Video showing how it works can be seen on YouTube at:

https://youtu.be/sCX2agoOm14
ACTIVE trial: 5 years later


**Table 2. Effect of Training on Cognitive Outcomes From Baseline to Year 5**

<table>
<thead>
<tr>
<th>Intervention Groups</th>
<th>Memory</th>
<th>Reasoning</th>
<th>Speed of Processing</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory (possible range: 0-192; n = 2790)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score at baseline, mean (SD)</td>
<td>81.0 (16.1)</td>
<td>80.7 (15.6)</td>
<td>80.9 (15.9)</td>
<td>79.4 (16.6)</td>
</tr>
<tr>
<td>Mean change from baseline to year 5</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 to 0.35)</td>
<td>0.05 (-0.07 to 0.17)</td>
<td>0.06 (-0.07 to 0.17)</td>
<td></td>
</tr>
<tr>
<td><strong>Reasoning (possible range: 0-75; n = 2802)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score at baseline, mean (SD)</td>
<td>25.9 (12.2)</td>
<td>25.2 (12.0)</td>
<td>25.6 (11.7)</td>
<td>24.5 (12.0)</td>
</tr>
<tr>
<td>Mean change from baseline to year 5</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 (-0.10 to 0.08)</td>
<td>0.26 (0.17 to 0.35)</td>
<td>0.02 (-0.06 to 0.11)</td>
<td></td>
</tr>
<tr>
<td><strong>Speed of processing (possible range: 0-1500; n = 2802)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score at baseline, mean (SD)</td>
<td>889.0 (272.5)</td>
<td>904.0 (264.5)</td>
<td>906.8 (260.6)</td>
<td>920.1 (267.3)</td>
</tr>
<tr>
<td>Mean change from baseline to year 5</td>
<td>79.1</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 to 0.13)</td>
<td>0.15 (0.01 to 0.29)</td>
<td>0.76 (0.62 to 0.90)</td>
<td></td>
</tr>
</tbody>
</table>

*Effect size defined as training improvement from baseline to year 5 minus control improvement from baseline to year 5 divided by the intrasubject SD of the Biom-transformed composite score. Positive effect sizes indicate improvement.

Abbreviation: CI, confidence interval.
ACTIVE trial: 10 years later

Ten-Year Effects of the Advanced Cognitive Training for Independent and Vital Elderly Cognitive Training Trial on Cognition and Everyday Functioning in Older Adults

George W. Rebok, PhD, Karlene Ball, PhD, Lin T. Guey, PhD, Richard N. Jones, ScD, Hae-Young Kim, DrPH, Jonathan W. King, PhD, Michael Marsiske, PhD, John N. Morris, PhD, Sharon L. Tennstedt, PhD, Frederick W. Unverzagt, PhD, and Sherry L. Willis, PhD, for the ACTIVE Study Group

Effect Size = 0.36
Risk of developing dementia

**Risk:**
- 331 participants developed dementia:
  - Control: 14%
  - 10 or fewer sessions: 12.1%
  - 11 to 14 sessions: 8.2%
- Speed training associated with a reduced risk for dementia by 8% per session
- HR, 0.52; CI 0.33 - 0.82; P = .005

Edwards JD, Xu H, Clark DJ, Ross LA, Unverzagt FW. The ACTIVE study: What have we learned and what is next? Cognitive training reduces incident dementia across ten years. ten years (2016). Presented at the meeting of the American Psychological Association. July, Denver, CO.
Can we enhance cognitive training?
Transcranial direct current stimulation (tDCS)

tDCS

Treatment

• Application of a small current across the scalp while doing a mental activity
• Multiple studies suggest enhancement of learning and memory
• Potential for treating depression
tDCS

Treatment
tDCS Treatment
tDCS for cognition in older persons with HIV

- Funded by the National Institute on Aging
  - R21AG056256, Ownby PI
- Three groups:
  - Active tDCS + Cognitive training
  - Sham tDCS + Cognitive training
  - Sham tDCS + Watching educational videos
- Six treatment sessions, 20 minutes, over two weeks
- Assessments at baseline, immediately after completing treatment, and one month later
tDCS for cognition in older persons with HIV

tDCS

Treatment

$p = 0.01$

$d = 0.97$
What about combining interventions?
Alzheimer Disease incidence, diet, and physical activity

No. at risk
Much PA + high diet 200 192 141 60 45 35 19
Some PA + high diet or much PA + middle diet 496 470 332 135 106 73 37
Some PA + middle diet, no PA + high diet, or much PA + low diet 573 526 374 168 121 82 35
Some PA + low diet or no PA + middle diet 421 377 241 99 72 48 27
No PA + low diet 190 165 103 39 27 18 9

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Combining exercise, diet, cognitive training, and vascular risk factor monitoring.

Figure 2: Change in cognitive performance during the 2 year intervention. Figure shows estimated mean change in cognitive performance from baseline until 12 and 24 months (higher scores suggest better performance) in the modified intention-to-treat population. Error bars are SEs. Mixed-model repeated measures analyses were used to assess between-group differences (group × time interaction) in changes from baseline to 24 months based on data from all participants with at least one post-baseline measurement. NTB=neuropsychiatric test battery.
Combined physical/cognitive training in aged MCI subjects: the Train the Brain study
Putting it together
Brain health and fitness interventions

Interventions

- Computer training, working memory training, brain games
- Crossword puzzles, learning a new language, learning a musical instrument, taking classes, working acrostics
- Walking, running, weight lifting
- MIND diet, Mediterranean diet, DASH diet, Nu-Age diet, social interaction
- Transcranial electrical stimulation
- Vitamin E, gingko biloba, acetyl-l-carnitine, alpha-lipoic acid, theanine, fish oil, many proprietary supplements
- Optimism, sense of purpose, other attitudes…
- Many more . . .
Tanzi SHIELD model

Interventions

- S (Sleep)
- H (Handle stress)
- I (Interact with others)
- E (Exercise)
- L (Learn new things)
- D (Diet)
Circle of Friends

Interventions

- Healthy lifestyle: reduced stress
- Strong social network
- Sense of purpose
- Aerobic and strength exercise
- Mental workout
- Heart-healthy diet

Belmont Village Senior Living
Barcelona Brain Health Model

Interventions

- Cognitive training
- Physical exercise
- Nutrition
- Life plan
- Comprehensive health
- Socialization
- Sleep

https://bbhi.cat/en/
Lancet Commission 2020

Interventions

- Minimize diabetes
- Treat hypertension
- Prevent head injury
- Stop smoking
- Reduce air pollution
- Reduce midlife obesity
- Maintain frequent exercise
- Reduce occurrence of depression
- Avoid excessive alcohol
- Treat hearing impairment
- Maintain frequent social contact
- Attain high level of education

www.thelancet.com Published online July 30, 2020 https://doi.org/10.1016/S0140-6736(20)30367-6
Designing a brain health program

Interventions

What should patients be told?

Hard for them to do everything

May make them less likely to do anything

Provide something simple that can easily be followed and revised
Cogtrastim model

- Cognitive Training
  - Mentally Stimulating Activities
  - Meditation
  - ↑ Educational Attainment
  - ↑ Cognitive Reserve

- Cognitive Training
  - Exercise
  - Meditation/Yoga
  - Transcranial Electrical Stimulation

- Treat Diabetes/Metabolic Syndrome
  - Treat Hypertension
  - Address Obesity
  - Mediterranean Diet
  - Improve Sleep
  - Exercise
  - CBT
  - Stress Management
  - Reduce Alcohol Use
  - Prevent Head Injury

Cogtrastim

- Cognitive Function
  - Brain Stimulation
  - ↑ BDNF

Outcomes

- Maintain Cognition
- Reduce Neuropathology
  - (amyloid/tau/vascular/inflammatory)
- Reduce Inflammation
  - ↓ “Bad” Cytokines
  - Oxidative Stress

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Three key mechanisms of brain health

Interventions

Maintain or improve cognition

Brain stimulation = ↑ BDNF

Reduce inflammation
BDNF

Brain Derived Neurotrophic Growth Factor

- Increases number of brain cells in areas important for memory
- Key in brain plasticity
- Other positive effects – may be mechanism by which antidepressants work
Choosing activities for a program

Effect size: “Bang for buck”

Consistent findings

Twofers, even threelfers

Multiple mechanisms
Cognitive Training

- Brain training
  - Brain HQ, Lumosity, AARP, Cognifit, many others
- Meditation
- Learn a new language
- Learn a musical instrument
- Video games
- “If it doesn’t challenge you, it doesn’t change you.”
Interventions

- Aerobic exercise (↑ BDNF)
- Weight training (↑ BDNF)
- Cognitive training (↑ BDNF)
- Transcranial electrical stimulation (↑ BDNF)
Cogtrastim Model

Reducing inflammation

- Exercise
- Sleep
- Stress management
- Weight loss
- Diet
- Antioxidants?
Cogtrastim Model

Interventions

Cognitive Training
- Computer Training
- Meditation
- Electronic Games
- Learn a Language
- Learn a Musical Instrument

Brain Stimulation
- Aerobic Exercise
- Resistance Training
- Transcranial Electric Stimulation
- Others (?)

Reduce Inflammation
- Stress Management
- Diet
- Sleep
- Aerobic Exercise
- Weight Loss
- Supplements (?)

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Cogtrastim Model

Brain health training program?

Interventions

Focus on one activity from each group, preferably daily

Choose activities that work for the person
Brain health training program

Interventions

Daily

Aerobic exercise
Mentally stimulating activities
Meditation
Mediterranean diet
Sleep
Brain health training program

Weekly

- Cognitive training at least 3 times/week
- Strength training at least 3 times/week
Bottom line
Dementia prevention is possible through promoting brain health.

Specific types of cognitive training, exercise and diet may slow cognitive aging and reduce dementia incidence.

A brain health plan should be part of a comprehensive strategy for senior health.
## Contact:

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Psychiatry and Behavioral Medicine  
Nova Southeastern University  

Blog at: www.cogtrastim.com

<table>
<thead>
<tr>
<th>Cognitive Training</th>
<th>Brain Stimulation</th>
<th>Reduce Inflammation</th>
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<tbody>
<tr>
<td>Computer Training</td>
<td>Aerobic Exercise</td>
<td>Stress Management</td>
</tr>
<tr>
<td>Meditation</td>
<td>Resistance Training</td>
<td>Diet</td>
</tr>
<tr>
<td>Electronic Games</td>
<td>Transcranial Electric Stimulation</td>
<td>Sleep</td>
</tr>
<tr>
<td>Learn a Language</td>
<td>Others (?)</td>
<td>Aerobic Exercise</td>
</tr>
<tr>
<td>Learn a Musical Instrument</td>
<td></td>
<td>Weight Loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Supplements (?)</td>
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