How does exercise benefit people at risk for dementia?

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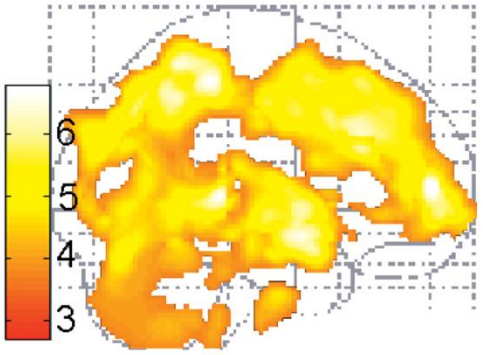
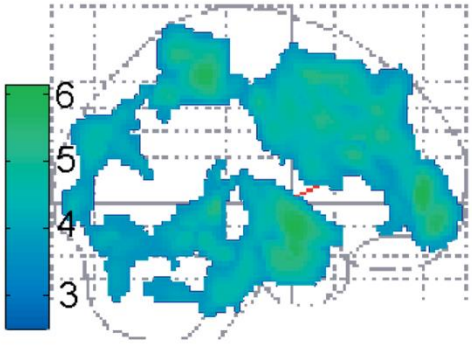
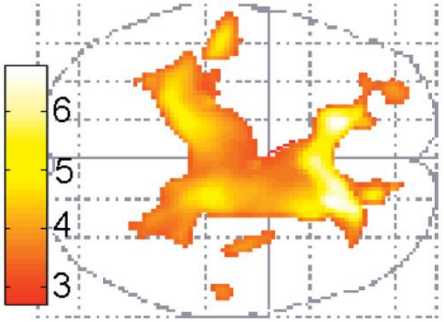
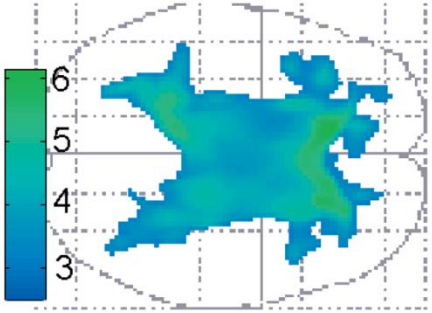
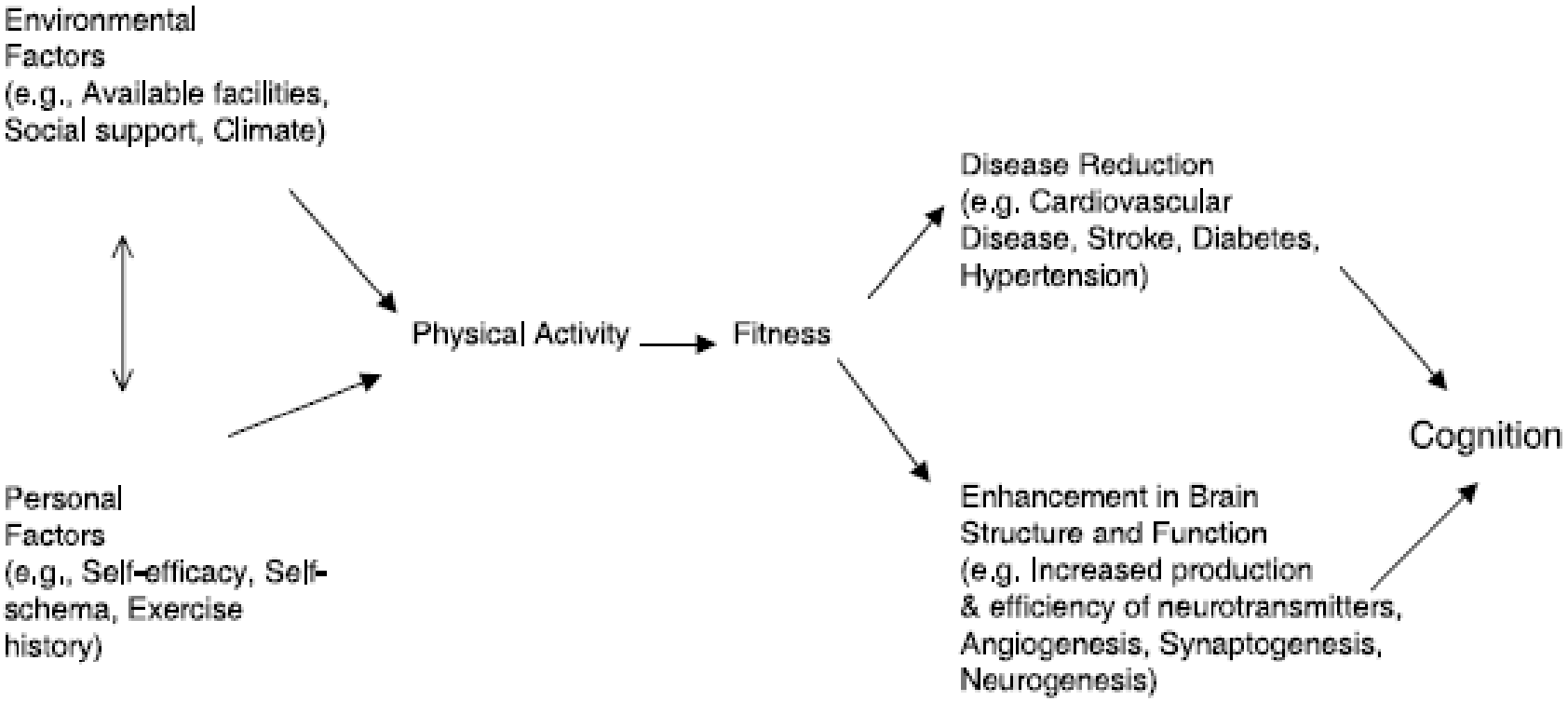
- Brain processes that show greatest rates of decline remain highly plastic (Colcombe 2004)
- Exercise and physical fitness can impact both brain structure and brain function

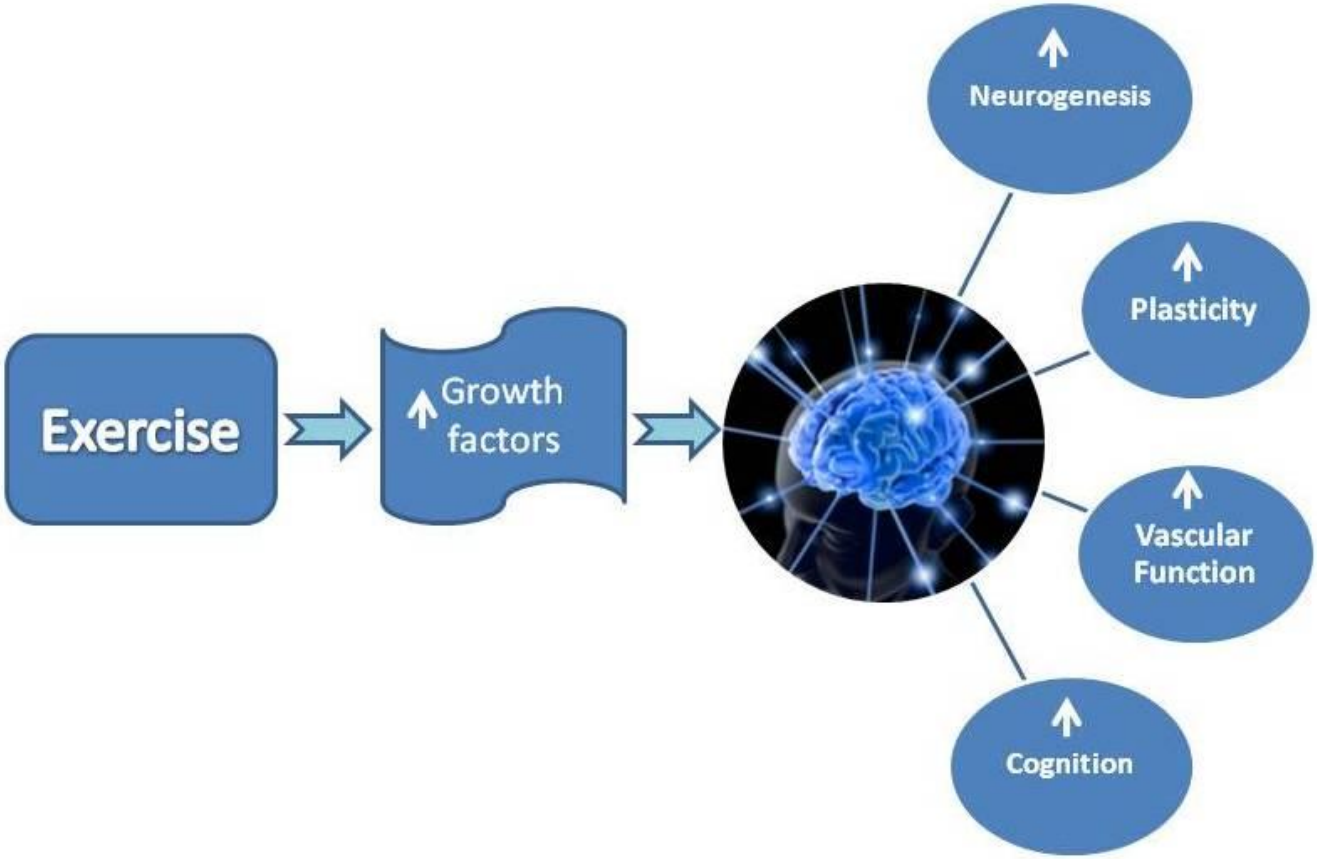
	Age-Related Declines	Amelioration by Fitness
Gray Matter		
	Map of gray matter showing regions that shrink with age. Clusters with largest peaks are evident in the frontal/prefrontal cortex (BAs 46/9,6), parietal cortex (BAs 40,21,5) and temporal cortex (BAs 21,38).	Map of gray matter revealing regions that show preservation with cardiovascular fitness. Clusters with largest peaks are in frontal/prefrontal cortex (BAs 46,9,6), parietal cortex (BA 40) and temporal cortex (BAs 21,22,38).
White Matter		
	Map of white matter showing greatest age-related changes in the anterior white matter tracts and the more posterior tracts in the parietal lobes.	Map of white matter showing regions of relative preservation from age-related decline with fitness. Most regions that show age-related decline also show sparing with fitness.

Colcombe et al. J Gerontol: Medical Sciences, 2003; 58a(2): 176-80

Theoretical Model of relationship between physical activity and cognition



McAuley et al. Brain, Behavior, and Immunity, 2004; 18:214-220.


Exercise
↑ Growth factors
↑ Neurogenesis
↑ Plasticity
↑ Vascular Function
↑ Cognition

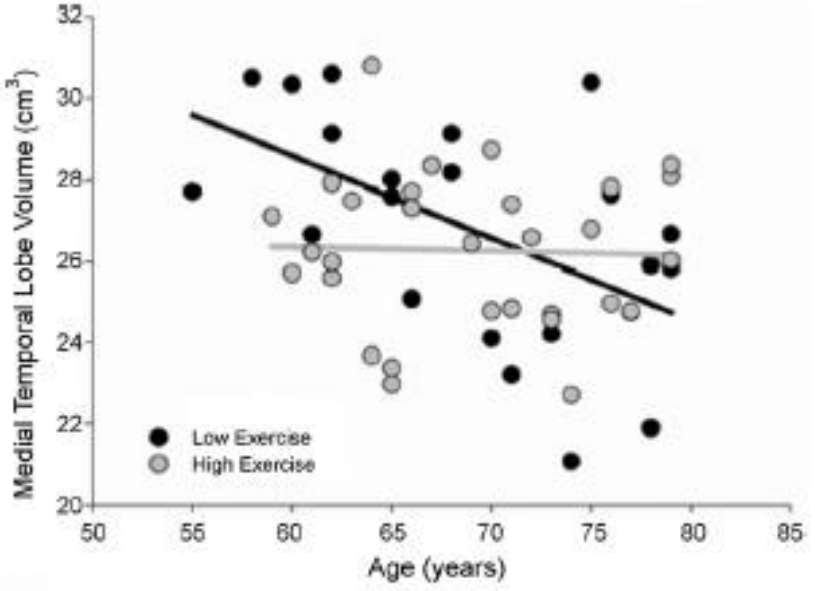
Brain structure:

- Maintaining cardiorespiratory fitness may protect the brain from tissue loss associated with Alzheimer's disease(Honea, 2009)

Physical activity

- Brain tissue loss in older adults who engaged in less than the average physical activity

- No brain tissue loss in older adults who engaged in more than the average

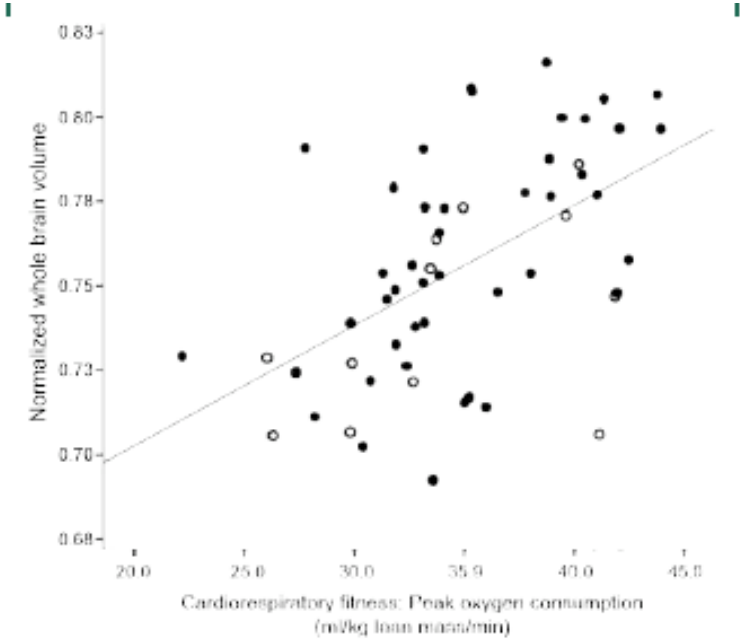


Bugg JM, Head D. Exercise moderates age-related brain atrophy of the medial temporal lobe. Neurobiology of aging, 2009.

Whole Brain Volume & Cardiorespiratory Fitness (VO_2^{peak})

Dementia: Very mild & mild

Brain Volume

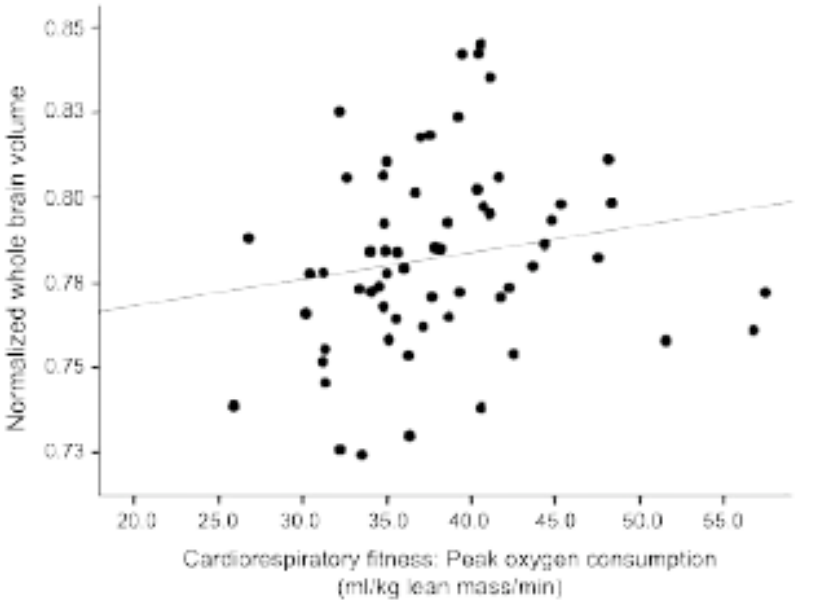


VO_2^{peak}

r = 0.54, p < 0.001

No Dementia

Brain Volume



VO_2^{peak}

r = 0.18, p=0.17

* adjusted for age

(Burns, et al., *Neurology*, 2008,v. 71)

- Aerobic exercise training program can increase the size of the hippocampus, and improve memory.
  - Walking for about 30 minutes at 50-75% of max HR 3 times per week

Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock l, et al. Exercise training increases hippocampus and improves memory. Proc Natl Acad Sci USA. 2011; 108: 3017-22.

- Brain function:
  - Compelling evidence that exercise improves functional connections between the hippocampus and other important regions of the brain
  - These “networks” tend to deactivate with age, but this deactivation process can be mediated by high levels of exercise and physical fitness
  - One 12-month trial demonstrated improved connectivity in older adults who performed an aerobic “walking” program

Voss MW, Prakash RS, Erickson KI, et al. Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. Frontiers in aging neuroscience, 2010.

Cognitive Function & Physical Activity
Cross sectional studies

Higher physical activity is associated with better cognitive performance:

- ✓Reasoning
- ✓Working memory
- ✓Reaction time
- ✓Accuracy
- ✓Executive function
- ✓Global cognitive function

Clarkson-Smith & Hartley (1989); Hillman et al., 2006; Bixby et al., (2007); Angevaren et al.,2007

Cognitive Function & Physical Activity: *Older women across the life course*

- *Physically active as teenagers:* Highest cognitive performance & lowest rates of cognitive impairment (CI).

- *Physically active 30, 50, or late life (inactive as teenagers):* 50% lower rate of late-life CI compared to women who remained inactive.

- *Physically active at any age:* Less likely to have CI.

Middleton et al., 2010

- Biceps curls
- Triceps extension
- Seated rowing
- Pull-down exercises
- Leg presses
- Hamstring curls
- Calf-raises
- Minisquats
- Minilunges
- Lunge walks

- 2 sets of 6-8 reps
- Increase in load when above completed with proper form and without discomfort

Liu-Ambrose T, Nagamatsu LS, Graf P, Beattie BL, Ashe MC, Handy TC. Resistance training and executive functions: a 12-month randomized controlled trial. Arch Intern Med. 2010; 170: 170-8

- In humans, resistance training improves executive function
  - reduced serum homocysteine and
  - increased concentrations of insulin-like growth factor I (IGF-I)

Liu-Ambrose T, Donaldson MG. Exercise and cognition in older adults: is there a role for resistance training programmes? Br J Sports Med 2009;43:25-27.

Relationship between cardiovascular risk and cognitive impairment

- Hypertension – risk factor for stroke
- Prior to clinical event has a more subtle impact on cognitive function
- Hypertension related to poorer performance
  - tests of attention
  - learning and memory
  - executive functions
  - visuospatial skills
  - psychomotor abilities
  - perceptual skills

Hypertension

- Reduced cerebral blood flow and metabolism, particularly in the frontal and temporal lobes and subcortical regions
- Reduced blood flow during memory tasks
- Damage to smaller blood vessels leads to white matter disease
- People with hypertension have more brain atrophy
- People who are medicated have less white matter disease than those who are not

Waldstein. Current Directions in Psychological Science, 2003; 12(1): 8-12

Hypertension

- Higher midlife blood pressure seems to be more strongly related to cognitive decline than concurrent blood pressure
- Systolic hypertension seems to be more risky than diastolic hypertension
- Antihypertensive therapy seems to have a strong protective effect, in fact people on hypertensive therapies for 12 years had a risk similar to normotensives

Grodstein. Alz and Dement, 2007; 3: S16-S22.

Dyslipidemia

- Higher HDL is associated with decreased risk and lower LDL is associated with increased risk.
- Supported by several large epidemiological studies

Diabetes

- Persons with diabetes decline in cognitive function 1.2-1.5 times faster than controls.
- OR for dementia is 1.6
- Hyperinsulinemia increases risk even in those who do not have overt diabetes

Inflammation

- Among high-functioning elders without cognitive impairment, those with metabolic syndrome and elevated inflammatory markers have an increased risk of developing cognitive impairment over four years. (RR 1.66)
- Serum markers (IL6 and CRP) are also prospectively related to decline in cognitive function

Yaffe et al. JAMA, 2004; 292(18): 2237-2242.
Yaffe et al. Neurology, 2003. 61(1):76-80.

Type 2 DM

Hypertension

Dyslipidemia

Inflammation

The good news

- Exercise recommendations for dementia and cognitive impairment are the same as for other chronic diseases such as diabetes, heart disease, and osteoarthritis.

Maintain a physically active lifestyle

- Exercise through the life span. Younger is better, but it's never too late!
- Focus should be on both regular physical activity and decreasing time spent in sedentary activities.
- Transgenerational programs may be an effective way to encourage physical activity.

Aerobic (endurance) activity

- Minimum of 30 minutes of moderate physical activity at least five days per week, OR
- Minimum of 20 minutes of vigorous physical activity at least three days per week.

- Relative to one's level of fitness
- Can be accrued in 10 minute bouts

- Moderate physical activity
  - 5-6 on a 10 point scale
  - Moderate increase in HR and breathing
- Vigorous physical activity
  - 7-8 on a 10 point scale
  - Marked increase in HR and breathing

Training Characteristics:

- Combined strength + aerobic showed greater improvement than aerobic alone.
- Long-term training showed the greatest improvement.
- Short bouts of ex (< 30 min) had little impact on cognitive function.

(normal aging, not cognitively impaired)

Colcombe and Kramer. Psychological Science, 2003: 14(2); 125-130.