

Brain health promotion strategies: Separating evidence-based hope from hopeless pseudo-medicine

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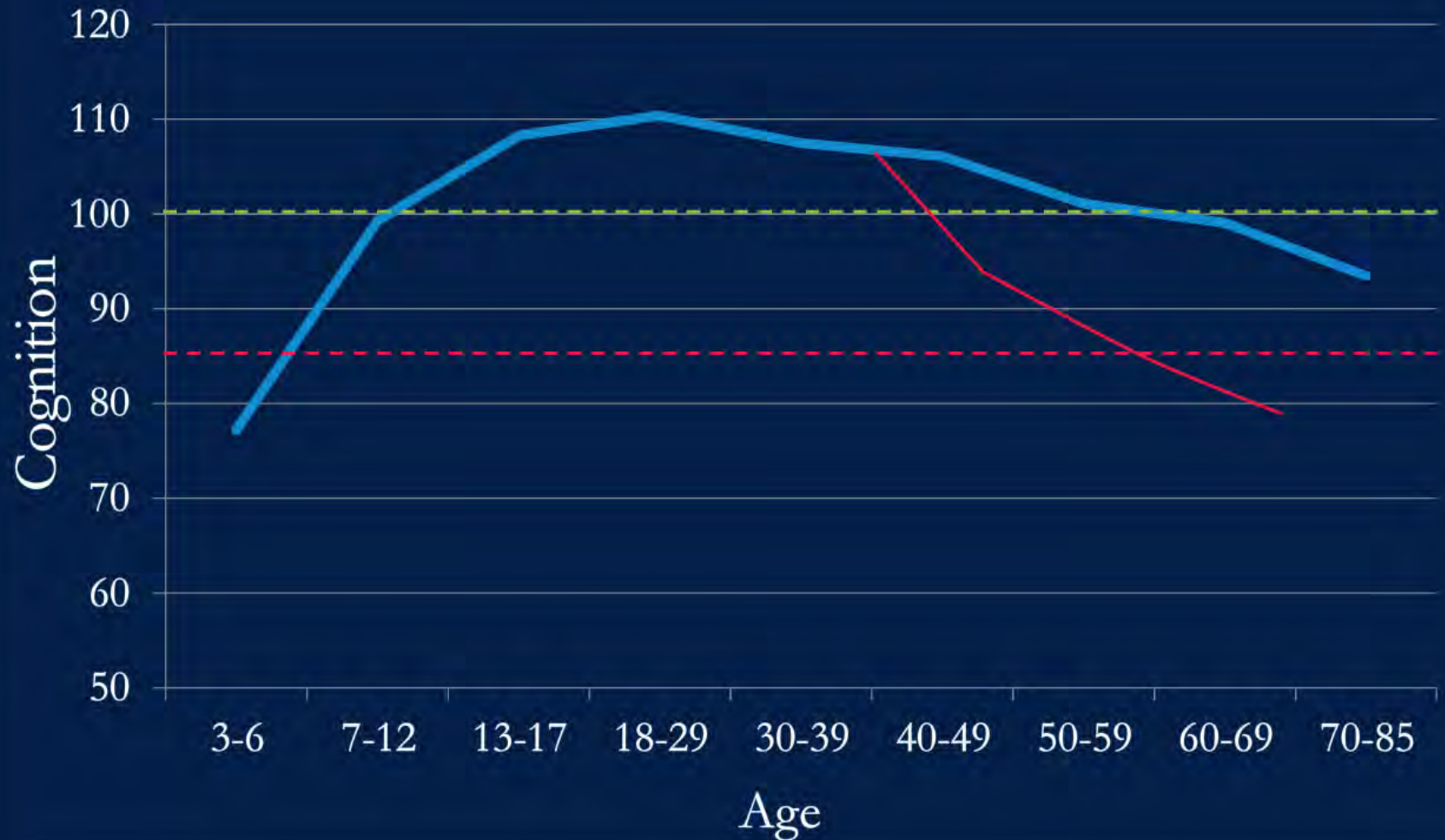


University of California
San Francisco



**GLOBAL
BRAIN HEALTH
INSTITUTE**

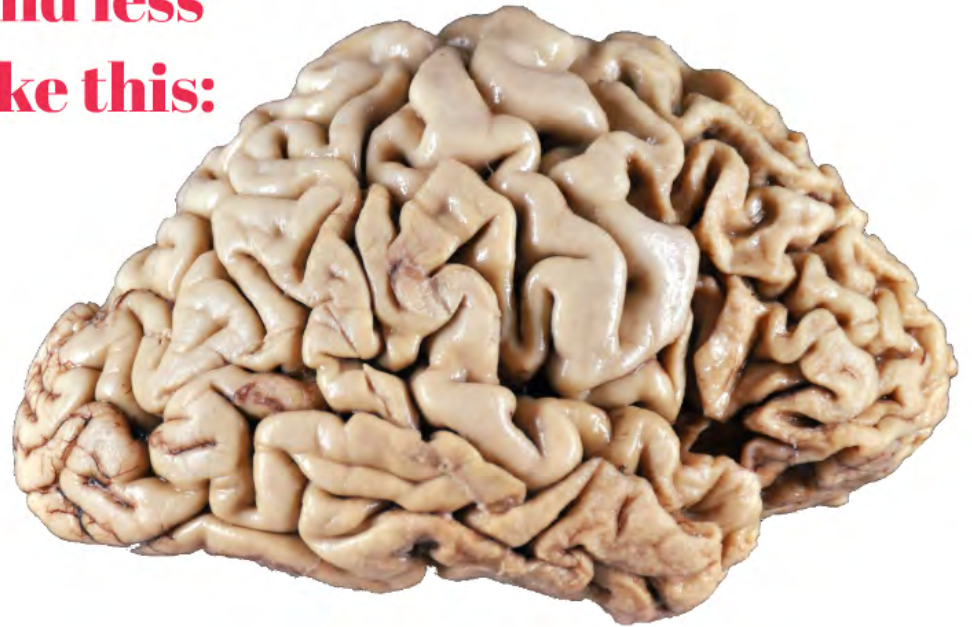
What is “Typical” Cognitive Aging?



**How do we keep our
brains looking more
like this:**



**And less
like this:**





Non-modifiable factors

Age
Biological sex
Family history
Head trauma

Modifiable factors

Hypertension
Hyperlipidemia
Diabetes
Depression
Smoking

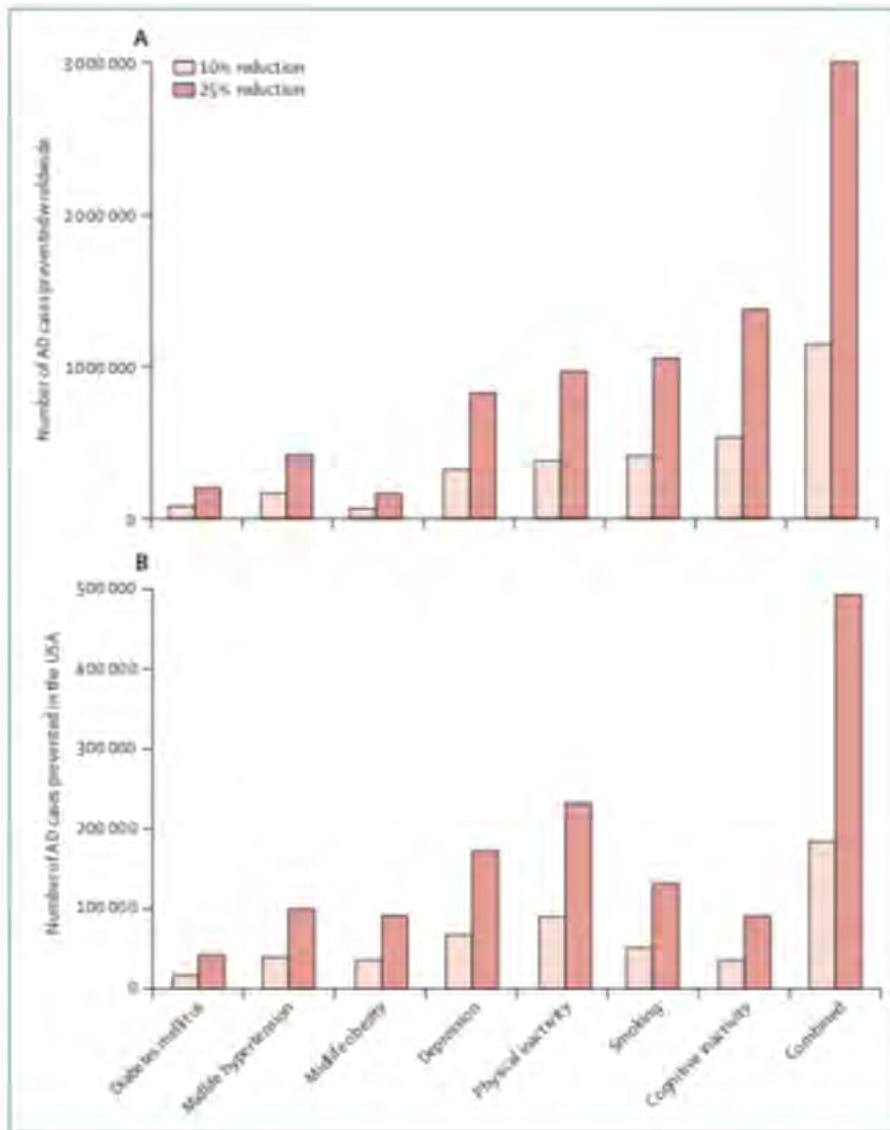


Lifestyle factors:
cognitive stimulation
Social isolation/loneliness
physical activity
healthy sleep
nutrition

The projected effect of risk factor reduction on Alzheimer's disease prevalence

Deborah E Barnes, Kristine Yaffe

At present, about 33·9 million people worldwide have Alzheimer's disease (AD), and prevalence is expected to triple over the next 40 years. The aim of this Review was to summarise the evidence regarding seven potentially modifiable risk factors for AD: diabetes, midlife hypertension, midlife obesity, smoking, depression, cognitive inactivity or low educational attainment, and physical inactivity. Additionally, we projected the effect of risk factor reduction on AD prevalence by calculating population attributable risks (the percent of cases attributable to a given factor) and the number of AD cases that might be prevented by risk factor reductions of 10% and 25% worldwide and in the USA. Together, up to half of AD cases worldwide (17·2 million) and in the USA (2·9 million) are potentially attributable to these factors. A 10–25% reduction in all seven risk factors could potentially prevent as many as 1·1–3·0 million AD cases worldwide and 184 000–492 000 cases in the USA.



Approximately 30% of cases of dementia may be attributable to key modifiable risk factors:

- uncontrolled vascular disease
- sedentary lifestyle
 - * mental and physical
- depressed mood/stress
- dietary factors and alcohol

What is the relationship between uncontrolled vascular disease, obesity, and dementia?



High triglycerides/cholesterol, Hypertension, diabetes/insulin resistance, smoking, obesity, all increase our risk of cerebrovascular disease and dementia.

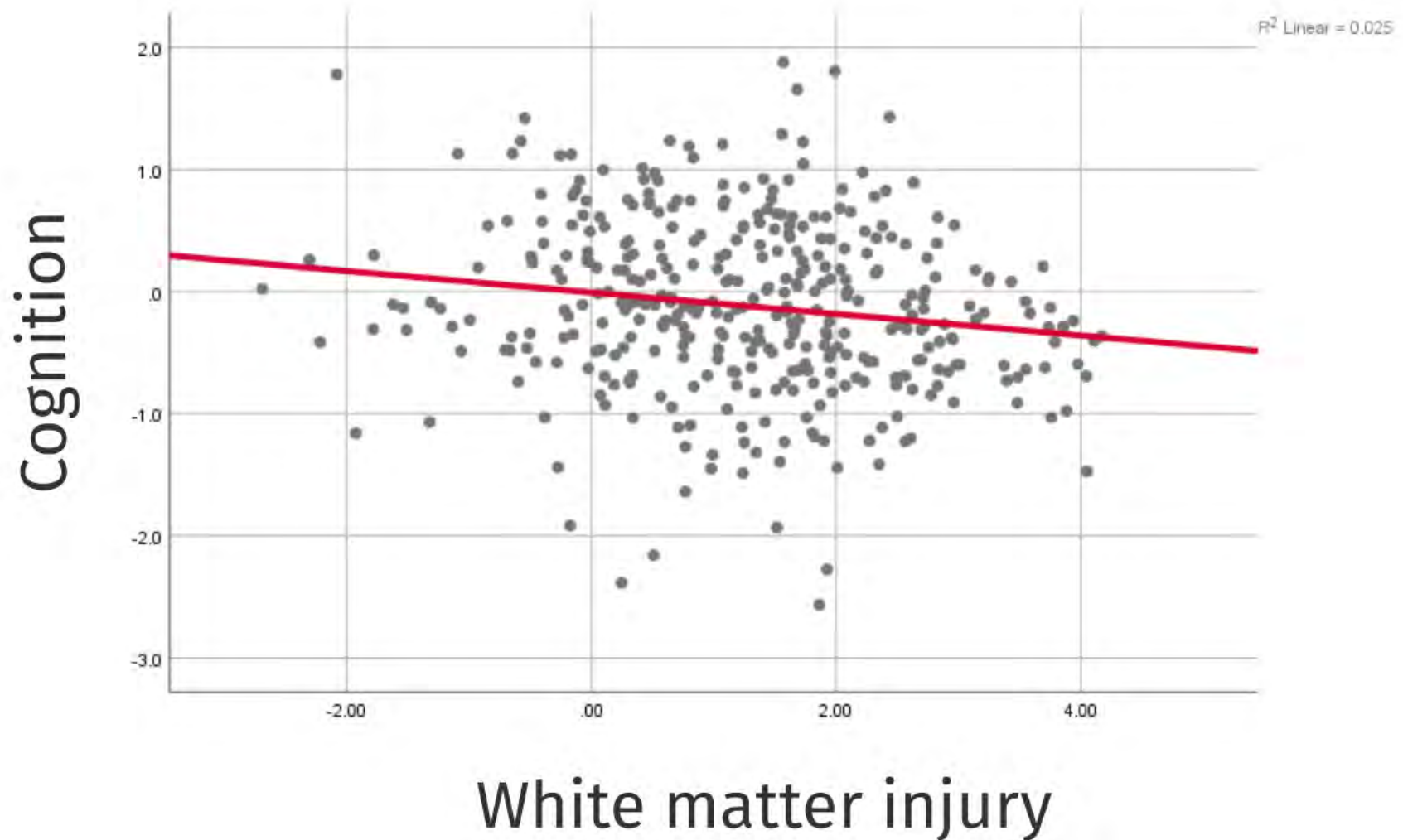


**Obesity in midlife is
associated with 3x risk of
Alzheimer disease, and 5x risk of
dementia, in late life.**

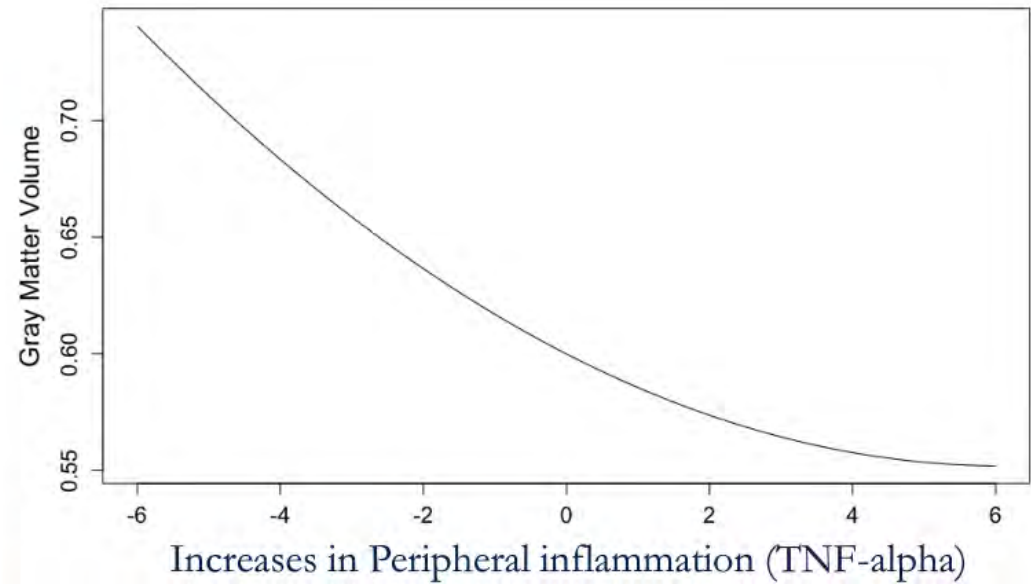
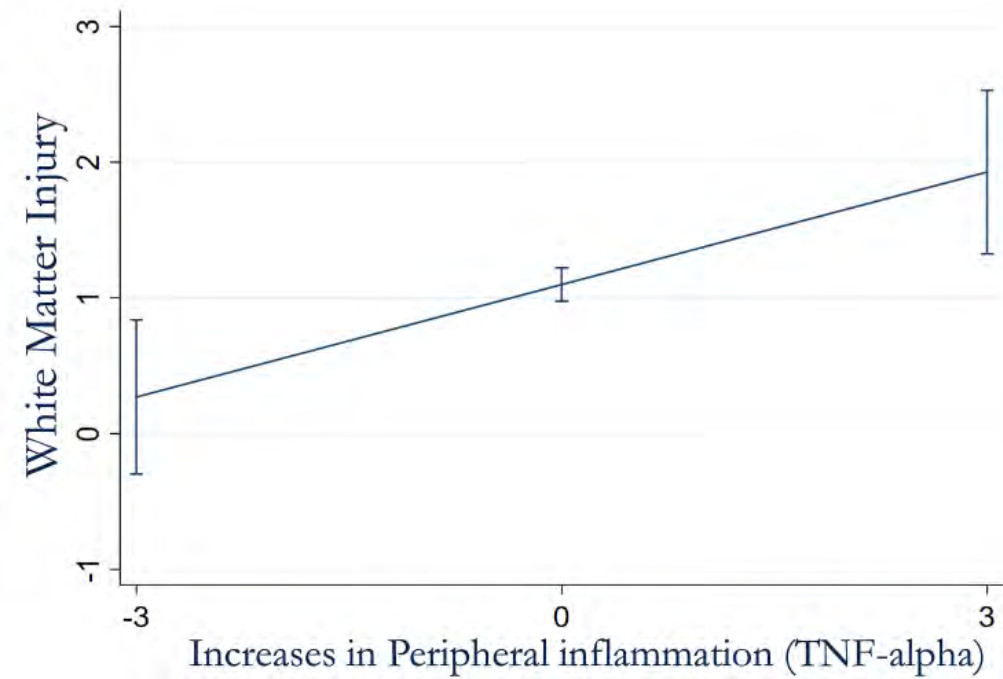
Whitmer RA, et al. Neurology. 2008

Whitmer RA, et al. BMH. 2005

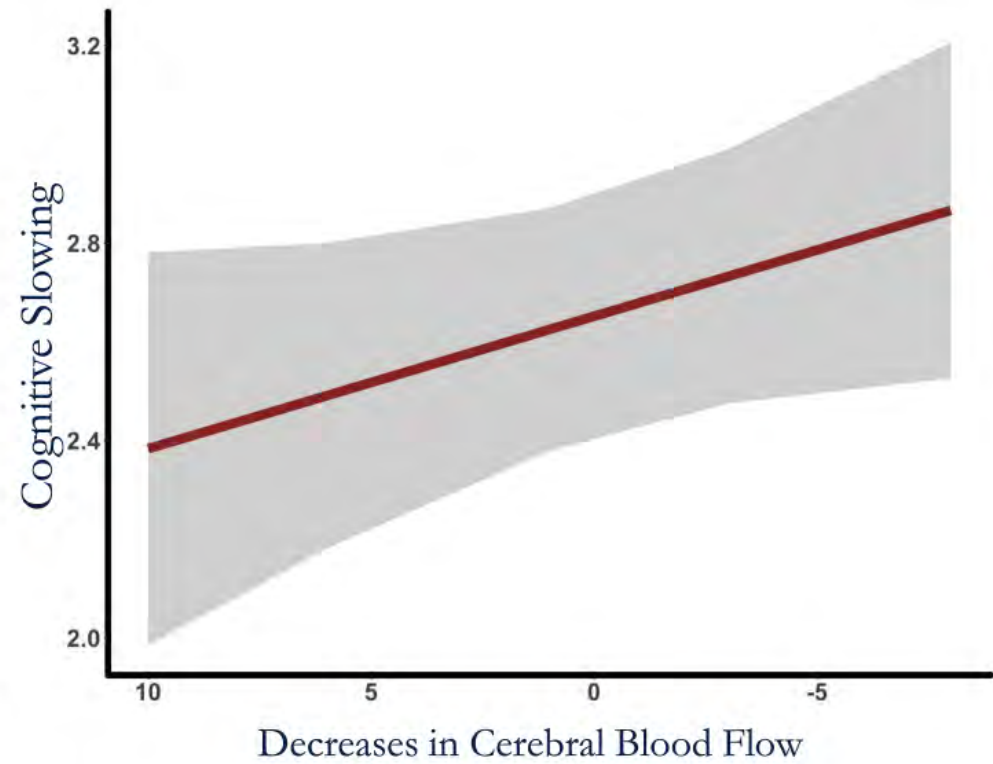
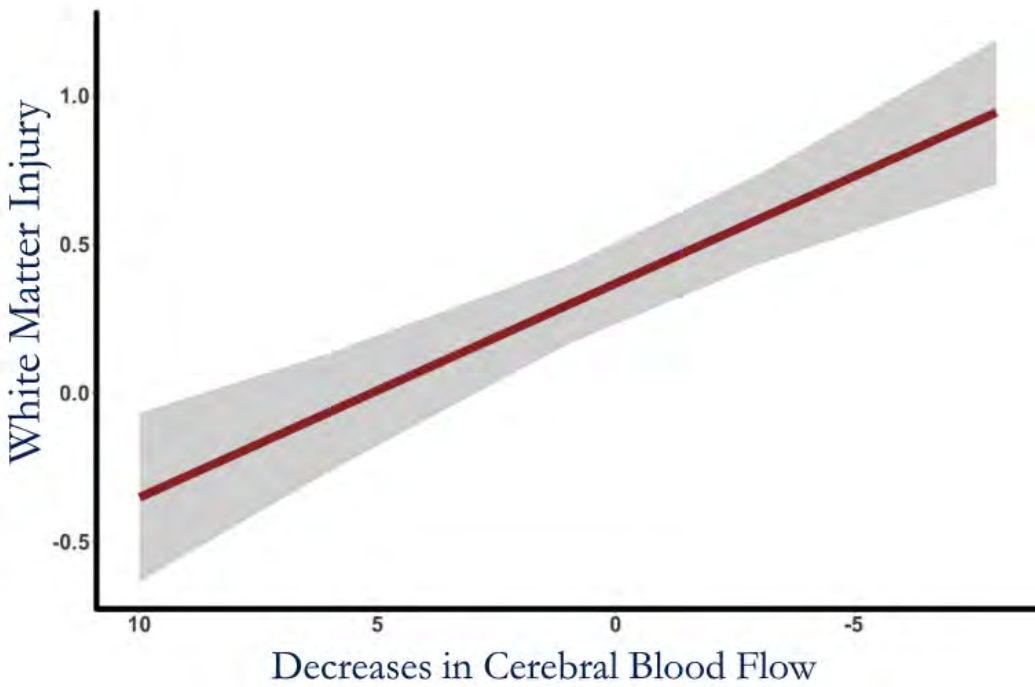
White matter injury is strongly associated with cognitive impairment



Mechanisms?



Lindbergh et al,
under review



Staffaroni et al.,
in press, Human Brain Mapping

**Physical
Activity
Promotes
Better Brain
Aging!**



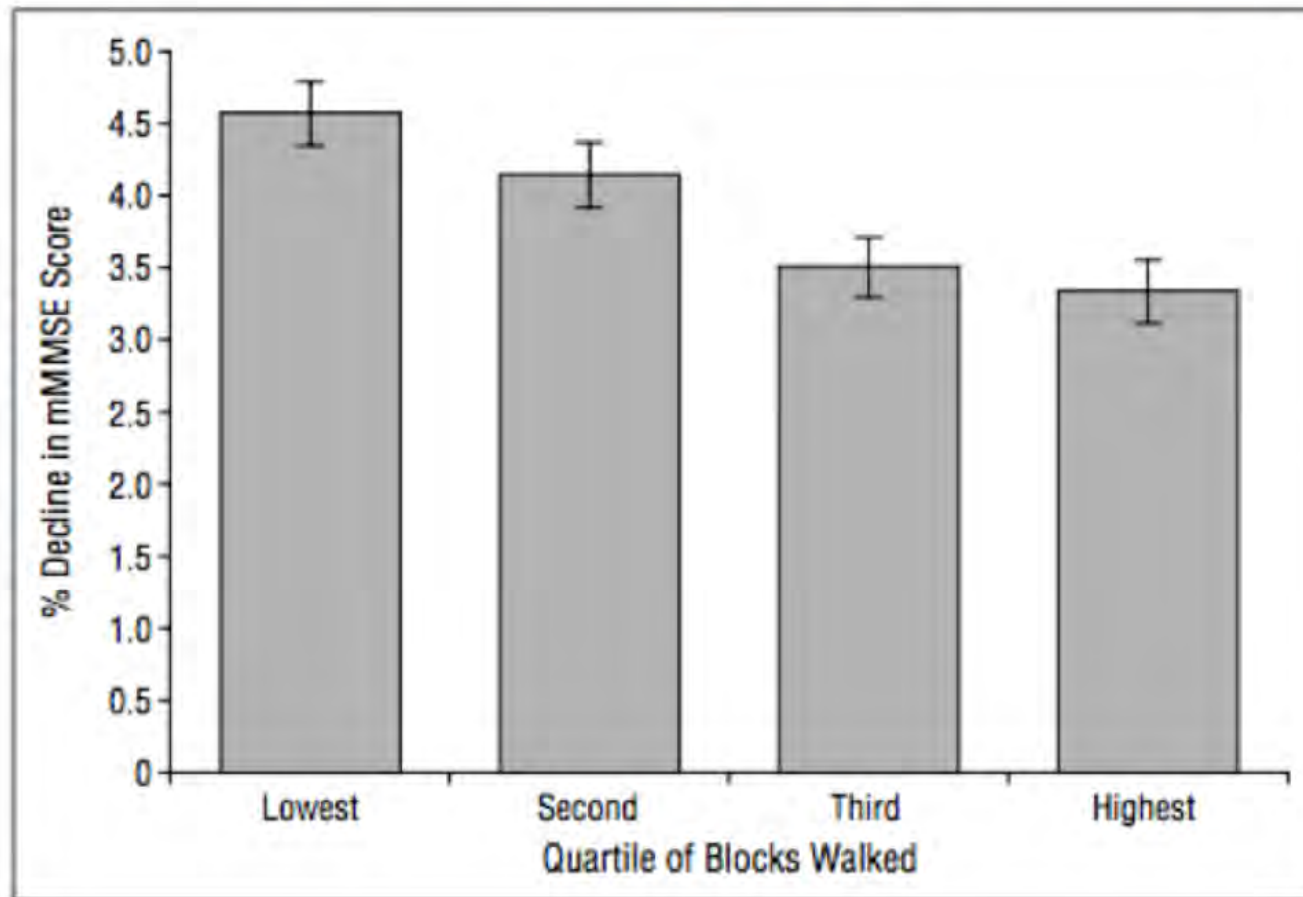
Any type is better than being sedentary.

Moderate intensity is the goal, for 150 minutes per week!

High midlife (45 to 65 years old) fitness associated with 88% reduced risk of dementia over 44 years AND, among those who developed dementia, onset was delayed on average 5 years.

Horder, et al. 2018

Walking counts!



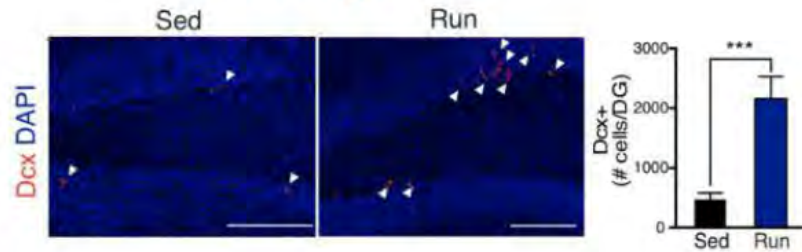
33% reduced risk of decline over 6 to 8 years.

Yaffe et al., 2001

Physical Activity Promotes Better Brain Aging



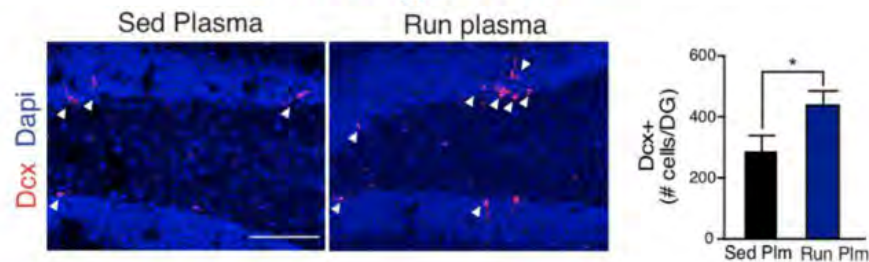
Neurogenesis



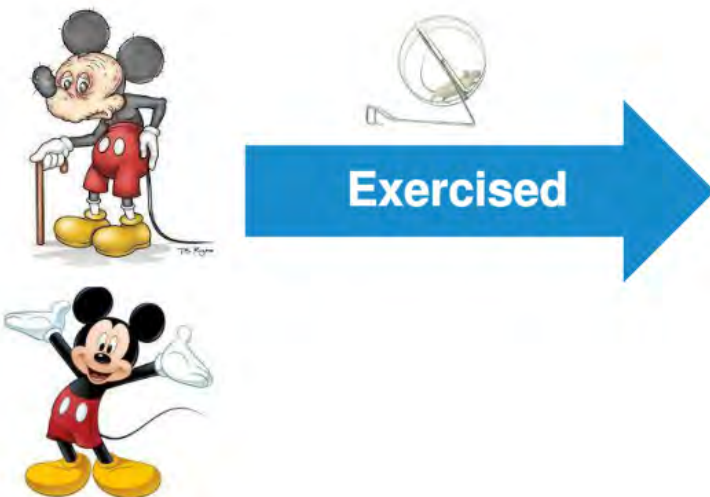
S. Villeda



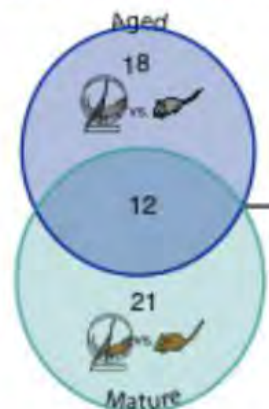
Neurogenesis



A. Horowitz



Blood Factors

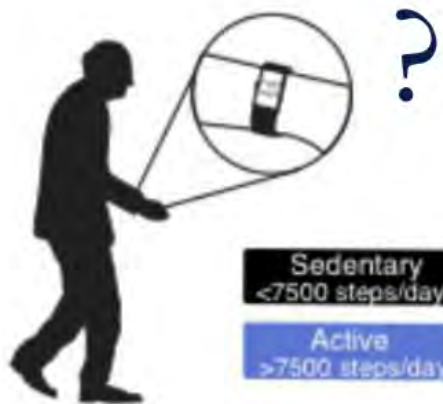
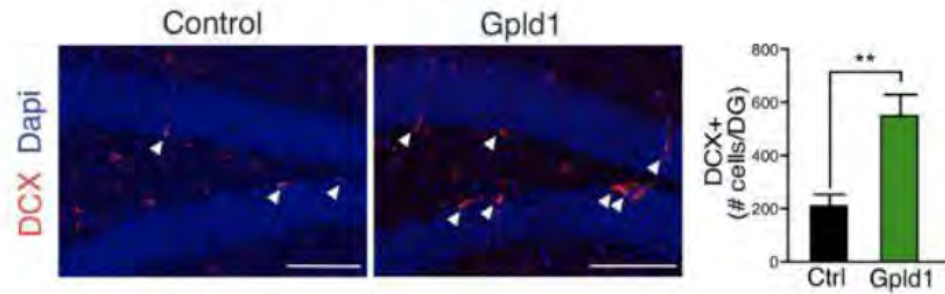


Physical Activity Promotes Better Brain Aging

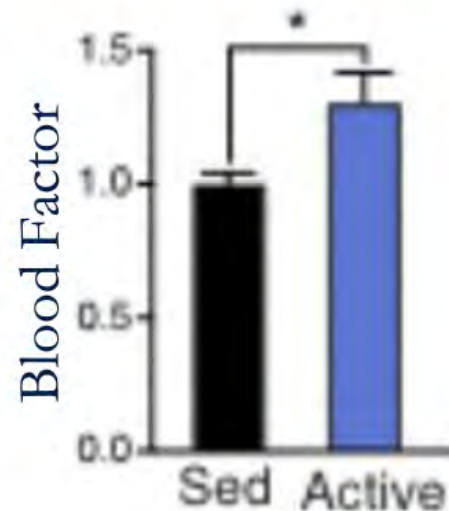


1 blood factor

Neurogenesis



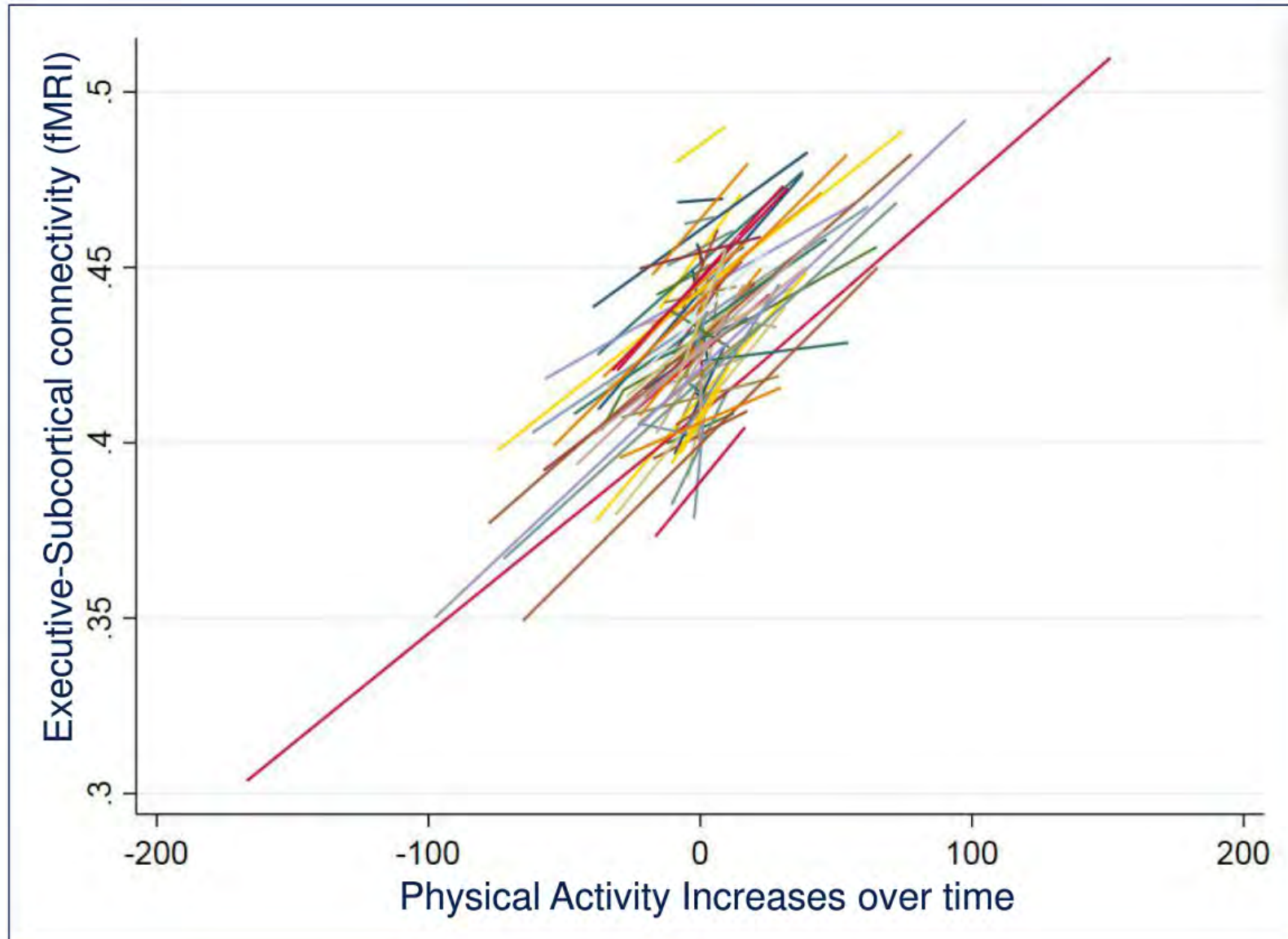
Fitbit Study: Healthy Older Adults



Horowitz et al. *under review*

Never too late!

Increases in Physical Activity over time relate to better brain network synchrony



K. Dorsman et al.

Cognitive Stimulation & "Brain Training"

Journal of Gerontology: PSYCHOLOGICAL SCIENCES
2005, Vol. 60B, No. 5, P251–P258

Copyright 2005 by The Gerontological Society of America

Complexity of Work and Risk of Alzheimer's Disease: A Population-Based Study of Swedish Twins

Ross Andel,¹ Michael Crowe,² Nancy L. Pedersen,^{3,7} James Mortimer,⁴
Eileen Crimmins,⁵ Boo Johansson,⁶ and Margaret Gatz^{3,7}

Main finding: those who engaged in more complex work with people had more than 5 times reduced odds of developing Alzheimer disease.

Cognitive activities delay onset of memory decline in persons who develop dementia



C.B. Hall, PhD
R.B. Lipton, MD
M. Sliwinski, PhD
M.J. Katz, MPH
C.A. Derby, PhD
J. Verghese, MB, BS

ABSTRACT

Background: Persons destined to develop dementia experience an accelerated rate of decline in cognitive ability, particularly in memory. Early life education and participation in cognitively stimulating leisure activities later in life are 2 factors thought to reflect cognitive reserve, which may delay the onset of the memory decline in the preclinical stages of dementia.

Methods: We followed 488 initially cognitively intact community residing individuals with epidemiologic, clinical, and cognitive assessments every 12 to 18 months in the Bronx Aging Study. We assessed the influence of self-reported participation in cognitively stimulating leisure activities on the onset of accelerated memory decline as measured by the Buschke Selective Reminding Test in 101 individuals who developed incident dementia using a change point model.

Main findings: late life cognitive activities influence "cognitive reserve" independently of level of education. Each additional self-reported day of cognitive activity at baseline delayed the onset of memory decline by 0.18 years.

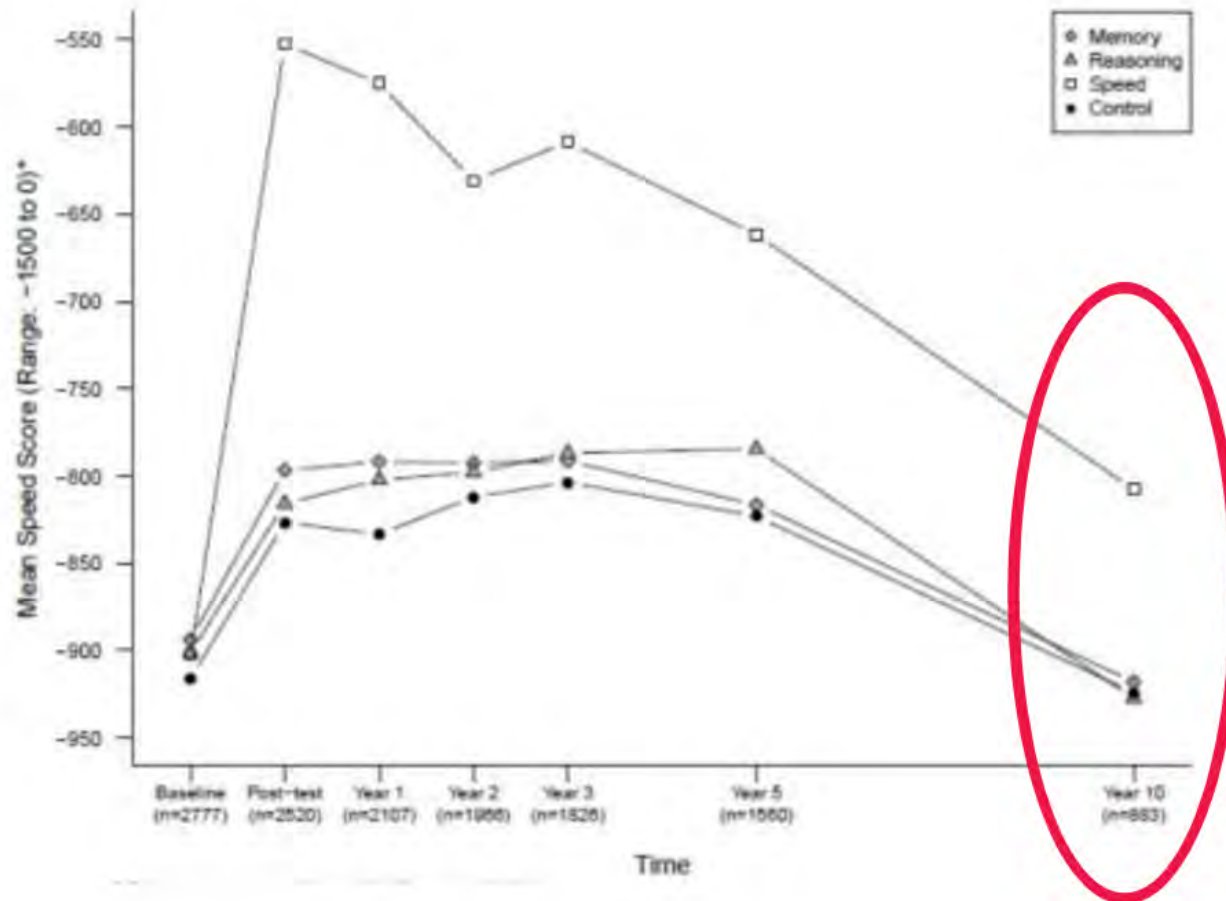
Take home message:

Late life cognitive activities (e.g., playing games) may promote cognitive stability (beyond baseline education/occupation).

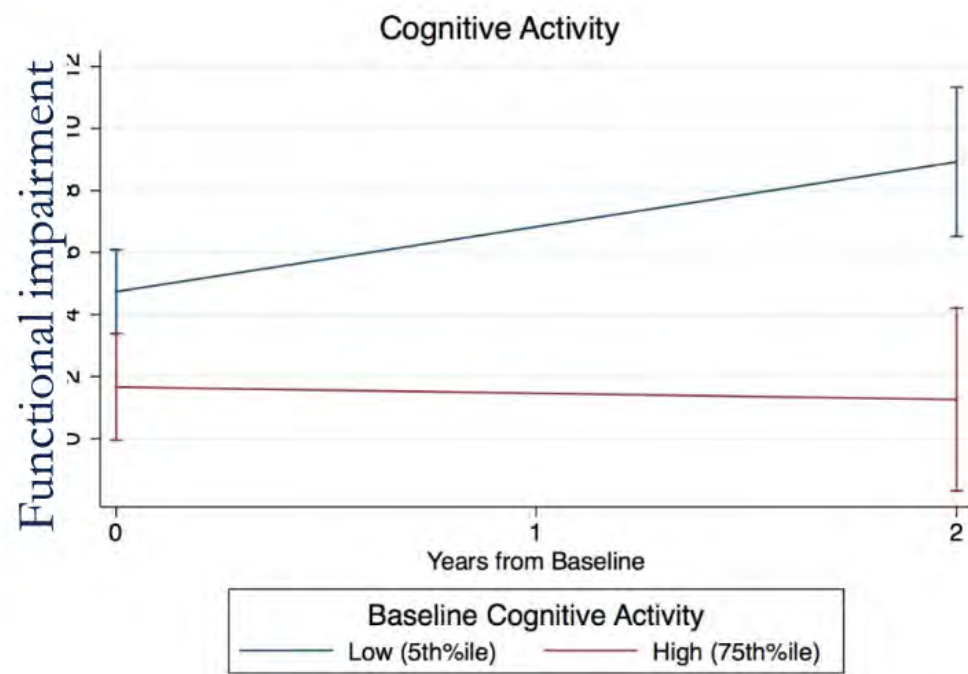
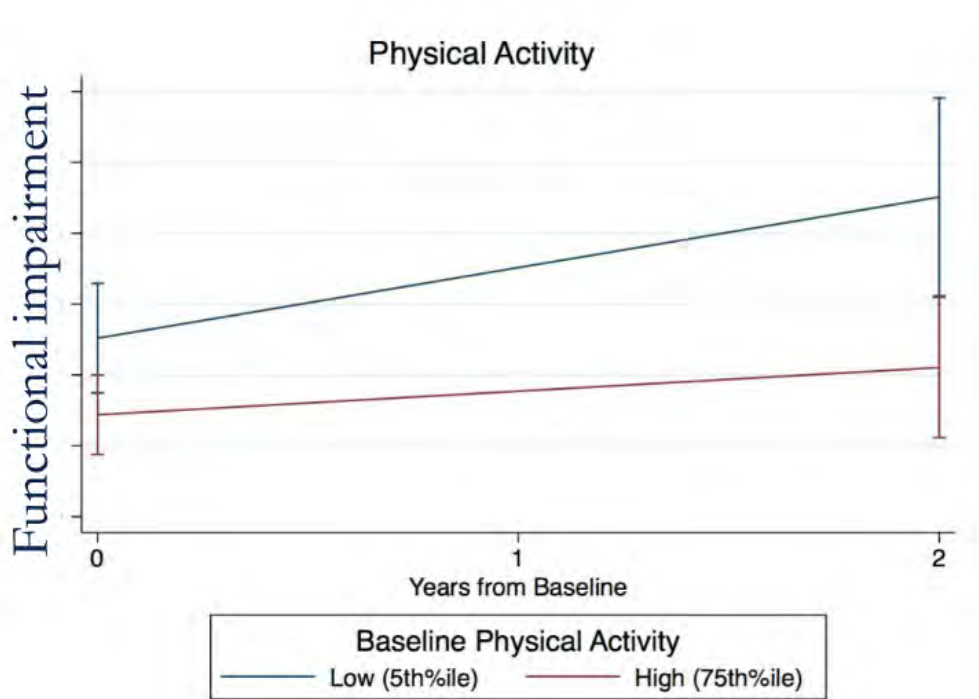
Jonaitis et al., 2013)



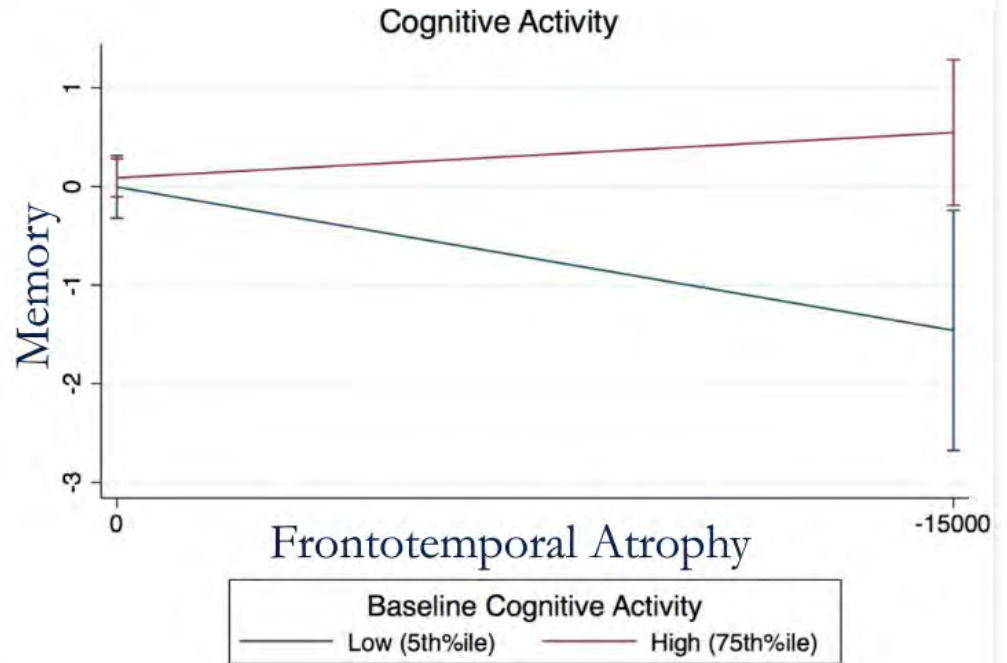
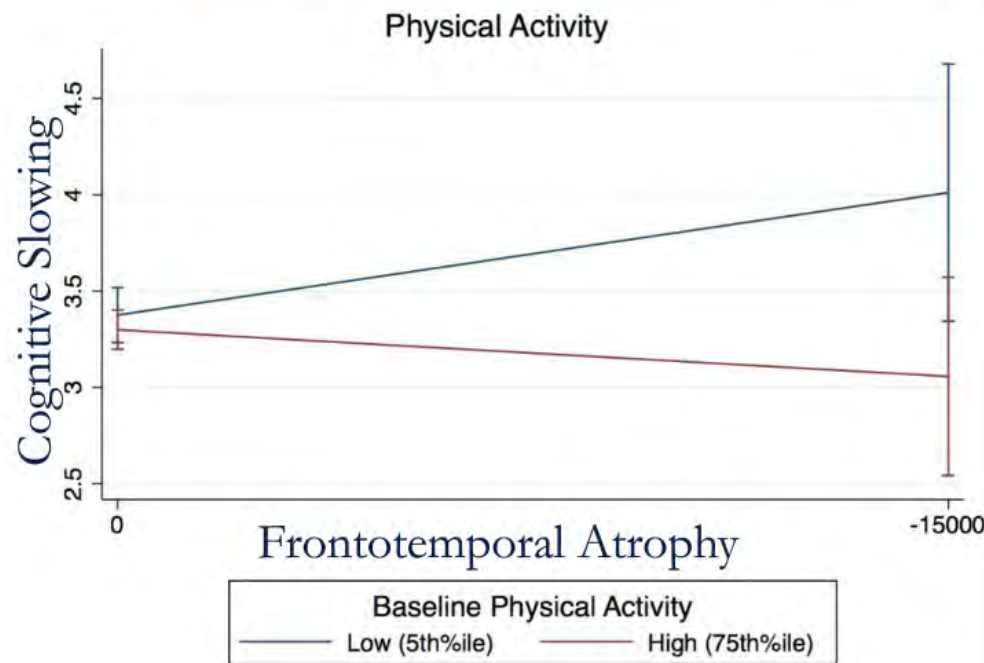
ACTIVE Study: 10-year benefits of processing speed/reasoning training
(Rebok et al., 2014)



Active Lifestyles are associated with $>60\%$ less cognitive and functional decline in patients with genetic forms of neurodegeneration (FTD)



Genetic FTD Carriers with Active Lifestyles “Outperform” their Brains



Casaletto et al, *under review*

How can I promote "cognitive stimulation"?

Should I buy a "brain training" program?

Novel and challenging.

Many forms...



Stress, age, and inflammation

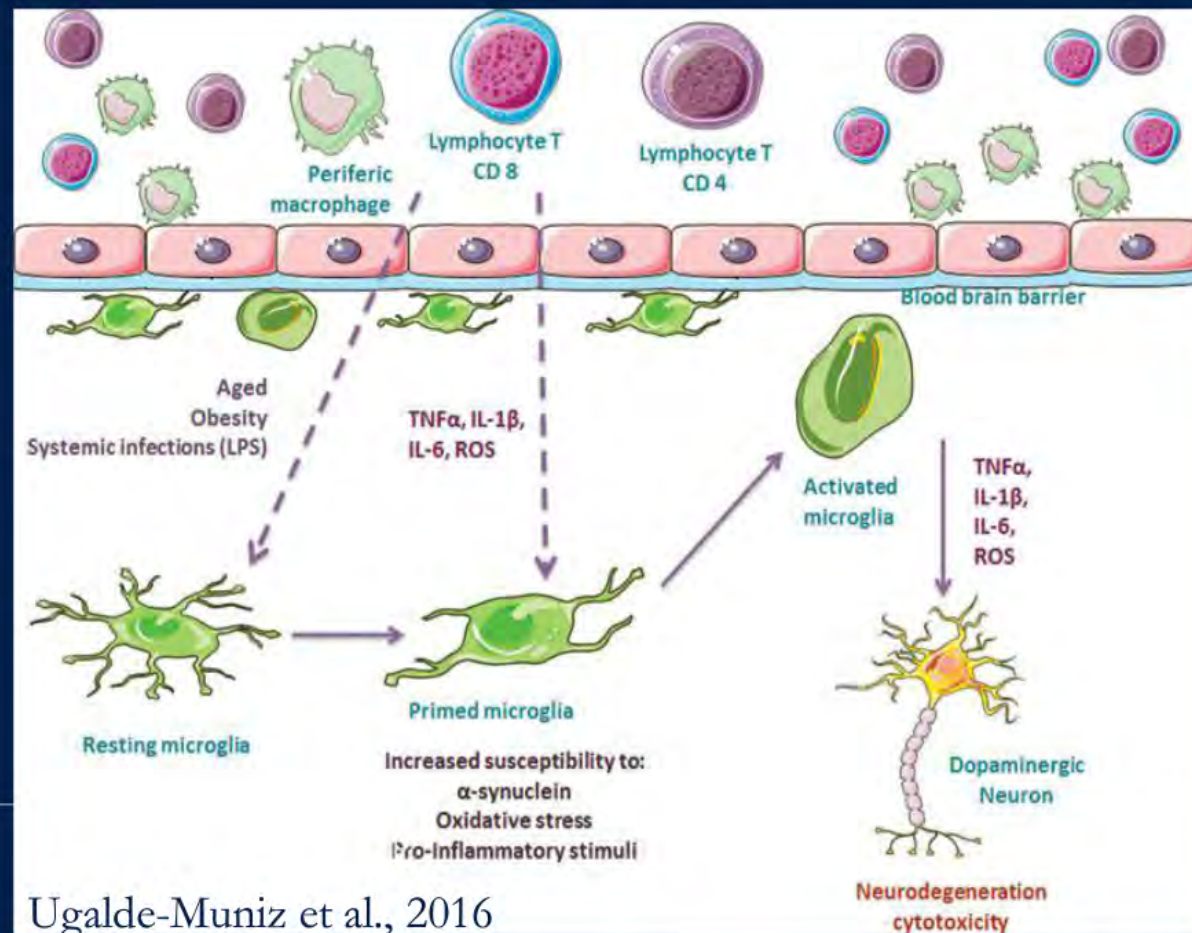
“Double-hit” Hypothesis

Aging

Perceived Stress

Inflammation

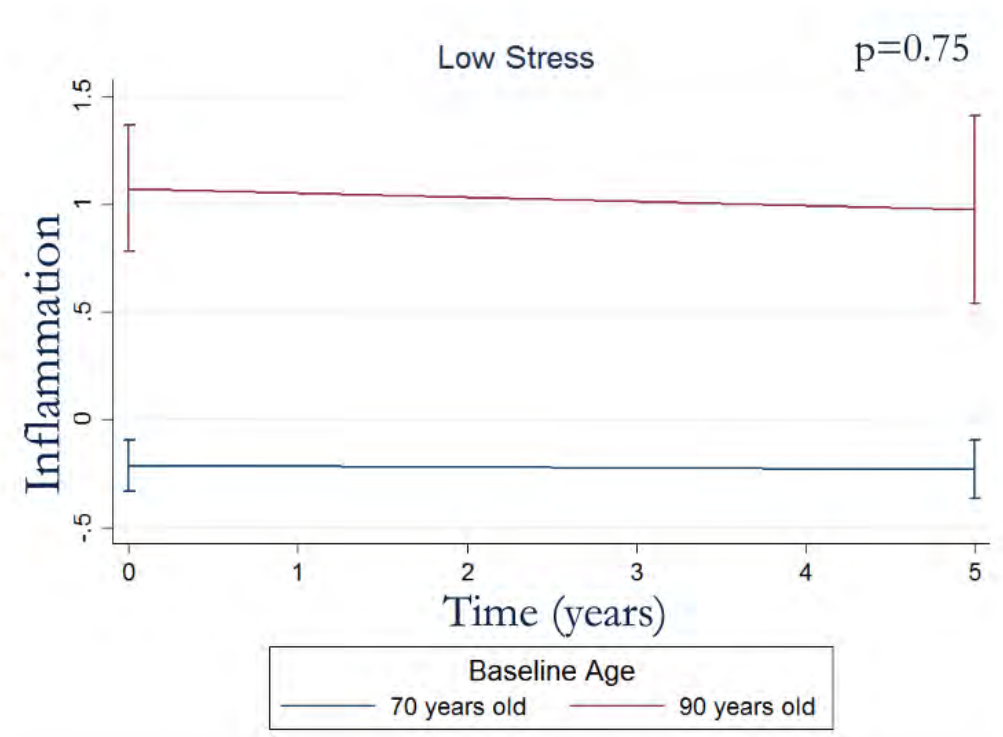
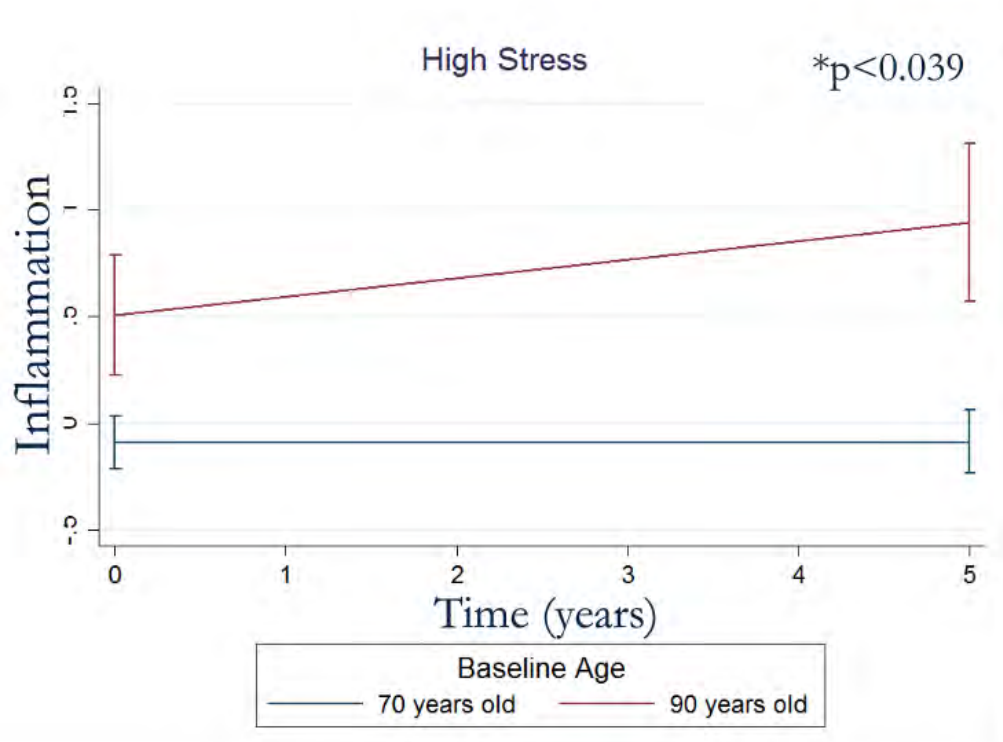
Cognition



Franceschi et al., 2000; Sparkman & Johnson, 2008; Gomez et al., 2005

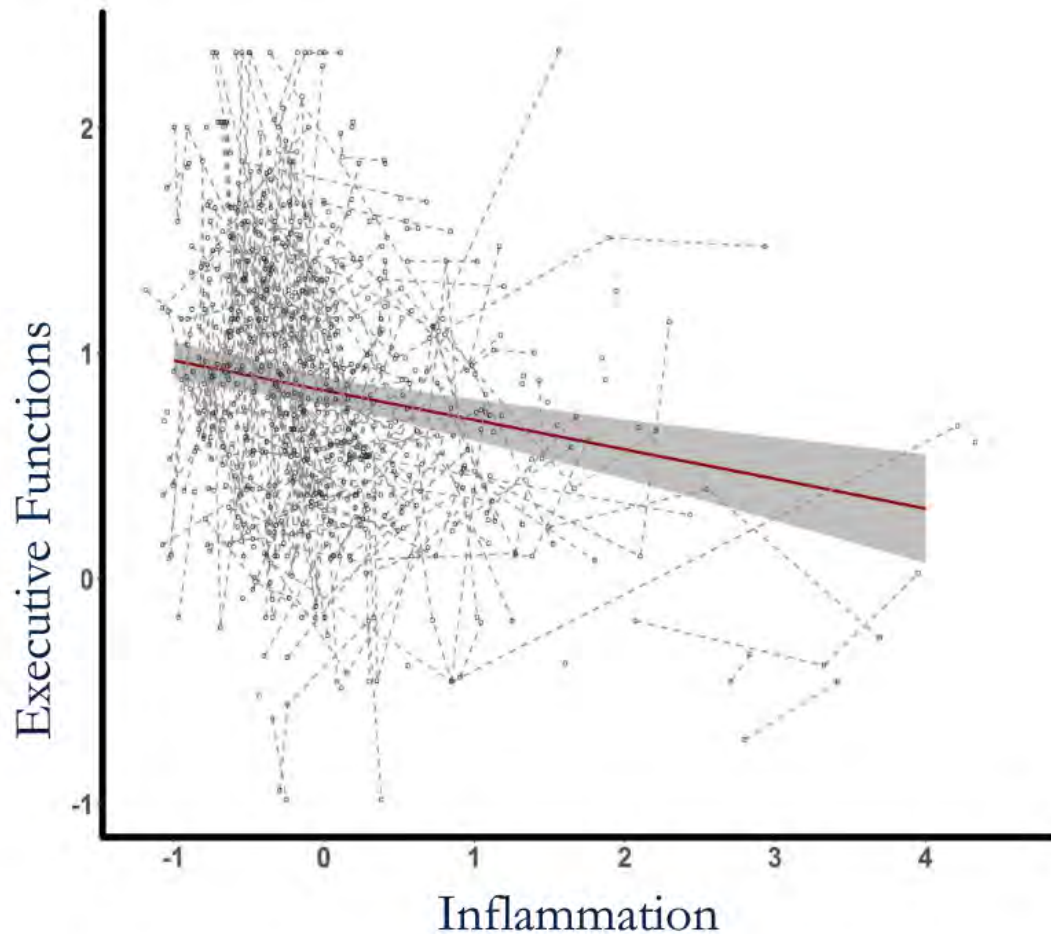
Ugalde-Muniz et al., 2016

High Perceived Stress Accelerates Immune Activation Aging Trajectories



Casaleto et al., 2018, AJGP

Changes in Inflammation Track with Changes in Cognition



Casaletto et al., 2018, AJGP

Strategies to reduce stress

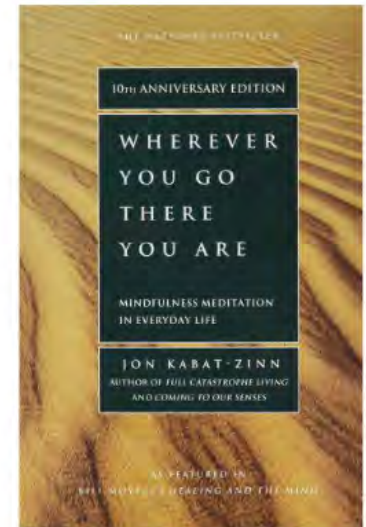


Deep breathing/Progressive muscle relaxation

Mindfulness-based Stress Reduction (MBSR)

Exercise

Simplifying environment/responsibilities



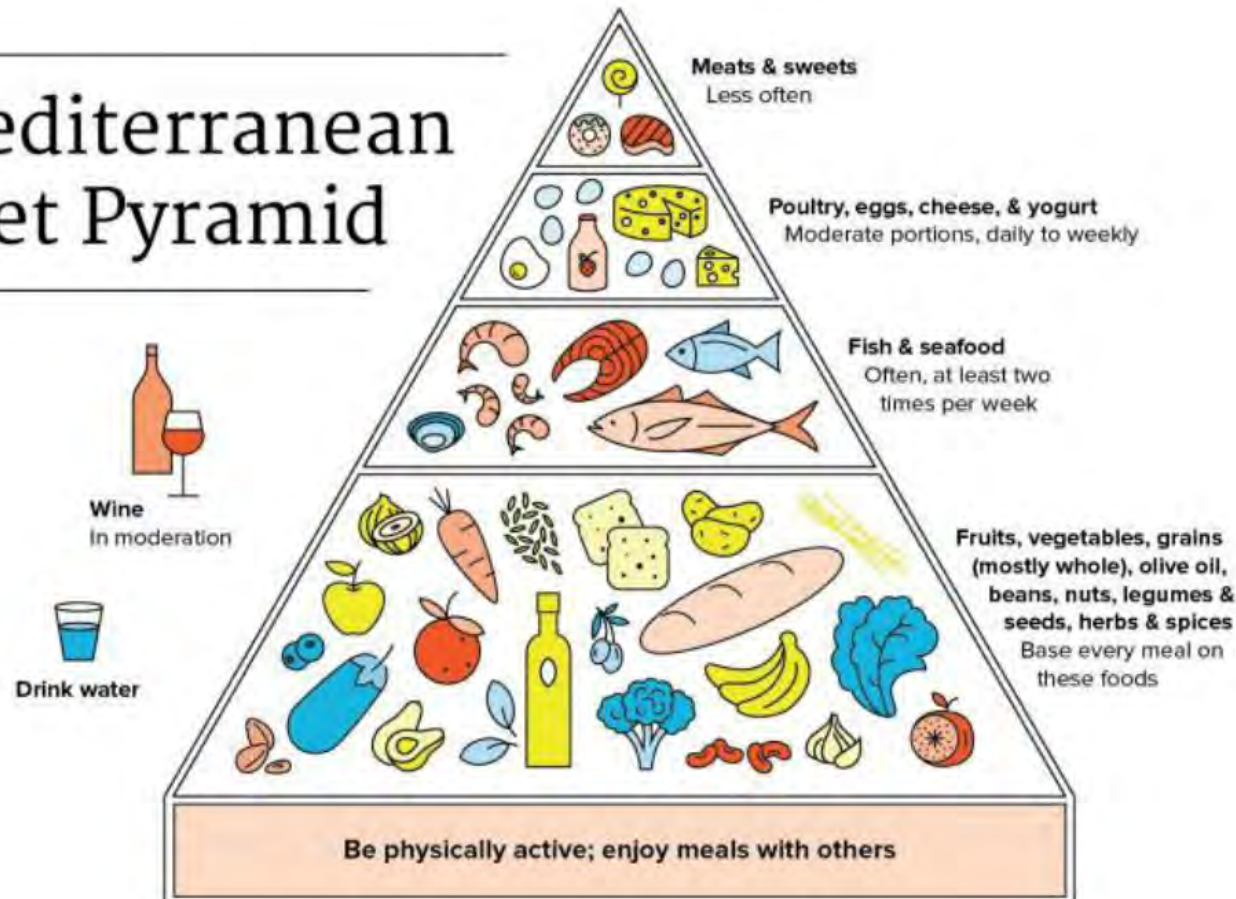
Mediterranean Diet/Whole Fruits & Vegetables

Higher adherence = Better cognitive outcomes

~30% reduced risk of cognitive decline and dementia

~30% reduced risk of stroke

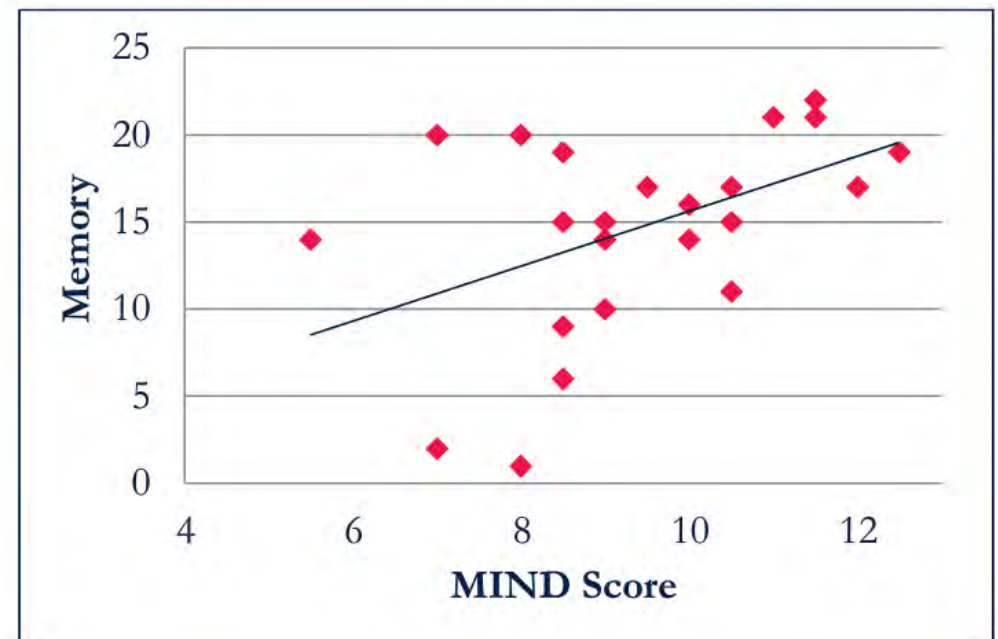
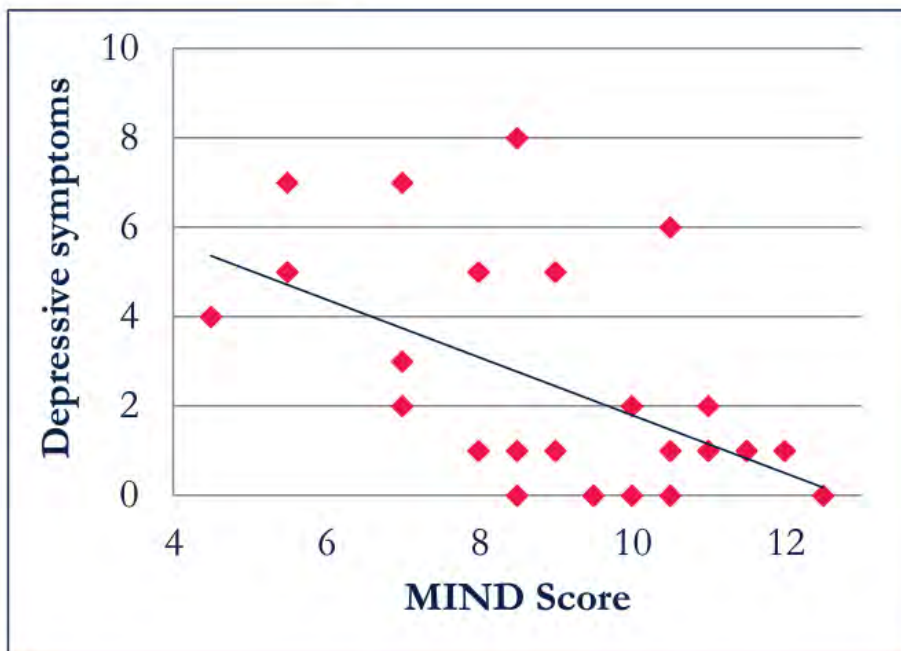
Mediterranean Diet Pyramid



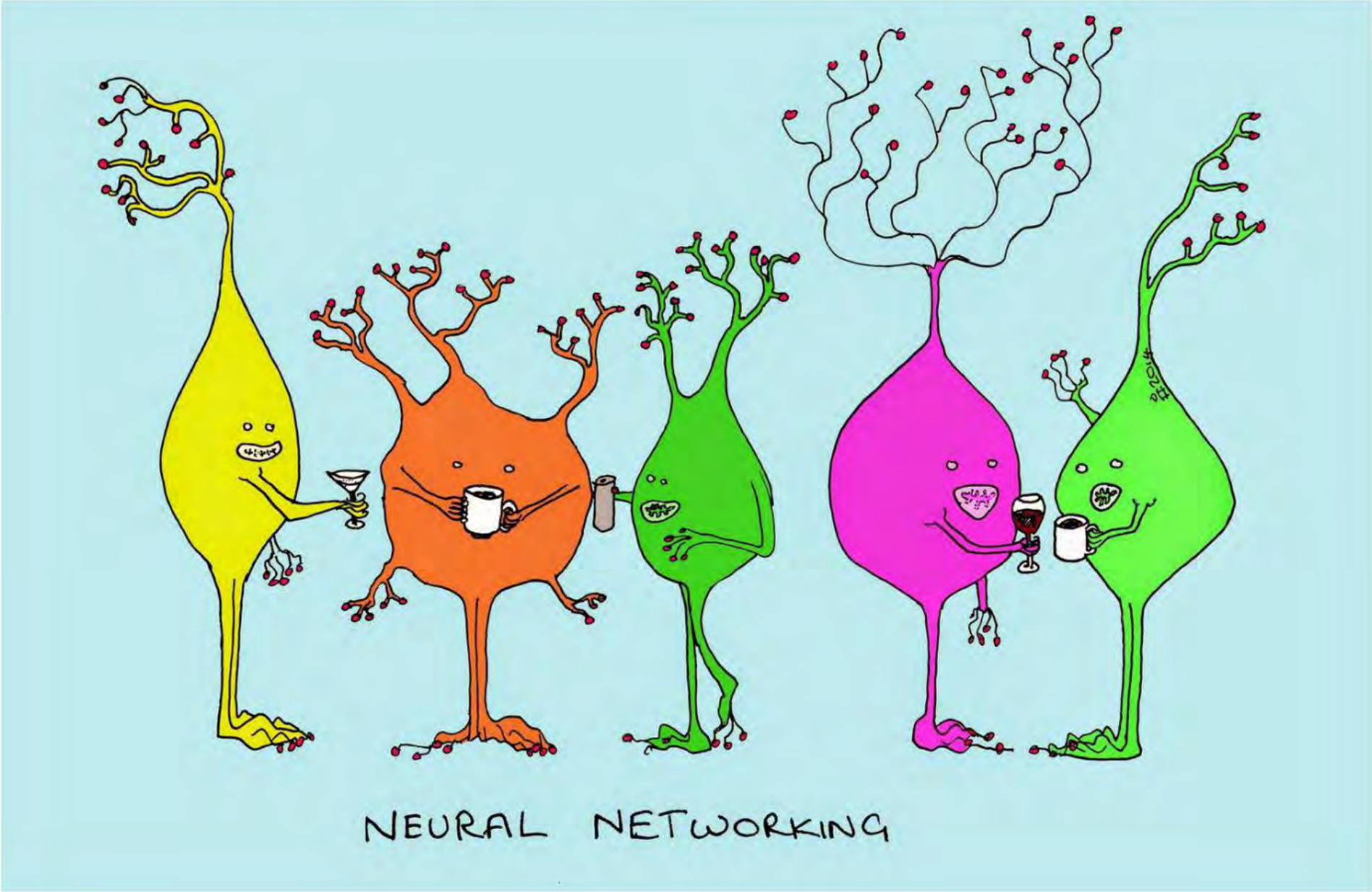
MIND Diet is associated with Fewer Alzheimer-like Symptoms in Typically Aging Adults



Fox et al., *under review*



Challenge your brain and support it with nutrients!



Studies currently enrolling!

Fitbit Healthy Brain Aging

How much exercise? Biology associated with exercise?

Activities for Aging Neurogenesis (ActAN) Study

*What brain-related pathways **change** with lifestyle behaviors?*

Contact us! Kaitlin.Casaletto@ucsf.edu or
Nina.djukic@ucsf.edu

THANK YOU

Hillblom Aging Network

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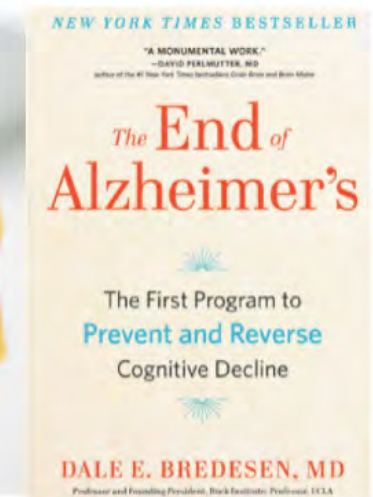
UCSF Weill Institute for Neurosciences

Memory and Aging Center

How to decode direct-to-consumer interventions for brain health

Joanna Hellmuth, MD, MHS

How to know what to trust?



How does the government regulate supplements?

Dietary Supplement Health and Education Act, 1994,
dictates how the Food and Drug Administration (FDA)
regulates supplement safety and efficacy.

Dietary Supplement Health & Education Act

Safety of supplements

- Supplements are NOT tested by the FDA for safety
- Supplements are considered “safe” until proven otherwise
- They can only be found “unsafe” after causing harm
- Only gives the FDA permission to stop a company from making a supplement when the agency can prove it poses a significant risk to public health
- Opposite of the FDA process for drug approval

Dietary Supplement Health & Education Act

Safety of supplements

- Supplements may be marketed as "natural" but still may contain hazardous compounds
- Supplement contents may cause side effects or unwanted symptoms
- Supplement compounds may interact with existing medications and medical conditions

Supplement efficacy for brain health

Supplement efficacy for brain health

- No dietary supplement has been shown to prevent cognitive decline or dementia

Dietary Supplement Health & Education Act

Efficacy of supplements

- Claims allowed: **statements of structure or function**
 - "Calcium can improve bone strength"
 - "Supplement X can improve memory and concentration"
- FDA does not see or review data supporting these claims
- Companies are supposed to have evidence their claims are true, but FDA is not permitted to examine it

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Dept. Health Human Services 2012 study assessing structure/function claims

- Evaluated 127 supplements to review the extent substantiating data complied with FDA standards
- “Overall, substantiation...for the sampled supplements were inconsistent with FDA **guidance** on competent and reliable scientific evidence.”
- “These results raise questions about the extent to which structure/function claims are truthful and not misleading.”

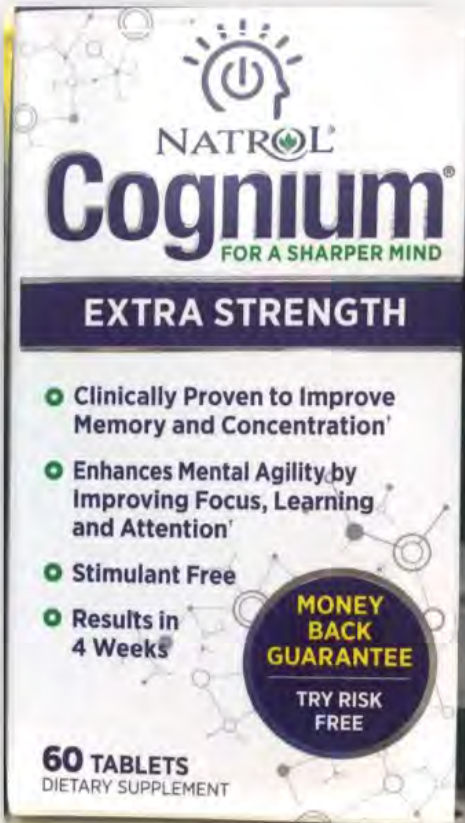
https://www.nutriwatch.org/09Reg/oig_2012.pdf

Dietary Supplement Health & Education Act

Efficacy of supplements

- Claims that are illegal: statements of prevention, treatment, or cure of a disease process
 - “Calcium can improve *osteoporosis*”
 - “Supplement X can improve *Alzheimer’s symptoms*”

How are these statements perceived?



“Clinically proven to improve memory”

“Clinically proven to improve Alzheimer’s symptoms”

How
would
you
interpret
this label
now?

BRAIN HEALTH



NATROL
Cognium
FOR A SHARPER MIND

EXTRA STRENGTH

- Clinically Proven to Improve Memory and Concentration*
- Enhances Mental Agility by Improving Focus, Learning and Attention*
- Stimulant Free
- Results in 4 Weeks*

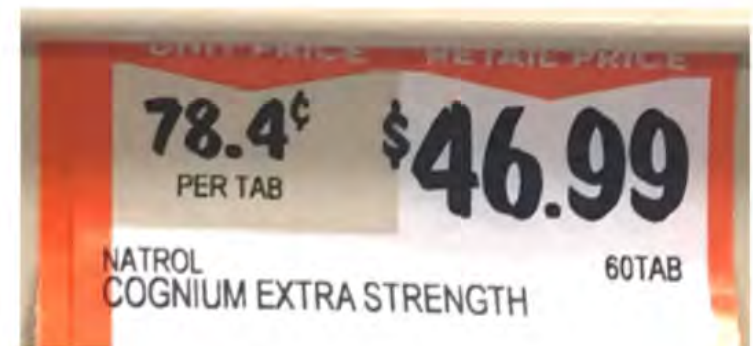
MONEY BACK GUARANTEE
TRY RISK FREE

60 TABLETS
DIETARY SUPPLEMENT

78.4
PER TA

NATROL
COGNIMUM

How
would
you
interpret
this label
now?



VIEWPOINT

The Rise of Pseudomedicine for Dementia and Brain Health

Joanna Hellmuth, MD, MHS

Memory and Aging Center, Department of Neurology, University of California, San Francisco.

Gil D. Rabinovici, MD
Memory and Aging Center, Department of Neurology, University of California, San Francisco.

Bruce L. Miller, MD
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The US population is aging, and with it is an increasing prevalence of Alzheimer disease, which lacks effective approaches for prevention or a cure.¹ Many individuals are concerned about developing cognitive changes and dementia. With increasing amounts of readily accessible information, people independently seek and find material about brain health interventions, although not all sources contain quality medical information.

This landscape of limited treatments for dementia, concern about Alzheimer disease, and wide access to information have brought a troubling increase in "pseudomedicine." Pseudomedicine refers to supplements and medical interventions that exist within the law and are often promoted as scientifically supported treatments, but lack credible efficacy data. Practitioners of pseudomedicine often appeal to health concerns, promote individual testimony as established fact, advocate for unproven therapies, and achieve financial gains.

With neurodegenerative disease, the most common example of pseudomedicine is the promotion of dietary supplements to improve cognition and brain health. This \$3.2-billion industry promoting brain health

to describe endeavors that follow "...the apparent precepts and forms of scientific investigation, but they're missing something essential...."⁶ Cargo cult science is apparent in material promoting some brain health supplements; "evidence" is presented in a scientific-appearing format that lacks actual substance and rigor. Feynman suggested 1 feature of scientific integrity is "bending over backwards to show how [the study] may be wrong..." which is a feature that is often lacking when interventions are promoted for financial gain.⁶

A similarly concerning category of pseudomedicine involves interventions promoted by licensed medical professionals that target unsubstantiated etiologies of neurodegenerative disease (eg, metal toxicity; mold exposure; infectious causes, such as Lyme disease). Some of these practitioners may stand to gain financially by promoting interventions that are not covered by insurance, such as intravenous nutrition, personalized detoxification, chelation therapy, antibiotics, or stem cell therapy. These interventions lack a known mechanism for treating dementia and are costly, unregulated, and potentially harmful.

Shortly after...



FDA U.S. FOOD & DRUG ADMINISTRATION

Beware of unproven Alzheimer's treatments like these!

False Promises About So-Called Alzheimer's Cures
Unfortunately, when faced with a serious health issue, even the most rational person can be led to believe implausible claims.

1 2 3



WARNING & ONLINE ADVISORY LETTERS:

Products making illegal, unproven claims about Alzheimer's treatment

FDA

The New York Times

Supplement Makers Touting Cures for Alzheimer's and Other Diseases Get F.D.A. Warning

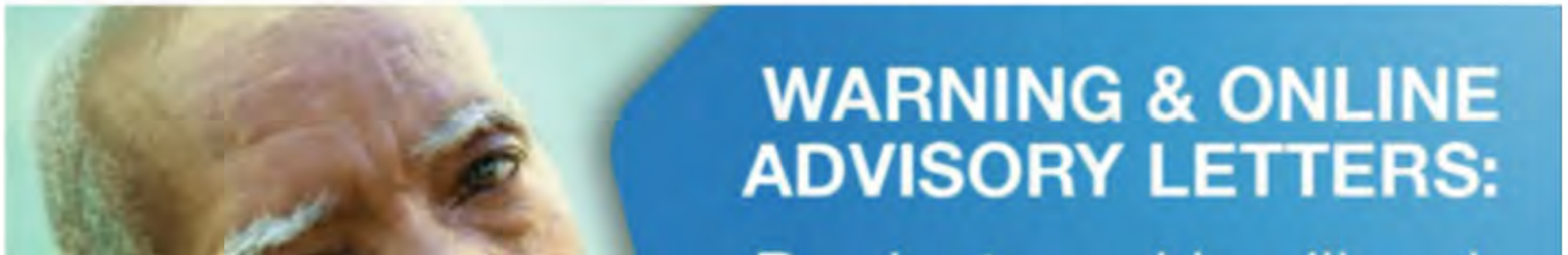


The F.D.A. also suggested that Congress strengthen its authority over the \$40 billion industry, which sells as many as 80,000 kinds of powders and pills with little federal scrutiny. Robert K. Chin/Alamy

What was in the FDA action?



- **Warning letters to 17 supplement manufacturers**
- **Strong consumer warning**
 - “fly in the face of true science”
 - “offered by...scam artists”
 - “These products are a waste of money”



What was in the FDA action?



- **Warning letters to 17 supplement manufacturers**
- **Strong consumer warning**
“fly in the face of true science”
“offered by...scam artists”
“These products are a waste of money”



WARNING & ONLINE ADVISORY LETTERS:

Products making illegal, unproven claims about Alzheimer's treatment



Supplements like these are still legally sold without review of safety or efficacy



BRAIN HEALTH



NATROL Cognium
FOR A SHARPER MIND

- Clinically Proven to Improve Memory and Concentration*
- Stimulant Free
- Results in 4 Weeks

MONEY BACK GUARANTEE
TRY RISK FREE

60 TABLETS
DIETARY SUPPLEMENT

BRAIN HEALTH



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MONEY BACK GUARANTEE
TRY RISK FREE

60 TABLETS
DIETARY SUPPLEMENT

UNIT PRICE	RETAIL PRICE
55.0¢ PER TAB	\$32.99

UNIT PRICE	RETAIL PRICE
78.4¢ PER TAB	\$46.99



Jarrow Neuro Optimizer
DIETARY SUPPLEMENT



BURIED TREASURE
Liquid Nutrients

Neuro NECTAR
Thought Provoking

Whole Food Complex • 16 FL OZ (473 mL)
Dietary Supplement

43.4¢ PER FL OZ	\$51.99
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2.06 PER FL OZ	\$32.99
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Limitations of the FDA

- FDA ultimately has limited enforcement due to the Dietary Supplement Health and Education Act of 1994
- Limited resources to act on even on the illegal claims
- Doesn't impact the supplements we are most often asked about (perfectly legal but misleading structure/function claims)

What can do you?

What can do you?

- Understand that supplements may or may not be safe for you
- Know that supplement manufacturers can make broad claims about improving **brain function** and do not provide evidence to the FDA supporting these claims
- Empower your friends and family to accurately interpret the labels on supplements
- Consider focusing your resources on interventions with evidence supporting brain health

If you want to learn more...

The New York Times

PERSONAL HEALTH

Brain Booster in a Bottle? Don't Bother

To support brain health as you age, start with the same foods that can help to keep your heart healthy.



KQED NEWS

forum

FORUM

FEB 21

UCSF Researchers Call Out Brain Health Supplements as 'Pseudomedicine'

Dietary supplements that purport to improve brain health are "pseudomedicine," according to a recent paper published in JAMA by a team of UCSF researchers. They say that although there is no known nutritional supplement

U.S. News & World Report

HEALTH

Do Nutritional Supplements Fight Dementia?

Forbes

Science Versus Pseudo-Science: What Really Works to Prevent Cognitive Decline?

UCSF Memory and Aging Center



Thank you!