Vancouver Coastal Health Research Institute

Djavad Mowafaghian CENTRE FOR BRAIN HEALTH

CENTRE for HIP Health and Mobility

Exercise for Healthy Aging

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COGMOB
Aging, Mobility, and Cognitive Neuroscience Lab

UBC a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA

Overview

Context

- Impaired cognitive function and mobility are "geriatric giants" that significantly increase morbidity and mortality
- Often co-exist and thus, likely share common pathophysiology
  - Cerebral small vessel disease
  - Amyloid

Cerebral Small Vessel Disease

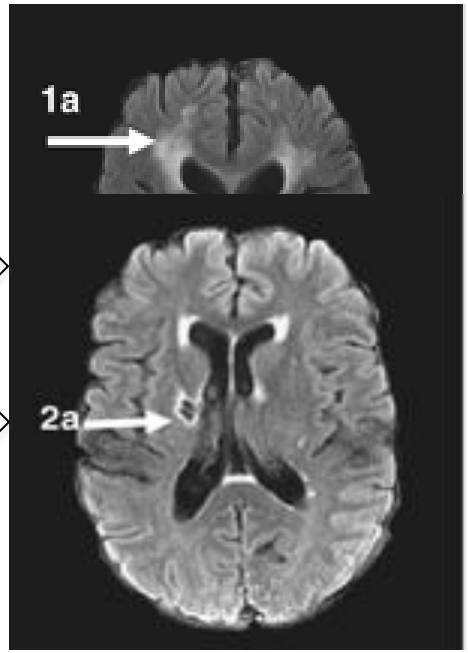
Risk factors

- Age
- Hypertension
- Diabetes
- Dyslipidemia

Small Vessel Disease

White Matter Lesions

Lacunes

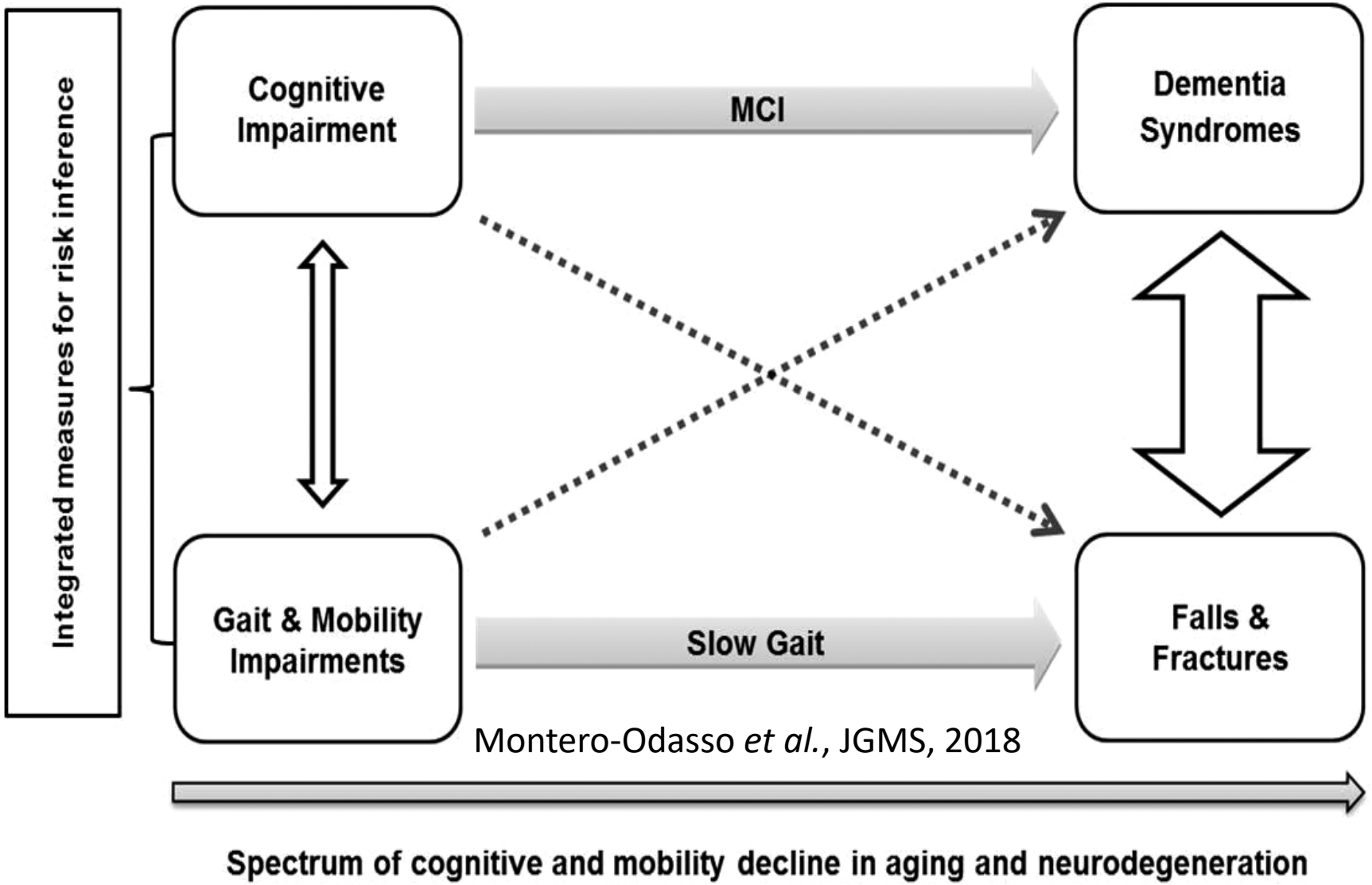


These “silent” lesions are associated with increased risk of stroke, slow gait, falls, and dementia.

Cerebral Amyloid-Beta

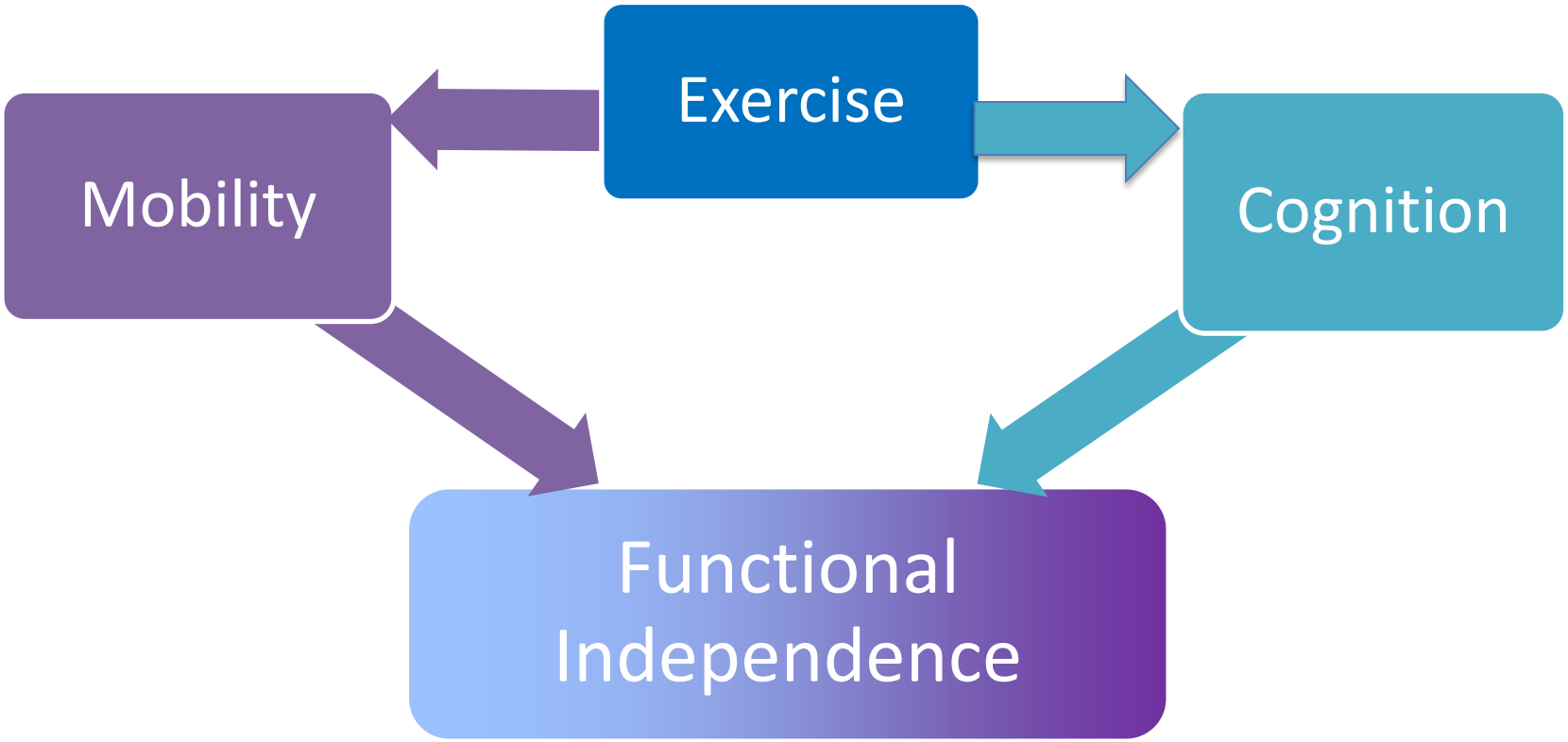
- Cerebral Aβ (PiB-PET) in older adults without dementia is associated with:
  - Falls over 12 months
    - » Stark *et al.,* Neurology, 2013
  - Slow gait
    - » Nadkami *et al.*, JAMA Neurology, 2017
  - Age-related mobility decline
    - Decreased cadence and increased double support time
      - » Wennberg *et al.*, J of Geron, 2018

Interplay: Cognition & Mobility

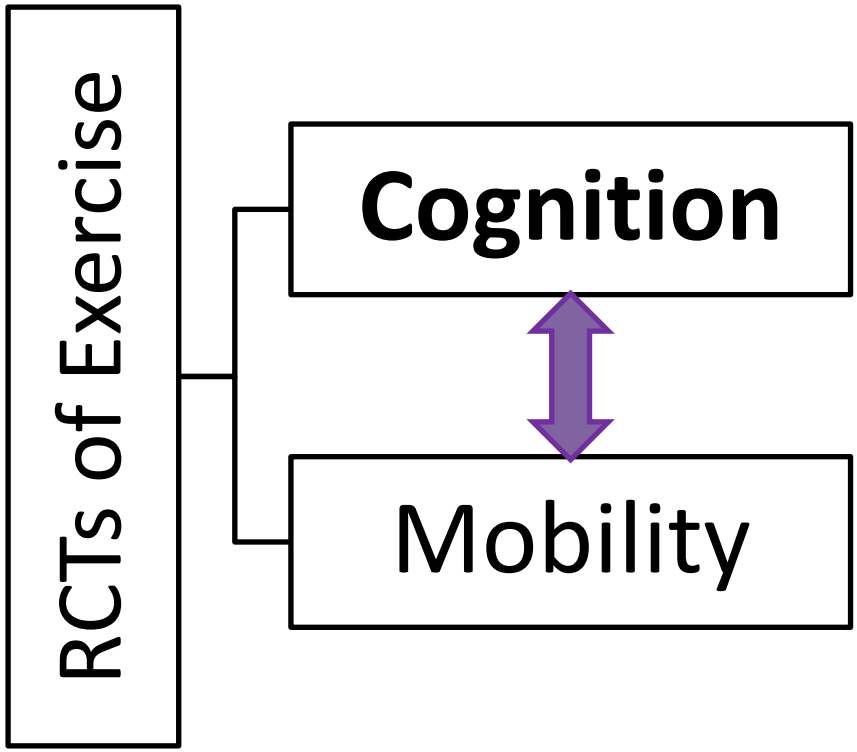


Montero-Odasso *et al.*, JGMS, 2018

Context




Context
Studies
Conclusions


RCTs of Exercise
Cognition
Mobility

Global Council on Brain Health Releases Consensus Report on Exercise and Brain Health

Research shows exercise causes positive changes in brain structure and function and lowers risk of cognitive decline.

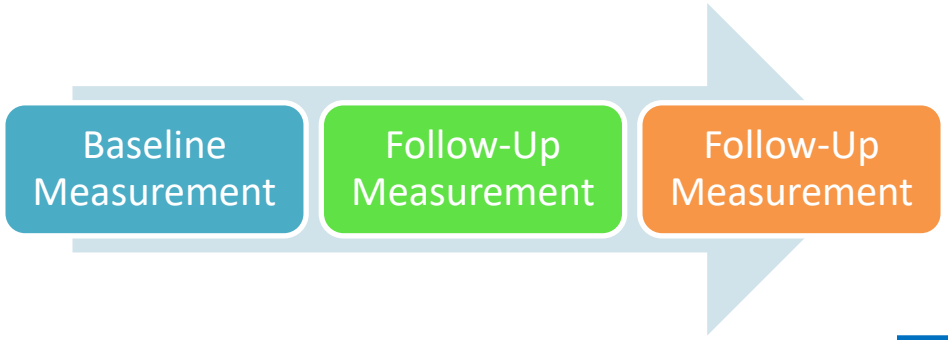
AARP®
Real Possibilities

NEWS PROVIDED BY
AARP →
Jul 21, 2016, 08:00 ET

GCBH experts agree that brain health is positively affected by physical activity. Purposeful exercise is proven to benefit brain structure and functioning, while an active lifestyle is proven to lower risk of cognitive decline.

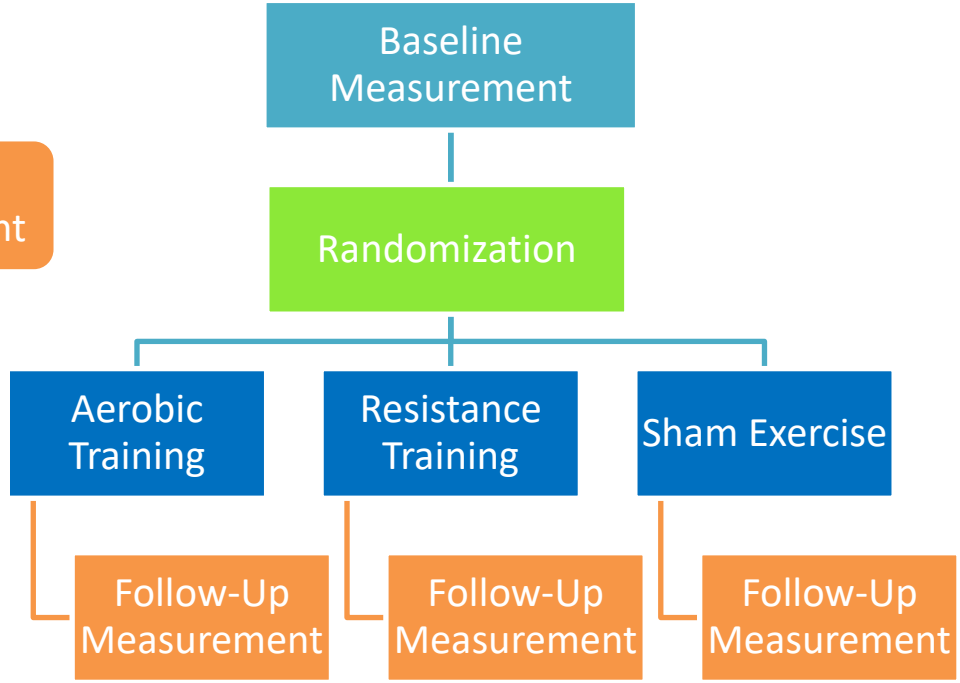
Cohort

- No prescribed treatment/intervention
- **Physical activity level**
  - Questionnaires
  - Accelerometry data

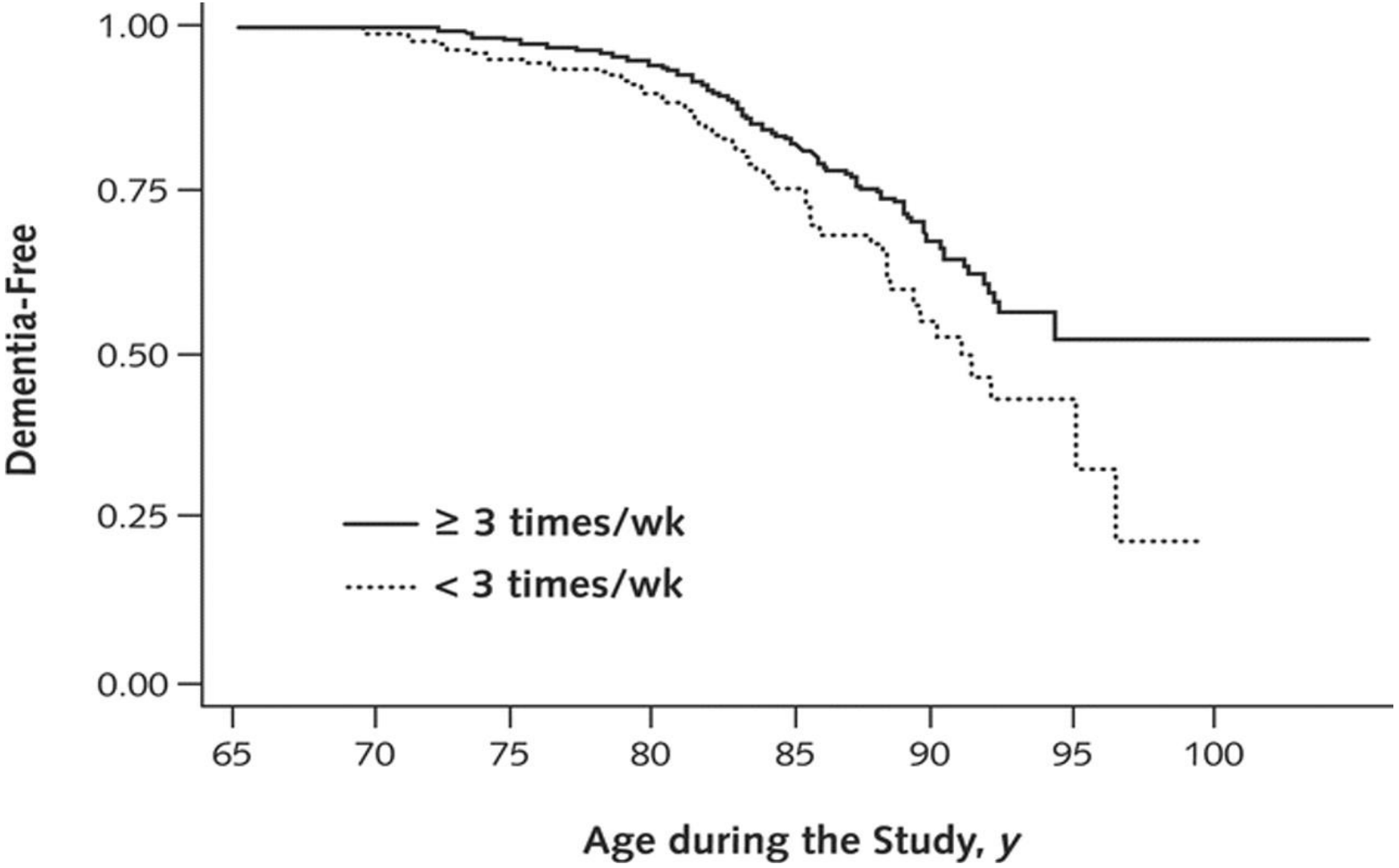


Randomized Controlled Trials

- Treatments/interventions are randomly prescribed
- **Purposeful exercise**



Physical Activity & Dementia Risk



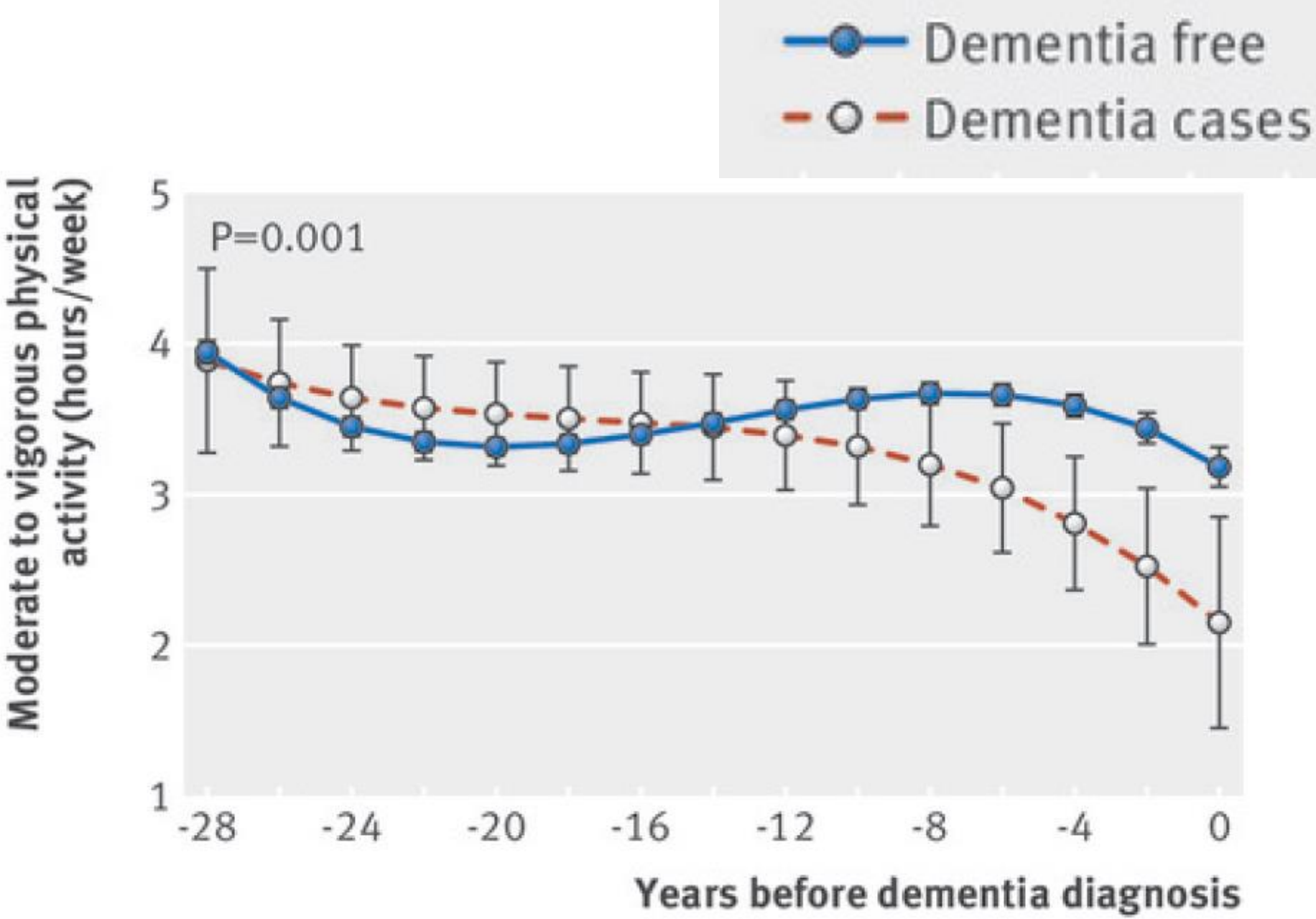
Larson *et al.*, Annals of Internal Medicine, 2006

Physical activity, cognitive decline, and risk of dementia: 28 year follow-up of Whitehall II cohort study

Séverine Sabia *research associate*[1 2], Aline Dugravot *statistician*[1], Jean-François Dartigues *professor*[3], Jessica Abell *research associate*[1 2], Alexis Elbaz *research professor*[1], Mika Kivimäki *professor*[2], Archana Singh-Manoux *research professor*[1 2]

[1]Centre for Research in Epidemiology and Population Health, INSERM U1018, Université Paris-Saclay, Hôpital Paul Brousse, Paris, France; [2]Department of Epidemiology and Public Health, University College London, London, UK; [3]INSERM U1219, University of Bordeaux, Bordeaux, France

Results — Mixed effects models showed no association between physical activity and subsequent 15 year cognitive decline. Similarly, Cox regression showed no association between physical activity and risk of dementia over an average 27 year follow-up (hazard ratio in the "recommended" physical activity category 1.00, 95% confidence interval 0.80 to 1.24). For trajectories of hours/week of total, mild, and moderate to vigorous physical activity in people with dementia compared with those without dementia (all others), no differences were observed between 28 and 10 years before diagnosis of dementia. However, physical activity in people with dementia began to decline up to nine years before diagnosis (difference in moderate to vigorous physical activity −0.39 hours/week; P=0.05), and the difference became more pronounced (−1.03 hours/week; P=0.005) at diagnosis.



BMJ 2017;357:j2709 doi: 10.1136/bmj.j2709 (Published 22 June 2017)

Physical activity, cognitive decline, and risk of dementia: 28 year follow-up of Whitehall II cohort study


OPEN ACCESS

Séverine Sabia *research associate*[1 2], Aline Dugravot *statistician*[1], Jean-François Dartigues *professor*[3], Jessica Abell *research associate*[1 2], Alexis Elbaz *research professor*[1], Mika Kivimäki *professor*[2], Archana Singh-Manoux *research professor*[1 2]

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- Previous findings showing a lower risk of dementia in physically active people may be attributable to reverse causation – that is, due to a decline in physical activity levels in the preclinical phase of dementia.

BMJ 2017;357:j2709 doi: 10.1136/bmj.j2709 (Published 22 June 2017)

Cohort

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- **Physical activity level**
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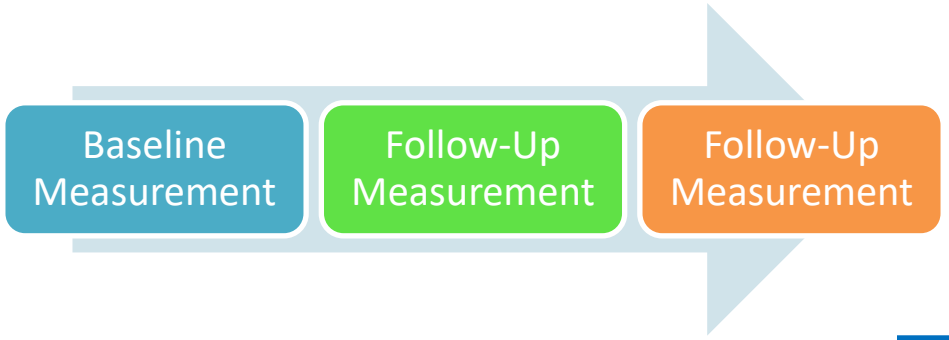
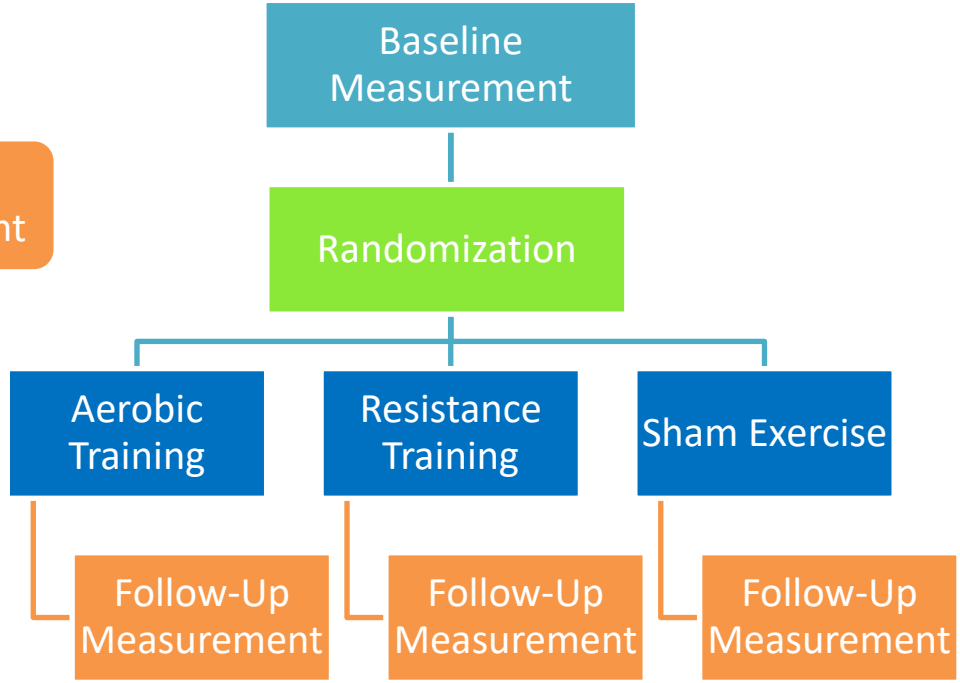


Randomized Controlled Trials

- Treatments/interventions are randomly prescribed
- **Purposeful exercise**



Exercise is Medicine

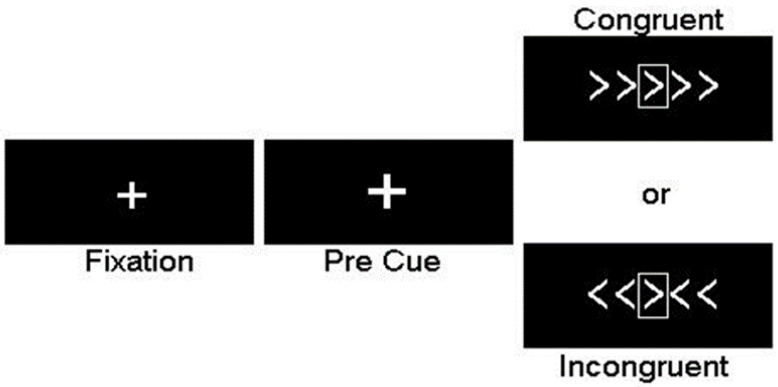
- Exercise
  - Subcategory of PA
- Types of Exercise
  - **Aerobic Training**
  - **Resistance Training**
  - Anaerobic Training
  - Balance/Agility Training
  - Multimodal
  - Others: Yoga, Tai Chi, dance

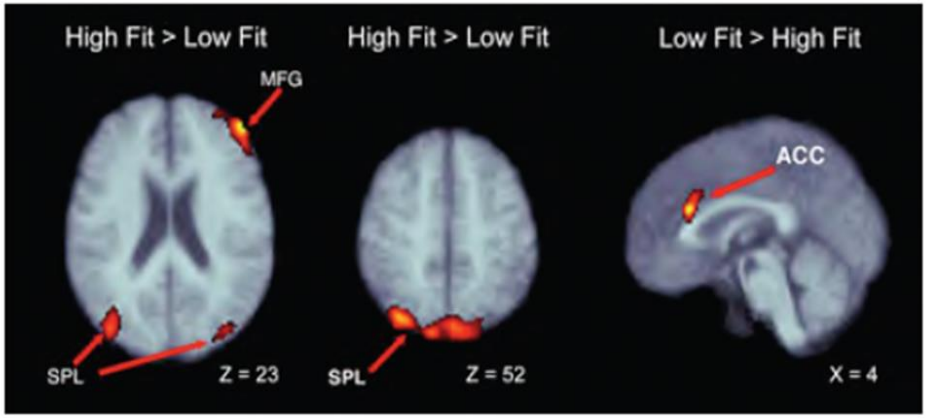
Domains of Cognition

- Hippocampal-Dependent **Memory**
  - Impairment common in dementia
  - Impairment associated with conversion from mild cognitive impairment (MCI) to AD
- **Executive Functions**
  - Planning, decision making, multi-tasking
  - Sensitive to aging effects
  - Impairment common in dementia

Aerobic Training Improves Executive Functions and Associated Functional Plasticity

- A 6-month, 3x/week (moderate-intensity) walking program improved:





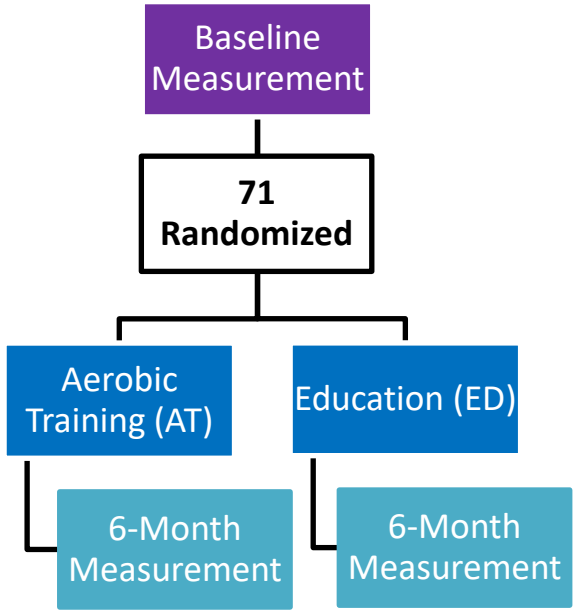
- Selective attention and response inhibition (Ericksen Flanker Task)
  - » Colcombe *et al.*, PNAS, 2004
- Functional plasticity associated with Flanker Task performance
- Neural efficiency

Aerobic Training Improves Memory and Increases Hippocampal Volume

- A 12-month, 3x/week (moderate-intensity) walking program improved/increased:
  - Cognitive performance of spatial memory
  - Hippocampus volume by 2%
    - Reversing age-related loss in volume by 1-2 years
      - » Erickson *et al.*, PNAS, 2011

Aerobic Training and Mild VCI*

- A 6-month, 3x/week (moderate-intensity) walking program improved/increased:
  - Memory performance (ADAS-Cog)
  - Neural efficiency (Flanker Task)
    - » Liu-Ambrose *et al.*, Neurology, 2016
    - » Hsu *et al.*, BJSM, 2017

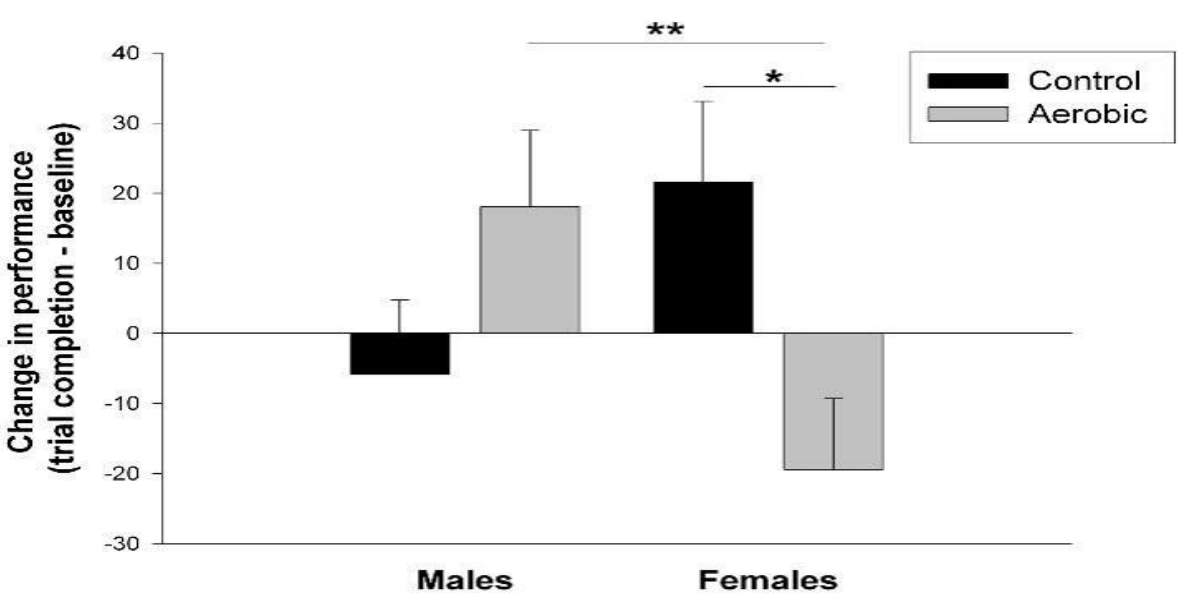


* VCI = Vascular Cognitive Impairment
  - Neuroimaging evidence of cerebral small vessel disease
  - MoCA < 26/30
  - No impairment in iADLs

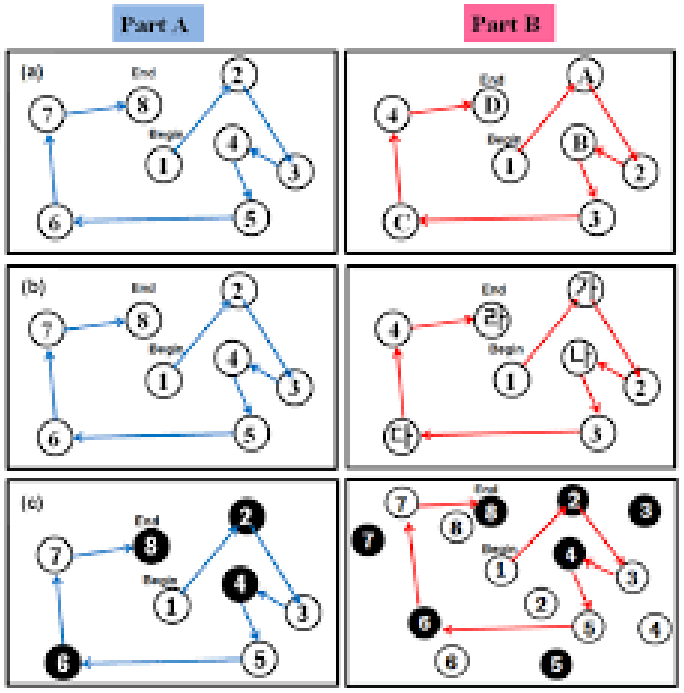
HEART & STROKE FOUNDATION

Heart&Stroke

Aerobic Training may be Particularly Beneficial for Females

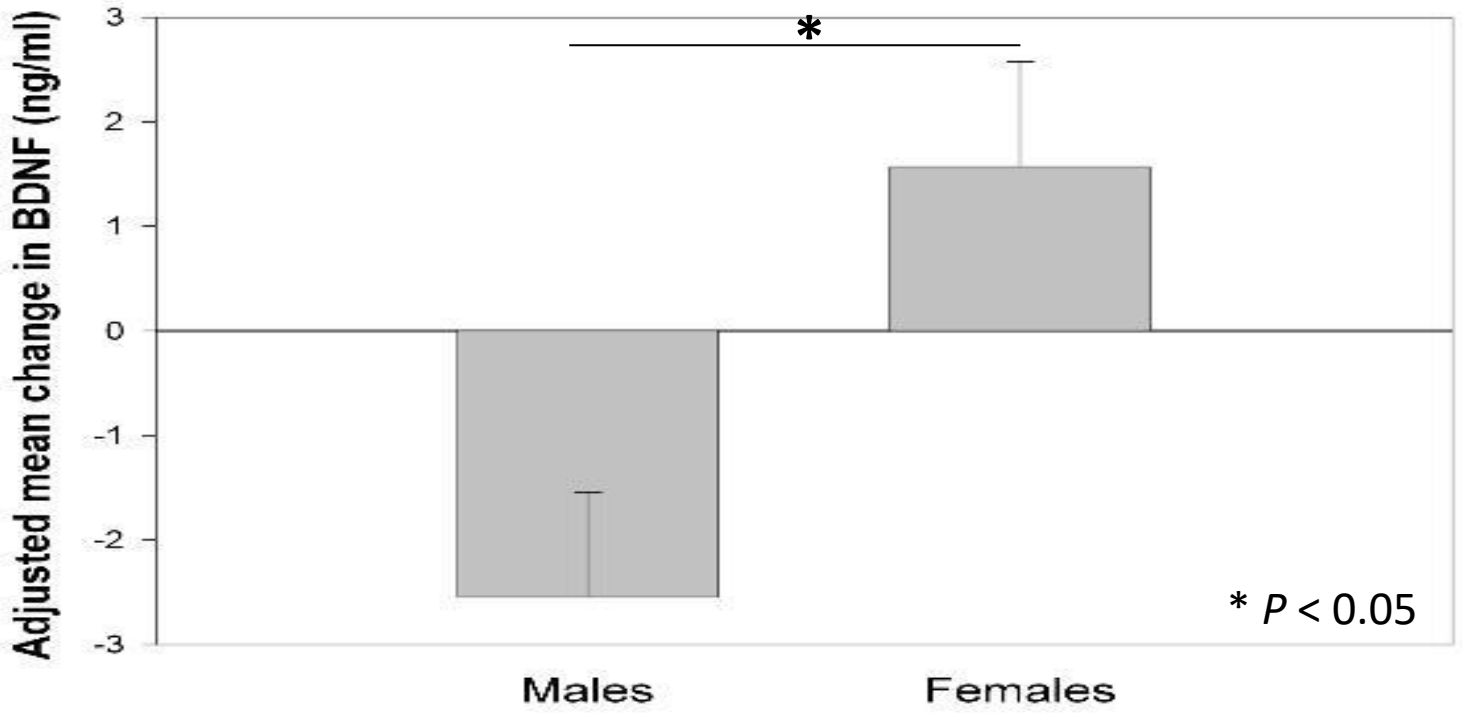


Barha *et al.*, JAD, 2017



Trail Making B-A

Aerobic Training Promotes Circulating BDNF Levels (in Females)



BDNF=brain derived neurotrophic factor

Barha *et al.*, JAD, 2017

What about **resistance training**?

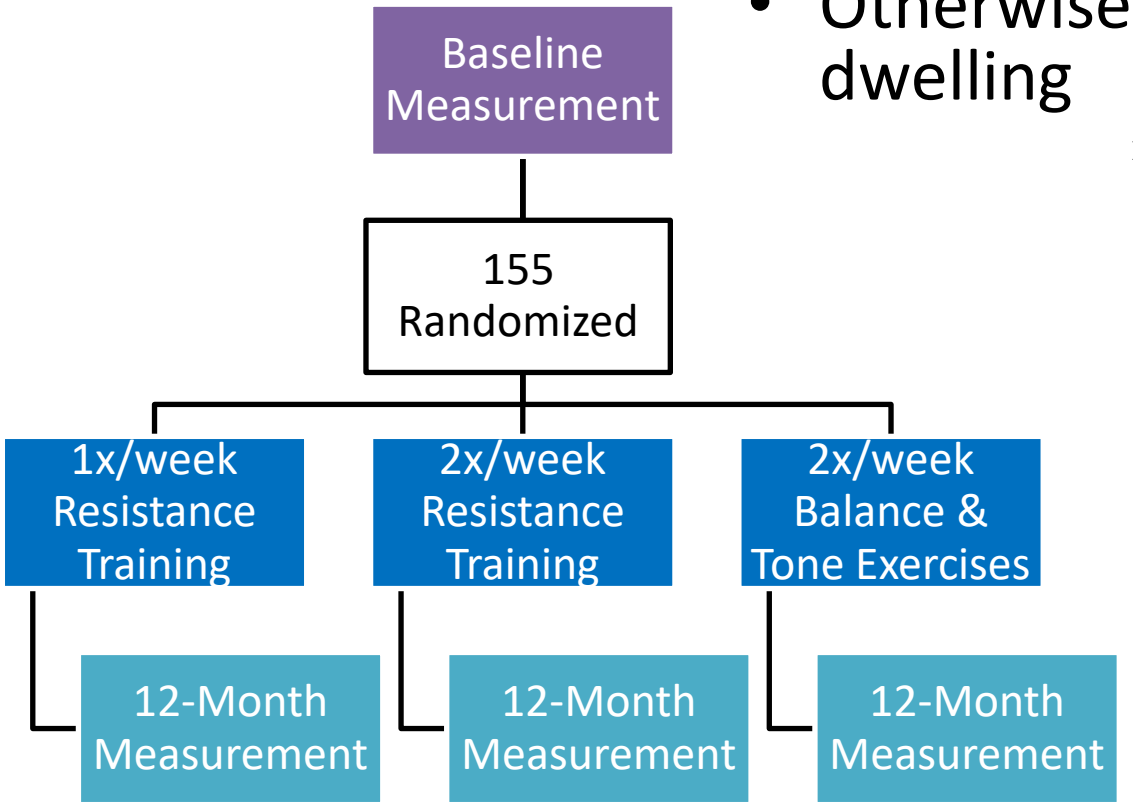
Resistance Training for Brain Health

Liu-Ambrose *et al.*, 2010 & 2011
Nagamatsu *et al.*, 2012 & 2013
Bolandzadeh *et al.*, 2015

Resistance Training for Brain Health

- Women aged 65 to 75 years
- Otherwise healthy & community-dwelling

» Liu-Ambrose *et al.*, 2010 & 2011



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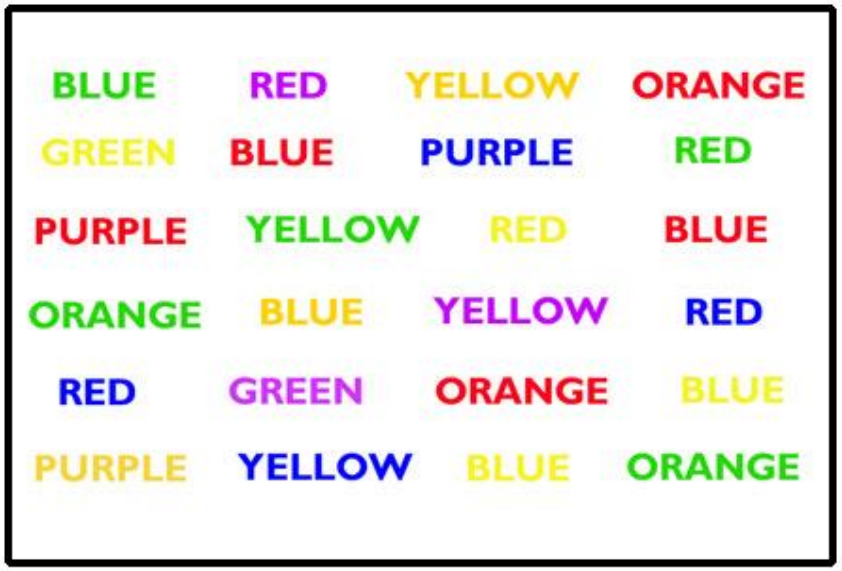
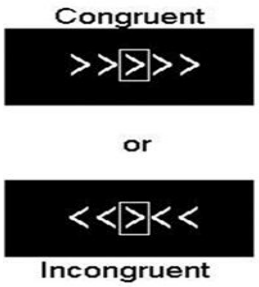
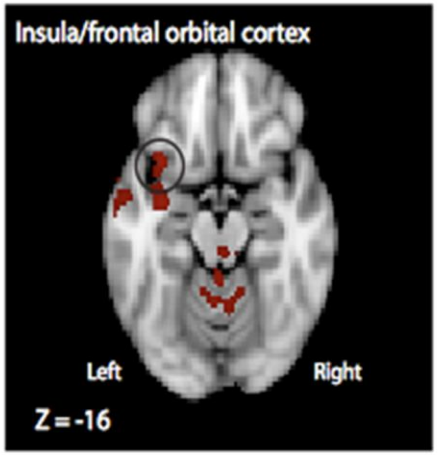
Resistance Training Improves Executive Functions and Functional Plasticity

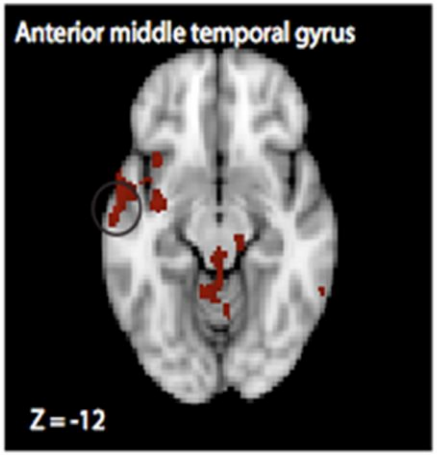
- Lifting weights 1x/week or 2x/week significantly improved executive functions.



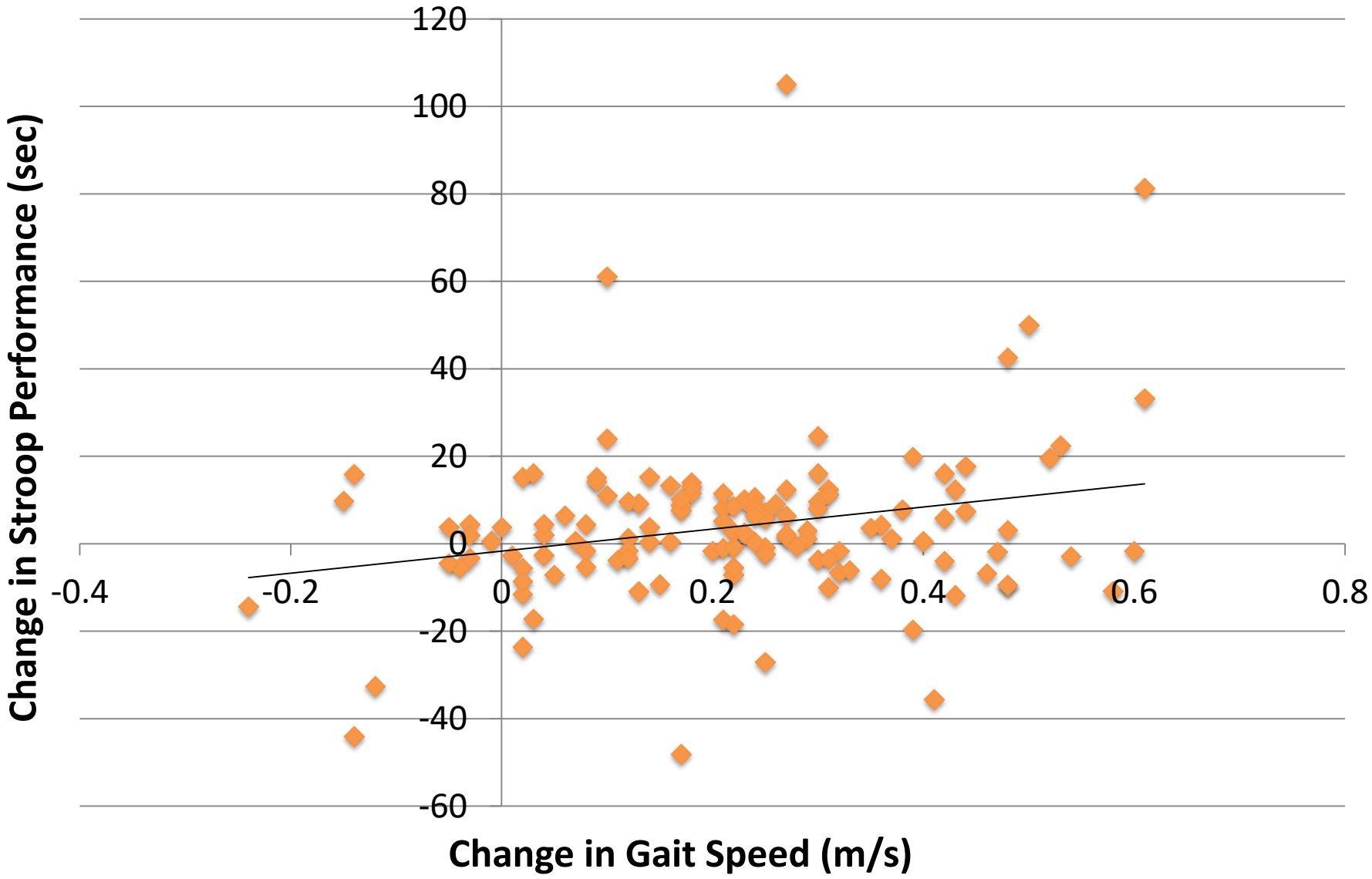
- Lifting weights 2x/week induced functional plasticity during the Flanker task







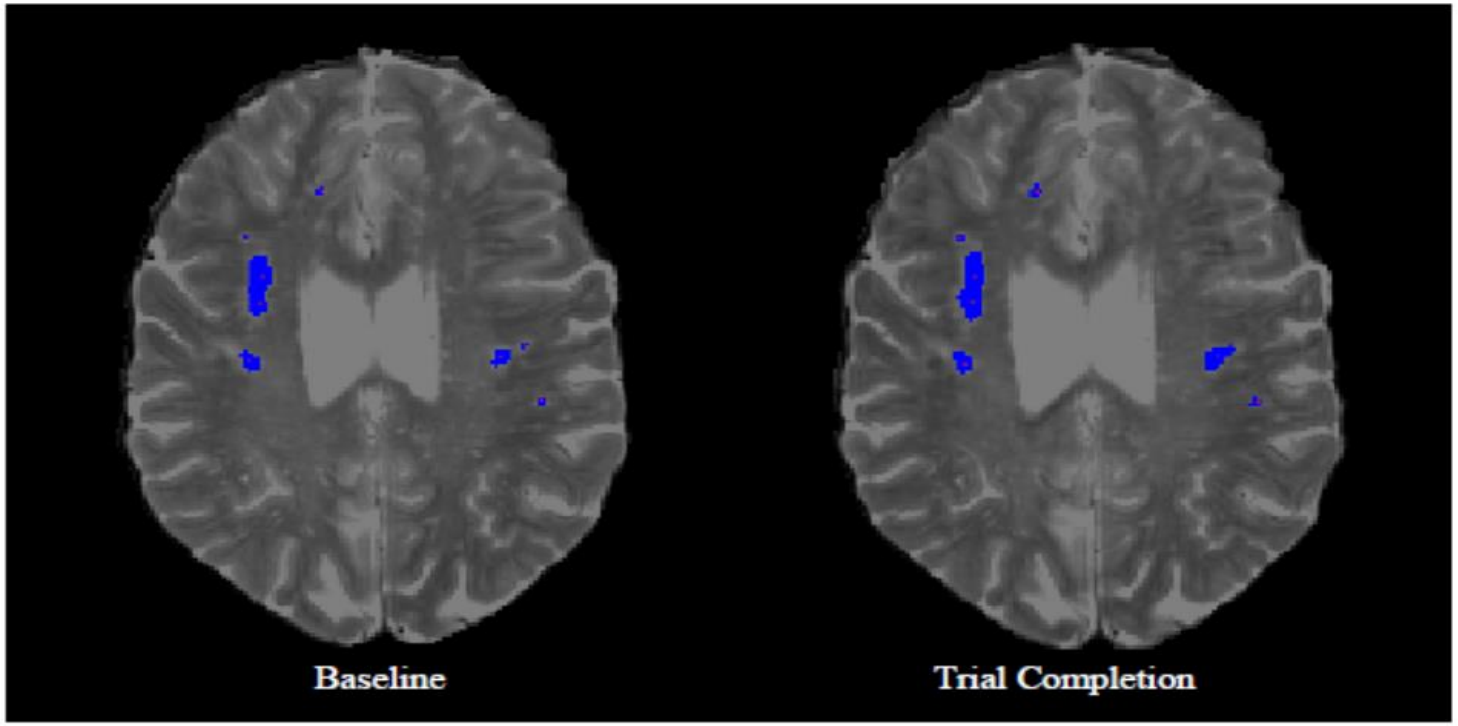
Improved cognitive performance significantly associated with increased gait speed (r=0.24; p<0.01).



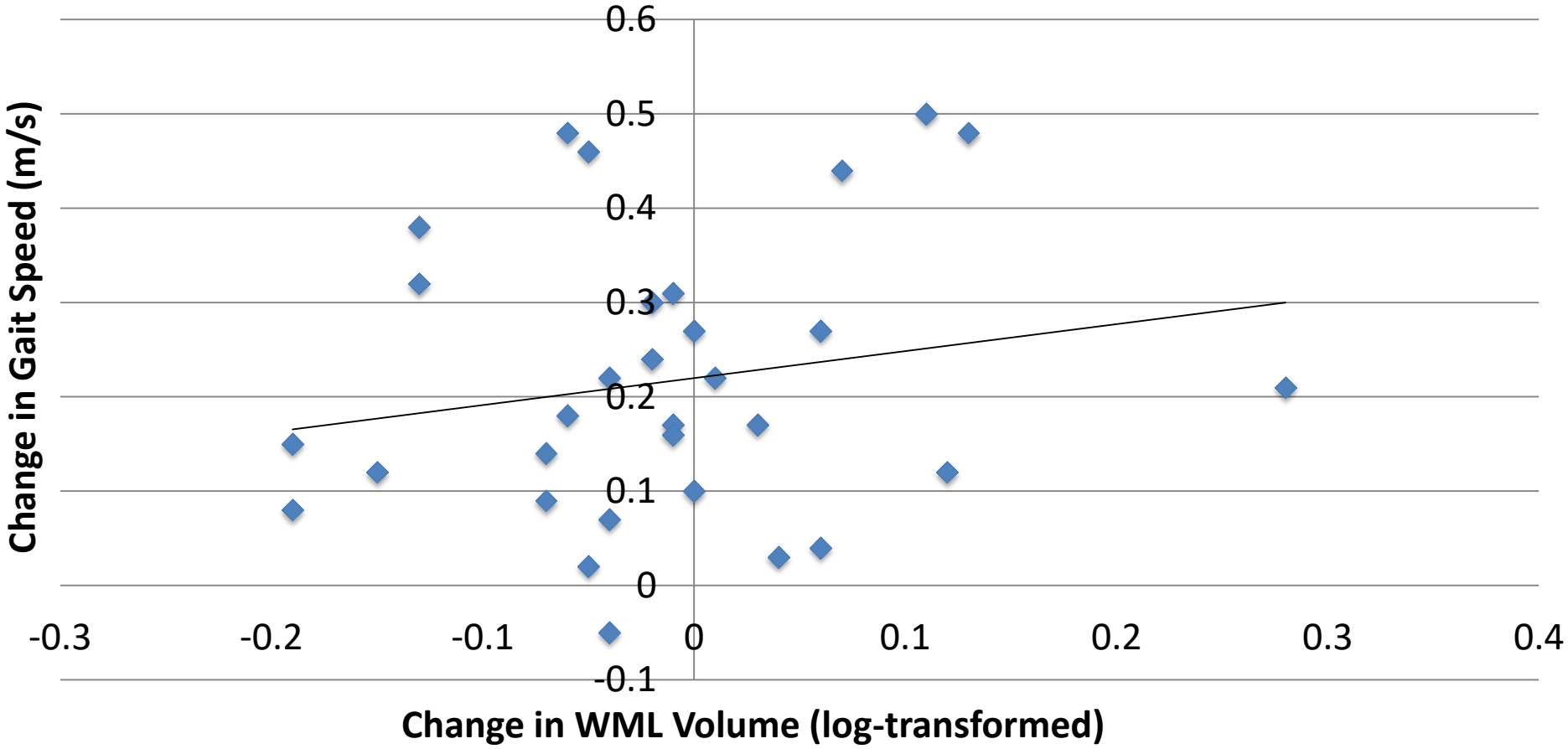
Resistance Training Moderates Disease Progression

Lifting weights 2x/week significantly reduced progression of white matter lesions.

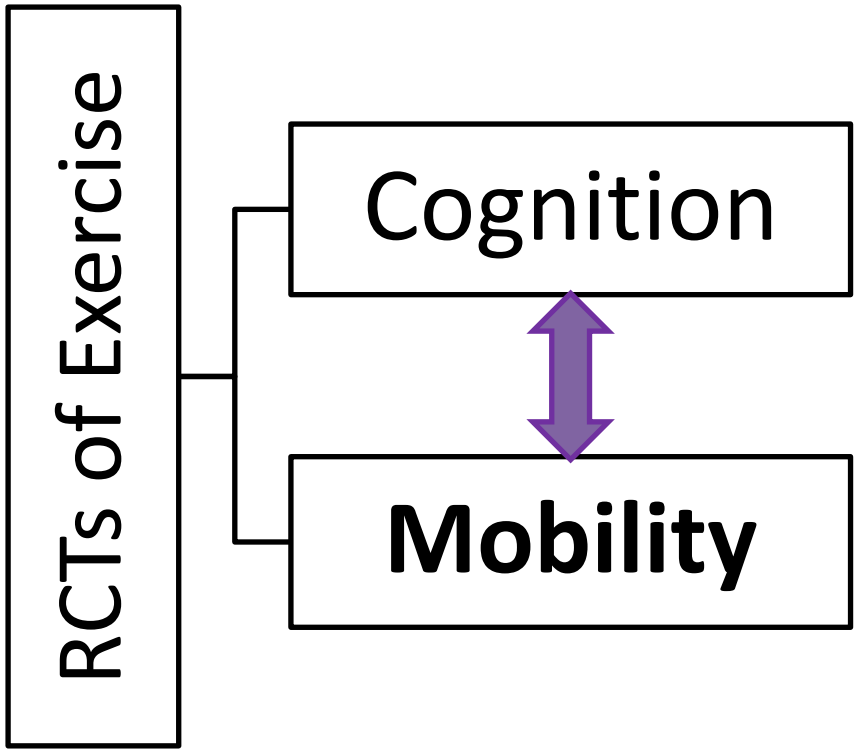
» Bolandzadeh *et al.*, JAGS, 2015



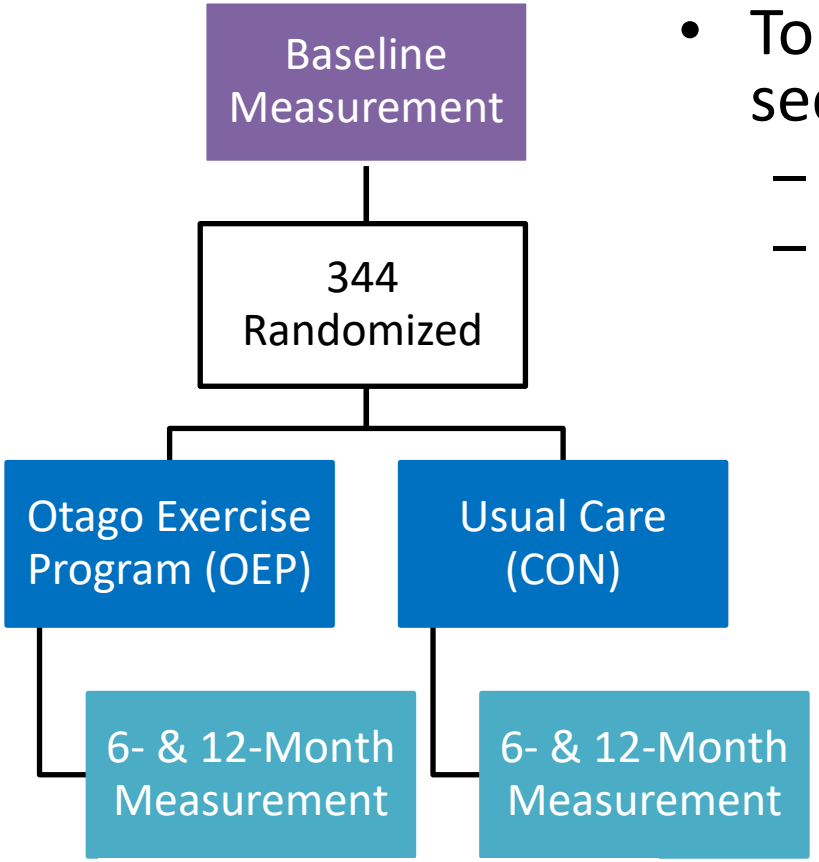
Reduced WML progression was associated with maintenance of gait speed (r=0.31, p=0.04) and to a lesser degree, with improved Stroop Test performance (r=0.30, p=0.06)




Context
Studies
Conclusions


RCTs of Exercise
Cognition
Mobility

Action! Seniors



- To assess the efficacy of exercise as a secondary falls prevention strategy
  - Aged 70 years and older
  - Presented to a health care provider (ED or GP) due to a fall
    - » Liu-Ambrose *et al.*, JAMA, 2019
    - » Liu-Ambrose *et al.*, JAGS, 2008

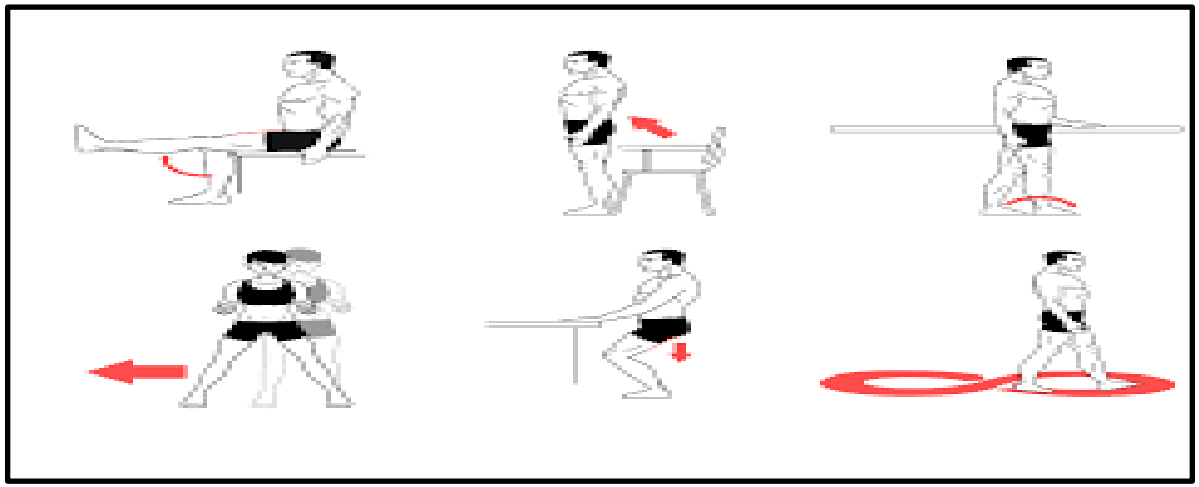
CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Participants

- All were patients of the Vancouver Falls Prevention Clinic (www.fallsclinic.ca)
- Referrals to the Vancouver Falls Prevention Clinic are from physicians for older adults who sought medical attention after a fall
- In addition, demonstrate risk for future falls based on clinic screening measures

Otago Exercise Program (OEP)

- Home-based, delivered by PT
  - 5 home visits over 6 months
  - Progressive strength and balance retraining (3x/week)
  - Walking (2x/week)



Primary Outcome

- Self-reported number of falls over 12 months
- Documented prospectively on monthly calendars
- Monthly phone calls to verify calendar information and circumstances of falls

Secondary Outcomes

- Executive Functions
  - Stroop Colour-Word Test
  - Trail Making Test (A and B)
  - Verbal Digits Span, Forward and Backward
  - Digit Symbol Substitute Test
- Physiological Profile Assessment (PPA)
- Timed Up and Go Test (TUG)
- Short Physical Performance Test (SPPB)

Results

Variable	CON n = 172	OEP n = 172
Age, years	81.9 (6.0)	81.2 (6.1)
Sex, male	53 (31%)	62 (36%)
Number of Falls 12M Prior, n (%)	3.0 (4.3)	2.8 (2.3)
Number of Fall-Related Fractures 12M Prior, n (%)	32 (19)	33 (18)
Use of Walker, Brace, or Cane, n (%)	37 (22%)	46 (27%)
Geriatric Depression Scale	3.0 (2.6)	2.8 (2.4)
Functional Comorbidity Index	4.0 (2.0)	4.1 (2.2)
Instrumental Activities of Daily Living	7.4 (1.1)	7.2 (1.2)
Mini-Mental State Examination (30 pts max)	27.9 (1.6)	27.7 (1.7)
Montreal Cognitive Assessment (30 pts max)	23.4 (3.3)	22.9 (3.4)
Timed-Up and Go Test, sec	16.9 (6.4)	16.3 (7.0)
Short Physical Performance Battery (12 pts max)	7.8 (2.3)	7.9 (2.2)
Gait Speed, m/s	0.8 (0.2)	0.9 (0.2)
OEP Compliance	NA	63%

Results

- Compared with the CON group, the OEP group:
  - Experienced 36% fewer falls (Incident Rate Ratio = 0.64, 95% CI: 0.46, 0.90, p = .009)
  - Improved executive functions, specifically processing speed (p = .047)
  - No significant differences in PPA, TUG, or SPPB

Results

- Improved processing speed was a significant mediator of the OEP on:
  - Moderately-injurious falls

- No physical performance measures were mediators.

» Liu-Ambrose *et al.*, 2020, JGMS

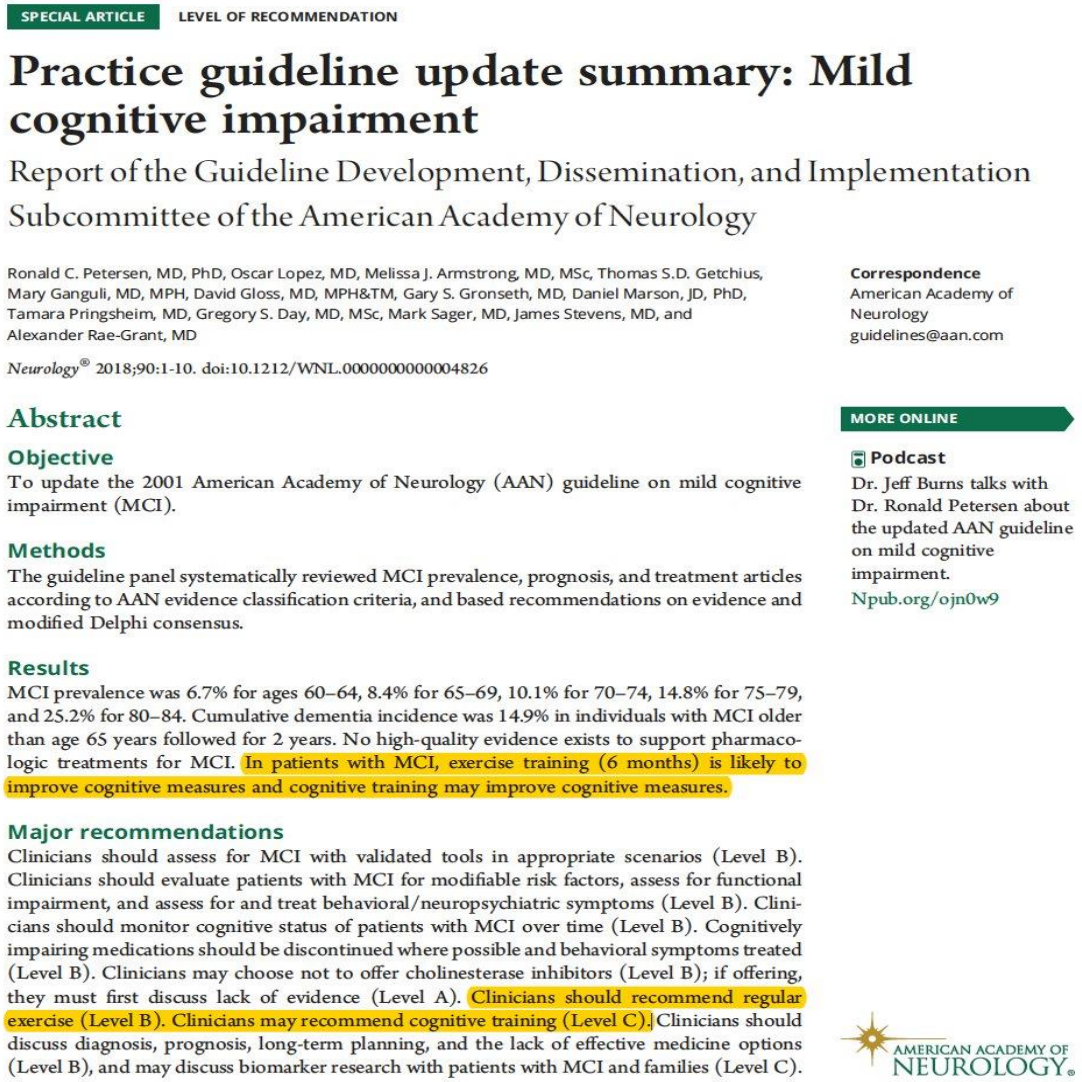
Results

- Improved cognition may be unrecognized pathway by which exercise improves mobility and reduces falls
  - » Liu-Ambrose *et al.*, BJSM, 2012
- Processing speed, as measured by DSST, is a predictor of future falls among older fallers
  - » Davis *et al.*, JAGS, 2017

Overview

Conclusions: Cognition

- Sufficient evidence for exercise to be included in practice guideline on mild cognitive impairment



SPECIAL ARTICLE LEVEL OF RECOMMENDATION

Practice guideline update summary: Mild cognitive impairment

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Ronald C. Petersen, MD, PhD, Oscar Lopez, MD, Melissa J. Armstrong, MD, MSc, Thomas S.D. Getchius, Mary Ganguli, MD, MPH, David Gloss, MD, MPH&TM, Gary S. Gronseth, MD, Daniel Marson, JD, PhD, Tamara Pringsheim, MD, Gregory S. Day, MD, MSc, Mark Sager, MD, James Stevens, MD, and Alexander Rae-Grant, MD

Correspondence
American Academy of Neurology
guidelines@aan.com

Neurology® 2018;90:1-10. doi:10.1212/WNL.0000000000004826

Abstract

Objective
To update the 2001 American Academy of Neurology (AAN) guideline on mild cognitive impairment (MCI).

Methods
The guideline panel systematically reviewed MCI prevalence, prognosis, and treatment articles according to AAN evidence classification criteria, and based recommendations on evidence and modified Delphi consensus.

Results
MCI prevalence was 6.7% for ages 60–64, 8.4% for 65–69, 10.1% for 70–74, 14.8% for 75–79, and 25.2% for 80–84. Cumulative dementia incidence was 14.9% in individuals with MCI older than age 65 years followed for 2 years. No high-quality evidence exists to support pharmacologic treatments for MCI. In patients with MCI, exercise training (6 months) is likely to improve cognitive measures and cognitive training may improve cognitive measures.

Major recommendations
Clinicians should assess for MCI with validated tools in appropriate scenarios (Level B). Clinicians should evaluate patients with MCI for modifiable risk factors, assess for functional impairment, and assess for and treat behavioral/neuropsychiatric symptoms (Level B). Clinicians should monitor cognitive status of patients with MCI over time (Level B). Cognitively impairing medications should be discontinued where possible and behavioral symptoms treated (Level B). Clinicians may choose not to offer cholinesterase inhibitors (Level B); if offering, they must first discuss lack of evidence (Level A). Clinicians should recommend regular exercise (Level B). Clinicians may recommend cognitive training (Level C). Clinicians should discuss diagnosis, prognosis, long-term planning, and the lack of effective medicine options (Level B), and may discuss biomarker research with patients with MCI and families (Level C).

MORE ONLINE

Podcast
Dr. Jeff Burns talks with Dr. Ronald Petersen about the updated AAN guideline on mild cognitive impairment.
Npub.org/ojn0w9

AMERICAN ACADEMY OF NEUROLOGY

Conclusions

- Multimodal training likely provides the most benefit

Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis

Joseph Michael Northey,[1,2] Nicolas Cherbuin,[3] Kate Louise Pumpa,[1,2] Disa Jane Smee,[2] Ben Rattray[1,2]

Table 1 Results of moderator analysis

Moderator	No. of effect sizes	Estimate Mean (95% CI)
Exercise moderators		
Mode		
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)

BMJ

Northey JM, *et al*. *Br J Sports Med* 2018;**52**:154–160. doi:10.1136/bjsports-2016-096587

Conclusions

- Physical activity is a legitimate medical therapy for promoting cognitive health
  - Degree of benefit equal or exceeds that of pharmaceutical agents
  - Minimal adverse effects
- Reducing physical inactivity by 25% could prevent one million cases of dementia worldwide

» Barnes and Yaffe, Lancet Neurol, 2011

Conclusions: Falls

- Exercise reduces falls by promoting physical and cognitive function
- Growing interest in:
  - Pairing cognitive training with exercise training
    - Sequential or concurrent
  - Adding or increasing cognitive load to exercise
    - Tai Chi
- The inclusion of measures of cognitive function in falls risk screening, especially in high-risk groups

"Refusing to go to the gym is not the same thing as resistance training."

Conclusions

- Common barriers to physical activity/exercise uptake and adherence are magnified among those with impaired cognition (even without dementia) and mobility

Conclusions

- Facilitate compliance
  - Personalize as appropriate
  - Encourage problem-solving and discussion
  - Establish achievable goals, monitor progress, and provide feedback often
  - Make it bite size/manageable = exercise “snacks”
    - Bouts of activity can be very beneficial
- Make it fun and enjoyable
  - Socialization

Conclusions

- Change perspective

Limiting our daily sitting/lying to just 23.5 hours: too ambitious?

Karim Khan

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up the freeway embankment, stepping over the steel barriers, dashing hopefully across breaks in eight lanes of Hummers

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