Advancing Cognitive Training for Older Adults: Long-Term Results from the ACTIVE Trial and Beyond
The design of the ACTIVE trial was largely pre-specified by the National Institute on Aging and the National Institute of Nursing Research in RFA-AG-96-001.

Three major emphases of the request for applications were:
1. Common intervention protocols at multiple sites
2. Primary outcomes: *functional competence*, focus on everyday independence
3. Focus of interventions: *basic cognitive abilities*. 
ACTIVE: Primary Aim

To test the efficacy of three cognitive interventions to improve or maintain the cognitively demanding activities of daily living.
Simplified Conceptual Model

Participant Characteristics ➞ Training ➞ Cognitive Abilities ➞ Daily Function
Interventions

Three cognitive training interventions:
- Memory
- Reasoning
- Speed of Processing
Intervention Protocol

- Initial Training: 10 90-min sessions
- Booster: 4 90-min sessions
  - 1 yr after training
  - 3 yr after training
- Trained in small groups at local facility
- Memory & Reason –
  - strategy-based training
The ACTIVE study differed from prior cognitive training research in several ways:

1. multi-site, randomized controlled, single-blind trial,
2. intent-to-treat analytical approach that included all randomized participants rather than only those compliant with the intervention,
3. primary outcome measures of everyday functioning, and
4. a more socioeconomically and racially diverse study sample.
Study Design

1. Ineligible
2. Screen for Eligibility
   - Refused
3. Eligible and Consenting
4. Baseline Measurements
5. Randomize to Training
   - Memory
   - Reasoning
   - Speed
   - No Contact
6. Post-Test (PT)
   - Booster
     - Yes
     - No
   - Booster
     - Yes
     - No
   - Booster
     - Yes
     - No
7. 1-Yr Test (A1)
8. 2-Yr Test (A2)
9. 3, 5 10-Yr Tests (A3 and A5 and A10)
ACTIVE Steering Committee

- University of Alabama- Birmingham
  Karlene Ball, Ph.D.
- Hebrew Senior Life, Boston
  John Morris, Ph.D.
- Indiana University
  Fredrick Unverzagt, Ph.D.
- Johns Hopkins University
  George Rebok, Ph.D.
- Pennsylvania State University
  Sherry Willis, Ph.D.
- University of Florida / Wayne State University
  Michael Marsiske, Ph.D.
- New England Research Institutes, Coordinating Center
  Sharon Tennstedt, Ph.D.
- National Institute on Aging
  Jeffrey Elias, Ph.D.
- National Institute of Nursing Research
  Kathy Mann-Koepke, Ph.D.
Targeted Population

• Diverse sample age $\geq 65$ years
• Heterogeneous sample
  – Urban and Rural
  – Oversample African American
  – Age 65 – 94
  – Wide SES range
• Cognitive normal
• Living independently
• At risk of loss of independence
Baseline Characteristics (n=2,802)

- Mean Age: years 73.6 (5.9) Range 65-94
- Gender: Female 75.9%
- Race: African American 26.0% (over sampled)
- Education: H.S. diploma 88.6%
- Marital Status: Married 35.9%
- Cognitive Status: MMSE score 27.3 (2.0)
Training Effects on Cognitive Abilities

• Immediate effect
Reliable individual effect: Memory 26%, Reason 74%, Speed 87%

• Durability of Effects
Memory: 5 years
Reason & Speed: 10 years

• Training Specific to Ability Trained
Effect of Training on Cognitive Abilities

![Bar chart showing standardized training effect size for Memory trained, Reasoning trained, and Speed trained groups.](image)
FIGURE 4. 10-year Trajectory of Memory, Separately by Training Group

- Memory
- Reasoning
- Speed
- Control

Mean Memory Score (Range: 0 to 132)

Time:
- Baseline (n=2801)
- Post-test (n=2362)
- Year 1 (n=2135)
- Year 2 (n=2020)
- Year 3 (n=1875)
- Year 5 (n=1568)
- Year 10 (n=943)
Reason: 10 Yr Trajectory
Speed: 10 Yr Trajectory

FIGURE 6. 10-year Trajectory of Speed of Processing, Separately by Training Group

Mean Speed Score (Range -1500 to 0)*

* Scores were reversed to graphically present decline

Time

Baseline (n=1777) Post-test (n=1520) Year 1 (n=1207) Year 2 (n=1200) Year 3 (n=1200) Year 5 (n=1000) Year 10 (n=853)
Normal Memory vs Memory Impaired: Impact on Training on Memory, Reasoning, Speed

<table>
<thead>
<tr>
<th>Interven</th>
<th>Time</th>
<th>Memory</th>
<th>Reasoning</th>
<th>Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>PT</td>
<td>.300***</td>
<td>-.009</td>
<td>-.050</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.254***</td>
<td>.033</td>
<td>-.061</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>.214***</td>
<td>.052</td>
<td>-.057</td>
</tr>
<tr>
<td>Reason</td>
<td>PT</td>
<td>.001</td>
<td>.477***</td>
<td>0.025</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.013</td>
<td>.416***</td>
<td>-.026</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.003</td>
<td>.262***</td>
<td>-.021</td>
</tr>
<tr>
<td>Speed</td>
<td>PT</td>
<td>.004</td>
<td>-.017</td>
<td>-1.488***</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.004</td>
<td>.009</td>
<td>-1.238***</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.024</td>
<td>-.013</td>
<td>-0.886***</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interven</th>
<th>Time</th>
<th>Memory</th>
<th>Reasoning</th>
<th>Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>PT</td>
<td>-.012</td>
<td>-.117</td>
<td>0.105</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>-.175</td>
<td>-.163</td>
<td>0.107</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.100</td>
<td>-.015</td>
<td>0.400*</td>
</tr>
<tr>
<td>Reason</td>
<td>PT</td>
<td>-.048</td>
<td>.573***</td>
<td>-0.277</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>-.230</td>
<td>.208</td>
<td>-0.155</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.331</td>
<td>.276*</td>
<td>-0.434*</td>
</tr>
<tr>
<td>Speed</td>
<td>PT</td>
<td>-.108</td>
<td>-.111</td>
<td>-1.420***</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>-.168</td>
<td>-.097</td>
<td>-1.100***</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.298</td>
<td>.079</td>
<td>-0.755***</td>
</tr>
</tbody>
</table>
Effects of Booster Training

• Significant Booster Effect:

  • Speed: Booster Effect through 5 yr follow-up
  • Reason & Speed: Booster through 10 yr follow-up
Training Effects on Daily Function

- Self Reported IADL Difficulty:
- 5 yr Follow-up: Reason report significant less difficulty
- 10 yr Follow-up – All training groups report significant less difficulty

- Training had no effect on performance-based measures of function. However, booster speed training improved performance in Everyday Speed.
FIGURE 7. 10-year trajectory of Self-rated IADL Trajectory, Separately by Training Group

* Scores were reversed to graphically present decline.
Speed & Reason Effects: Reduced Crashes & Less Driving Cessation

- **Speed vs Control**
  - Speed vs Control
  - Cumulative Survival
  - Time (months) to driving Cessation or Crash

- **Reason vs control**
  - Reasoning vs Control
  - Cumulative Survival
  - Time till State-reported At-fault Crash (months)
Selectivity of Attrition at 5 Years

- Retained 67% (n = 1,877) of initial sample
- Attrition higher if male, older, lower MMSE, lower Reasoning and Memory Scores, less education, and more health problems at baseline
- No differences across treatment groups
Thank you
Goals of Presentation

• To review the 5-year results of the ACTIVE trial and their implications
• To summarize major themes from ACTIVE publications
• To discuss next steps for ACTIVE
• To identify challenges and suggest approaches for future training studies
Excluded

- Age < 65 years
- Substantial cognitive decline
  - MMSE < 23
  - self-reported Alzheimer's disease
- Substantial functional decline
  - Assistance with dressing, personal hygiene, bathing
  - Specified predisposing medical conditions (e.g., CVA)
- Severe sensory losses
- Communicative difficulties
- Similar cognitive training
- Unlikely availability
- Non-English speaking
Five-Year Results from the ACTIVE Trial

- Published in lead article in *JAMA*, December 20, 2006
- *JAMA*'s most read/most e-mailed article
- Extensive media coverage – *NPR, New York Times, Washington Post*
- *The Washington Post*'s most viewed and most e-mailed story
Sample: Unique Characteristics

Unusually heterogeneous sample for cognitive aging
- Minority elders (WSU, IU, JHU)
- Low income elders (PSU)
- Very old adults (HRCA)
Effect of Training on Function: Self-Reported IADLs

Mean IADL Difficulty Score over Time for different training groups:
- Memory trained
- Reasoning trained
- Speed trained
- Control

Baseline (N=2802) to Year 5 (N=1877)
Cognitive Abilities

**Reasoning**
- Word Series
- Letter Series
- Letter Sets

**Memory**
- Auditory Verbal Learning Test
- Hopkins Verbal Learning Test
- Rivermead Paragraph Recall

**Visual Processing Speed**
- Useful Field of View

Daily Function

**Everyday Problem Solving**
- Observed Tasks of Daily Living
- Everyday Problems Test

**ADL / IADL Functioning**
- Perceived IADL Performance
- Perceived IADL Capacity
- Perceived ADL Performance

**Everyday Speed**
- Complex Reaction Time
- Timed IADL Test
Effects of Booster Training

![Bar chart showing standardized booster effect size for memory, reasoning, and speed composite measures across three training groups: memory boosted, reasoning boosted, and speed boosted.](chart)
Major Areas of ACTIVE Publications (published, in press, submitted)

1. Short-term and long-term evaluations of training effects and real-world transfer / Effects of training on quality of life
   - Ball et al., JAMA, 2002
   - Wolinsky et al., J of Gerontol: Psych Sci, 2006
   - Wolinsky et al., J or Gerontol: Med Sci, 2006

2. Predictors of training responsiveness / Individual differences in training response / Applications of new methods for the study of longitudinal change (growth models, mixed effects longitudinal models)
   - Jones et al., Exp Aging Research, 2005
   - Unverzagt et al., submitted

3. Cognitive status and its association with training outcomes and functional changes
   - Crowe et al., International J of Geriatric Psychiatry, in press
   - Cook et al., submitted

4. Race/ethnicity effects on test performance, test bias and cognitive change
   - Aiken Morgan et al., Exp Aging Research, in press
   - Aiken et al., submitted
5. Physical factors / morbidity as predictors of cognitive function and change
   – Kuo et al., *J of Am Geriatr Soc*, 2005

6. Measurement studies (functional status, self-reported medications)
   – Owsley et al., *Gerontology*, 2002
   – Caskie et al., *Gerontologist*, 2004
   – Diehl et al., *J of Applied Gerontology*, in press

7. Mental health and well-being
   – Gallo et al., *Aging and Mental Health*, 2003
   – Yen et al., submitted
New Challenges for Advancing Cognitive Training

• Are there new ways to train people so that results generalize to multiple areas of daily function?
• What should be the accepted transfer target(s)?
• What is the expected time course?
• What is the best way to extend cognitive training to the cognitively impaired?
• Can we match interventions to individual risk profiles?
Next Steps for ACTIVE

• Proposed follow-up at 10 years to assess:
  – Protective effects on cognitive abilities, daily function, quality of life, driving safety, and health service use
  – Individual difference factors that moderate response to intervention, including low cognitive function, engagement, and APOE genotype
  – No additional intervention (booster training)
Next-Step Training Approaches

• Multi-faceted interventions that combine skill-based training and other behavioral and non-behavioral intervention techniques

• Hybrid approaches that target cognitive and functional abilities

• High-intensity, high-exposure interventions
  - activity-based (e.g. Baltimore Experience Corps)
  - life-style management
  - web-based, computerized
  - in-home, self-administered
Primary Analysis: Mixed Effects Model

- Dependent Variables: cognitive abilities and daily function
- Independent Variables: basic design features
  - treatment group
  - booster training
  - field site
  - replicate within site
  - time x training (net effect of trial)
  - time x booster (non-specific effects of additional social contact in booster)
  - time x training x booster (training-specific effects of booster)
### Effect of Training on Cognitive Abilities

<table>
<thead>
<tr>
<th>Abilities</th>
<th>Memory</th>
<th>Reasoning</th>
<th>Speed</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>-1.0</td>
<td>-4.8</td>
<td>-5.3</td>
<td>-4.0</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>0.23 (0.11, 0.31)</td>
<td>0.05 (-0.07, 0.17)</td>
<td>0.05 (-0.17, 0.17)</td>
<td></td>
</tr>
<tr>
<td><strong>Reasoning Change</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>4.3</td>
<td>8.1</td>
<td>4.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>-0.01 (-0.01, 0.08)</td>
<td>0.26 (0.17, 0.35)</td>
<td>0.02 (-0.06, 0.11)</td>
<td></td>
</tr>
<tr>
<td><strong>Speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>-19.1</td>
<td>119.6</td>
<td>241.8</td>
<td>-96.1</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>-0.01 (-0.15, 0.13)</td>
<td>0.15 (0.01, 0.29)</td>
<td>0.76 (0.62, 0.90)</td>
<td></td>
</tr>
</tbody>
</table>
## Effect of Training on Function

<table>
<thead>
<tr>
<th>Function</th>
<th>Memory</th>
<th>Reasoning</th>
<th>Speed</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IADL Difficulty</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>-0.7</td>
<td>-0.4</td>
<td>-0.3</td>
<td>-1.2</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>0.20 (-0.06, 0.46)</td>
<td>0.29 (0.03, 0.55)</td>
<td>0.26 (-0.002, 0.51)</td>
<td></td>
</tr>
<tr>
<td><strong>Everyday Problem Solving</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>1.5</td>
<td>1.8</td>
<td>1.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>0.15 (-0.28, 0.02)</td>
<td>-0.08 (-0.21, 0.05)</td>
<td>-0.05 (-0.18, 0.07)</td>
<td></td>
</tr>
<tr>
<td><strong>Everyday Speed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean change BL to 5 years</td>
<td>0.1</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Effect size (99% CI)</td>
<td>0.04 (-0.09, 0.17)</td>
<td>0.09 (-0.04, 0.22)</td>
<td>0.08 (-0.05, 0.21)</td>
<td></td>
</tr>
</tbody>
</table>
## A Taxonomy of Behavioral and Non-Behavioral Intervention Strategies
(adapted from Baltes)

<table>
<thead>
<tr>
<th>Goal</th>
<th>Level</th>
<th>Target</th>
<th>Type</th>
<th>Mode</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrich</td>
<td>Individual</td>
<td>Cognitive ability (e.g., memory,</td>
<td>Cognitive training-practice</td>
<td>Single component</td>
<td>Laboratory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>attention, executive function)</td>
<td></td>
<td></td>
<td>Clinic</td>
</tr>
<tr>
<td>Prevent</td>
<td>Small group (e.g., n =3-5)</td>
<td>Cognitive complaints</td>
<td>Cognitive rehabilitation</td>
<td>Multiple component</td>
<td>Hospital</td>
</tr>
<tr>
<td></td>
<td>Large group (e.g., n &gt; 5)</td>
<td>Efficacy beliefs</td>
<td>Phamaco-therapy</td>
<td></td>
<td>Home</td>
</tr>
<tr>
<td>Remediate</td>
<td>Neighborhood</td>
<td>Functional skills</td>
<td>Life-style modification</td>
<td></td>
<td>School</td>
</tr>
<tr>
<td></td>
<td>Community</td>
<td></td>
<td>(e.g., exercise, health</td>
<td></td>
<td>Workplace</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>habits, diet, stress</td>
<td></td>
<td>Community center</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>reduction)</td>
<td></td>
<td>Internet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Multiple settings (e.g.,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinic + Internet; clinic + home)</td>
</tr>
</tbody>
</table>
| Compensate    |                        |                                     |                           |                              |}

<table>
<thead>
<tr>
<th>Goal</th>
<th>Level</th>
<th>Target</th>
<th>Type</th>
<th>Mode</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Laboratory</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Home</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>School</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Workplace</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Community center</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Internet</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Multiple settings (e.g.,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinic + Internet; clinic + home)</td>
</tr>
</tbody>
</table>
Technology-Based: In-Home Video Training Study

• Developed and evaluated a modification of the standardized Speed of Processing training protocol for home use.

• Emphasis on accessibility and affordability.
Standard versus Home-based Training

- **STANDARD**
  - Lab-based
  - Trainer-facilitated
  - Computer-based
  - 8-10 sessions
  - 5 weeks

- **HOME-BASED**
  - Home-based
  - Self-administered
  - Videotape-based
  - 8-10 sessions
  - 5 weeks
FIGURE 2. Study Design

- Ineligible
- Screen for Eligibility → Refused
  - Eligible and Consent
  - Baseline Measurements
  - Randomize to Training
    - Memory
    - Reasoning
    - Speed
    - No Contact
  - Randomize to Training
    - Booster
      - Yes
      - No
    - Booster
      - Yes
      - No
    - Booster
      - Yes
      - No
  - 1-Year (A1) and 2-Year (A2) Tests
    - Booster
    - Booster
    - Booster
  - 3-Year (A3), 5-Year (A5), and 10-Year (A10) Tests


<table>
<thead>
<tr>
<th>Intervention</th>
<th>Time</th>
<th>Composite Outcome Measures</th>
<th></th>
<th></th>
<th>Memory-impaired</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Memory-normal</td>
<td>Memory</td>
<td>Reasoning</td>
<td>Speed</td>
</tr>
<tr>
<td>Memory</td>
<td>PT</td>
<td>.300**</td>
<td>-.009</td>
<td>-.050</td>
<td>-.012</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.254**</td>
<td>.033</td>
<td>-.061</td>
<td>-.175</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>.214**</td>
<td>.052</td>
<td>-.057</td>
<td>-.100</td>
</tr>
<tr>
<td>Reasoning</td>
<td>PT</td>
<td>.001</td>
<td>.477**</td>
<td>.025</td>
<td>-.048</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.013</td>
<td>.416**</td>
<td>-.026</td>
<td>-.230</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.003</td>
<td>.262**</td>
<td>-.021</td>
<td>-.331</td>
</tr>
<tr>
<td>Speed</td>
<td>PT</td>
<td>.004</td>
<td>-.017</td>
<td>-1.488**</td>
<td>-.108</td>
</tr>
<tr>
<td></td>
<td>A1</td>
<td>.004</td>
<td>.009</td>
<td>-1.238**</td>
<td>-.163</td>
</tr>
<tr>
<td></td>
<td>A2</td>
<td>-.024</td>
<td>-.013</td>
<td>-1.886**</td>
<td>-.298</td>
</tr>
</tbody>
</table>

*Note.  PT = post-test, A1 = first annual assessment, A2 = second annual assessment.  
* p < .05  
** p < .001