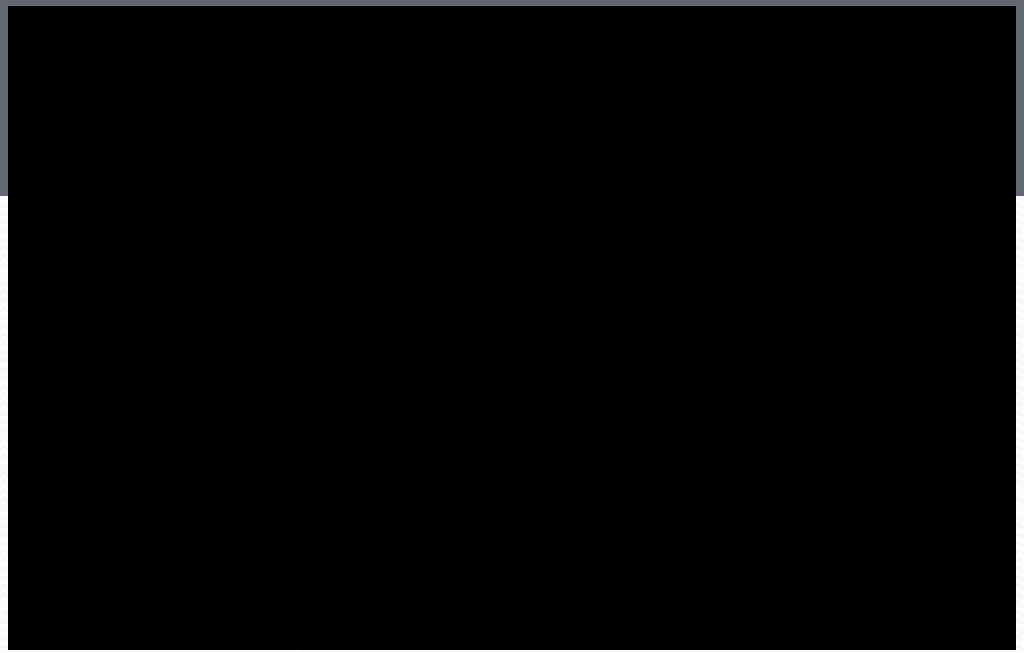
Brain Fitness for Positive Aging

Ray Ownby, MD, PhD

Interprofessional Geriatrics Training Institute

July 7, 2017



Overview

Cognitive aging and what we can do about it.

Positive Aging

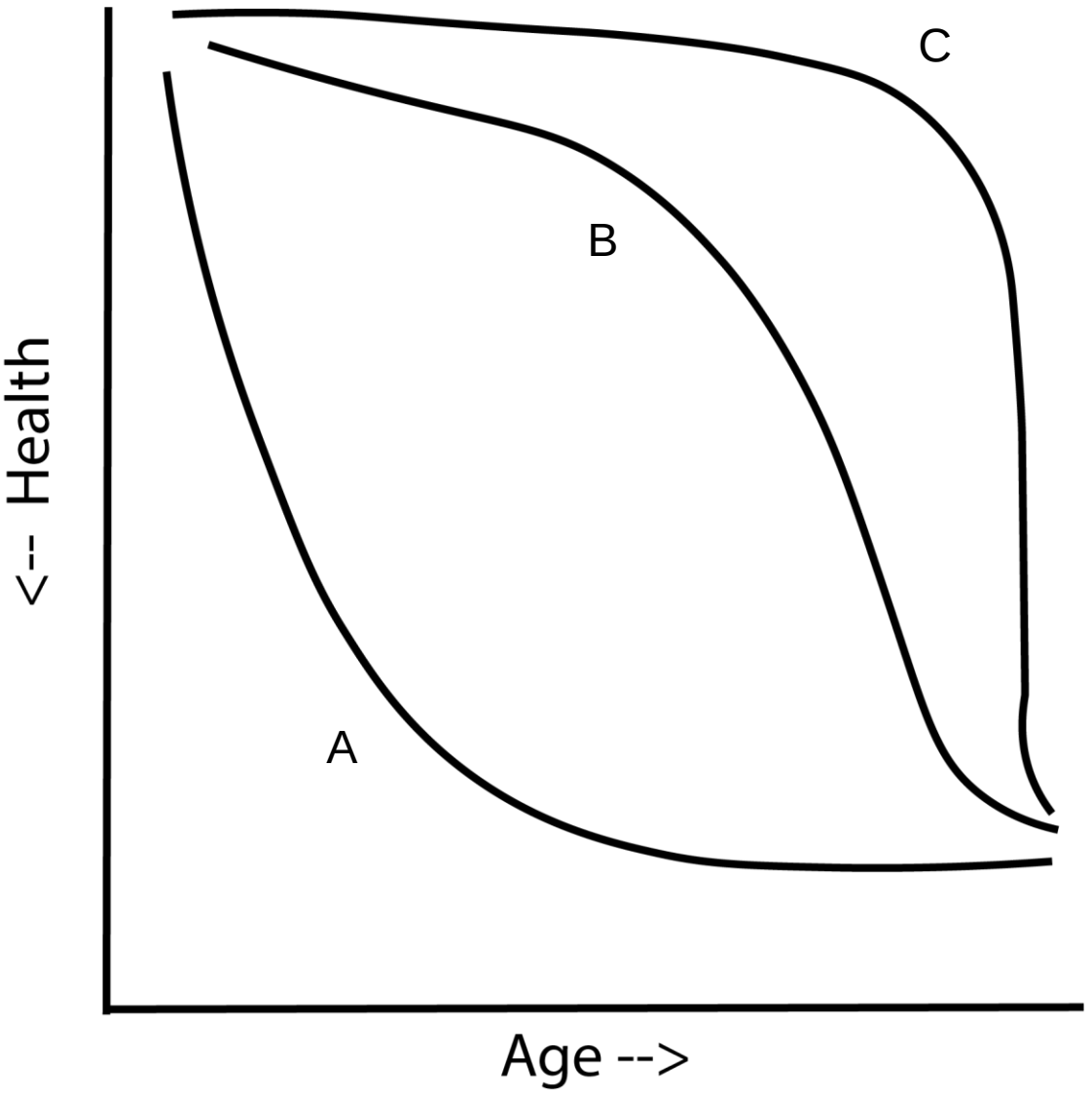
Optimal Cognitive Function
Optimal Physical Function
Absence of Disease

Brain Fitness

Brain structure
Brain function

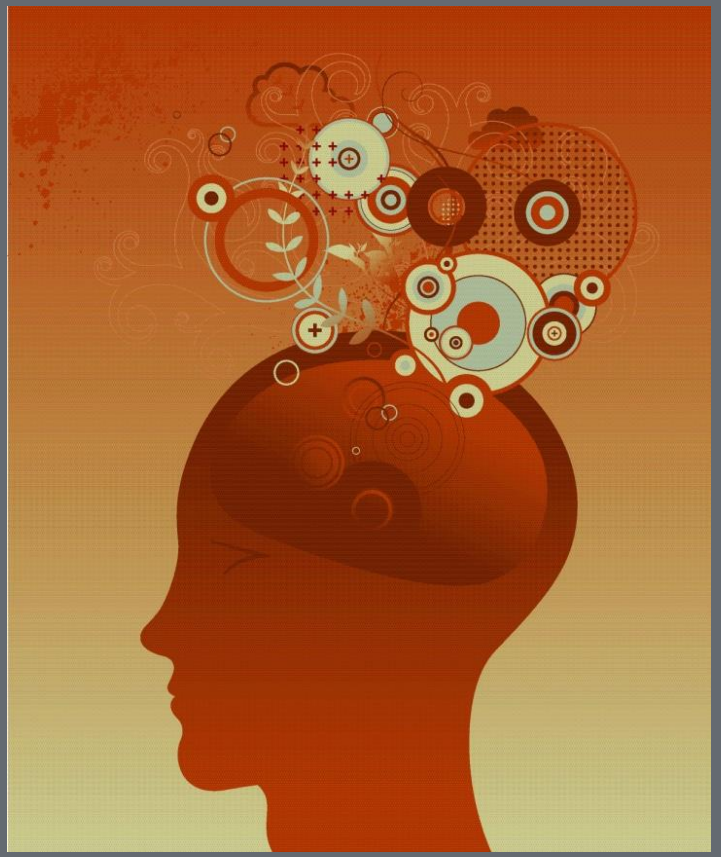
Overview

Cognitive aging and what we can do about it.



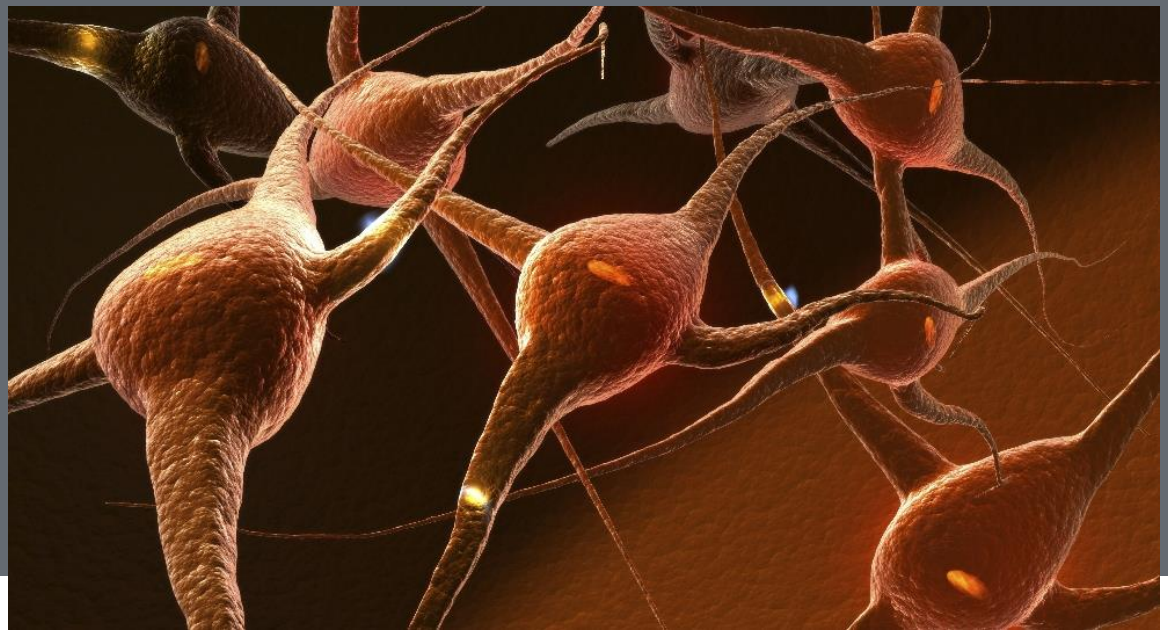
Cognitive Aging

What changes with age

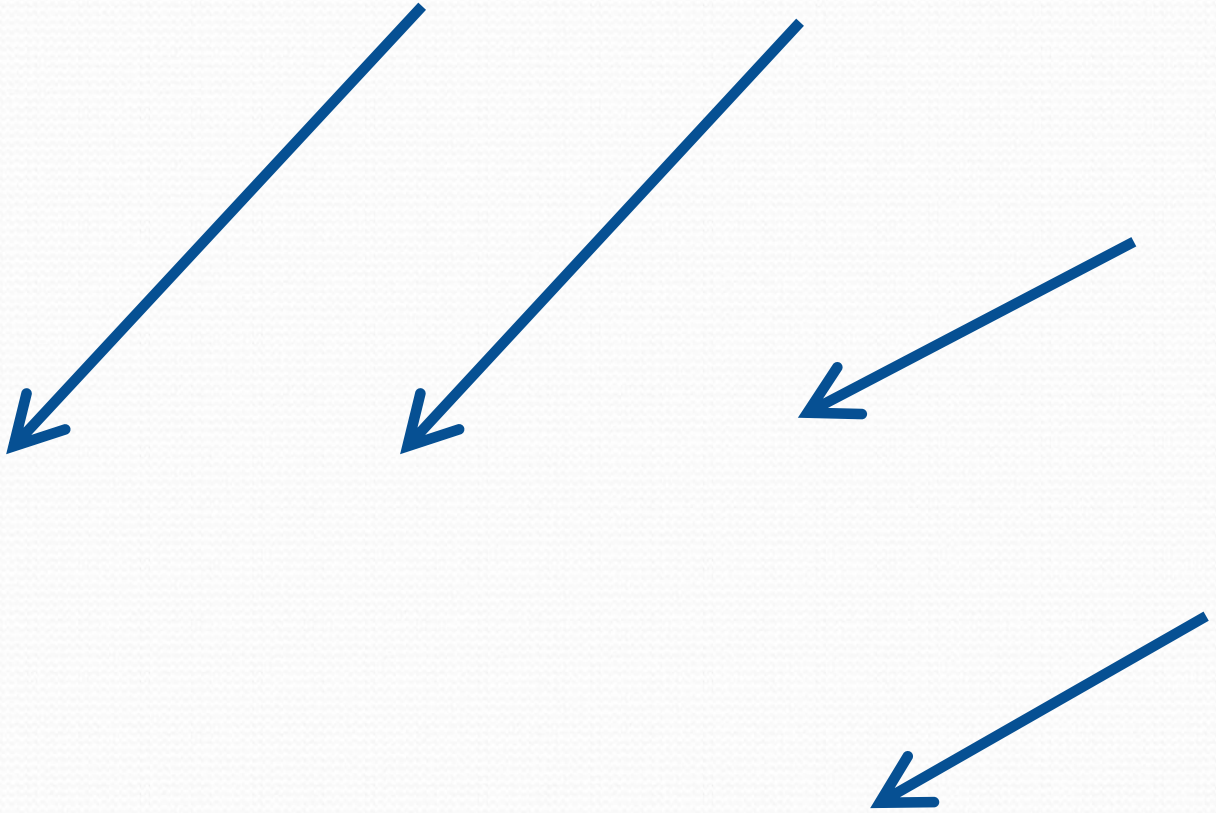


What causes the changes?

The science of memory and cognition



Structural and functional changes



Plaques and tangles

Risk factors

Cognitive aging and what we can do about it.

Amyloid predicts cognitive decline

Research

CONCLUSIONS AND RELEVANCE Exploratory analyses of a cognitively normal cohort followed up for a median of 3.1 years suggest that elevation in baseline brain amyloid level, compared with normal brain amyloid level, was associated with higher likelihood of cognitive decline, although the findings are of uncertain clinical significance. Further research is needed to assess the clinical importance of these differences and measure longer-term associations.

Michael C. Donohue, PhD; Reisa A. Sperling, MD, MMSc; Ronald Petersen, MD, PhD; Chung-Kai Sun, MS; Michael W. Weiner, MD; Paul S. Aisen, MD; for the Alzheimer's Disease Neuroimaging Initiative

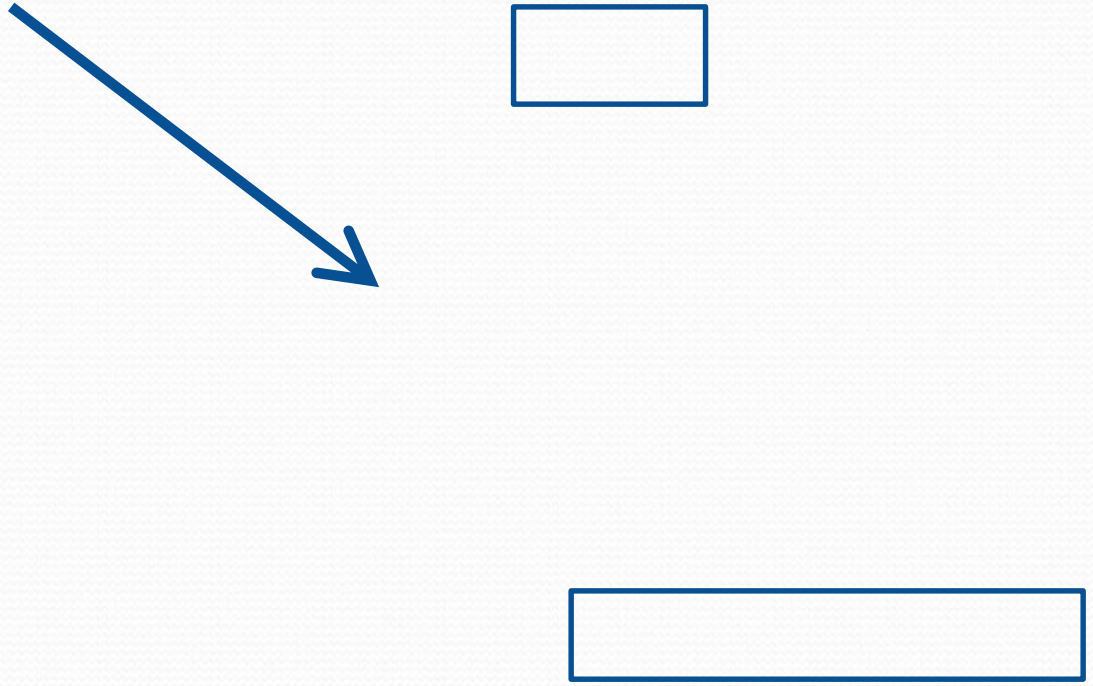
Donohue MC et al (2017). Association between elevated brain amyloid and subsequent cognitive decline among cognitively normal persons. *JAMA* 317(22):2305-2316.

Nun Study

Cognitive aging and what we can do about it.

Nun Study

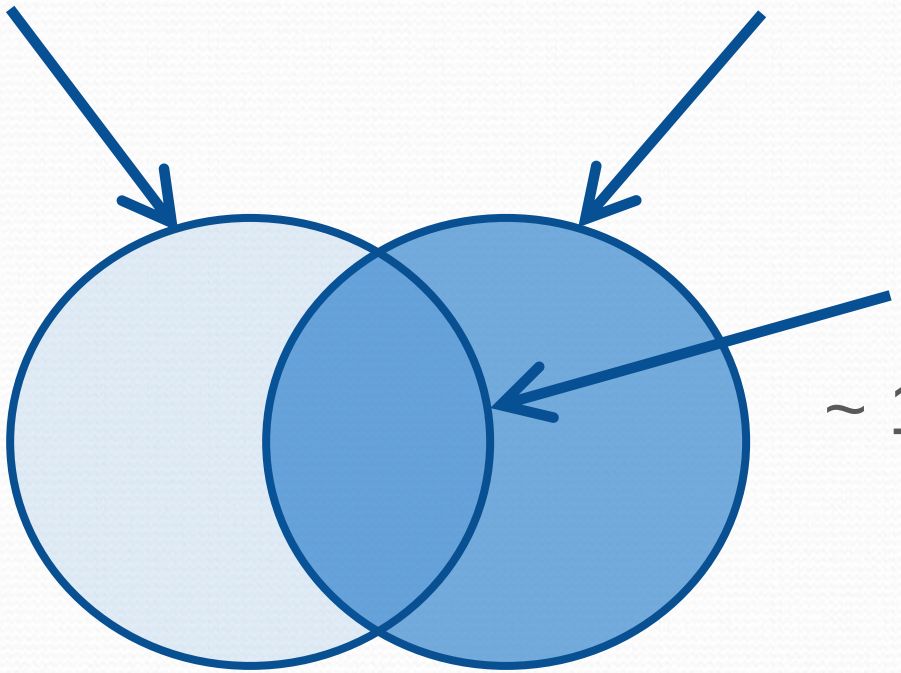
Cognitive aging and what we can do about it.



Riley KP et al (2002). Alzheimer's neurofibrillary pathology and the spectrum of cognitive function: Findings from the Nun Study. *Annals of Neurology,* 51, 567–577.

Nun Study

Cognitive aging and what we can do about it.



Correlation = 0.57

Correlation squared = 0.32

About a third overlap

What about the other 2/3?

So what else causes cognitive aging?

Neuroinflammation

ORIGINAL ARTICLE

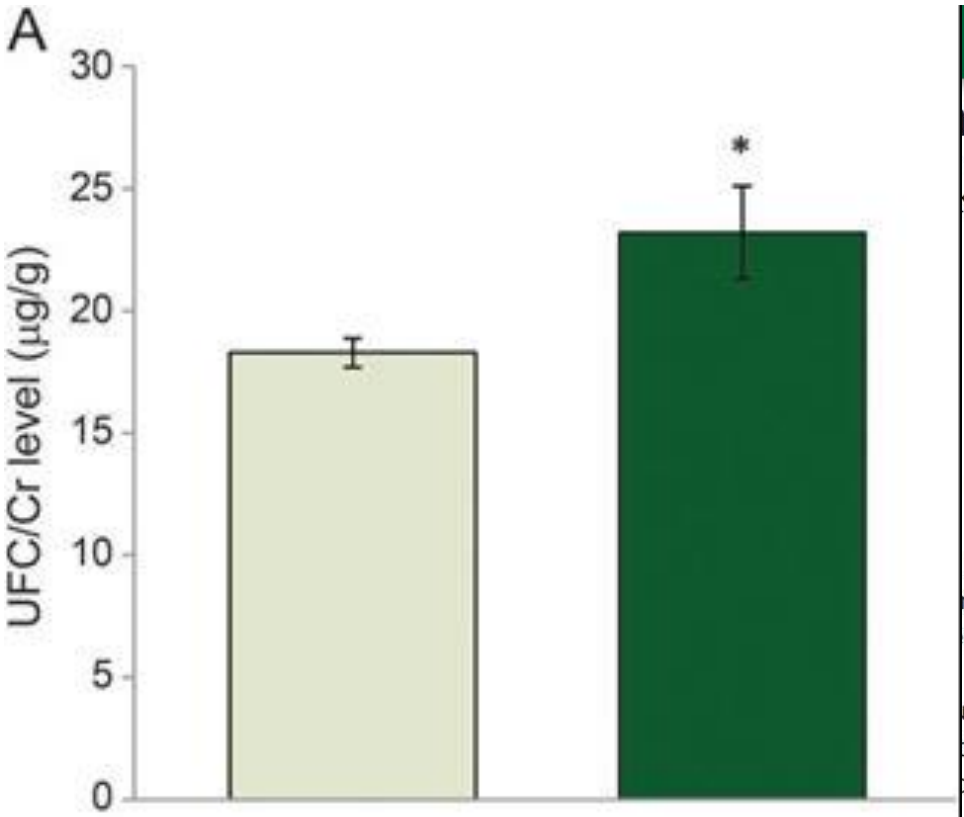
Depression and Risk for Alzheimer Disease

Systematic Review, Meta-analysis, and Metaregression Analysis

Raymo
Vineeth

Conclusions: A history of depression may confer an increased risk for later developing AD. This relation may reflect an independent risk factor for the disease.

Arch Gen Psychiatry. 2006;63:530-538



easures predict

k

measures of cortisol predict Alzheimer disease

design to examine whether cortisol dysregulation
n the Baltimore Longitudinal Study of Aging (BLSA)
s over an average interval of 10.56 years. Urinary
measured, and a UFC/Cr ratio was calculated to
ulation, we used within-person UFC/Cr level (i.e.,
time (i.e., within-person slope), and UFC/Cr variabil-
on). Cox regression was used to assess whether

but not UFC/Cr slope, were significant predictors of

Differences in UFC/Cr level control and future participants with AD controlling for baseline age. *$p < 0.05$; UFC/Cr = urinary free cortisol/creatinine.

Long-term cortisol measures predict Alzheimer disease risk.
Ennis, Gilda; An, Yang; Resnick, Susan; Ferrucci, Luigi; MD, PhD; OBrien, Richard; MD, PhD; Moffat, Scott Neurology. 88(4):371-378, January 24, 2017.

Wolters Kluwer Health | OvidSP

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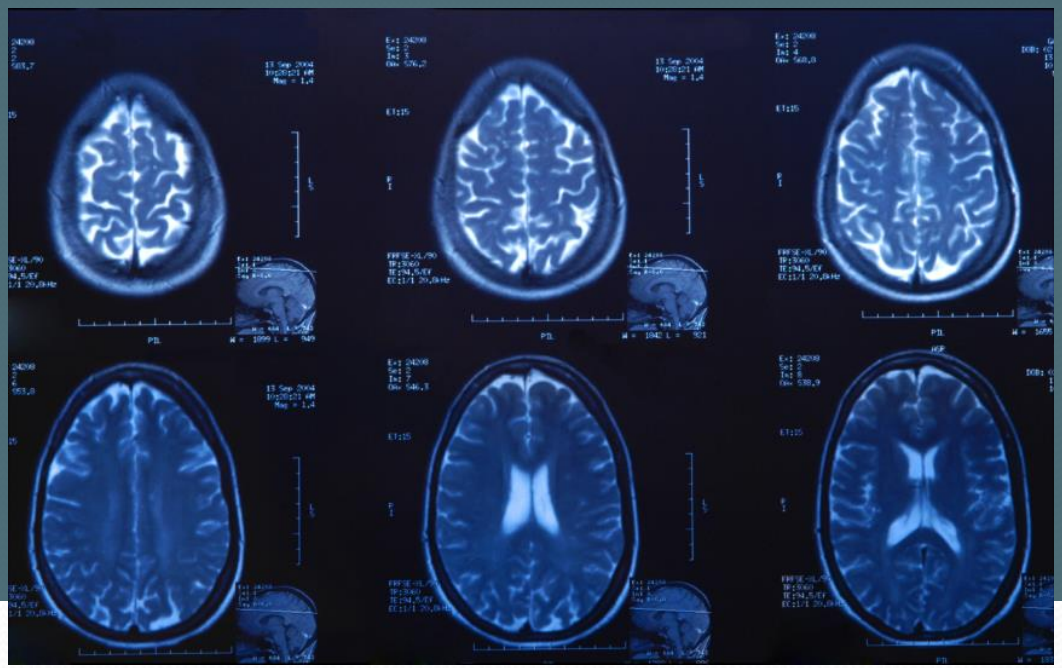
What can be done?



Overview

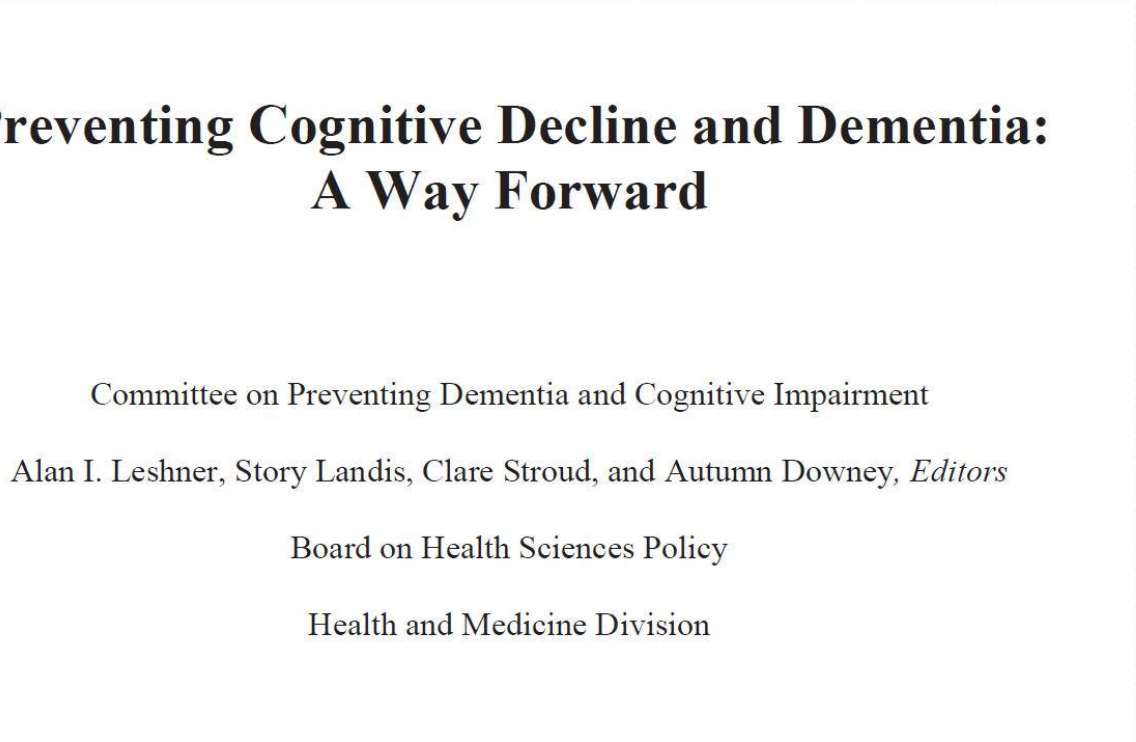
Cognitive aging and what we can do about it.

What we can do about it

- Exercise
- Diet
- Stress management
- Mood
- Sleep
- Purpose in life
- Social engagement
- Cognitive training
- tDCS

Risk factors

Cognitive aging and what we can do about it.



National Academy of Sciences, June, 2017

Also see: Interventions to prevent age-related cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia. Agency for Health Research and Quality, Comparative Effectiveness Report Number 188, March 2017.

Treatment

Cognitive aging and what we can do about it.

NBC Nightly News with Lester Holt, June 22, 2017

National Academy of Sciences, June, 2017

Also see: Interventions to prevent age-related cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia. Agency for Health Research and Quality, Comparative Effectiveness Report Number 188, March 2017.

Treatment?

Cognitive aging and what we can do about it.

Highest priority areas:

Cognitive training

Blood pressure management

Physical activity

National Academy of Sciences, June, 2017

Also see: Interventions to prevent age-related cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia. Agency for Health Research and Quality, Comparative Effectiveness Report Number 188, March 2017.

Exercise

Meta-analysis of effects

Hillman et al., Nat Rev Neurosci, 2008 , 9, 58-65.

Issues

Promoting brain health

PNAS

Exercise training increases size of hippocampus and improves memory

Kirk I. Erickson[a], Michelle W. Voss[b,c], Ruchika Shaurya Prakash[d], Chandramallika Basak[e], Amanda Szabo[f], Laura Chaddock[b,c], Jennifer S. Kim[b], Susie Heo[b,c], Heloisa Alves[b,c], Siobhan M. White[f], Thomas R. Wojcicki[f], Emily Mailey[f], Victoria J. Vieira[f], Stephen A. Martin[f], Brandt D. Pence[f], Jeffrey A. Woods[f], Edward McAuley[b,f], and Arthur F. Kramer[b,c,1]

[a]Department of Psychology, University of Pittsburgh, Pittsburgh, PA 15260; [b]Beckman Institute for Advanced Science and Technology, and [f]Department of Kinesiology and Community Health, University of Illinois, Champaign-Urbana, IL 61801; [c]Department of Psychology, University of Illinois, Champaign-Urbana, IL 61820; [d]Department of Psychology, Ohio State University, Columbus, OH 43210; and [e]Department of Psychology, Rice University, Houston, TX 77251

Edited* by Fred Gage, Salk Institute, San Diego, CA, and approved December 30, 2010 (received for review October 23, 2010)

Erickson KI et al. (2011). *Proceedings of the National Academy of Sciences, 108,* 3017-3022.

Diet

Mediterranean diet

- The Mediterranean diet emphasizes olive oil, fish, cheese and yogurt, as well as fresh fruits and vegetables
- Beans, legumes, and nuts are important
- Whole grain breads and pastas

Mediterranean Diet

Risk of cognitive impairment

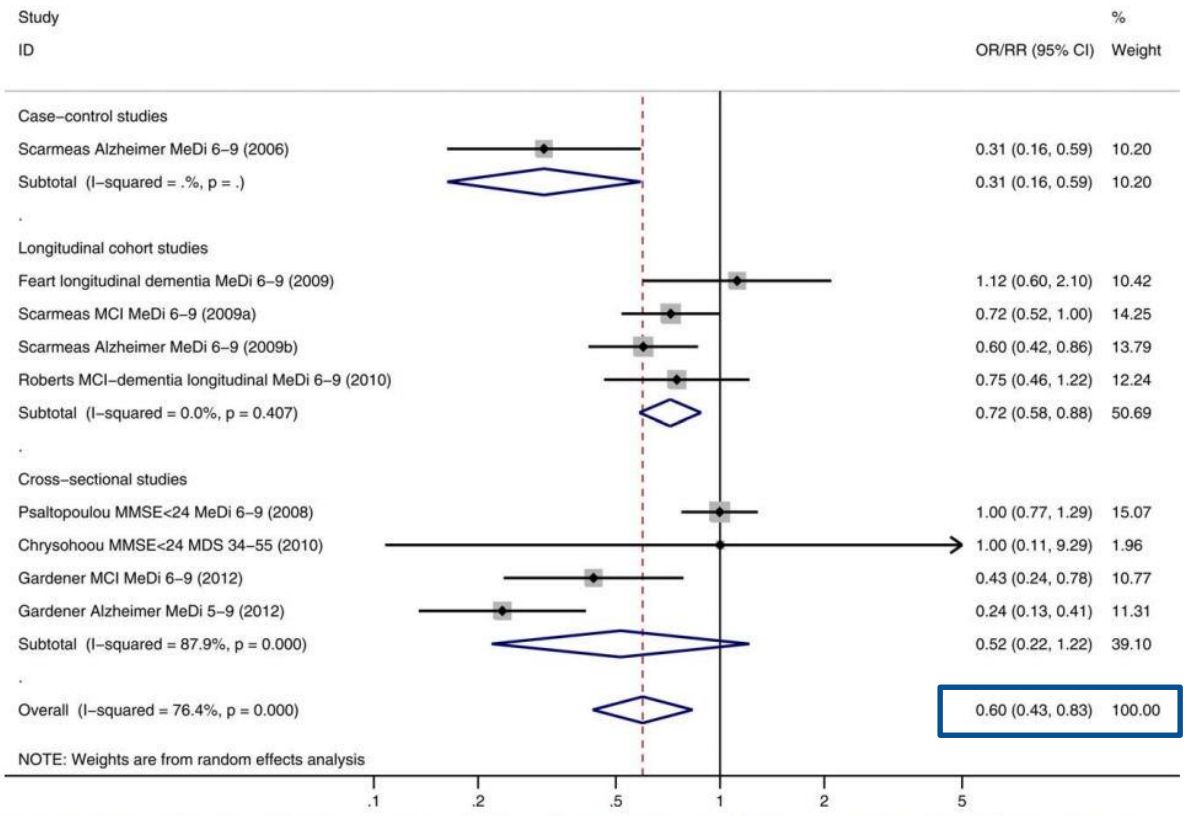
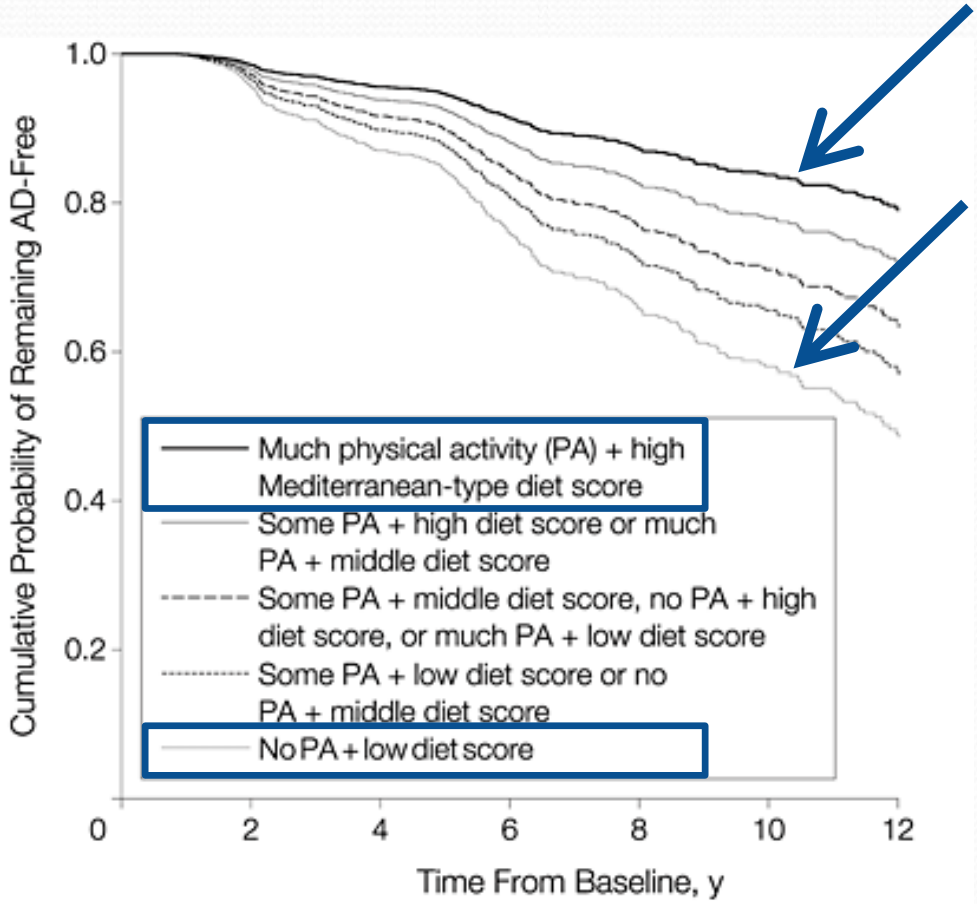


FIGURE 3: Forest plot describing the association between high adherence to Mediterranean diet and risk for cognitive impairment. Apart from the overall analysis, the subanalyses on case–control (upper panels), longitudinal cohort (middle panels), and cross-sectional studies (lower panels) are presented. CI = confidence interval; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; OR = odds ratio; RR = relative risk. [Color figure can be viewed in the online issue, which is available at www.annalsofneurology.org.]

Psaltopoulou T et al (2013). Mediterranean diet, stroke, cognitive impairment, and depression: A meta-analysis. *Annals of Neurology,* 74, 580-591.

What about exercise *and* diet?

Alzheimer Disease (AD) Incidence in Individuals by No, Some, or Much Physical Activity and Low, Middle, and High Mediterranean-Type Diet Adherence Scores



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

Scarmeas, N. et al. JAMA 2009;302:627-637.

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JAMA

Cognitive training

Life moves pretty fast. If you don't stop and look around once in awhile, you could miss it.

--Ferris Bueller

Cognitive Training

Treatment

Cognitive training

- Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study
- Six sites
- 2,832 participants
- National Institute on Aging
- Key intervention:
- Speed of processing
  - Useful Field of View

Effects of Cognitive Training Interventions With Older Adults

A Randomized Controlled Trial

Karlene Ball, PhD
Daniel B. Berch, PhD
Karin F. Helmers, PhD
Jared B. Jobe, PhD
Mary D. Leveck, PhD
Michael Marsiske, PhD
John N. Morris, PhD
George W. Rebok, PhD
David M. Smith, MD
Sharon L. Tennstedt, PhD
Frederick W. Unverzagt, PhD
Sherry L. Willis, PhD
for the ACTIVE Study Group

Context Cognitive function in older adults is related to independent living and need for care. However, few studies have addressed whether improving cognitive functions might have short- or long-term effects on activities related to living independently.

Objective To evaluate whether 3 cognitive training interventions improve mental abilities and daily functioning in older, independent-living adults.

Design Randomized, controlled, single-blind trial with recruitment conducted from March 1998 to October 1999 and 2-year follow-up through December 2001.

Setting and Participants Volunteer sample of 2832 persons aged 65 to 94 years recruited from senior housing, community centers, and hospital/clinics in 6 metropolitan areas in the United States.

Interventions Participants were randomly assigned to 1 of 4 groups: 10-session group training for memory (verbal episodic memory; n=711), or reasoning (ability to solve problems that follow a serial pattern; n=705), or speed of processing (visual search and identification; n=712); or a no-contact control group (n=704). For the 3 treatment groups, 4-session booster training was offered to a 60% random sample 11 months later.

Main Outcome Measures Cognitive function and cognitively demanding everyday functioning.

Results Thirty participants were incorrectly randomized and were excluded from the analysis. Each intervention improved the targeted cognitive ability compared with baseline, durable to 2 years ($P<.001$ for all). Eighty-seven percent of speed-, 74% of reasoning-, and 26% of memory-trained participants demonstrated reliable cognitive improvement immediately after the intervention period. Booster training enhanced training gains in speed ($P<.001$) and reasoning ($P<.001$) interventions (speed booster, 92%; no booster, 68%; reasoning booster, 72%; no booster, 49%), which were maintained at 2-year follow-up ($P<.001$ for both). No training effects on everyday functioning were detected at 2 years.

Conclusions Results support the effectiveness and durability of the cognitive training interventions in improving targeted cognitive abilities. Training effects were of a magnitude equivalent to the amount of decline expected in elderly persons without dementia over 7- to 14-year intervals. Because of minimal functional decline across all groups, longer follow-up is likely required to observe training effects on everyday function.

JAMA. 2002;288:2271-2281 www.jama.com

NEARLY HALF OF COMMUNITY-dwelling persons aged 60 years and older express concern about declining mental abilities.[1] Although there is substantial evidence that many cognitive abilities and processes are related to measures of functional status, need for care, and quality of life, few studies have addressed whether improving cognitive functions might have short- or long-term effects on activities related to living independently. Interventions designed to delay or prevent the need for nursing homes, home care, and hospital stays can save health care costs

ACTIVE trial: 5 years later

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

	Intervention Groups			
	Memory	Reasoning	Speed of Processing	Control Group
Memory (possible range: 0-132; n = 2790)				
Score at baseline, mean (SD)	81.0 (16.1)	80.7 (15.6)	80.9 (15.8)	79.4 (16.6)
Mean change from baseline to year 5	–1.0	–4.8	–5.3	–4.0
Effect size (99% CI)*	0.23 (0.11 to 0.35)	0.05 (–0.07 to 0.17)	0.05 (–0.07 to 0.17)	
Reasoning (possible range: 0-75; n = 2802)				
Score at baseline, mean (SD)	25.9 (12.2)	25.2 (12.0)	25.6 (11.7)	24.5 (12.0)
Mean change from baseline to year 5	4.3	8.1	4.2	5.2
Effect size (99% CI)*	–0.01 (–0.10 to 0.08)	0.26 (0.17 to 0.35)	0.02 (–0.06 to 0.11)	
Speed of processing (possible range: 0-1500; n = 2802)				
Score at baseline, mean (SD)	899.0 (272.5)	904.0 (264.5)	906.8 (260.6)	920.1 (267.3)
Mean change from baseline to year 5	79.1	119.6	241.8	–96.1
Effect size (99% CI)*	–0.01 (–0.15 to 0.13)	0.15 (0.01 to 0.29)	0.76 (0.62 to 0.90)	

Abbreviation: CI, confidence interval.
*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 Blom-transformed composite score. Positive effect sizes indicate improvement.

Willis et al (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *JAMA, 296,* 2805–2814.

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,[a,b] Karlene Ball, PhD,[c] Lin T. Guey, PhD,[d] Richard N. Jones, ScD,[e] Hae-Young Kim, DrPH,[d] Jonathan W. King, PhD,[f] Michael Marsiske, PhD,[g,h] John N. Morris, PhD,[e] Sharon L. Tennstedt, PhD,[d] Frederick W. Unverzagt, PhD,[i] and Sherry L. Willis, PhD,[j] for the ACTIVE Study Group

Rebok et al (2014). *Journal of the American Geriatrics Society,* 62, 16-24.

Effect Size = 0.36

Cognitive training in ACTIVE trial

Cognitive Training

Treatment

Risk for dementia:

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

Brooks M (2016). Brain training protects against cognitive decline, dementia. *Medscape.* http://www.medscape.com/viewarticle/866577#vp_2 [Report of presentation at the Alzheimer Association International Conference, 2016].

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.

Cognitive training in ACTIVE trial

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Cognitive training in ACTIVE trial

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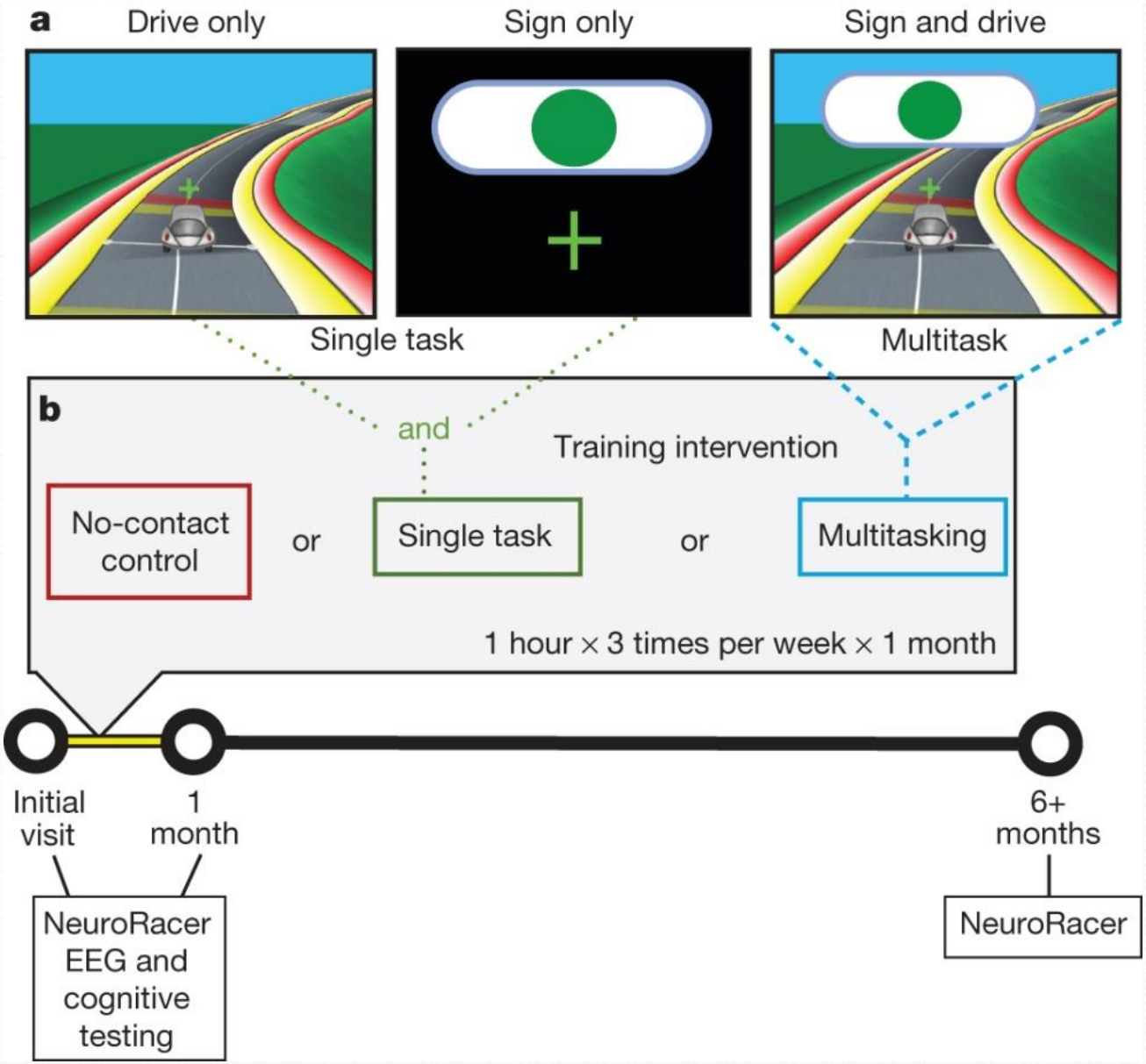
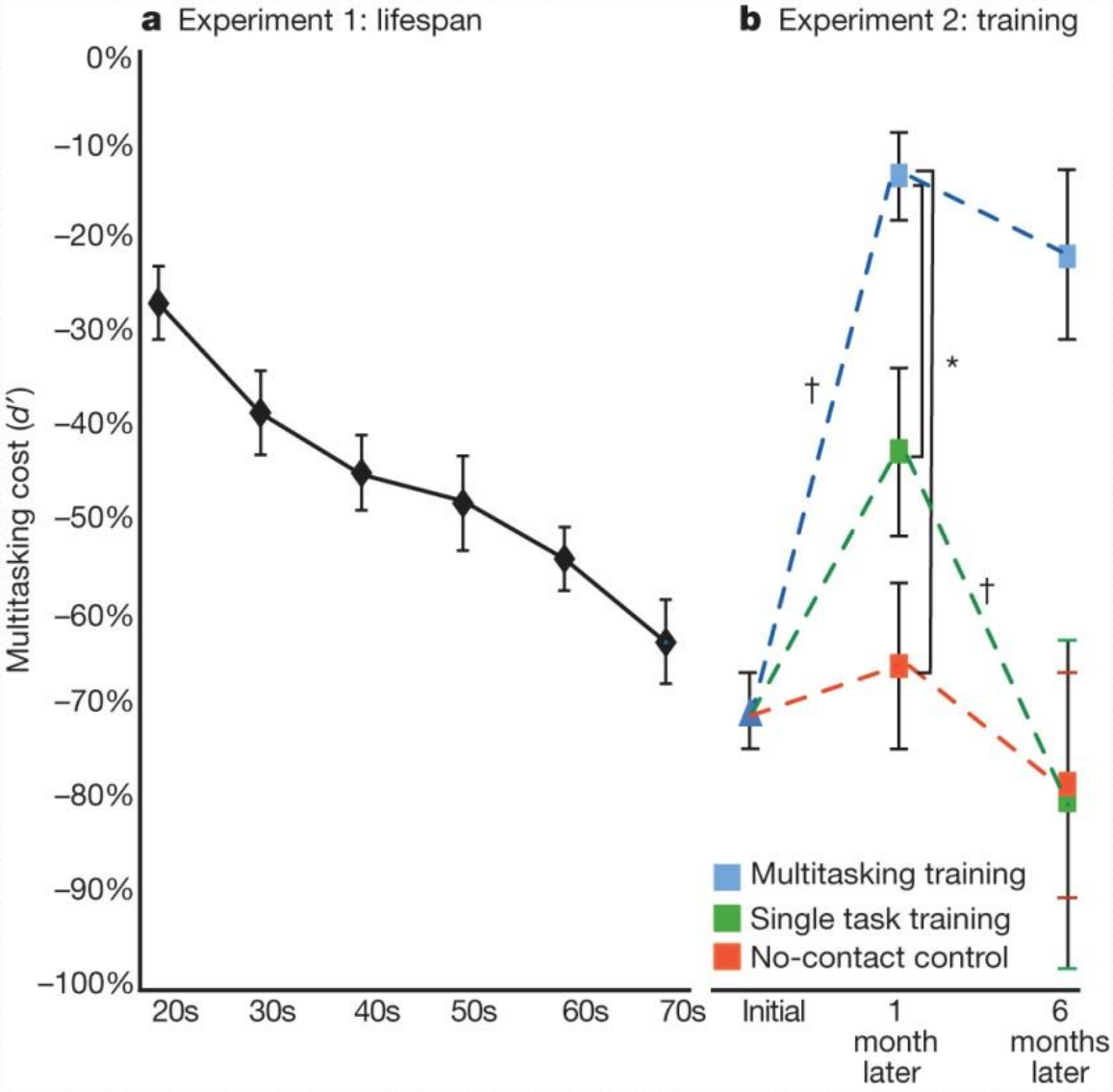
Cognitive Training

Treatment

Anguera JA et al (2013). Video game training enhances cognitive control in older adults. *Nature, 501(7465),* 97-101.


a
Drive only
Sign only
Sign and drive
Single task
Multitask
b
and
Training intervention
No-contact control
or
Single task
or
Multitasking
1 hour × 3 times per week × 1 month
Initial visit
1 month
6+ months
NeuroRacer EEG and cognitive testing
NeuroRacer

nature


a Experiment 1: lifespan
b Experiment 2: training
Multitasking cost (d′)
0%
−10%
−20%
−30%
−40%
−50%
−60%
−70%
−80%
−90%
−100%
20s
30s
40s
50s
60s
70s
Initial
1 month later
6 months later
†
*
†
Multitasking training
Single task training
No-contact control

nature

Can we enhance cognitive training?

tDCS

Treatment

Transcranial direct current stimulation

- 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

Treatment

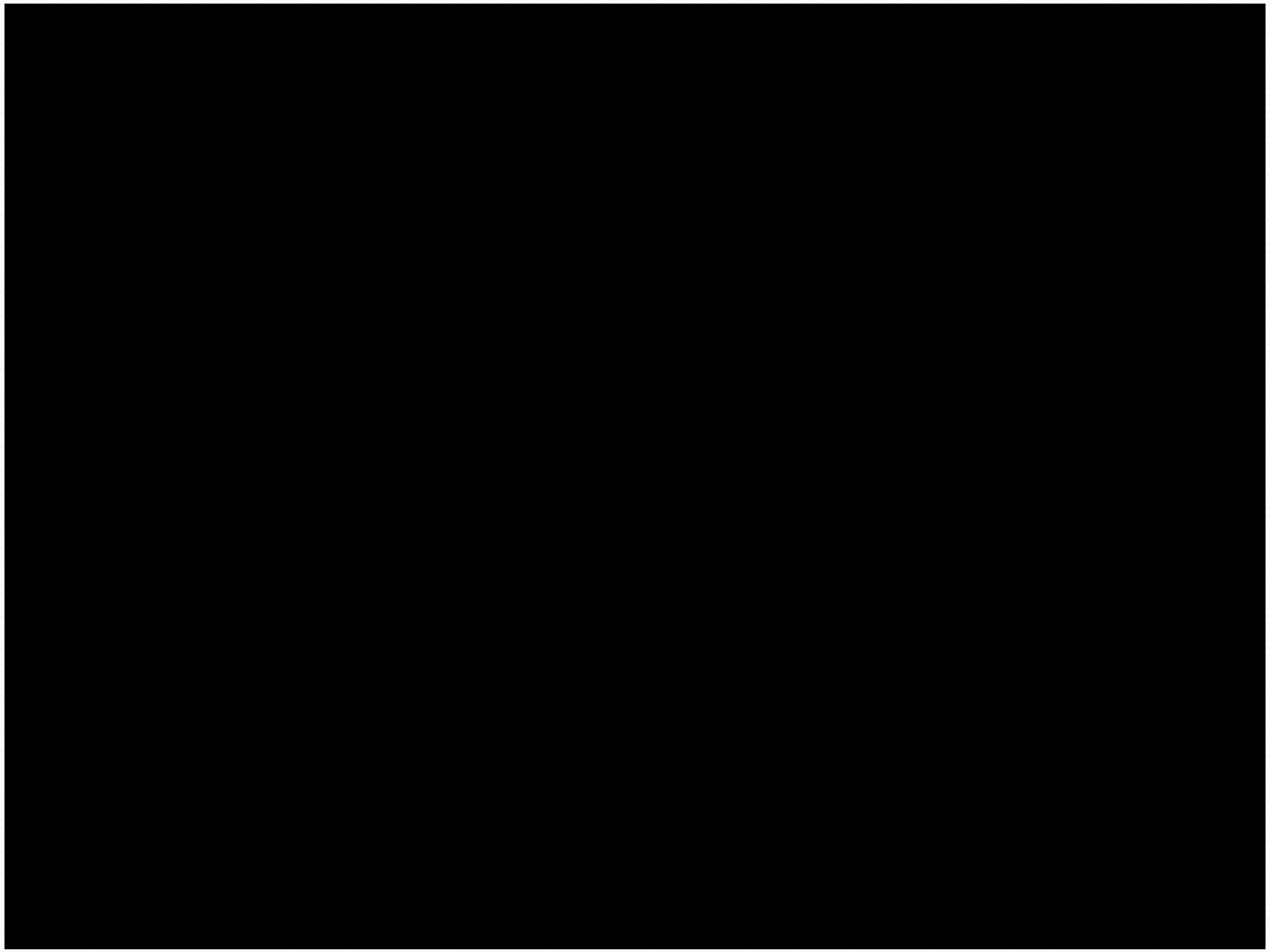
tDCS for cognition in older persons with HIV

- Pilot study
- Combined with speed of processing cognitive training
- Results suggest enhancement of learning and memory
- Pending funding from the National Institute on Aging

GT Racing 2 – Gameloft, Paris

tDCS

Treatment

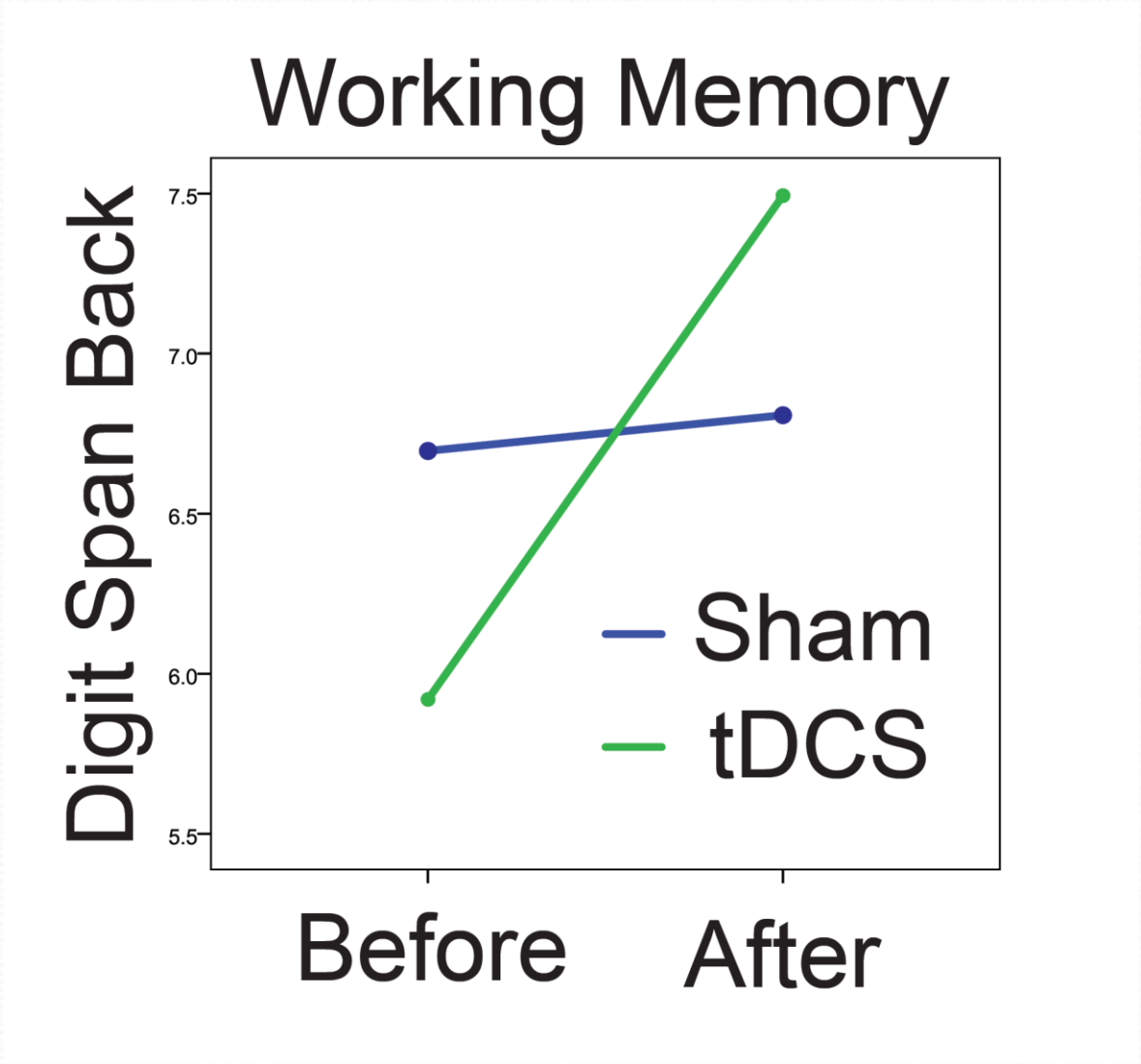


tDCS for cognition in older persons with HIV

tDCS

Treatment

Ownby RL, Acevedo A (2016). A pilot study of cognitive training with and without transcranial direct current stimulation to improve cognition in older persons with HIV-related cognitive impairment. *Neuropsychiatric Disease and Treatment, 12*, 2745-2754.



Will tDCS work in normal elderly?

tDCS

Treatment

Augmenting cognitive training older adults: The ACT trial

- Funded by National Institute on Aging for 5 years
- Sites at University of Florida, University of Miami, and University of Arizona
- $5.7 million dollars
- Adam Woods, PhD, Principal Investigator
- Status: Recruiting

Bottom line

Overview

Cognitive aging and what we can do about it.

What we can do about it

- Exercise
- Diet
- Stress management
- Mood
- Sleep
- Purpose in life
- Social engagement
- Cognitive training
- tDCS

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Cognitive Aging

Treatment

No pill fixes cognitive aging, and it doesn't look like one is going to come along soon.

Cognitive Aging

Treatment

Specific types of diet, exercise and cognitive training *may* slow cognitive aging.

Cognitive Aging

Treatment

More research is needed.

Contact:

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Memory Disorders Program