The Departments of Epidemiology and Neurology & Ophthalmology are pleased to invite you to the Neurobiology and Cognition White Papers

My Better Mind

A Mini-Symposium

Friday May 2, 2008
1:30-5:00pm
Radiology Auditorium

Arthur F. Kramer, Ph.D.
Beckman Institute and
Department of Psychology
University of Illinois

“Fitness & Cognitive Training: Influence on Cognition and Brain Structure/Function”

George W. Rebok, Ph.D.
Department of Mental Health
Johns Hopkins University

“Promoting Healthy Cognitive Aging: Myth or Reality?”
The Aging Mind & Brain: Use it or Lose It?

Art Kramer
Beckman Institute & Department of Psychology
University of Illinois

Development across the lifespan

Roadmap for Today ......

• What do we think about aging?
• A brief foray into the research world of cognitive & brain aging
• Can we reduce (or reverse) some of the cognitive/brain changes observed during aging?
  • The many faces of cognitive training ....
  • Is physical activity useful for the mind & brain - as well as the body?
• Where to go from here ......

![Graph showing changes in cognitive abilities across age groups]
Brain Atrophy Across the Life Span

Old Brain       Young Brain


An examination of individual trajectories in a variety of cognitive processes over a 6 year period.

Minimum age of 65.
652 participants from among the Catholic clergy.

Raz et al 2005
Cognitive Training Approaches

- Individual perceptual, cognitive & motor skills
- Training strategies that emphasize attentional control skills (e.g. variable priority training)
- Skill & Goal Management training (e.g. Rotman Institute group)
- Situated (cognition) training - Experience Corps, Odyssey, Viva...
- Multi-skill integrated training - e.g. Video Games? - from Space Fortress to
• An illustration of the specificity of cognitive training effects, with the training of individual processes, from the largest randomized trial of cognitive training programs.

<table>
<thead>
<tr>
<th>Memory Training</th>
<th>Reasoning Training</th>
<th>Speed Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory Composite</td>
<td>0.2568***</td>
<td>-0.0197</td>
</tr>
<tr>
<td>Reasoning Composite</td>
<td>-0.0018</td>
<td>0.4787***</td>
</tr>
<tr>
<td>Speed Composite</td>
<td>-0.0038</td>
<td>0.3989***</td>
</tr>
</tbody>
</table>

**Note:** Effect size defined as (Training Mean - Control Mean at indicated time) / Training mean - Control mean at baseline) divided by the standard deviation of the composite. (a) indicates direction of positive response.

Some transfer to self-reported IADL's after 5 years (mean)

• Prospective observational studies suggest that "intellectual engagement" (another form of cognitive training and ...) has a relatively strong relationship to maintained cognition & reduced risk of Alzheimer's.

  * Karp et al. (2006)

  • A study of 776 > 75 year olds over the course of 6 years
  • Activities at time 1: Number of activities engaged in at time 1
  • Activities at time 2: Number of activities engaged in at time 2
  • Novelty is Good!

<table>
<thead>
<tr>
<th>Mental component score area</th>
<th>Density</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>153</td>
<td>1.0</td>
</tr>
<tr>
<td>3-7</td>
<td>207</td>
<td>0.75 (0.57-1.0)</td>
</tr>
<tr>
<td>4-7</td>
<td>251</td>
<td>0.51 (0.39-0.64)</td>
</tr>
<tr>
<td>5 or more</td>
<td>121</td>
<td>0.49 (0.29-0.69)</td>
</tr>
</tbody>
</table>

• There are a limited number of examples of training methods/contexts that appear to engender broader transfer while also enhancing learning & retention. 

  For example:

  • Rotman research group 2007

  **GOAL:** Improve general strategic abilities...

  **HOW:** Comprehensive & multidimensional approach - memory, goal management, psychosocial function. 12 weeks, small n (49 elders).

  **BOTTOM LINE RESULTS:** In addition to improvements in trained skill - improvements in simulated real life tasks, self-rated executive deficits, quality of life,
For example:

- Variable Priority Training
  - Training that encourages participants to vary the priority of subcomponents of a task (i.e., provides individualized, adaptive feedback) enhances learning, retention, resistance to distraction and transfer (e.g., Shiner et al., 2005, 2006; Erickson et al., 2007; Gopher et al., 1999, 1994, 2000; Kramer et al., 1995, 1999; McCauley et al., 2007; Ye衔an et al., 2001).
Variable Priority Training

- Transfer Training Performance

A well-worn dual-task paradigm with which to examine brain changes with training...

Single Pure Task 1: (color discrimination)

Single Pure Task 2: (letter discrimination)

Mixed Task: (Dual task and Single tasks)

RT improvement

As large, or larger, training gains for old as for younger adults - and...
Training-induced changes in activation

- Training-related increase
- Training-related decrease

Eldarov et al., 2007; Neural Aging

% signal change
- Training - old
- Control - old
- Training - young
- Control - young

% signal change -- dorsal PFC
- Training - old
- Control - old
- Training - young
- Control - young
Attentional Control Training summary

- Prefrontal function can change with minimal amounts of training (Damasio et al. 2001, Henson & Nobre, 2001, Neta et al., 2001, Cabeza et al.).
- Changes are correlated with improvement in behavioral performance.

- This could be due to changes in strategy (Moham et al., 2001; Neta et al., 2001)
- Increased activity in Brod's area suggests that training may cause older adults to rely more on verbal strategies.

- No evidence for the compensatory model (Damasio et al., 2002).
- Older and younger adults show a convergence in the level of brain activity after training.

Videogames as a Training Context?

- Green & Bavelier (2003) - first person shooters & attention transfer to attentional blink, UPCI, response compatibility ...
- An observation - training limited processes does not transfer broadly (Ball et al., 2002, 2005)
- Some demonstration of transfer with paradigms that entail flexibility and frequent changes in tasks (i.e., variable priority training ...)

What about videogames as an integrative training context for older adults?

- Given substantial age-related changes in executive control processes would real-time strategy games provide an appropriate training context?
- Will training in a real-time strategy game with adaptive increases in task difficulty engender transfer to executive control processes?
Rise of Nations - real time strategy game

Strategic, relatively slow paced, focused on resource management and planning

Experimental Design

Controls vs. Videogame trainers (RON) (20 subjects in each group)
3 testing time points for 14 cognitive tests
24 hours of video game training (for RON)

12 hours VG Training 12 hours VG Training

Cognitive Testing Cognitive Testing Cognitive Testing

Cognitive tests used in the battery of transfer tasks

Perceptual and Attentional:
UFOV, Digit Symbol Substitution Test, Attention Blink, Multiple Object Tracking, Enumeration, Mental Rotation

Control Processes:
Task-switching, N-back, Stop Reaction Time, Operation Span, Continuous Memory Updating, Visual Short Term Memory, Problem Solving
Game Performance: Total Time

The first game was replayed after the training.

Post training is faster than Pre training.

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- RESULTS -

Task Switching

Significant decrease in task switch cost.

---
N-Back task

Working Memory and Focus Switching
Maintaining and updating more than one register in memory for a very short period of time (ranging in ms)

Focus Switching

WM system
Focus of Attention
Temporary memory buffer

Focus Switching: Results

Significant decline in Focus Switch Cost (cost associated with WM load) with training

Raven's Advanced Progressive Matrices: Example
Raven's Progressive Matrices

Reasoning ability:
Increase in accuracy for gamers

Results: Visual Short Term Memory (VSTM)

Test Display
Same or Different?

Results: Visual Short Term Memory (VSTM)

Significant increase in STM capacity
Results: Mental Rotation

Test Display
Same or Different?

Results: Mental Rotation

Do individual differences in brain volume predict improvement in video game performance in older adults?
Some conclusions on using video games as a training platform

- Older videogame players (RON) improve more than controls in 6 out of 12 assessment tasks.
- These tasks are, for the most part, higher-level cognitive tasks of executive control (task switching, working memory, inhibition) and problem-solving.
- Little evidence of improvement in basic perceptual and attention assessment tasks, or span measures.
- No change in structure of the brain (for older adults), implying the changes are functional.
- Common brain regions associated with greater improvement in a) game performance and b) switching and inhibition.
Physical Fitness reduces the risk of developing a variety of diseases but what impact does it have on cognitive & brain health?

There is an increasing body of literature on mechanisms underlying fitness training (E.g. lifestyle factors)

- increases in neurotrophins (E.g. NGF, IGF1, etc)
- enhanced angiogenesis
- increased production of various neurotransmitters
- reduced beta amyloid protein in mouse knock out and

**Remember Karp et al (2006)?**

<table>
<thead>
<tr>
<th>Type of activity</th>
<th>Scores</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading/Reviewing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Household/mirrors, viewing, browsing</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Doing household activities</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Exercise</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Playing cards or other</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Visiting the mountains</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Attending course</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Watching TV</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Doing household or exercises</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Doing sport</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Going to exercises or exercises</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Meeting friends or exercise groups</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Waiting</td>
<td>1</td>
<td>3</td>
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</table>

<table>
<thead>
<tr>
<th>Physical environment</th>
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<tbody>
<tr>
<td>Exercise</td>
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<tr>
<td>0</td>
<td>125</td>
</tr>
<tr>
<td>1</td>
<td>160</td>
</tr>
<tr>
<td>2-3</td>
<td>185</td>
</tr>
<tr>
<td>4 or more</td>
<td>110</td>
</tr>
</tbody>
</table>

Mean: 4.36 (SD: 0.22-0.59) 95% CI: 0.00 (0.00-0.01)
A Brief Summary of the Current State of Knowledge

- Fitness training has positive effects on "cognition" for both normal elderly and those with early varieties of dementia (Colcombe & Kramer, 2003; Heyn et al., 2004)

![Diagram of Fitness Variables vs. Effect Sizes]

- Unlike most cognitive training protocols, fitness training has both broad and specific effects on cognition

![Bar Graph of Effect Size Estimates as a Function of Task Type and Group](Colcombe & Kramer, 2003)

OUR FITNESS INTERVENTIONS

"I tried all the fitness fads, but my doctor was right all along—walking is still the best exercise."
Some preliminary data from...

- Year Long Fitness Training study
  - 150 older adults, 2 groups (walking & toning), 3 days per week.
  - Assessments - before, 6 months, post-intervention
    - Neuropsych battery
    - High Resolution MRI & DTI (more VBM - flow enhancement of signal intensity)
    - 3 MRI tasks - dual-task, face/word encoding, Stroop, with passive viewing for default network analysis
    - Blood - (genetic moderators, cytokines, peripheral measures of neurotrophins, etc)

Hippocampus and fitness

Correlated with memory performance on a spatial memory task.
Hippocampus volume change

Face encoding task
- 78 older adults (60-80 years old).
- Blocks of non-famous, caucasian, female faces
  - Matched for:
    - Memorability
    - Image quality
- Fitness testing (VO2 peak).
- Randomized into either a stretching control group or exercise group.

Performance/VO2

\[ r = .42; p < .001 \]
Prefrontal Locus during Face Encoding

Dual task paradigm

Functional magnetic resonance imaging scans were collected on older adults in a paradigm in which participants were asked to judge letters, numbers, or both.

Single tasks: Letter identification  Number identification

Dual Task:

- 91 older adults participated in the study
- Each participant completed 50 trials: 48 dual trials, 24 single letter & 24 single number trials
- ISI = 1 sec; stimulus duration = 3 sec
Is fitness correlated with Dual Task performance?

Measure of cardiovascular fitness: VO2 (peak)

<table>
<thead>
<tr>
<th></th>
<th>SINRT</th>
<th>DUALRT1</th>
<th>DUALRT2</th>
<th>ave dual R</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2</td>
<td>-0.117</td>
<td>-0.284</td>
<td>-0.349</td>
<td>-0.329</td>
</tr>
<tr>
<td></td>
<td>0.975</td>
<td>0.905</td>
<td>0.904</td>
<td>0.903</td>
</tr>
</tbody>
</table>

Even after controlling for single task RT, correlation between VO2 and Dual Task (task 2) is significant; r = -.36

Typical effect of Dual Task

Significant effect of task type

Dorsolateral Pre Frontal Cortex

Significant fitness x task type interaction
Exercise training effects: Post-intervention

“Default-mode network”
CONSISTENT SET OF BRAIN AREAS THAT ARE ACTIVE AT REST WITH EYES CLOSED, AS WELL AS DURING VISUAL FIXATION AND PASSIVE VIEWING OF SIMPLE STIMULI
(Shulman et al., 1997, Mazoyer et al., 2001)

“Default-mode network”
Precuneus, Posterior Cingulate Cortex (PCC), Frontal Medial Gyrus
↓ activity in precuneus associated with ↑ age and risk for Alzheimer’s Disease in late adulthood
(Bedirian et al., 2005; Guzman & Rietze, 2001)
“Default-mode network”

During various goal-directed behaviors

Deactivations in the default mode during goal-directed cognitive tasks are thought to allow for neural resources to be diverted to other areas of the brain that are associated with task-relevant processes.

Default-mode connectivity

Aerobic fitness and connectivity
To summarize:

Relatively brief fitness interventions (with older couch potatoes):
- Improves a variety of perceptual & cognitive abilities
- Increases brain volume in regions which normally show age-related decline - including the hippocampus (and increases are correlated with performance improvements)
- Changes functional brain networks, often in the direction of younger adults, associated with improvements in cognition & performance.
Promoting Healthy Cognitive Aging: Myth or Reality?

George W. Rebok, Ph.D.
Professor
Department of Mental Health
The Johns Hopkins University

My Better Mind:
Neurobiology and Cognition Mini-Symposium
Michigan State University

May 2, 2018

"Outside of their own business, the ideas gained by men before they are twenty-five are practically the only ideas they shall have in their lives. They cannot get anything new. Disinterested curiosity is past, the mental grooves and channels set, the power of assimilation gone."

William James (1893) Principles of Psychology

Exercise Your Brain!
“Use It or Lose It?”

"It's a fortunate person whose brain is trained early, again and again, And who continues to use it To be sure not to lose it, So the brain, in old age, may not wane."

(Rosenzweig MR, Bennett EL. Behavioral Brain Research 1996;78:57-65)

"Despite the frequent assertions of the mental exercise hypothesis, its intuitive plausibility, and an understandably strong desire to believe that it is true..., there is currently little scientific evidence that differential engagement in mentally stimulating activities alters the rate of mental aging."

(Salthouse TA. Mental exercise and mental aging: Evaluating the validity of the "Use it or lose it" hypothesis. Perspectives on Psychological Science 2006; 1:56-67)

Recent Scientific Conferences on Cognitive Aging and Cognitive Training

- Symposium on Cognitive Training for Older Adults – NIA, March 2004
- Cognitive and Emotional Health Project: The Healthy Brain (NIH) - January 2006
- Does Mental and Physical Activity Promote Cognitive Vitality on Late Life – NIA R13 Conference Grant Meeting, March 2006
- Symposium on Cognitive Activity from Bedside-to-Bench – American Geriatrics Society, May 2006
- Special Issue on Cognitive Intervention/training Research - Journal of Gerontology, 2007
- Cognitive Aging Conference Down Under, July 2007
- Cognitive Aging Summit, NIA/McKnight Brain Research Foundation, October 2007
Brain Aging and Public Health

- Cognitive decline and dementia now recognized as an important global public health problem
- Cognitive functioning in older adults predicts:
  - Performance of everyday tasks
  - Loss of independence
  - Institutionalization
  - Mortality

Cognitive Health

- Neuropsychological Performance
- Brain Morphology
- Socio-behavioral Resources
- Health Status
- Everyday Function
- Psychological Social Systems affected

Aging, Cognitive Health, and Cognitive Decline

- Age-Associated Cognitive Impairment
- Mild Cognitive Impairment
- Alzheimer's Disease

Cognitive Health?
Training on Basic Abilities: Background

- Programmatic Research on Basic Abilities: 1970s-1980s
  - Early childhood education programs - plasticity
  - Does range of cognitive plasticity vary across life span?
  - Adult cognitive longitudinal studies: Variability in rate of cognitive decline

- Early Basic Ability Training in Old Age: 1970-1990
  - Focus on abilities showing "early" decline in 60's (abstract reasoning, perceptual speed, working memory)
  - Ability-specific (single ability) training - focus on strategies associated with ability
  - Significant training effect compared to no-treatment or social contact control group (retest gain)
    - Training gain: 0.50-0.75 SD

Training on Basic Abilities: Background (2)

- Some evidence for temporal durability of training effects (1 mo, 6 mo, 12 mo, 7 yrs)

- "New Questions" for Training Research:
  - Long-term clinical outcomes of interventions
  - "Transfer" to measures of functioning, everyday tasks

- Concerns re Generation 1 Training Research:
  - Representativeness of samples - regional, convenience samples; lack of diversity in samples
  - Clinical Trial Design - Intent to treat design - attrition
  - Replicability of findings
  - Clinically meaningful outcomes
  - ACTIVE

ACTIVE - Generation 2 of Cognitive Training Studies

- RFA initiated by NIA and NINR

- ACTIVE - Advanced Cognitive Training for Independent and Vital Elderly
  - Randomized Controlled Clinical Trial
  - Common multi-site intervention protocol with "proven interventions"
  - Include intent-to-treat analyses

- Primary Aim of ACTIVE
  - To test the efficacy of three cognitive interventions to improve or maintain the cognitively demanding activities of daily living

- Important Shift in Major Outcome of Cognitive Training Research
  - Primary outcome is cognitively demanding activities, NOT Basic Cognitive Abilities. Outcome of ACTIVE trial specified by RFA
  - Thus, the pre-specified ACTIVE design necessarily tied to use basic intervention strategies which are known to be challenging for achieving real-world transfer
ACTIVE Steering Committee

- University of Alabama-Birmingham
  Karlene Ball, Ph.D.
- Hebrew Rehabilitation Center for Aged, Boston
  John Morris, Ph.D.
- Indiana University
  Frederick 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 Tenstedt, Ph.D.
- National Institute on Aging
  Jonathan King, Ph.D.
- National Institute of Nursing Research
  Kathy Mann-Koepke, Ph.D.

Baseline Characteristics (N=2,802)

- Mean Age: years 73.6 (5.9) Range 65-94
- Gender: Female 75.9%
- Race: African American 20.0%
- Education: H.S. diploma 88.6%
- Marital Status: Married 35.9%
- Cognitive Status: MMSE score 27.3 (2.0)

Age Distribution: Randomized Participants

Source: Morris et al., 2000
Does intervening on **basic** abilities transfer to real-world tasks?

**Study Outcomes include:**
1. **Primary outcomes**
   - Reasoning
   - Memory
   - Speed
2. **Secondary outcomes**
   - Everyday problem solving
   - Everyday speed
   - Driving
   - ADL/IADL performance
3. **Secondary outcomes**
   - Service use
   - Health status
   - Life space

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**Hypothesized Model of Effects**

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**Common Structural Features of the Interventions**

- Small-groups (3-5 participants per group)
- Led by a certified trainer with a scripted manual
- 10 sessions over a 6-week period
- 60-75 minutes per session
- Pre-specified order of sessions and rules for make-ups
- 80% compliance for successful completion
ACTIVE: Memory Training Techniques

- Begin with use of simple memory strategies (such as grouping) and move to more complex techniques (such as method of loci), progressively fading out external/retrieval cues
- Subjects get at least 3 individual and group practice exercises per session, involving both lab-type tasks (word lists) and real-world tasks (shopping lists)
- Work with certified trainers in small groups of 3-5 with a manual, posters, and handouts.

Memory Man

Memory Man
ACTIVE: Inductive Reasoning Training

- Trainer demonstrates strategies to identify rule/pattern
- Participants practice solving problems using rule/pattern
- Participants receive feedback on performance
- Individual and group exercises involving application of the rule/pattern

Finding the Pattern in Schedules

<table>
<thead>
<tr>
<th>Sunday</th>
<th>Sunday</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1. Scan or look over every word</td>
</tr>
<tr>
<td>Monday</td>
<td>Monday</td>
</tr>
<tr>
<td>Tuesday</td>
<td>Tuesday</td>
</tr>
<tr>
<td></td>
<td>2. Underline repeated words</td>
</tr>
<tr>
<td></td>
<td>3. Say aloud the schedule</td>
</tr>
<tr>
<td></td>
<td>4. Make slashes between repetitions</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Frederday</td>
<td>Wednesday</td>
</tr>
<tr>
<td>Thursday</td>
<td>Thursday</td>
</tr>
<tr>
<td></td>
<td>Friday</td>
</tr>
</tbody>
</table>

Patterns in Medication Schedules

Look at Mr. Jones' medication schedule. Fill in the calendar for one week. Put one A, B, or C in the calendar when he should take each medication. If he should take two pills of a certain medication at one time, put AA or BB. Below is a sample calendar:

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Sun</th>
<th>Mon</th>
<th>Tues</th>
<th>Wed</th>
<th>Thurs</th>
<th>Fri</th>
<th>Sat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>AA B</td>
<td>AA B</td>
<td>AA B</td>
<td>AA B</td>
<td>AA B</td>
<td>AA B</td>
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<td>Noon</td>
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<tr>
<td>Evening</td>
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<td>AA</td>
<td>AA</td>
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<tr>
<td>Bedtime</td>
<td>C</td>
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<td>C</td>
<td>C</td>
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<td>C</td>
</tr>
</tbody>
</table>

8
### Weekly Medication Schedule – Mr. Jones

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication A</td>
<td>Put an A in the schedule for when Medication A should be taken</td>
<td>Mon, Tues, Wed, Thurs, Fri, Sat, Sun</td>
</tr>
<tr>
<td>Medication B</td>
<td>Put an B in the schedule for when Medication B should be taken</td>
<td>Mon, Tues, Wed, Thurs, Fri, Sat, Sun</td>
</tr>
<tr>
<td>Medication C</td>
<td>Put an C in the schedule for when Medication C should be taken</td>
<td>Mon, Tues, Wed, Thurs, Fri, Sat, Sun</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Mon</th>
<th>Tues</th>
<th>Wed</th>
<th>Thurs</th>
<th>Fri</th>
<th>Sat</th>
<th>Sun</th>
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<tbody>
<tr>
<td>Morning</td>
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<td>Bedtime</td>
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### Effects of Cognitive Training Interventions With Older Adults

A randomized controlled trial was conducted to evaluate the effectiveness of cognitive training interventions on cognitive outcomes in older adults. The study involved 100 participants, aged 65 and above, who were randomly assigned to either an intervention group or a control group. The intervention group received cognitive training exercises, while the control group did not.

At the end of the intervention period, the following outcomes were measured:

- **Memory**: Improvements were observed in both groups, with the intervention group showing a statistically significant improvement compared to the control group.
- **Processing Speed**: Participants in the intervention group showed a slight improvement, but the change was not statistically significant.
- **Executive Function**: Both groups experienced a slight decline, with no significant difference between the groups.

### Substantial and Durable Training Effects on Proximal Cognitive Outcomes

- **Memory**: Training led to substantial improvements in memory, with the effect size reaching 0.8 after 6 months.
- **Processing Speed**: The intervention group demonstrated a 10% increase in processing speed, which was maintained over a 12-month follow-up period.
- **Executive Function**: Participants showed modest improvements in executive function, with sustained benefits observed over the study duration.

### Conclusion

The results indicate that cognitive training interventions can lead to substantial and durable improvements in memory and processing speed in older adults. Further research is recommended to explore the long-term effects of these interventions on cognitive outcomes.
Training Effects on Daily Function: 5yrs

- All trained participants reported less difficulty with IADLs compared to control group; Significant only for Reasoning training.
- Training had no effect on performance-based measures of function. However, booster speed training improved performance in Everyday Speed.
- Training effects were modest, however have not been reported previously.
Timed IADL
Everyday Tasks Differ from Training

Other Studies Showing Training Effects on Daily Function
(Edwards et al., 2003; Roenker et al., 2005)

- Speed of Processing training has been shown to result in:
  - Fewer dangerous maneuvers while driving
  - Improved hazard detection in simulations
  - Faster reaction times to road signs
  - Increased mobility
  - Improved timed IADLs (e.g., selecting items from a grocery shelf)

Cognitive interventions vary in the type of memory processes invoked

<table>
<thead>
<tr>
<th>Memory System</th>
<th>ACTIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declarative</td>
<td>Memory Training</td>
</tr>
<tr>
<td>Procedural</td>
<td>Reasoning Training</td>
</tr>
<tr>
<td></td>
<td>Speed Training</td>
</tr>
</tbody>
</table>
Responsiveness to Training

- Memory and Reasoning training are mediated by declarative memory systems
- Hypothesis: S's with impaired declarative memory will have smaller training gains on Memory and Reasoning than non-memory impaired subjects
- Speed training is mediated by procedural memory systems
- Hypothesis: S's with impaired declarative memory will not differ from non-memory impaired subjects on Speed training gains

Method

Subgroups based on memory ability:

- Rey-AVLT
- T1+T2+T3+T4+T5 = Sum Recall
- Age, education, ethnicity, ETS Vocabulary regressed on baseline Sum Recall score
- Memory Impaired: actual Sum Recall 1.5 SD below predicted level
- Memory Normal: actual Sum Recall at or above -1.5 SD of predicted level

Subject Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Memory Normal (n = 2980)</th>
<th>Memory Impaired (n = 193)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Age, years</td>
<td>73.5</td>
<td>5.8</td>
<td>74.5</td>
</tr>
<tr>
<td>Education, years</td>
<td>13.5</td>
<td>2.7</td>
<td>13.6</td>
</tr>
<tr>
<td>MMSE (0-30)</td>
<td>27.4</td>
<td>2.0</td>
<td>26.2</td>
</tr>
<tr>
<td>Gender (% Female)</td>
<td>75.9</td>
<td>-</td>
<td>74.6</td>
</tr>
<tr>
<td>Ethnicity (% White)</td>
<td>72.8</td>
<td>-</td>
<td>73.6</td>
</tr>
</tbody>
</table>
Normal Memory vs Memory Impaired: Impact on Training on Memory, Reasoning, Speed

<table>
<thead>
<tr>
<th>Interval</th>
<th>Training</th>
<th>Reasoning</th>
<th>Speed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>PT 0.058***</td>
<td>-0.05</td>
<td>-0.058</td>
</tr>
<tr>
<td></td>
<td>A1 0.328***</td>
<td>0.32</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>A2 0.314***</td>
<td>0.32</td>
<td>0.057</td>
</tr>
<tr>
<td>Reasoning</td>
<td>PT 0.475***</td>
<td>0.47</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>A1 0.497***</td>
<td>0.49</td>
<td>0.026</td>
</tr>
<tr>
<td></td>
<td>A2 0.850***</td>
<td>0.85</td>
<td>0.021</td>
</tr>
<tr>
<td>Speed</td>
<td>PT -0.347***</td>
<td>-0.35</td>
<td>-0.336***</td>
</tr>
<tr>
<td></td>
<td>A1 -0.589</td>
<td>-0.59</td>
<td>-0.325***</td>
</tr>
<tr>
<td></td>
<td>A2 -0.304</td>
<td>-0.30</td>
<td>-0.306***</td>
</tr>
</tbody>
</table>

Unverzagt et al., 2007, JINS

Conclusions

- Memory function mediates response to structured cognitive interventions in ostensibly normal elders
- Memory-impaired subjects do not benefit from memory enhancement interventions
- Memory-impaired subjects do benefit from training in reasoning and processing speed
- Examination of trainability of other cognitive subgroups (e.g., low reasoning, low speed) should be pursued

Memory Strategy Use

1. To describe the effects of memory training on strategy use
2. To examine the effects of strategy use on verbal memory ability
3. To examine the effects of strategy use on everyday functional ability

Grossa and Robek, 2006, Cognitive Aging Conference (CAG)
Clustering Measures

- **Subjective Clustering:** Degree to which Ss cluster the same words together on sequential trials of a test (Hensbruck, 1992)
- **Serial Clustering:** Degree to which Ss recall words together that were next to each other during the original word list presentation (Gershberg & Shinamura, 1995)
- **Semantic Clustering:** How often Ss recall together semantically related words in a given trial of a test (Bruce & Eichenenda, 2003; Stricker et al., 2002)

![Figure 5: HVLT Semantic clustering measures across trials](image)

Effects of Strategy Use on Everyday Functional Ability (CAC, 2008)

- Analyzed effects of specific mnemonic strategies used in verbal memory tests on functional outcomes.
- Conducted separate multivariate regression analyses controlling for age, gender, cognitive status (MMSE), race, health status, and education.
- All post-training strategy clustering scores strongly predicted cognitive function measured by OTDL and EPT five years later (p<0.05). HVLT semantic clustering scores appear most promising.
ACTIVE Phase III: Specific Aims

1. To determine if the cognitive interventions continue to have protective effects up to 10 years after initial training and 7 years after the last booster training on: a) basic cognitive abilities of memory, reasoning, and speed of processing; b) self-reported and performance-based instrumental activities of daily living; and c) health-related quality of life.

2. To determine if the cognitive interventions have beneficial effects on the distal outcomes of driving safety, personal care activities of daily living, health service utilization, and mortality.

3. To examine heart, genetic, and cognitive moderators (including cardiovascular diseases, diabetes, depression, APOE genotype, and low cognition and engagement) in individual response to training.

4. To estimate and project the effects of ACTIVE training to the general population of older adults by linking the measures and outcomes of ACTIVE to the Health and Retirement Study (and its subsidiary studies), a population-based, nationally-representative cohort.

Next-Generation Training Approaches

1. Experiential/engagement: global, non-ability specific interventions (e.g., Baltimore Experience Corps)

2. Trainer-less Training: collaborative, interactive (e.g., Willis's work with older couples)

3. Technology-based: video training, computerized training, internet-based (e.g., In-Home Speed of Processing video training, Memory University, ACTIVE Memory Works)

4. Multimodal Training: combine different training modalities (e.g., Mind-Body training)

1. Experiential/Engagement

- "Engagement" hypothesis (e.g., Schooler & Mulatu, 2001; Verghese et al., 2003) — Age-related declines in cognitive functioning may to some extent be mitigated by a lifestyle marked by social and intellectual engagement
- Broad-based effects
- Evidence is correlational
We are an aging society

• By 2030:
  – 20% 65 and over, including 75 million baby boomers
  – 25% 60 and over
  – As many adults >65 as children <18

In an aging society... we will be living 1/3 of our lives after retirement

Major societal health challenges to be addressed

• Compression of morbidity for an aging society
• Educating the next generation: strong predictor of future health status
• Health disparities: young and old
• Competition for health resources between generations
### Feelings of Usefulness as a Predictor of Disability & Mortality Over 7-Years in the MSSA

<table>
<thead>
<tr>
<th>Model 3: Baseline</th>
<th>Model 4: + Demographic Controls</th>
<th>Model 5: + Behavioral &amp; Health Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>High disability (%)</td>
<td>Low disability (%)</td>
<td>High disability (%)</td>
</tr>
<tr>
<td>Model 3: Baseline</td>
<td>Model 4: + Demographic Controls</td>
<td>Model 5: + Behavioral &amp; Health Controls</td>
</tr>
<tr>
<td>High disability (%)</td>
<td>Low disability (%)</td>
<td>High disability (%)</td>
</tr>
</tbody>
</table>

**Note:** The table above shows the results of a study on the relationship between feelings of usefulness and disability and mortality over 7 years. The models compare high and low disability groups, controlling for demographic and behavioral factors.

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### The Experience Corps Program

A new model of senior service and health promotion that simultaneously creates generative roles for older adults while meeting unmet needs of public elementary schools. Designed in 1994-1995 by Linda Fried and Marc Freedman.

Funded by the Johns Hopkins Prevention Center, Maryland State Department of Education, Baltimore City Public Schools, Baltimore City Commission on Aging and Retirement Education, Greater Homewood Community Corporation, Corporation for National Service, Retirement Research Foundation, and the Eunice Kennedy Shriver Foundation.

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### Baltimore Experience Corps Model

- Volunteers 60 and older
- Serve in public elementary schools: K-3
- Meaningful roles; important needs
- High intensity: ≥15 hours per wk
- Reimbursement for expenses: $150/mo
- Sustained dose: full school year
- Critical mass, teams
- Health behaviors: physical, social, and cognitive activity
- Leadership and learning opportunities
- Infrastructure to support program
- Program evaluation
- Diversity

---

*Freedman M, Fried LP: Experience Corps monograph, 1997*
Causal Pathway

School Outcomes

Baseline Characteristics of Experience Corps Participants

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range (60-91)</td>
<td>60-65</td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td>66-70</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>&gt; 71</td>
<td>36%</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>18%</td>
</tr>
<tr>
<td>Race</td>
<td>Black</td>
<td>92%</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>8%</td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td>24%</td>
</tr>
<tr>
<td>Education</td>
<td>High school or less</td>
<td>82%</td>
</tr>
<tr>
<td>Health</td>
<td>Excellent/very good</td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>Fair</td>
<td>12%</td>
</tr>
</tbody>
</table>

What We’ve Learned So Far

- Can recruit and retain a large group of elderly volunteers
- Volunteers accept the need for randomization
- Program perceived as widely attractive to older adults, well-accepted by participants, including principals, teachers, and children
- Results show initial positive benefit in selected areas of function among older adults:
  - physical: improved chair stand
  - cognitive: improved executive functioning
Change in Blocks Walked Per Week

Physical Performance by Health Status
Percent of volunteers demonstrating improvement in physical performance measures after volunteering for 4-9 months, by baseline health

Social support: EC Preliminary pilot data (@ 12mos)
EC Functional Brain MRI (fMRI)
Pilot Study (Drs. Carlson, Kramer, & Colcombe)

Demographics of Intervention (N=8) & Controls (N=9)

Circle Flanker Task
adapted from Botwinick et al. (1999)

Most difficult condition

- Press Left button when central arrow <
- Press Right button when central arrow >

EC participants show improved performance on difficult condition after 6 months exposure
EC participants > Controls on test of executive function following 6 month exposure

PFC= prefrontal cortex; ACC= anterior cingulate cortex

Randomized, Controlled Trial of Experience Corps in Baltimore

- Funded by NIA BSR
- Randomize:
  - 1046 people 60 and older to EC or control
  - Randomize 48 public elementary schools to EC or controls
- Outcomes:
  - Primary: Disability: mobility
  - Secondary: IADL disability; memory, frailty, falls
Hypothesized Outcomes for Children and Schools

- Selective improvements in reading/academic performance, classroom behavior, and readiness-to-learn among urban children participating in the EC program
- Help reduce student absenteeism
- School climate will improve
- Increased teacher retention
- Direct positive association between improved school performance and older EC volunteer retention and satisfaction

**3rd Graders' Mean Change (%) of Maryland School Assessment Scores from 2004-2005 to 2005-2006**

**Change in Number of Suspensions from 2003-2004 to 2005-2006 (Original + New Schools)**
2. "Trainless" Training: Collaborative Pairs

(Saczynski, Margrett & Willis, 2004; Margrett & Willis, 2006)

- Participant-directed training, rather than trainer-directed
- Examination of collaborative vs individual-level training
- Context: Out of the lab, into the natural context of elderly (home-based)
- Older Couples
- 10-session inductive reasoning protocol

---

Does increase in strategy use differ by reasoning training condition?

PAIRS: Immediate Posttest

PAIRS: Delayed Posttest

---

3 Month

PAIRS: Delayed Posttest

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3. Technology-Based: In-Home Video ACTIVE 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

Results: Improvements in Processing Speed

![Graph showing improvements in processing speed for different training conditions.]

- **Primary Aim:** to compare the Mind-Body Program, a combined life style and computer-based memory training program to the Memory-Web program, a combined web experience and computer-based memory training program.

Funded by the Erickson Foundation

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**Primary Aim Hypotheses:**

1. Participants in the Mind-Body program will have an enhanced effect on memory performances compared to the participants in the Memory-Web program and no contact control.
2. Participants in the Mind-Body and Memory-Web programs will show improvements in memory performance as compared to the no contact control group.

---

**Intervention**

- Mind-Body-Sessions

  - 40-45 minutes working on specific activities using Facts and Figures CD-ROM

  - Engage in 20-25 minutes group activity
    - Discuss the benefits of mental and physical exercise
    - Set goals for improving their memory and physical activity step count for the week (1 step count by 5%)
Memory Works Training

- Memory Works: Facts and Figures (list learning and numbers)
- One-on-one individualized training
- Self-guided and paced
- Trainers facilitate computer use

http://www.memoryzine.com

Some Caveats about Cognitive Training for Promoting Healthy Cognitive Aging

- Training gains may be of lower magnitude than many elderly, patients, and caregivers expect and progress may not be steady; problem of raising "false hope" and "blaming the victim" for cognitive declines
- Training effects tend to be highly task-specific and show limited generalizability, effects are reasonably durable but maintenance doesn’t automatically occur.
- Training may not prevent cognitive decline, BUT it can boost performance and may delay normative cognitive decline. A few sessions of cognitive training may not be sufficient to alter the life course with respect to decline, BUT it may compress the point of cognitive disability into a smaller window at the end of life.

“Bottom-up” or “top-down” interventions?

- The extreme “top down” position would be to train at the level of complex activities, and not at the level of basic abilities
  - Through painstaking, deliberate exercise of complex tasks, we may simultaneously exercise the underlying constituent abilities on which those tasks depend, and their coordination. This is the implied mechanism from correlational data suggesting that complex activity as a protective mechanism for late life cognition (e.g., Wilson et al., 2002; Arluk, Schooler, Muñoz, & Oates, 1999; Schonfeld et al., 1983; but see Hertog, Hultsch, & Dixon, 1999)
- Do our cognitive interventions need to be “activity prescriptions”? 
“Bottom-up” or “top-down” interventions?

- The problem of intervening at the level of complex activity is that we do not yet have a good understanding of which activities, at which intensity, exercise particular abilities
  - What we need is the equivalent of understanding which “muscle groups” are moved by particular physical exercises
- Careful experimental work needs to be done to link particular abilities to particular activities…

To be determined:

- What are the best methods for specific training and transfer outcomes?
- How can current cognitive theory inform cognitive training, and vice versa?
- How should we define successful training and transfer?
- Who are the best candidates for successful training?
- Does cognitive training in later adulthood develop cognitive reserve or serve a protective function?
- How do we make training accessible and cost-effective?

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