RECOMMENDED READING LIST

Systematic Reviews


Intervention Studies


Basic Mechanisms

Prescribing Exercise to Improve Cognitive Function among Those at Risk for Decline

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Increasing Aging Population

Aging & the Brain

Brain regions that reduce in volume with age.

Brain regions with minimal reduction or stable volume with age.

Raz et al., Cerebral Cortex, 2005

Aging & the Brain

Lindenberger et al., Frontiers in Neuroscience, 2008

Worldwide, one new case of dementia is detected every 4 seconds.


Much Variability Observed

McArdle, Advances in Statistical Analysis, 2011
What is good for your body, is good for your brain!

- The brain is the best customer of your heart and lungs
  - All of 3 lbs but consumes 20%
- A physically healthy body provides the basis for a healthy brain
  - Reduction of risk factors such as hypertension and diabetes
  - Growth factors

Exercise is Medicine

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

Road Map

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Exercise is Medicine:
- Aerobic Training
- Resistance Training
- Recommendations
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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

What are the effects of aerobic exercise on cognitive and brain health in older adults?
Meta Analysis of Aerobic Training

Colcombe and Kramer, 2002

Aerobic Training: Benefits both Cognitive and Brain Outcomes

- A 6-month, 3x/week walking program improved:
  - Cognitive performance of executive functions
  - Brain function as assessed by fMRI (Flanker)

  Colcombe et al., PNAS, 2004

Relevant to AD, Aerobic Training Increases Hippocampal Volume

- A 12-month, 3x/week (moderate-intensity) walking program improved/increased:
  - Cognitive performance of spatial memory
  - Hippocampus volume by 2%

  Erickson et al., PNAS, 2011

Mild Cognitive Impairment (MCI)

- A clinical state, can be transient
  - Associated with increased risk of dementia
- NIH Alzheimer’s Association (NIH-AA) criteria:
  1. Subjective memory complaints
  2. Objective cognitive impairment
  3. No significant functional impairment (i.e., intact IADL)
  4. No dementia

Albert et al., Alzheimers Dement, 2011
Benefits of Aerobic Training Extend to those at Greater Risk for Dementia (MCI)

- A 6-month, 4x/week walking program:
  - Improved cognitive performance of executive functions (women only!)
  - Reduced fasting plasma levels of insulin and cortisol

  > Baker et al., Arch Neurol, 2010

Aerobic Training Maintains Hippocampal Volume and Improves Memory in MCI

- A 6-month, 2x/week (moderate-intensity) walking program improved/increased:
  - Cognitive performance of verbal & spatial memory
  - Hippocampus volume by 4%

  > ten Brinke et al., BJSM, 2014

Cochrane Review: Exercise Interventions for People with Dementia

- 17 RCTs included, 1067 participants
- Meta-analysis suggest no clear evidence of benefit for exercise on cognitive function
  - Heterogeneous
  - Low quality of evidence
- However, benefit for ADLs

  > Forbes et al., Cochrane Database Syst Rev, 2015

What about Resistance Training?

- Important for healthy aging
  - Promotes favorable energy balance and reduced visceral fat deposition by enhancing basal metabolism
  - Counteracts age- and disease-related muscle wasting
  - Improves insulin sensitivity
  - Improves lipid profile
  - Reduces falls risk
  - Improves bone health
- More feasible than aerobic training in older adults with mobility issues

Road Map

- "Exercise is Medicine": Evidence from RCTs
  - Aerobic Training
  - Resistance Training
  - Recommendations

What are the effects of resistance training on cognitive and brain health in older adults?
**Pump your Muscles & Pump up the Brain**

- Both 3x/week moderate- and high-intensity resistance training for 6 months significantly improved/increased:
  - Cognitive performance of memory (verbal and spatial) & executive functions
  - IGF-1 (growth factor) levels
- Men aged 65 to 75 years old
  » Cassilhas et al., MSSE, 2007

**Brain Power Study**

**Primary Aim:** Assess the efficacy of resistance training on executive functions.

**Brain Power: Intervention**

- Certified instructors
- 60-minute classes
  - 40 minutes of training
- Resistance Training
  - Progressive loading using 8RM
    » 2 sets of 8 reps
- Balance and Tone
  - 2x/week
  - No progressive loading

**Brain Power: Outcomes**

- Neuroimaging
  - Functional MRI
  - Structural MRI
    » White matter lesions (WMLs)
    » Volumes
Compared with BAT, 1x/week and 2x/week RT significantly improved Stroop Test performance.

Compared with BAT, 2x/week RT increased functional activation in regions that support Flanker Task performance.

Compared with BAT, 2x/week RT significantly reduced WML progression.  
> Bolandzadeh et al., JAGS, 2015

• Lesions in subcortical white matter due to small vessel disease increases risk of:
  – A clinical stroke
  – Cognitive impairment and dementia
  – Conversion from MCI to dementia

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 ($r=0.30, p=0.06$).

At 2-year follow-up, both frequencies of RT promoted executive function compared with BAT
• 2x/week RT > BAT in memory, peak muscle power, and reduced cortical white matter atrophy
> Best et al., JINS, 2015
**ExCEL Study**

**Primary Aim:** Assess the efficacy of both resistance training and aerobic training on cognitive function among those with probable MCI.

Benefit of Resistance Training Extend to those with MCI

- **Benefits of Resistance Training Extend to those with MCI**
  - Compare with BAT, 2x/week RT significantly improved associative memory performance.
  - Also, increased functional activation of regions that support associative memory performance.

And the Evidence Keeps Building...

- **SMART (Study of Mental Activity & Regular Training)**
  - Gates et al., BMC Geriatrics, 2011
  - Suo et al., Mol Psychiatry, 2016
- 100 older adults with MCI
- 6 months of training; 2x/week; 3 sets of 8 reps

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**Who Participated**

- Women (N=86)
- 70 to 80 year-old
- Community dwelling
- Not partaking in resistance training or aerobic training
- No contraindications to exercise
- No history of stroke or neurodegenerative disease
- Have objective cognitive deficits
- Have not been diagnosed with dementia
- Subjective memory complaints

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**Nagamatsu et al., 2012 & 2013**

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**15/06/2016**
**Road Map**

- Exercise is Medicine: Evidence from RCTs
  - Aerobic Training
  - Resistance Training
  - Recommendations

**How Much Activity is Necessary?**

- The Cardiovascular Health Study – Pittsburgh Site
- Cohort study of heart disease and dementia
- “How many city blocks do you walk per week?”

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**Good News:**
A little/day can go a long way...

- Walking > 1 km/day maintains brain volume and reduces the risk of cognitive impairment over 9 years
  - Erickson et al., Neurology, 2010

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**Good News:**
A little/day can go a long way...

- What does 1 km/day look like?
  - ~10 city blocks in Vancouver
  - ~2.5 times around a standard track
  - For a healthy older adult, 13 minutes
    - Gait speed of 1.35 m/sec
  - For a frail older adults, 26 minutes
    - Gait speed of 0.65 m/sec

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**Amount vs. Intensity**

- Intensity of exercise needs to be considered as well as amount of exercise
- Of sufficient challenge to induce the underlying physiological response/cascades
  - Moderate-intensity

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**Type of Exercise: Does it Matter?**

- Evidence support both types of training
- Match to person’s personal preference and ability
- In the future, genetics may play a factor
  - Brain-derived neurotrophic factor polymorphism
### Prescription Guidelines

**Resistance Training**
- 2 to 3 sets of 8 to 15 reps
- 2 to 3 times per week with a rest day in between

**Aerobic Training**
- 2 to 3x/week
- Start at 45% Heart Rate Reserve (HRR) and work to 70-75% HRR
  - Brisk walk to jogging
- For safety, use both objective and subjective measures of exertion

### Considerations

- Common barriers to exercise uptake and adherence are magnified among those with cognitive impairment and dementia

### Considerations

- Clear communication to minimize anxiety and confusion, repeat often
- Facilitate compliance
  - Personalize as appropriate
  - Encourage problem-solving and discussion
  - Establish achievable goals, monitor progress, and provide feedback often
  - Make it bite size/manageable
    - 15-minute bouts x 3/day

### Considerations

- Supportive environment
  - Involve caregivers and friends (as appropriate)
  - Encourage socialization

- Creating a positive experience initially is important
  - Exercise augments regions of the brain that promote adherence to recommendations

  » Best et al., Under Review, 2016

### Summary: Exercise is Medicine for the Brain

- Physical activity is a legitimate medical therapy for promoting cognitive health
  - Degree of benefit 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
Summary:
Exercise is Medicine for the Brain

• Starting to exercise in late life is not futile: even those who are sedentary can improve function
  – In fact, those who are more frail may benefit the most

  » Sink et al., JAMA, 2015