



## The Impact of Exercise on Resilience in Dementia

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WISCONSIN  
ALZHEIMER'S DISEASE  
RESEARCH CENTER



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SCHOOL OF MEDICINE AND PUBLIC HEALTH



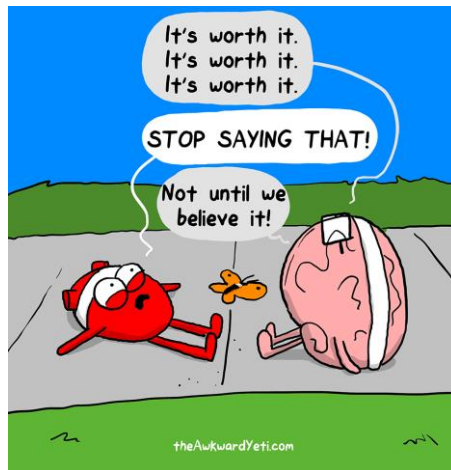
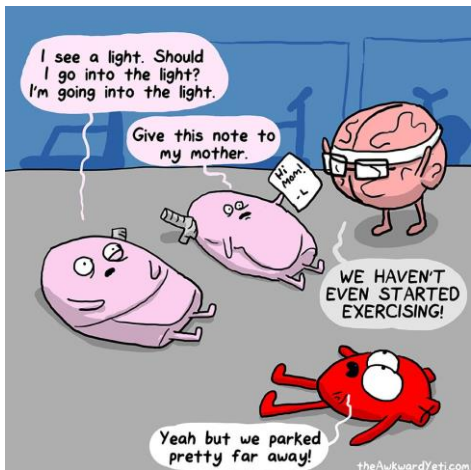
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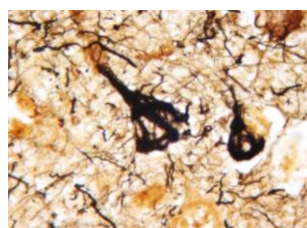
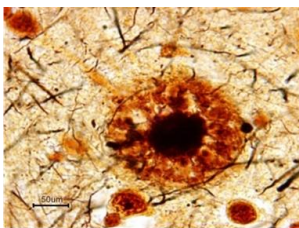
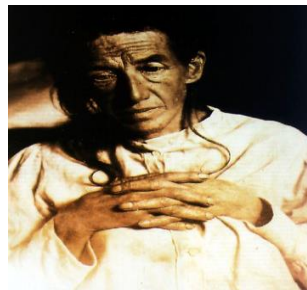
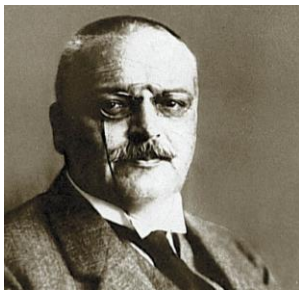
## Conflict of Interest

- None



# Alzheimer's Disease: The Origins

.. or if you prefer – A tale of a man, a woman, and two pesky proteins



## The Curious Case Of ...

### Observations on the Brains of Non-Demented Old People

B. E. TOMLINSON, G. BLESSED AND M. ROTH

*Medical Research Council Group on the Relationship between Functional and Organic Psychiatric Illnesses, Department of Psychological Medicine, University of Newcastle upon Tyne, and Department of Pathology,*

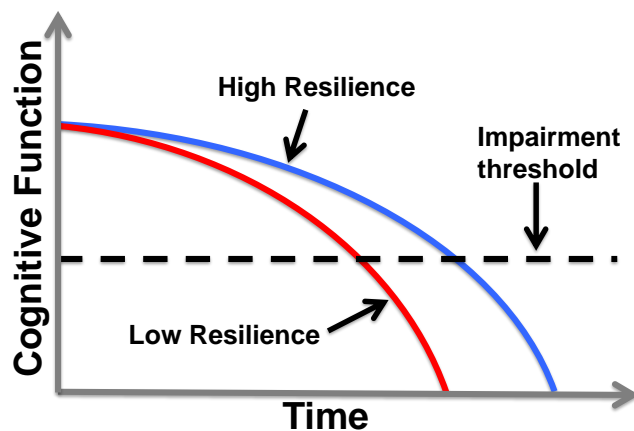
### Clinical, Pathological, and Neurochemical Changes in Dementia: A Subgroup with Preserved Mental Status and Numerous Neocortical Plaques

Robert Katzman, MD,\* Robert Terry, MD,\* Richard DeTeresa, BS,\* Theodore Brown, PhD,<sup>†</sup>  
Peter Davies, PhD,<sup>§§</sup> Paula Fuld, PhD,<sup>‡</sup> Xiong Renbing, MA,<sup>†</sup> and Arthur Peck, MD<sup>‡</sup>

## Resilience to AD

- Substantial number of persons with pathology but no symptoms
- Concept of resilience (or reserve) put forward to explain mismatch
  - Brain able to tolerate more pathology before reaching critical threshold
  - Interplay of genetic and environmental factors

## Resilience to AD



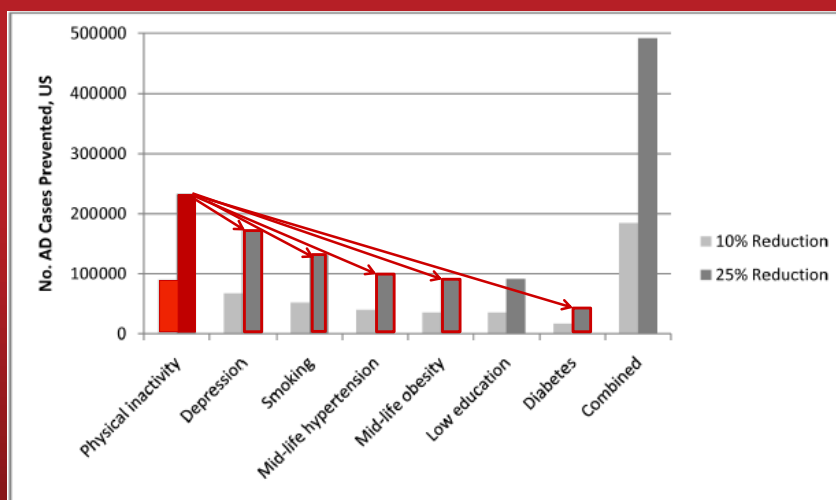
## Factors Contributing to Resilience

- Education
- Complex occupation
- Socioeconomic status
- Leisure activities
- Sleep
- Diet
- Social interaction
- Mentally-stimulating activities
- Physical activity

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## Why Physical Activity?



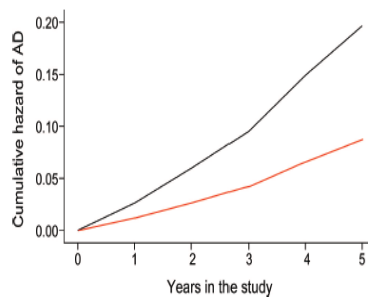
## A Word about Terminology

- Physical Activity
  - Bodily movement that results in energy expenditure
- Exercise
  - Subset of physical activity
  - Planned, structured, repetitive, intentional
- Cardiorespiratory Fitness
  - Capacity of circulatory, respiratory, and musculo-skeletal systems to support sustained work
  - VO<sub>2</sub>peak

## PHYSICAL ACTIVITY

## Total daily physical activity and the risk of AD and cognitive decline in older adults

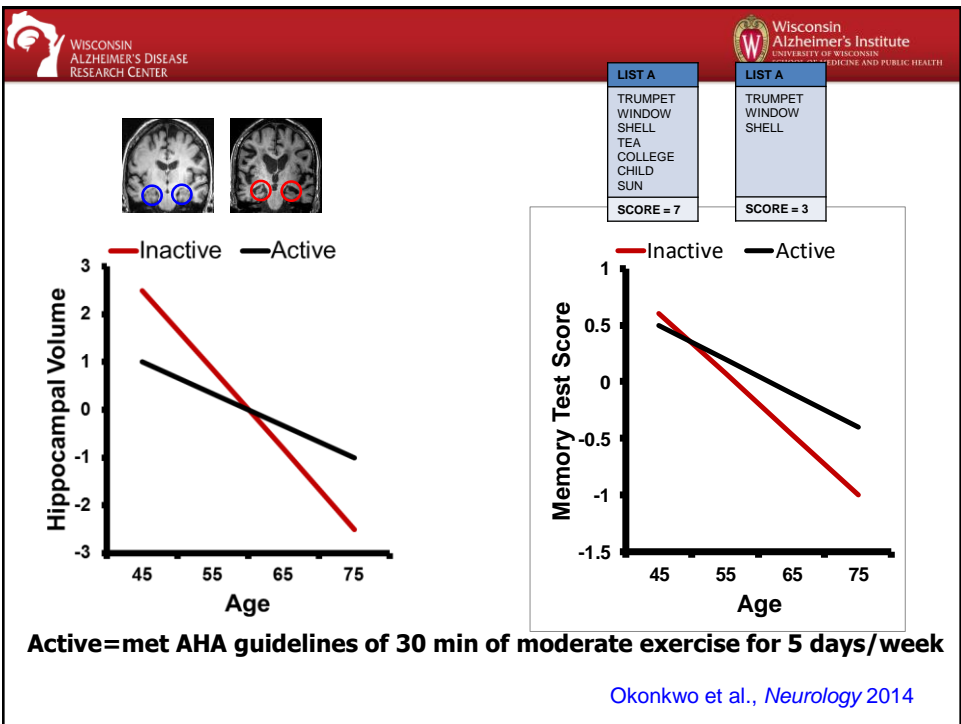
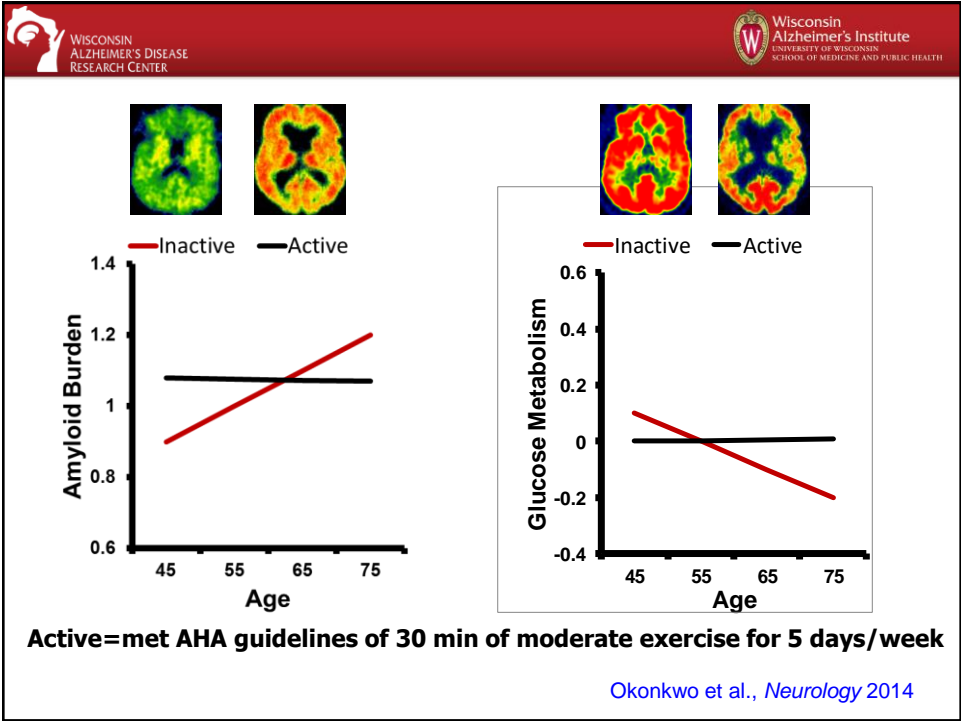
Figure 2 Total daily physical activity and risk of AD in old age



Buchman et al, Neurology 2012

## QUESTION

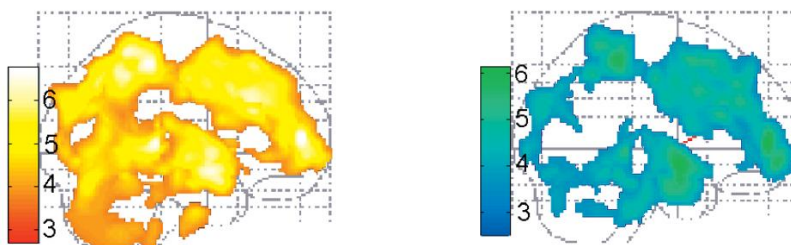
- Does engagement in physical activity attenuate age-associated changes in core AD biomarkers?
  - amyloid- $\beta$  burden
  - glucose metabolism
  - hippocampal volume
  - episodic memory





# CARDIORESPIRATORY FITNESS

## Aerobic Fitness Reduces Brain Tissue Loss in Aging Humans



**THE NEGATIVE EFFECT OF AGING ON THE BRAIN  
WAS DIMINISHED BY CRF**

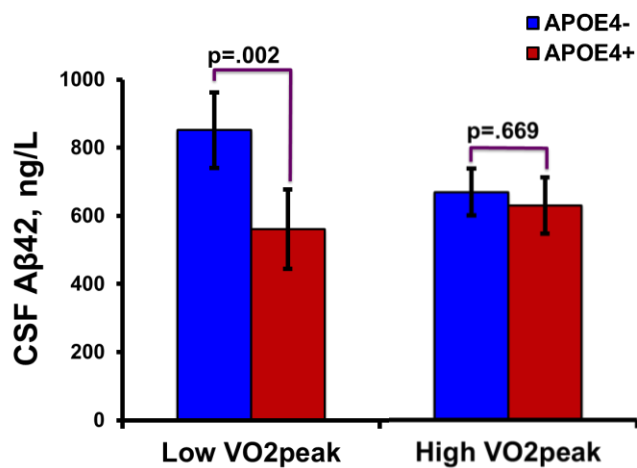
## Cardiorespiratory Fitness

### Graded Exercise Test



- Does higher CRF modify the effect of *APOE4* on CSF biomarkers of AD?

## Cardiorespiratory Fitness



Schultz et al., *Neurology* 2017

## Story So Far ...

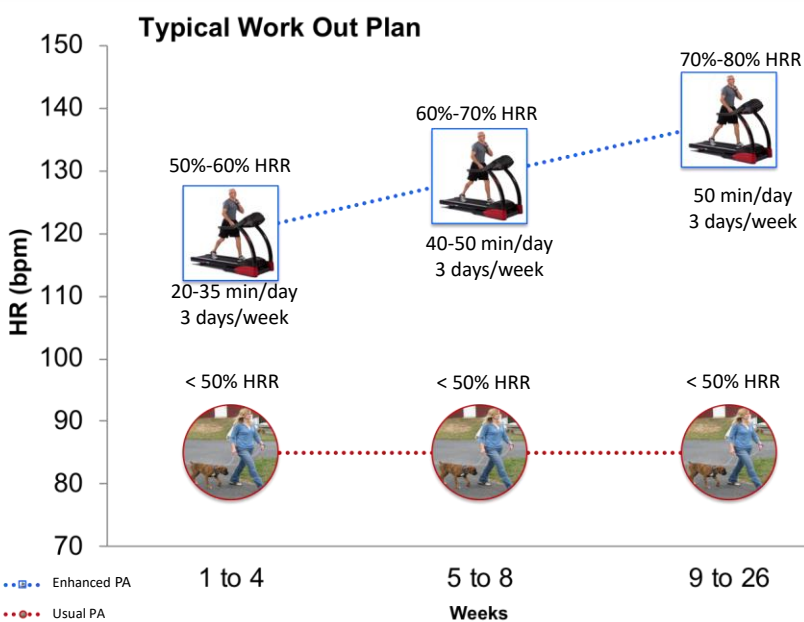
- Physically-active lifestyle may forestall AD
  - Attenuates influence of aging on brain and cognition
  - Modifies effect of genetics on biomarkers
- *“firm conclusions cannot be drawn about the association of any modifiable risk factor with AD ... [however] individuals should continue to aim for a physically and mentally active lifestyle”*
  - National Institute on Aging, State-of-the-Science Conference, 2010
- Randomized studies needed for causal link and mechanisms

## EXERCISE

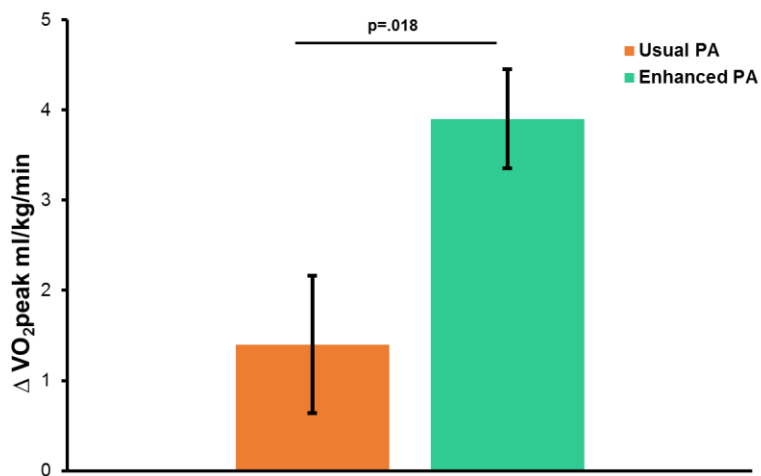
## REACH Study

- ae**R**obic **E**xercise **A**nd **C**ognitive **H**ealth pilot (REACH; NCT02384993)
- **Objective:** feasibility and acceptability of 6-month aerobic exercise intervention in middle-aged adults with FH of AD
  - Preliminarily assess (a) **effect on glucose metabolism and cognition**, (b) biological mechanisms and individual differences
- Eligibility
  - FH of AD
  - Physically inactive
  - Physician's consent
- Block-randomized (age, sex) → Usual Physical Activity vs. Enhanced Physical Activity

## REACH Study

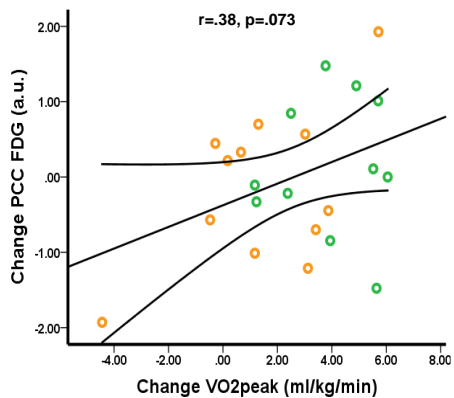
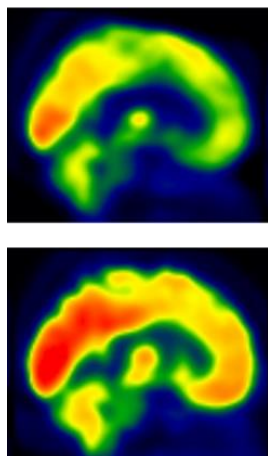


## REACH Study



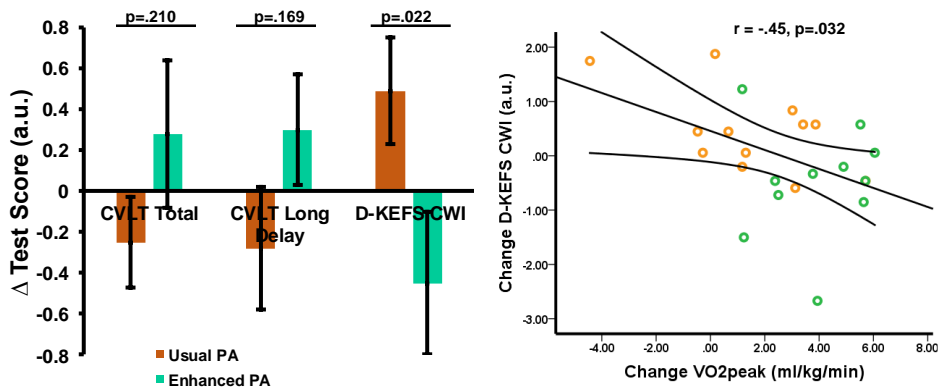
Gaitan et al., *Brain Plasticity* 2019

## REACH Study



Gaitan et al., *Brain Plasticity* 2019

## REACH Study



Gaitan et al., Brain Plasticity 2019

## Conclusion

- AD poses public health crisis
- Lack of disease-modifying agents
- Need for alternative approaches for halting global crisis
- **EXERCISE**

## Take Home

- Never too late to begin
- Check with PCP
- Start small, then build (frequency, intensity, duration)
  - Sitting less, parking farther away, taking stairs, walking around while on phone)
- Variety: aerobic, strength, balance
- **PERSIST!**

## NIA Website for Physical Activity

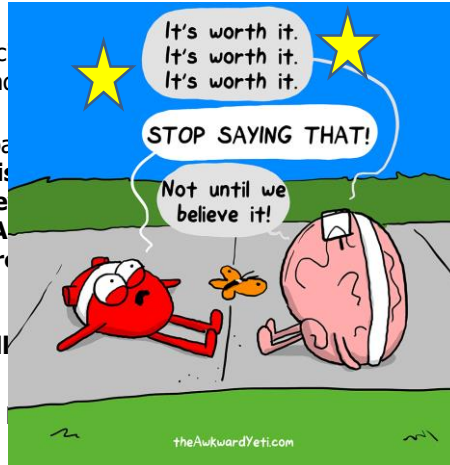
<http://go4life.nia.nih.gov/>



- General Information
- Helpful Tips
- Online Coaching
- Free Resources
  - Booklets, CDs

## ACKNOWLEDGEMENTS

- **Funding**  
NIH-NIA  
Alzheimer's Assoc  
Extendicare Found
- Staff and Participa  
**Wisconsin Regis**  
**Alzheimer's Pre**  
**the Wisconsin A**  
**Disease Resear**
- **Numerous Coll**
- **The Okonkwo**



[medic.wisc.edu](http://medic.wisc.edu)

THANK YOU!!