ActiveBrain: Using physical activity to explore, understand, and optimise brain function

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ACT MS Symposium 2021

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Overview

ACTIVE BRAIN | UNIVERSITY OF CANBERRA | RESEARCH INSTITUTE FOR SPORT & EXERCISE

1. **The Active Brain Lab**
2. **The case for moderate intensity as the key to brain health**
3. **The case for why concurrent training might actually be the key to brain health ☺**
4. **Potential applications for MS**

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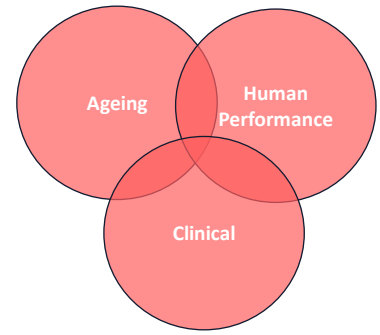
Active Brain

Core members (mostly education/research) from exercise science, physiotherapy, and psychology backgrounds

Our research investigates the interrelationship between human movement and the brain, seeking to optimise health and performance.

- Cognitive and physical performance
- Brain health (cerebrovascular, functional connectivity, volume)
- Mechanisms – e.g. growth factors and markers of nerve damage
- Mental fatigue



Partners and collaborators which include:

- The Australian National University
- Laval University, Canada
- Vrije Universiteit Brussels, Belgium
- Australian Institute of Sport
- Defence Science and Technology Group
- The Australian Army

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Lab and Equipment

Sit within the world class facilities of the UC Research Institute for Sport and Exercise (UCRISE)

Brain and related monitoring

- Electroencephalogram (electrical activity)
- Transcranial Doppler Ultrasound (cerebral blood flow)
- Pupilometry (pupil diameter)
- fNIRS (cerebral oxygenation)
- Driving simulator
- Transcrannial magnetic stimulation
- Range of cognitive testing and training packages

Exercise science

- Including: environmental chamber, upright & recumbent cycle ergometers, various treadmills

Physiology

- Including: non-invasive blood pressure, ventilatory gas, ECG, physical activity monitors, routine and advanced blood analysis

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Age and Neurocognitive Decline

Generally, group into:
1. Cerebrovascular Function
2. Cellular and DNA changes
3. Oxidative Stress/
4. Accumulation of Waste products (e.g. plaques)

Structure and Function
↓ Gray matter volume
↓ White matter structure
↓ Functional activation of neural networks

-Frontal/temporal lobes and hippocampus particularly prone

Cognitive Function
↓ executive function
↓ memory
-episodic > semantic

-Declines greatest >60 years

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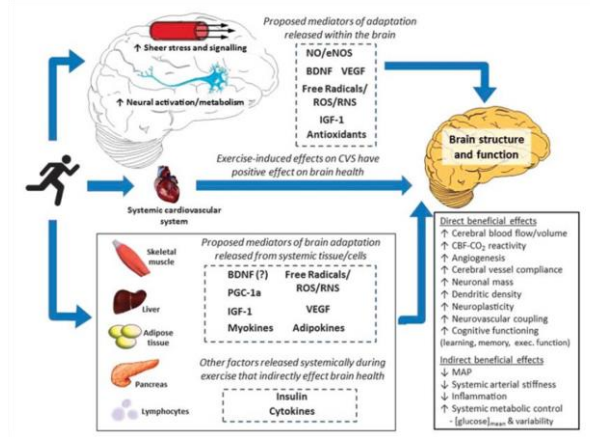
Physical Activity and Brain Health

Physical activity reduces the impacts of many risk factors for poor brain health whilst also creating a rich environment for positive brain adaptations

- **Reduces risk factors**
  - Diet
  - Cardiovascular disease
  - Cancer
  - Diabetes
  - History of depression
  - Head injury
  - Smoking
  - Low mental activity
- **Promotes neurotrophic environment**
  - Growth factors (e.g. BDNF)
  - Neurogenesis
  - Angiogenesis



1. Lucas, S. J., Cotter, J. D., Brassard, P., & Bailey, D. M. (2015). High-intensity interval exercise and cerebrovascular health: curiosity, cause, and consequence. *Journal of Cerebral Blood Flow & Metabolism, 35*(6), 902-911.

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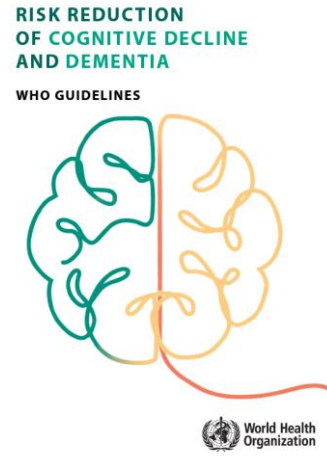
Guidelines for Cognitive Health

Physical activity interventions are recommended to adults with normal cognition to reduce the risk of cognitive decline

BUT, there is less certainty about the optimal dose of physical activity for brain health[2-3]



1. World Health Organization. Risk reduction of cognitive decline and dementia: WHO guidelines. 2019
2. Erickson KI, et al. Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines. *Med Sci Sport Exer*. 2019
3. Northey JM, et al. Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med.* 2018

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Is Moderate Intensity Key?

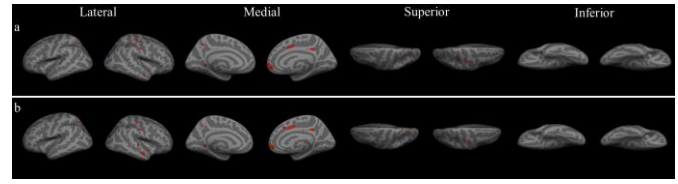
Older adults who accumulated more moderate intensity physical activity each week had greater brain volume

- **This translated to an ~2% greater brain matter volume for the average duration of moderate intensity PA per week**

BUT, no effects for light and vigorous intensity PA

Objectively measured physical activity is associated with dorsolateral prefrontal cortex volume in older adults

Joseph M. Northey [a, b, c, *], Ben Rattray [a, b, c], Kate L. Pumpa [a, b], Disa J. Pryor [b], Mark A. Fraser [c], Marnie E. Shaw [d], Kaarin J. Anstey [e, a, f], Nicolas Cherbuin [a]



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Is Moderate Intensity Key?

Meta-analysis showed exercise interventions improved cognitive function in adults over 50 years. But, dose seemed to be important particularly intensity[1]

Table 1 Results of moderator analysis

Moderator	No. of effect sizes	Estimate Mean (95% CI)	Q statistic	Omnibus test of moderators
Exercise moderators				
Mode			Q_{318}=781.68; p<0.01	Q_{4}=39.53; p<0.01
Aerobic	153	0.24 (0.10 to 0.37)		
Resistance training	80	0.29 (0.13 to 0.44)		
Multicomponent training	47	0.33 (0.14 to 0.53)		
Tai chi	25	0.52 (0.32 to 0.71)		
Yoga	28	0.13 (−0.10 to 0.36)		
Duration			Q_{318}=789.68; p<0.01	Q_{3}=27.83; p<0.01
Short (≤45 min)	36	0.09 (−0.28 to 0.46)		
Medium (>45 to ≤60 min)	263	0.31 (0.16 to 0.46)		
Long (>60 min)	24	0.33 (−0.04 to 0.65)		
Frequency			Q_{320}=804.58; p<0.01	Q_{3}=24.12; p<0.01
Low (≤2)	92	0.32 (0.13 to 0.52)		
Medium (3–4)	229	0.24 (0.07 to 0.40)		
High (5—7)	13	0.69 (0.10 to 1.28)		
Intensity			Q_{322}=264.61; p<0.01	Q_{3}=13.55; p<0.01
Low	71	0.10 (−0.02 to 0.23)		
Moderate	57	0.17 (0.03 to 0.33)		
High	83	0.16 (0.04 to 0.27)		
Length			Q_{320}=807.48 P<0.01	Q_{3}=23.32; p<0.01
Short (4–12 weeks)	78	0.31 (0.09 to 0.54)		
Medium (13–26 weeks)	170	0.28 (0.10 to 0.47)		
Long (>26 weeks)	86	0.27 (0.03 to 0.52)		

1. Northey JM, Cherbuin N, Pumpa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. Br J Sports Med. 2018;52:154-60.

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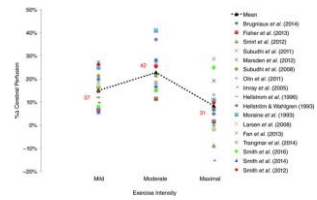
Mechanistic Support

So, what is it about moderate intensity physical activity?

Cerebral blood flow also displays an inverted U response to exercise intensity[1]

- Increased blood flow increases shear stress (great for vascular health)
- Carries circulating growth factors to active areas
  - Blood flow may be important for release of these growth factors[2]



Brain derived neurotrophic factor (BDNF)[3]

- Brain Derived Neurotrophic Factor (BDNF) is a neurotrophin found both centrally (within the brain) and peripherally (most abundantly circulating in blood)
- Essential for neurogenesis in the hippocampus (i.e. new cells in the brain)
- Blocking BDNF in animals negates the cognitive benefits of physical activity
- Current theory is that repeated exposure to exercise-induced transient increases in circulating BDNF lead to positive brain adaptations

1. Smith & Ainslie (2017). Regulation of cerebral blood flow and metabolism during exercise. Experimental Physiology. 102(11): 1356-1371.
2. Marie et al (2018). Brain-derived neurotrophic factor secreted by the cerebral endothelium: A new actor of brain function? JCBFM. 38(6): 935-949.
3. Walsh EI, Smith L, Northey J, Rattray B, Cherbuin N. Towards an understanding of the physical activity-BDNF-cognition triumvirate: a review of associations and dosage. Ageing Research Reviews. 2020:101044.

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Implications

The physical activity dose should provide a sufficient physiological stimulus and exposure time

Potential scenario is that moderate intensity is sufficient to optimise blood flow and release of growth factors. It is also able to be performed for a longer duration which means you get more exposure to these benefits i.e.

- More cerebral blood flow
- More BDNF release
- Sustained exposure to circulating BDNF to the brain

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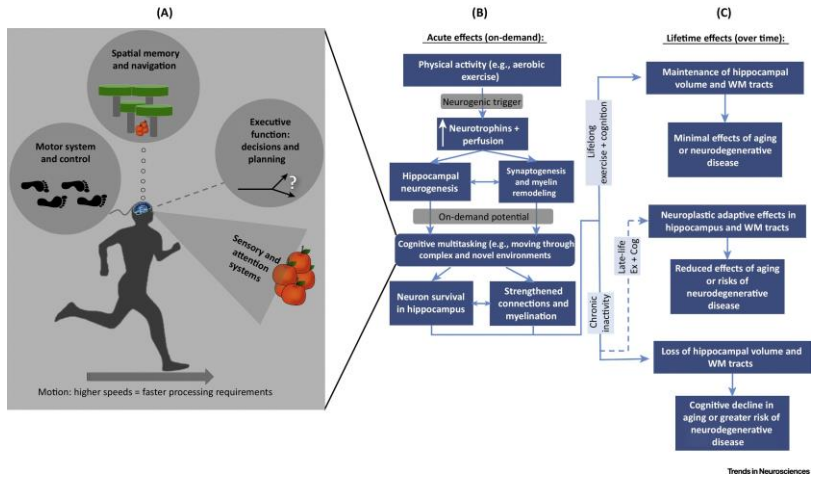
Concurrent Cognitive Tasks



"…senior orienteering may represent an ideal model in studies of healthy aging."[2]

1. Raichlen & Alexander (2017). Adaptive Capacity: An Evolutionary Neuroscience Model Linking Exercise, Cognition, & Brain Health. Trends in Neurosciences. 40(7): 408-421.
2. Östlund-Lagerström et al. (2015). Senior orienteering athletes as a model of healthy aging: a mixed-method approach. BMC Geriatr 15: 76.

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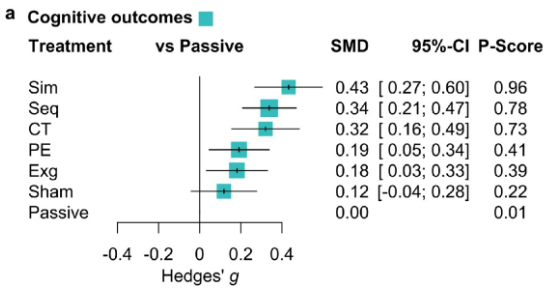
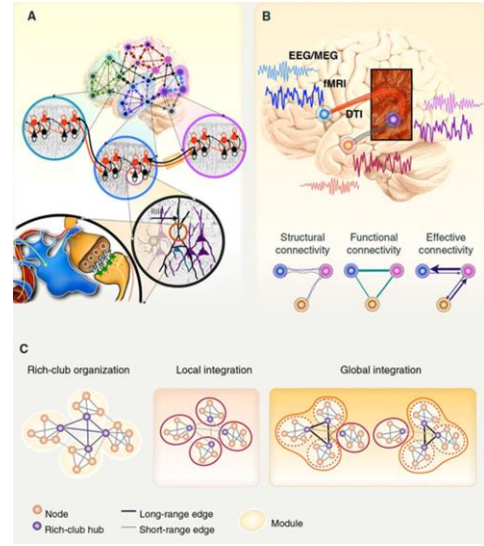
Combined PA and Cog Interventions





Above: Gavelin et al., (2021). Combined physical and cognitive training for older adults with and without cognitive impairment: A systematic review and network meta-analysis of randomized controlled trials. Ageing Research Reviews. 66: 101232.
Right: Park & Friston (2013). Structural and functional brain networks: from connections to cognition. Science. 342: 1238411

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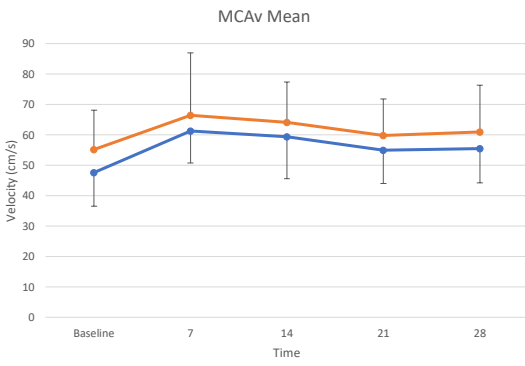
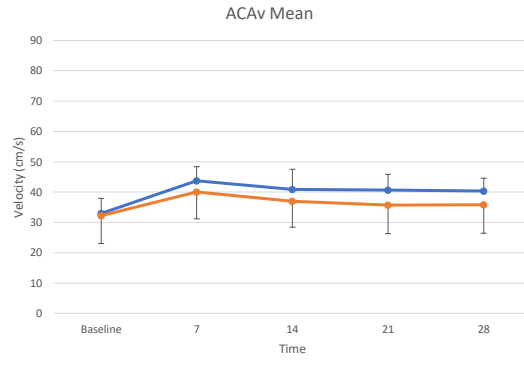
Combined PA and Cog Interventions



Exercise Only: (b = 5.56 cm/s; 95% CI 1.68 to 9.43)



Exercise Only: (b = -3.58 cm/s; 95% CI -6.15 to -1.01)

KEY:

Exercise-Only

Exercise-Cognitive

From UC Honours student – Vicki McCarthy (2021). The effect of a concurrent cognitive task on the cerebral blood flow response to exercise in older adults

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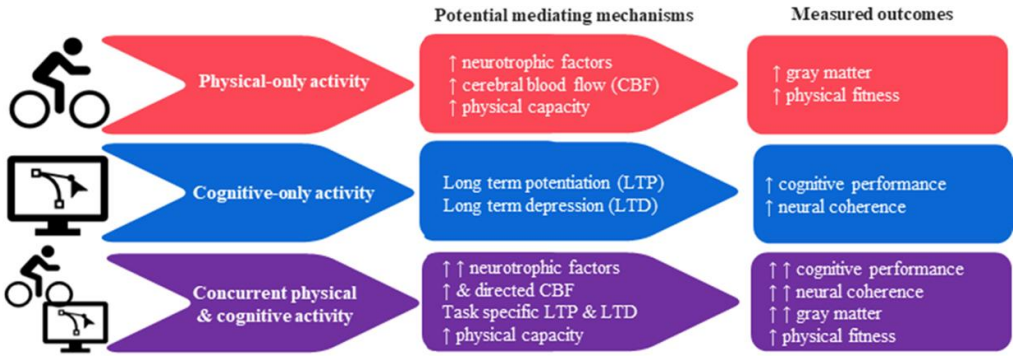
Combined PA and Cog Interventions



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Implications

To maximise benefits, consider the optimal dose of physical activity around cognitive challenges

Physical activity with cognitive challenges may be the most potent stimulus, though the desired outcome may impact what the cognitive challenge is

Examples may include:

- Learning new movement patterns (e.g., learning a new dance)
- Movement-based computer games
- Specific cognitive tasks during physical activity

Cognitive challenges following physical activity may also provide additional benefit

Taking advantage of the rich neurotrophic environment provided by physical activity when the richer environment is short-lived (maybe 30 min) and if physical activity is too fatiguing then may not support benefit

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How does this relate to MS?

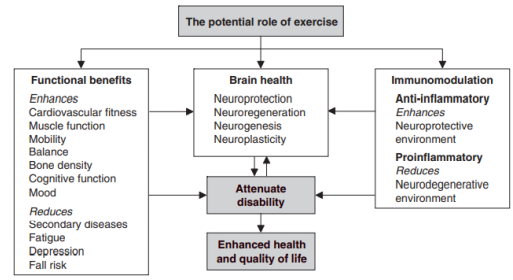
Mechanisms of action have the potential to benefit cognitive function from the early stages of MS[1]

Current evidence from cross-sectional research is promising, however randomised controlled trials are <u>emerging</u> and currently unclear[2]

- Poor methodological quality is noted e.g. insufficient intensity, frequency, and exercise testing[2]

Promote the benefits of physical activity to reduce the symptoms MS and manage comorbidities[3]

Recommend the utilisation of Accredited Exercise Physiologists who are trained in clinical exercise prescription



https://exerciseright.com.au/multiple-sclerosis/

1. White LJ, Castellano V. Exercise and brain health—implications for multiple sclerosis. Sports medicine. 2008 Feb;38(2):91-100.
2. Morrison JD, Mayer L. Physical activity and cognitive function in adults with multiple sclerosis: an integrative review. Disability and rehabilitation. 2017 Sep 11;39(19):1909-20.
3. Kalb R, Brown TR, Coote S, Costello K, Dalgas U, Garmon E, Giesser B, Halper J, Karpatkin H, Keller J, Ng AV. Exercise and lifestyle physical activity recommendations for people with multiple sclerosis throughout the disease course. Multiple Sclerosis Journal. 2020 Oct;26(12):1459-69.

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