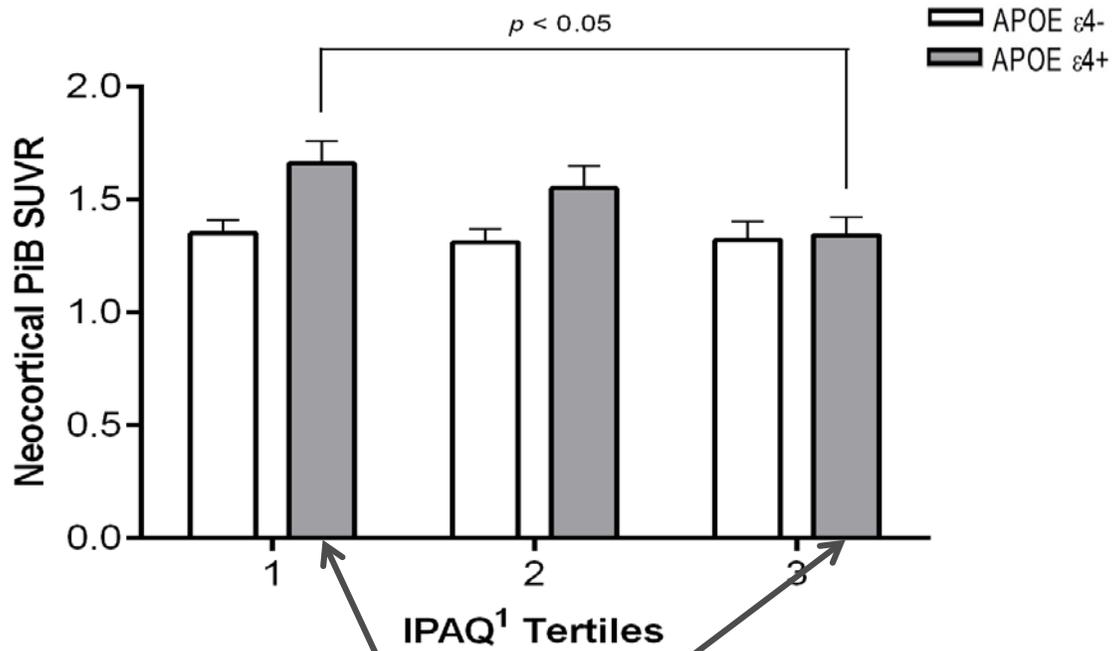


Exercise is associated with lower dementia pathology



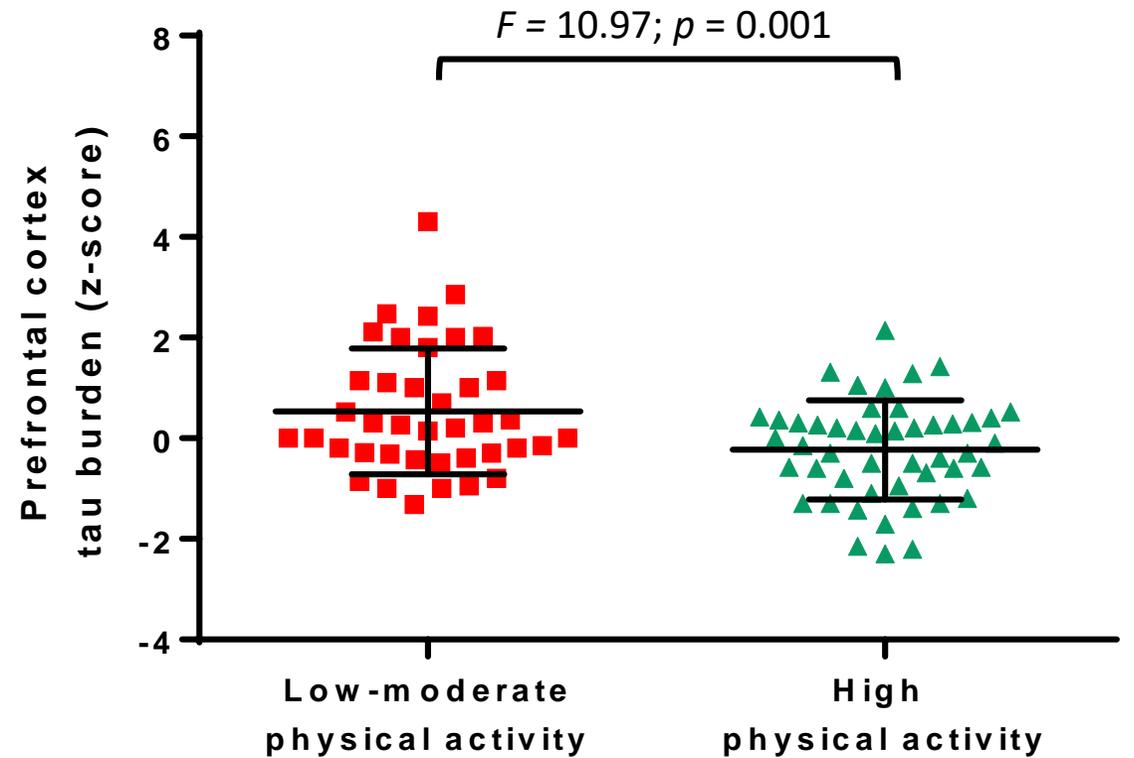
Brown, 2018, Ageing
Research Reviews

Exercise is associated with lower dementia pathology



Those that are sedentary and have the highest genetic risk, yet report high levels of physical activity, have "normal" levels of amyloid in the brain

Brown, 2013, Molecular Psychiatry



Brown, 2018, Journal of Alzheimer's disease

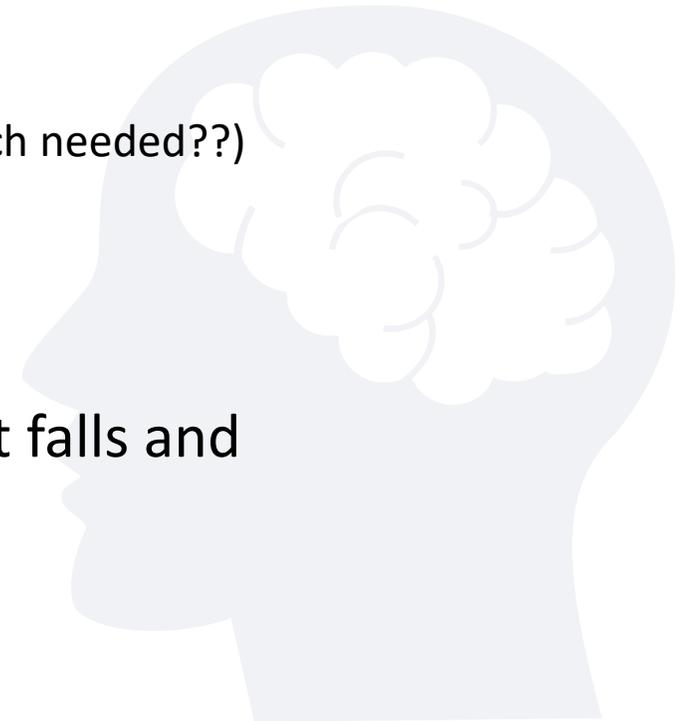
Individual variability

- Genetics
- Age
- Prior fitness levels
- Fitness response
- Diet
- Sleep



Can physical activity slow decline in dementia?

- Appealing approach → no current disease modifying drugs available
- Physical activity interventions can improve cognition in those with dementia
 - Undertaken in both community and care facility settings
 - Effect was shown across different types of dementia
 - Similar level of effect as seen with current drug treatments (combined approach needed??)
- Appears to be specific to aerobic exercise
- Resistance training important to maintain muscle tone, prevent falls and overall enhance quality of life



Future directions and conclusions

- Lots of evidence – but still not consistent enough
- Need large randomised controlled trials
- Better evaluation of individual variability
- Long-term tracking of individuals

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