COMBINING EXERCISE & COGNITIVE TRAINING TO IMPROVE EVERYDAY FUNCTIONING OF OLDER ADULTS

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Disclosures

Dr. Binder
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Studies of the effects of cognitive training and exercise training have shown mixed effects on measures of cognitive function.

Those studies that have shown positive effects have been on measures of specific cognitive tasks that do not always show transfer to other cognitive domains, and may not transfer to performance of everyday functional activities.
Key Features of Present Approach (EXACT)

- Improve cognitive training by:
  - Integrating ideas from the skill learning and memory literatures.
  - Considering the multi-process nature of everyday activities.

- Harness the effects of exercise to improve cognitive function in a staggered fashion.

- Evaluate the effects of training on proxies of everyday function.
Study Design

- 2 x 2 Factorial Design

- 4 Groups:
  1) Low Intensity Exercise/Health Education (Control)
  2) Low Intensity Exercise/Cognitive Training (Cognitive)
  3) Aerobic Exercise/Health Education (Exercise)
  4) Aerobic Exercise/Cognitive Training (Combined)

- Planned Enrollment = 96 subjects
Eligibility Criteria

- Ages 55-75 years
- English speaking
- Stable health
- Sedentary (exercise <3 times/wk x 20 min)
- Sufficient visual and auditory perception to complete testing
- Available informant
- Clinical Dementia Rating (CDR) score = 0
- BMI < 35 kg/m²
Exclusion Criteria

- Regular exercise (≥ 3 times per week for ≥ 20 min)
- Cognitive training program.
- Mild cognitive impairment (MCI) or dementia.
- Inability to walk on treadmill or ride exercise bike.
- Major or unstable medical, neurological or psychiatric disorder.
- Less than a 10th grade education.
- Cigarette smoking within the previous 12 months.
- History of alcohol or substance abuse.
- Inability to comprehend research tasks.
Screening Evaluations

- Telephone questionnaire
- Uniform Data Set (UDS) Clinical Battery
- Yale Physical Activity Questionnaire
- Physical exam, blood chemistries, CBC, ECG
- Treadmill exercise stress test
### Subjects Consented (n= 158)

- Randomized (n=96)
  - REFUSED: (n=22)
    - Time constraints (n=11)
    - Travel constraints (n=2)
    - Other reasons (n=9)
  - INELIGIBLE:
    - Medical conditions (n=9)
    - Too fit (n=7)
    - Abnormal stress test (n=4)
    - Cognitive impairment (n=5)
    - Physical limitations (n=6)
    - Can not speak English (n=3)
    - Multiple reasons (n=4)
    - Other (n=2)

### Telephone Screens (n=554)

### Randomized (n=96)

- **CONTROL** (n=25)
- **COGNITIVE** (n=23)
- **EXERCISE** (n=24)
- **COMBINED** (n=24)

### Follow-up Completion

- **Both Intervention & 6-month follow up Completed**
  - CONTROL: n=17
  - COGNITIVE: n=18
  - EXERCISE: n=20
  - COMBINED: n=19

- **6-month follow up Completed Only**
  - CONTROL: n=2
  - COGNITIVE: n=0
  - EXERCISE: n=3
  - COMBINED: n=0

- **Did not complete intervention & 6-mo Follow up**
  - CONTROL: n=6
  - COGNITIVE: n=5
  - EXERCISE: n=1
  - COMBINED: n=5
### Baseline Sample Characteristics (n=96)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=25)</th>
<th>Cognitive (n=23)</th>
<th>Exercise (n=24)</th>
<th>Combined (n=24)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs.</td>
<td>64 ± 7</td>
<td>64 ± 4</td>
<td>67 ± 6</td>
<td>65 ± 6</td>
<td>0.274</td>
</tr>
<tr>
<td>Female % (n)</td>
<td>60 (15)</td>
<td>70 (16)</td>
<td>71 (17)</td>
<td>67 (13)</td>
<td>0.856</td>
</tr>
<tr>
<td>Caucasian % (n)</td>
<td>96 (24)</td>
<td>78 (18)</td>
<td>71 (17)</td>
<td>88 (21)</td>
<td>0.080</td>
</tr>
<tr>
<td>Education, yr.</td>
<td>16 ± 2</td>
<td>17 ± 2</td>
<td>15 ± 2</td>
<td>16 ± 2</td>
<td>0.023</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 ± 5</td>
<td>28 ± 5</td>
<td>29 ± 5</td>
<td>29 ± 6</td>
<td>0.852</td>
</tr>
<tr>
<td>MMSE Score</td>
<td>29 ± 1</td>
<td>29 ± 2</td>
<td>29 ± 1</td>
<td>29 ± 1</td>
<td>0.209</td>
</tr>
<tr>
<td>GDS Score</td>
<td>1 ± 1</td>
<td>1 ± 2</td>
<td>1 ± 1</td>
<td>1 ± 2</td>
<td>0.866</td>
</tr>
</tbody>
</table>
Study Timeline

Randomized

- Cognitive
  - Home exercise
  - Health education
- Control
  - Home exercise
  - Cognitive training
- Exercise
  - Aerobic exercise
  - Health education
- Combined
  - Aerobic exercise
  - Cognitive training

Month:
0 1 2 3 4 5 6
Control=Home Exercise Protocol

- Home-based low intensity flexibility program.
- Instructed by exercise trainer at baseline.
- Instructed to perform 3x/week.
- Instructed not to perform any high intensity exercise including weight training, swimming, etc.
- Monthly session with trainer to review performance of exercises and exercise log.
**Control=Health Education Protocol**

- Started at Beginning of Month 5
- Weekly 1- hr session with Study Coordinator.
- Topics:  -Aging Skin
  -Hearing Problems,  
  -Problems with Smell  
  -Stroke,  
  -Taking Medications,  
  -Sleep and Aging,  
  -Eating Well  
  -Sleep and Aging.
Aerobic Exercise Protocol

- Supervised: treadmill walking or exercise bike
- 3 days/week for 6 months
- Exercise Goals:
  - 50-60% HRR, RPE=12-13, x 30 min by Week 4
  - 60-70% HRR, RPE=14-15, x 45 min by Week 12
  - 70-85% HRR, RPE=15-16, x 50 min for last 3 months

- Monitoring of training intensity with Polar™ HR monitors. Reviewed by WU research staff weekly.
Cognitive Training Protocol

Task Coordination

Prospective Memory

Retrospective Memory

- Spaced Training
- Interleaved Training
- Adaptive procedures (increasing difficulty of tasks)
- Utilized strategy training for prospective memory training
1. Task Coordination

- Attentional Priority (McKay-Brandt task; adapted from Kramer)
  - Number summing
  - Flower cutting

- Task Switching (Karbach & Kray)
You have to do two things. Use your mouse to cut the flower. It will appear at different locations on the screen.
And you will add the numbers that are presented in the box in the middle of the screen.
“You want to work on the Flower task and fill it with Blue.
The Number Bar is okay – it’s pretty full with Green.”
2. Prospective Memory

- Varied the ongoing activity
- Varied the prospective memory task
- Explicit strategy instruction
  - Nonfocal-monitoring
  - Focal-implementation intentions
  - Time-based-monitoring
3. Retrospective Memory

- Primary Component:
  Jacoby & Jennings’ Avoiding Repetitions Task

### STUDY: LIST OF WORDS
Thorn; Fable; Parch; Pun; Drop; Cap; Shark

### TEST PHASE

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Hand</td>
<td>New</td>
</tr>
<tr>
<td>Note</td>
<td>New</td>
</tr>
<tr>
<td>Thorn</td>
<td>Old</td>
</tr>
<tr>
<td>Note</td>
<td>Repeated Lure</td>
</tr>
<tr>
<td>Chin</td>
<td>New</td>
</tr>
<tr>
<td>Shark</td>
<td>Old</td>
</tr>
<tr>
<td>Cap</td>
<td>Old</td>
</tr>
<tr>
<td>Chin</td>
<td>Repeated Lure</td>
</tr>
</tbody>
</table>
Examples/Cognitive Training:
   - Apply implementation intentions to an everyday prospective memory challenge.

Example/Health Education:
   Apply what you learn in module to your own life situation.

Discussed with research staff each week.
### Adherence to Training Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Exercise (n=21)</th>
<th>Combined (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise Intervention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of sessions completed</td>
<td>68 ± 5</td>
<td>69 ± 5</td>
</tr>
<tr>
<td>(out of 72 possible sessions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent of sessions completed</td>
<td>95 ± 8</td>
<td>97 ± 7</td>
</tr>
<tr>
<td><strong>Cognitive Intervention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of sessions completed</td>
<td>22 ± 5</td>
<td>24 ± 0.5</td>
</tr>
<tr>
<td>(out of 24 possible sessions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent of sessions completed</td>
<td>90 ± 0.2</td>
<td>99 ± 0.02</td>
</tr>
</tbody>
</table>
## Treadmill / VO2 Data

<table>
<thead>
<tr>
<th>Training Condition</th>
<th>VO2 (ml/kg/min)</th>
<th>6-mo Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=17)</td>
<td>23 ± 4</td>
<td>0.4 ± 1.7</td>
</tr>
<tr>
<td>Cognitive (n=14)</td>
<td>23 ± 4</td>
<td>-0.5 ± 1.4</td>
</tr>
<tr>
<td>Exercise (n=21)</td>
<td>22 ± 4</td>
<td>+1.8 ± 3.3</td>
</tr>
<tr>
<td>Combined (n=19)</td>
<td>22 ± 5</td>
<td>+2.5 ± 2.8</td>
</tr>
</tbody>
</table>

P-value:
- Control vs Cognitive: 0.35
- Control vs Exercise: 0.002
- Control vs Combined: 0.35
- Cognitive vs Exercise: 0.002
- Cognitive vs Combined: 0.35
- Exercise vs Combined: 0.002
Everyday Transfer Measures
(Baseline and Post-Intervention)

- Virtual Week
- Cooking Breakfast
- Memory for Medical Information
Virtual Week Task

You need to roll an even number to continue!

1.13
Text: Monday 7:07 AM

Start Card
Perform Task
Event Card
Pause or Quit
Start
Memory for Medical Information

- Capture an everyday memory challenge for which age differences are apparent and memory control is needed.

- Develop two alternate versions that show comparable performance levels to be used during pre & post assessment period
  - Chagas Disease
  - Dwarfism
During the chronic phase, Chagas disease may be dormant.

Many people with Chagas disease may develop problems swallowing.

Chagas disease is not an endemic in the United States.
TEST

• 70 sentences (self-paced) that were old (30), new (30), or repeated lures (10)
• Judge if old (read aloud previously) or new (did not read aloud previously)

During the chronic phase, Chagas disease may be dormant.

OLD
PRESS 1

NEW
PRESS 2

If the subject responds “old”, then the source judgment follows

You indicated that the sentence was “old”. Which source was associated with the sentence?

Press 1
Press 2
Press 3
Press 4
I am unsure
Virtual Week: Regular PM

- Control
- Exercise
- Cognitive
- Combined

Proportion Correct

- Pre
- Post
Virtual Week: Irregular PM

Proportion Correct

Control | Exercise | Cognitive | Combined

Pre | Post
Cooking Breakfast: Time Range(s)

- Control
- Exercise
- Cognitive
- Combined

<table>
<thead>
<tr>
<th></th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
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<td></td>
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<tr>
<td>Exercise</td>
<td></td>
<td></td>
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<tr>
<td>Cognitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cooking Breakfast: Ideal Performance(s)

- Control
- Exercise
- Cognitive
- Combined

Seconds

Pre | Post
--- | ---

Control
Exercise
Cognitive
Combined
Cooking Breakfast: Table Setting

Number of Tables Set

- Control
- Exercise
- Cognitive
- Combined

Pre  Post
Memory for Health Information: Corrected Recognition (Hits - FAs)

- Control
- Exercise
- Cognitive
- Combined

Proportion Correct
Memory for Health Information: Source Memory

- Control
- Exercise
- Cognitive
- Combined

Proportion Correct

- Pre
- Post
Memory for Health Information: FAs to Repeated Lures

- Control
- Exercise
- Cognitive
- Combined

Proportion FAs

Pre  Post
Two months of cognitive training had a significant effect for improving a novel “real world” prospective memory task, but did not have an effect on performance of a “real world” task of cognitive control and working memory (cooking breakfast) or on remembering health-related information.
Study Strengths

- Careful screening to assess for mild cognitive impairment.
- Community-based intervention.
- Novel outcome measures to assess everyday function.
- Novel cognitive training protocol.
- Blinded study assessments.
Why did Cognitive Training not Transfer to Cooking, Health?

- Less overlap from training to target tasks

BUT consider Memory for Health Information

- Training tasks most aligned with cooking, health did not provide explicit strategies
- Training tasks did not involve a variety of contexts (and homework was difficult to apply to daily activities).
• Performance of the exercise training protocol may not have been sufficiently rigorous. However, fitness gains are in that range that Kramer’s group reports.

• Aerobic exercise my benefit executive/attention laboratory tasks but not everyday tasks that draw on an interplay of cognitive skills.

• May have targeted individuals who were too young to show benefit.
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Questions?
Supplementary Information
Laboratory Transfer Tasks

1) Processing Speed
   - Digit Symbol Substitution

2) Executive Function
   - Trails A/B; Fluency; Digit Span Backward
   - Stroop

3) Reasoning
   - WAIS Similarities
Study Measures

Functional Capacity
- Peak Aerobic Power ($\text{VO}_{2\text{peak}}$)
- Physical Performance Test (PPT)
- Senior Fit Test (SFT)
- Dual Task Walking Speed

Interview Instruments
- Short form (SF)-36 Questionnaire
- Late Life Function and Disability Index (LLFDI)
- Geriatric Depression Scale (GDS)