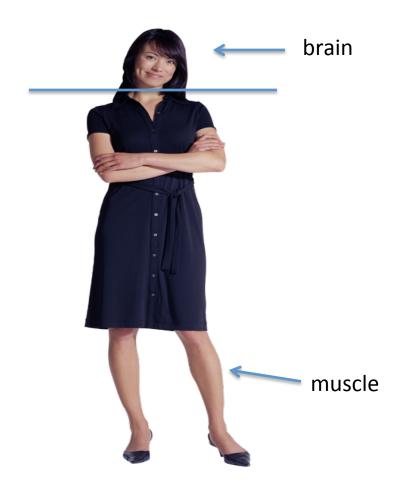
### Exercise & the brain

Bernard (Bob) Gutin, PhD

Emeritus professor Teachers College, Columbia University & Medical College of Georgia

# Is there an interaction between what is above & below the line?



• Acute effects of single bouts of exercise

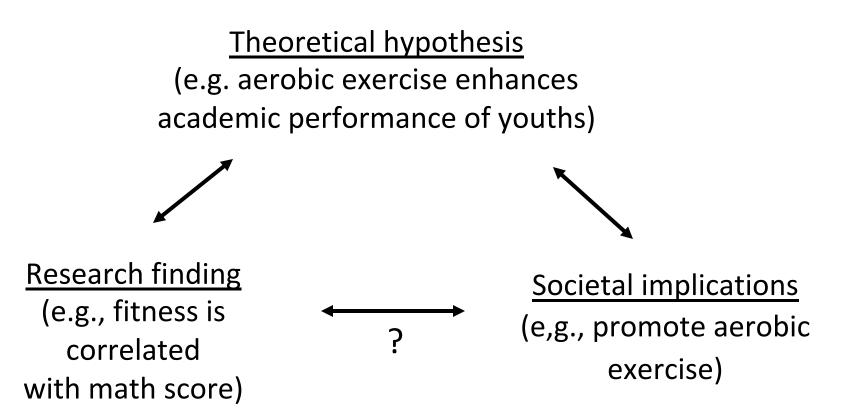
- Acute effects of single bouts of exercise
- Chronic effects of repeated bouts of exercise

- Acute effects of single bouts of exercise
- Chronic effects of repeated bouts of exercise
- Relation of exercise & fitness to mental health

- Acute effects of single bouts of exercise
- Chronic effects of repeated bouts of exercise
- Relation of exercise & fitness to mental health
- Effects of physical training on brain structure/ function

- Acute effects of single bouts of exercise
- Chronic effects of repeated bouts of exercise
- Relation of exercise & fitness to mental health
- Effects of physical training on brain structure/ function
- Traumatic effects of some sports on brain structure & function

How do we use research to cast light on personal behavior & public health practices?

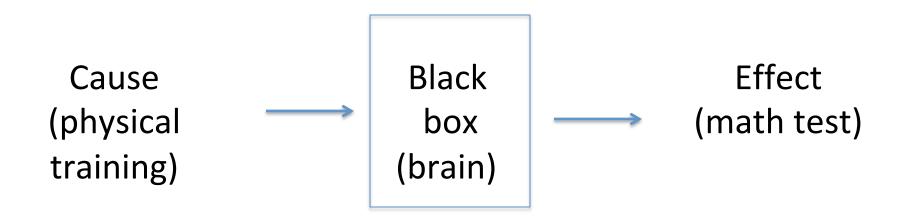


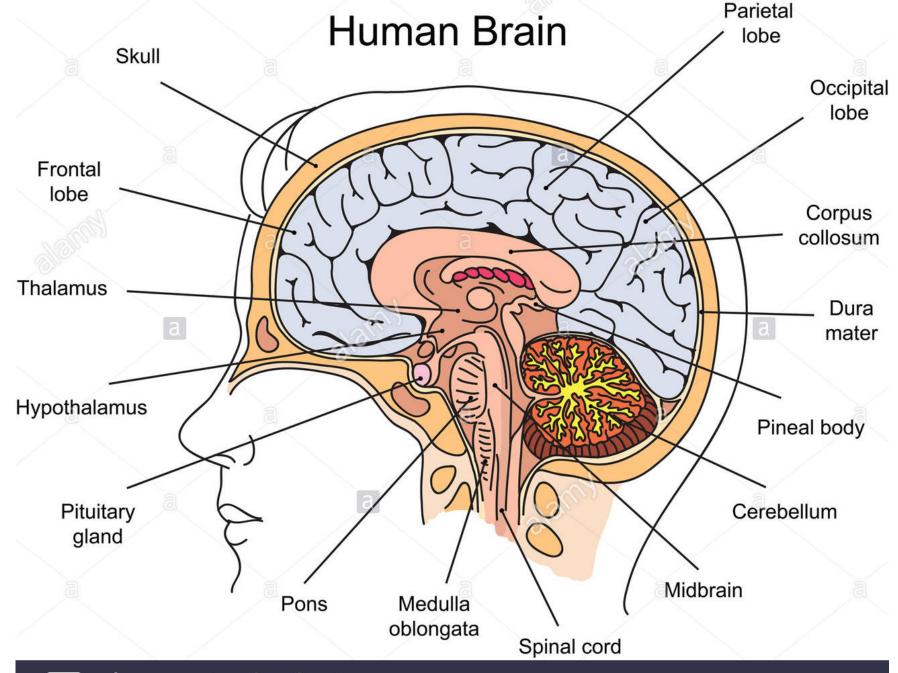
# General model for assessing relationships

Cause (e.g., physical training)

Effect (e.g., math test)

### What accounts for the relationships?





#### a alamy stock photo

C22XRW www.alamy.com

• Increase brain blood flow

- Increase brain blood flow
- Modulate general arousal level

- Increase brain blood flow
- Modulate general arousal level
- Delay age-related cognitive decline

- Increase brain blood flow
- Modulate general arousal level
- Delay age-related cognitive decline
- Enhance brain plasticity

- Increase brain blood flow
- Modulate general arousal level
- Delay age-related cognitive decline
- Enhance brain plasticity
- Up-regulate molecules related to brain activity

- Increase brain blood flow
- Modulate general arousal level
- Delay age-related cognitive decline
- Enhance brain plasticity
- Up-regulate molecules related to brain activity
- Influence systemic inflammation

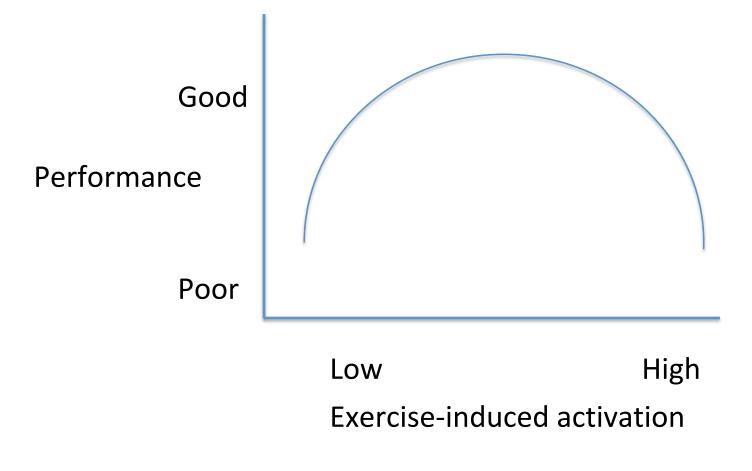
# Effects of single bouts of exercise (1960's & 70's at CUNY & Columbia U.)

- Effects of warm-up on performance
  - Application to sports (e.g., wrestling practice)
  - Application to cognitive performance

# Effects of single bouts of exercise (1960's & 70's at CUNY & Columbia U.)

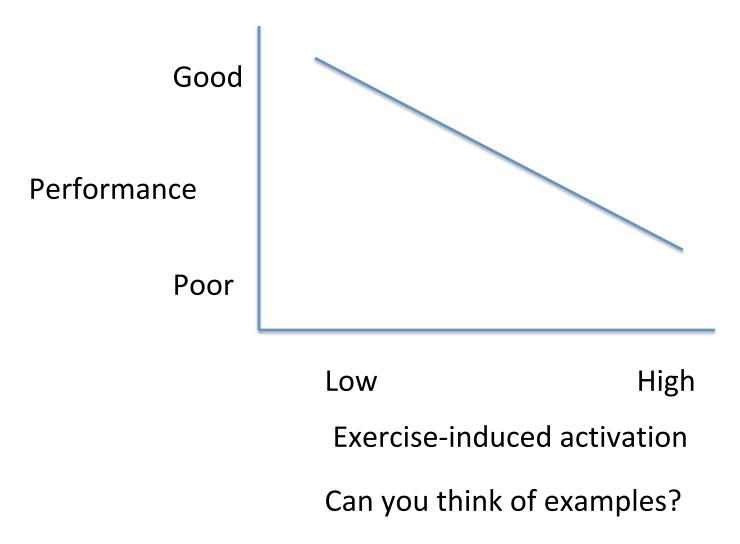
- Effects of warm-up on performance
  - Application to sports (e.g., wrestling practice)
  - Application to cognitive performance
- Various tasks
  - Running or cycling
  - Repeated addition & subtraction
  - Choice reaction time
  - Movement speed
  - Hand steadiness

# The inverted U-shaped relationship between activation & performance

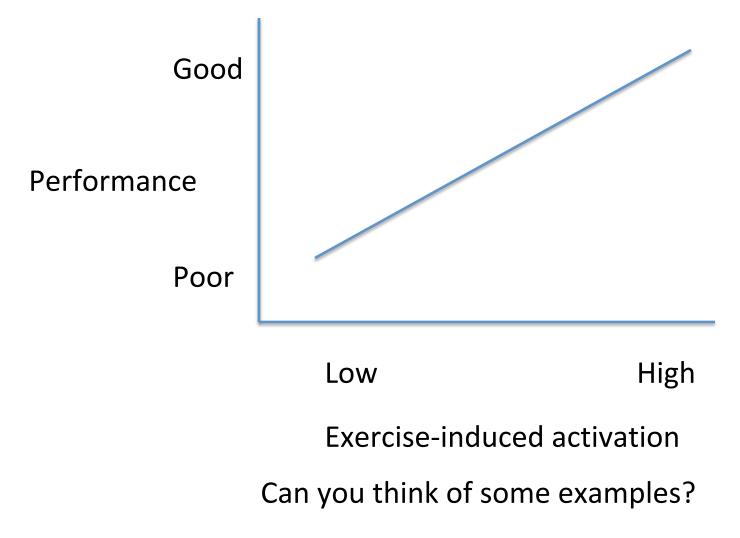


Is the "sweet spot" the same for all kinds of tasks?

# For tasks involving precision (inhibition), a low EIA is optimal



# For tasks involving <u>disinhibition</u>, a high level of activation is optimal



### Fast-forward to ~year 2000

- Catherine Davis, Phil Tomporowski in Georgia
- Kerry Stewart at Johns Hopkins
- Kramer & Hillman at Illinois
- Sophisticated measurements of cognition
- Brain-imaging studies

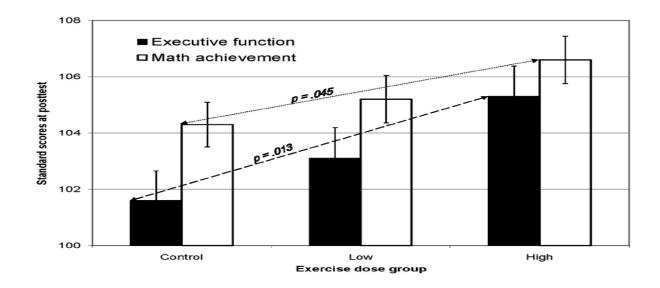
Subjects: 171 overweight 7-11 yr olds

- Subjects: 171 overweight 7-11 yr olds
- Physical training: 13 wk, 5 d/wk, 20 or 40 min/d, mean HR=166

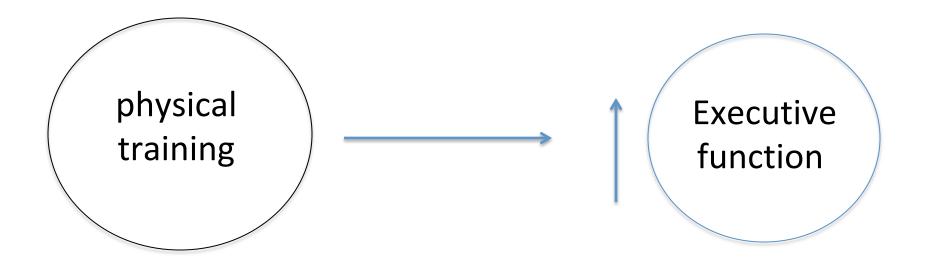
- Subjects: 171 overweight 7-11 yr olds
- Physical training: 13 wk, 5 d/wk, 20 or 40 min/d, mean HR=166
- Executive function: (select, organize, & initiate goal-directed actions)

- Subjects: 171 overweight 7-11 yr olds
- Physical training: 13 wk, 5 d/wk, 20 or 40 min/d, mean HR=166
- Executive function: (select, organize, & initiate goal-directed actions)
- Sub-study of functional MRI: measures blood flow to regions of brain

#### Effect of different doses of physical training on cognition in obese 7-11 yr olds (Davis, 2011)



During the executive function test, prefrontal cortex activity was increased & posterior parietal cortex activity was reduced, indicating greater focus on the planning task Cochrane Review of 18 studies, >2000 youths with obesity-overweight, 10 countries (Martin, 2018)



No significant effect for math, reading, inhibition control

## What are executive functions?

- Processes in which there is a need to overcome habitual responses
  - Planning/decision-making
  - Inhibition control
  - Dangerous/technically difficult situations

## What are executive functions?

- Processes in which there is a need to overcome habitual responses
  - Planning/decision-making
  - Inhibition control
  - Dangerous/technically difficult situations
- Among the last mental functions to reach maturity; reach peak at age 20-29

## What are executive functions?

- Processes in which there is a need to overcome habitual responses
  - Planning/decision-making
  - Inhibition control
  - Dangerous/technically difficult situations
- Among the last mental functions to reach maturity; reach peak at age 20-29
- Best predictor of functional decline in the elderly

## Physical activity & cognitive functioning of children: a systematic review (Biddzan-Bluma, 2018)

• 58 articles reviewed from 2000-2017

## Exercise & cognition in preadolescence: a meta-analysis (de Greeff, 2018)

- Acute PA improves attention (EIA)
- Physical training improves executive functions & academic performance

## Exercise & cognition in preadolescence: a meta-analysis (de Greeff, 2018)

- Acute PA improves attention (EIA)
- Physical training improves executive functions
  & academic performance
- Largest effects for interventions aiming for continuous PA over several weeks

## Exercise & cognition in preadolescence: a meta-analysis (de Greeff, 2018)

- Acute PA improves attention (EIA)
- Physical training improves executive functions
  & academic performance
- Largest effects for interventions aiming for continuous PA over several weeks

• Test of cognitive flexibility, & response inhibition

Red Blue Green Red Blue Green Red Blue Green

- Test of cognitive flexibility, & response inhibition
- Subjects identify color of the word on the screen

Red Blue Green Red Blue Green Red Blue Green

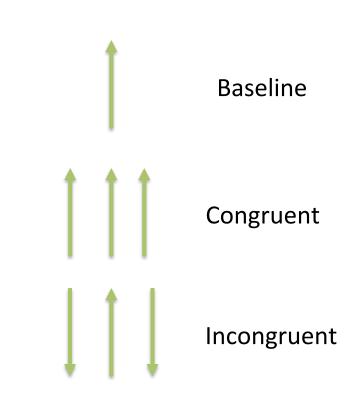
- Test of cognitive flexibility, & response inhibition
- Subjects identify color of the word on the screen
- In one condition, the words are color names that are either consistent or incompatible

RedBlueGreenRedBlueGreenRedBlueGreen

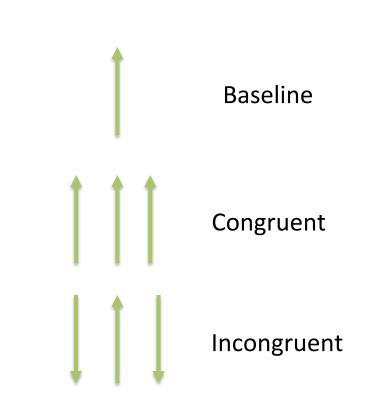
- Test of cognitive flexibility, & response inhibition
- Subjects identify color of the word on the screen
- In one condition, the words are color names that are either consistent or incompatible
- In another condition the words are color neutral & subject asked to identify color

RedBlueGreenRedBlueGreenRedBlueGreen

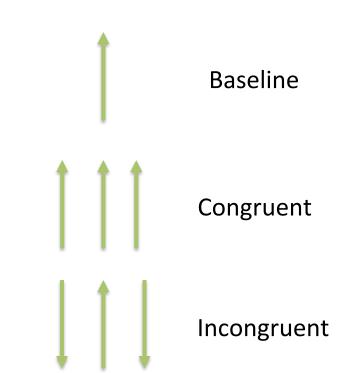
• Fixate on a plus-sign in center of screen



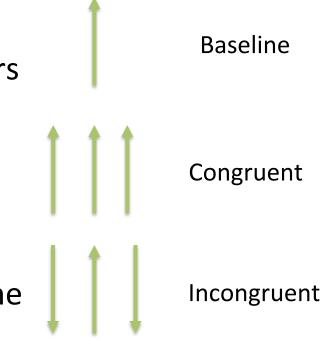
- Fixate on a plus-sign in center of screen
- An arrow pointing up or down appears & subjects identify direction



- Fixate on a plus-sign in center of screen
- An arrow pointing up or down appears & subjects identify direction
- Baseline condition, arrow appears alone



- Fixate on a plus-sign in center of screen
- An arrow pointing up or down appears & subjects identify direction
- Baseline condition, arrow appears alone
- In comparison condition, arrow is flanked by arrows pointing in the same or opposite direction of the center arrow



Mechanisms of exercise & the brain (Ratey, Spark)

- Improves cardiovascular function
- Improves function of neurons
- Stimulates brain-derived neurotrophic factor (BDNF) in hippocampus, area related to memory & learning
- BDNF promotes neuronal growth ("Miracle-Gro" of the brain)

Exercise in a mouse model of Alzheimer's disease (AD) (Choi, 2018)

 Adult hippocampal neurogenesis (AHN) is impaired before the onset of AD pathology Exercise in a mouse model of Alzheimer's disease (AD) (Choi, 2018)

- Adult hippocampal neurogenesis (AHN) is impaired before the onset of AD pathology
- Exercise enhances AHN, levels of brainderived neutrophic factor (BDNF) & cognitive performance

Exercise in a mouse model of Alzheimer's disease (AD) (Choi, 2018)

- Adult hippocampal neurogenesis (AHN) is impaired before the onset of AD pathology
- Exercise enhances AHN, levels of brainderived neutrophic factor (BDNF) & cognitive performance
- At early stages of AD, exercise & some pharmacological mimetics may protect against subsequent neuronal cell death

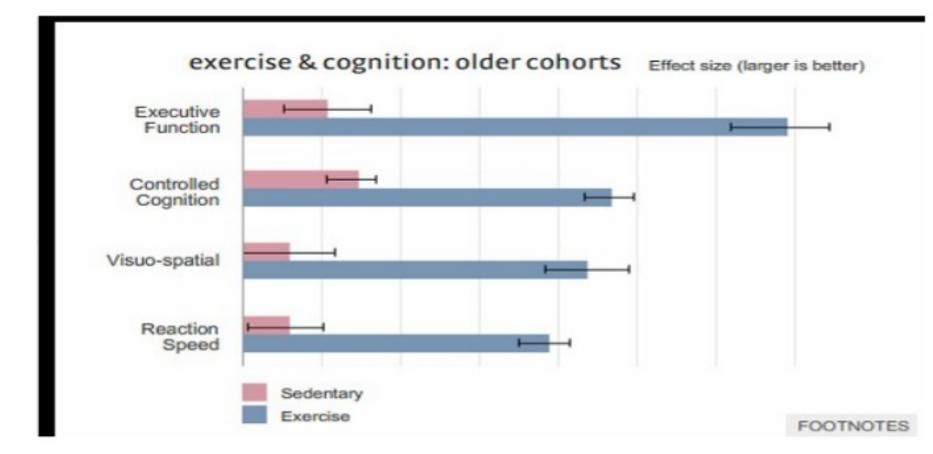
## Leg power & cognitive ageing after 10 yr in older female twins*, Gerontology,* 2015

 Protective relationship between muscle fitness (leg power) & both 10-yr cognitive change & subsequent total grey matter

## Leg power & cognitive ageing after 10 yr in older female twins*, Gerontology,* 2015

- Protective relationship between muscle fitness (leg power) & both 10-yr cognitive change & subsequent total grey matter
- Leg power predicts both cognitive ageing & global brain structure, despite controlling for common genetics & early life environment shared by twins

## The cognitive value of exercise



Source: Colcombe, S and Kramer, AF (2003) Fitness effects on the cognitive function of older adults: a meta-analytic study Psych Sci 14: 125 - 130 Exercise & cognition in aging (Gomes-Osman, 2018)

- Reviewed 98 RCTs
- Exercising for at least 52 hr —>↑ cognition
   global, speed, & executive function most stable

Exercise & cognition in aging (Gomes-Osman, 2018)

- Reviewed 98 RCTs
- Exercising for at least 52 hr →↑ cognition
   global, speed, & executive function most stable
- Effective exercise modes
  - aerobic
  - strength
  - mind-body
  - combinations

Whole brain volume (Esteban-Cornejo, 2017)

- Obesity is associated with structural differences in brain
- Studied overweight Spanish youths (8-11 yr)
- Higher aerobic fitness & speed-agility (but not muscular fitness) associated with
  - Better academic performance
  - Greater gray matter volume in several brain regions

# Hypothetical implication of Esteban-Cornejo results



Physical activity (PA) & cognition in adults at risk for Alzheimer disease (AD)

311 people with memory problems randomized to

- Usual care
- 24-wk home-based PA program (150 min/wk)

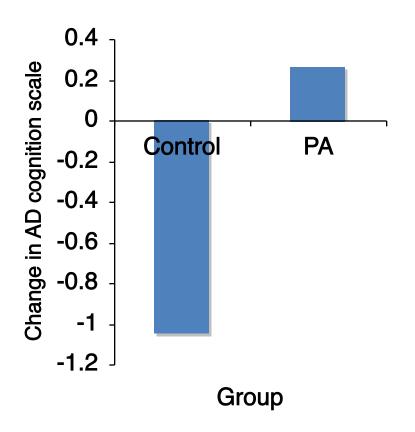
Main outcome - AD cognitive scale

Lautenschlager et al, JAMA, 2008

#### Physical activity (PA) & cognition in adults at risk for Alzheimer disease (AD)

- 311 people with memory problems randomized to
  - Usual care
  - 24-wk home-based PA program (150 min/wk)

# Main outcome - AD cognitive scale



Lautenschlager et al, JAMA, 2008

Physical training (PT) & the hippocampus (Erickson, 2011)

- Aging leads to shrinkage of hippocampus, leading to impaired memory & risk for dementia
- Fitter people have larger hippocampi
- Exercise increases hippocampal perfusion

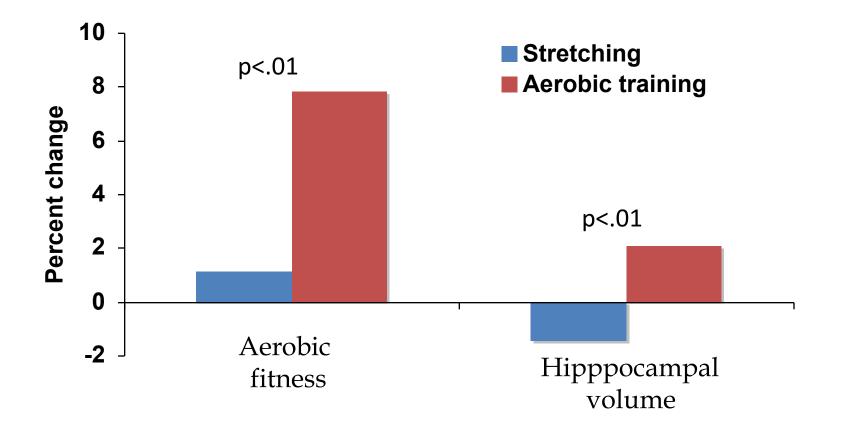
Effect of PT on aerobic fitness & hippocampus volume in adults (Erickson, 2011)

- 120 adults (mean age ~67)
- Randomly assigned to
  - Stretching
  - Aerobic training 3 days/wk for 12 mo

Effect of PT on aerobic fitness & hippocampus volume in adults (Erickson, 2011)

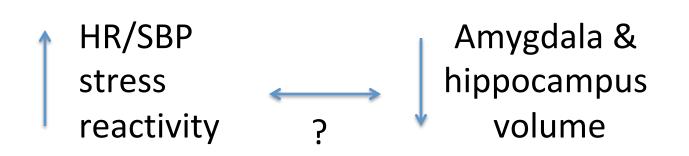
- 120 adults (mean age ~67)
- Randomly assigned to
  - Stretching
  - Aerobic training 3 days/wk for 12 mo
- Compared to the stretching group, the PT group increased in
  - Aerobic fitness
  - Hippocampal volume

Changes in fitness & hippocampal volume following 1 yr of intervention

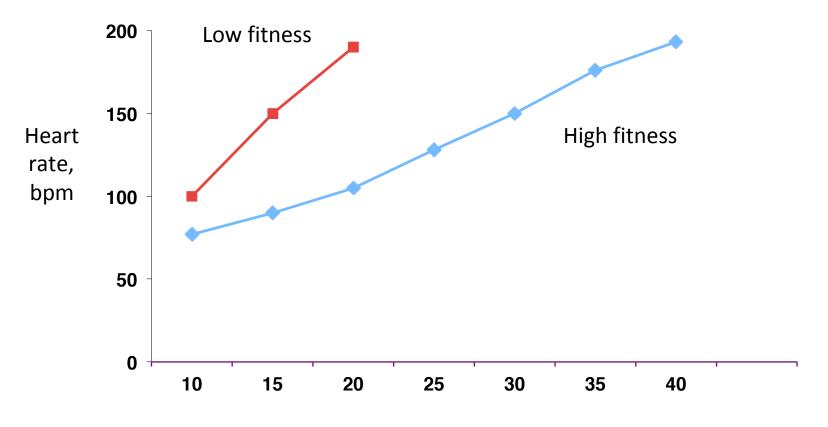


Erickson, PNAS, 2011

# CV reactivity to stressors & brain volumes (Trotman, 2018)



# Stress response to a variety of stressors is lower in people who are more fit



Oxygen consumption, ml/kg/min (or exercise workload)

# How might exercise play a role?



# Yesterday's NY Times (Velasques-Manoff, 2018)

#### Infections — Mental disease

?

Thinking while moving or moving while thinking? (Herold, 2018)

Incorporating cognitive tasks into motor tasks is the most promising way to enhance cognitive reserve

# Walk-station



Aging brain: effect of combined cognitive & physical training (CCPT) compared to each alone – a review (Joubert, 2018)

• CCPT >either alone

Aging brain: effect of combined cognitive & physical training (CCPT) compared to each alone – a review (Joubert, 2018)

- CCPT >either alone
- Good long-term maintenance (4-5 yr)

Aging brain: effect of combined cognitive & physical training (CCPT) compared to each alone – a review (Joubert, 2018)

- CCPT >either alone
- Good long-term maintenance (4-5 yr)
- Physical & cognitive training play different but complementary roles in brain plasticity

Acute & chronic effect of exercise on cognition in young people with ADHD: A review of intervention studies (Suarez-Manzano, 2018)

 20-30 min of moderate-intensity exercise acutely enhances processing speed, working memory, problem solving Acute & chronic effect of exercise on cognition in young people with ADHD: A review of intervention studies (Suarez-Manzano, 2018)

- 20-30 min of moderate-intensity exercise acutely enhances processing speed, working memory, problem solving
- Moderate-intensity PT (>30 min/d, >5 wk) improves attention, inhibition, emotional control, behavior, & motor control

# Slow-Wave Activity Enhancement to Improve Cognition (Wilckens, 2018)

 Slow-wave activity (SWA), & its coupling with other sleep features, reorganizes cortical circuitry, supporting cognition

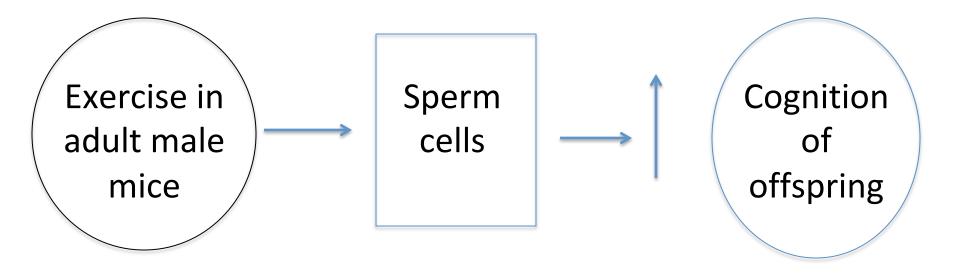
# Slow-Wave Activity Enhancement to Improve Cognition (Wilckens, 2018)

- Slow-wave activity (SWA), & its coupling with other sleep features, reorganizes cortical circuitry, supporting cognition
- Exercise (also meditation & sexual activity) enhances SWA sleep, improving
  - executive function
  - learning
  - memory

Interventional programs to improve cognition during healthy & pathological ageing: evidence for brain plasticity (Cespon, 2018)

Multi-modal programs are better than programs using a single interventional approach in healthy elderly & cognitively impaired subjects, including patients with mild cognitive impairment & Alzheimer's disease

# Is there an epigenetic effect of exercise? (Benito, 2018)



• Studied 353 participants, average age of 69 yr

- Studied 353 participants, average age of 69 yr
- Sarcopenia (low muscle mass) negatively influences cognition

- Studied 353 participants, average age of 69 yr
- Sarcopenia (low muscle mass) negatively influences cognition
- Sarcopenic effect is especially strong when combined with obesity

- Studied 353 participants, average age of 69 yr
- Sarcopenia (low muscle mass) negatively influences cognition
- Sarcopenic effect is especially strong when combined with obesity
- At-risk older adults may benefit from programs that maintain or improve strength & prevent obesity

• Studied >3000 adults >45 yr; mean=58 yr

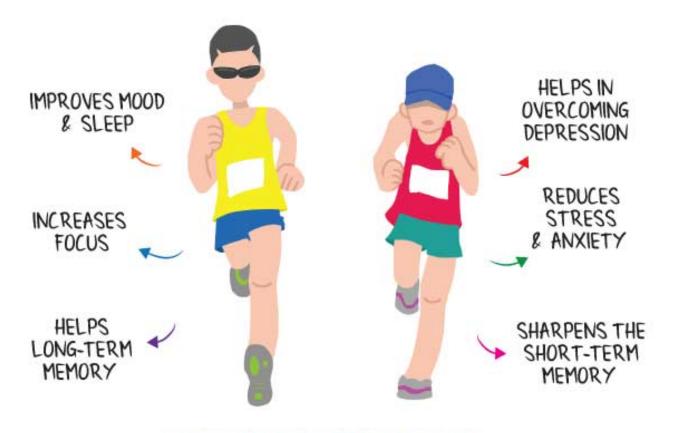
- Studied >3000 adults >45 yr; mean=58 yr
- 38% males overweight/obese; 52% of females

- Studied >3000 adults >45 yr; mean=58 yr
- 38% males overweight/obese; 52% of females
- Obese males (but not females) were <u>less</u> likely to become depressed

- Studied >3000 adults >45 yr; mean=58 yr
- 38% males overweight/obese; 52% of females
- Obese males (but not females) were <u>less</u> likely to become depressed
- Males judge a smaller body frame as less desirable than a larger, more muscular body

Physical activity & incident depression: meta-analysis of 49 prospective cohort studies; N=266,939 (Schuch, 2018)

Physical activity can confer protection against the emergence of depression regardless of age & geographical region



#### PHYSICAL EXERCISE IS THE KEY TO BRAIN HEALTH

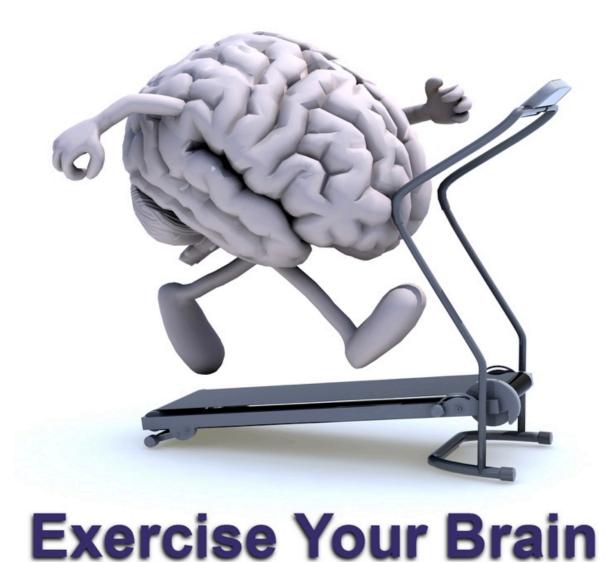
#### O DEVELOPINGHUMANBRAIN.ORG

**RESOURCES:** 

http://www.health.harvard.edu/blog/ regular-exercise-changes-brain-improve-memory-thinking-skills-201404097110 http://thebrainflux.com/brain-benefits-of-exercise/

# Unknowns

- Optimal doses/types of exercise for different tasks
- Optimal combinations of exercise & CNS activity for long-term learning
- Specific regions of brain & specific cognitive functions involved
- Carryover to normal life functions



# Are there any downsides to exercise for the brain?

# Longitudinal changes in linguistic complexity in professional football players (Berisha, 2017)

- Reductions in linguistic complexity associated with onset of neurological disorders
- Studied interviews over 8-yr period
- It declined more in players than in executives who have not played football
- For quarterbacks, it declined in proportion to the average number of times they were sacked/game

#### Chronic traumatic encephalopathy (CTE)

• Neurodegenerative disease, leads to aggression & dementia

#### Chronic traumatic encephalopathy (CTE)

- Neurodegenerative disease, leads to aggression & dementia
- Found in 110/111 (90%) of brains of former football players who had shown signs of pathology (Mez, 2017)

#### Chronic traumatic encephalopathy (CTE)

- Neurodegenerative disease, leads to aggression & dementia
- Found in 110/111 (90%) of brains of former football players who had shown signs of pathology (Mez, 2017)
- Should football (& other sports involving potential brain damage) be sponsored by parents & public agencies?

# Systematic review of mild traumatic brain injury in youths (Emery, 2016)

Few rigorous prospective studies have shown that psychological, behavioral and/or psychiatric problems persist beyond the short-term phase following mild traumatic brain injury

## Summary of exercise & brain function

 Exercise influences brain activation to have positive or negative effects on performance & learning

## Summary of exercise & brain function

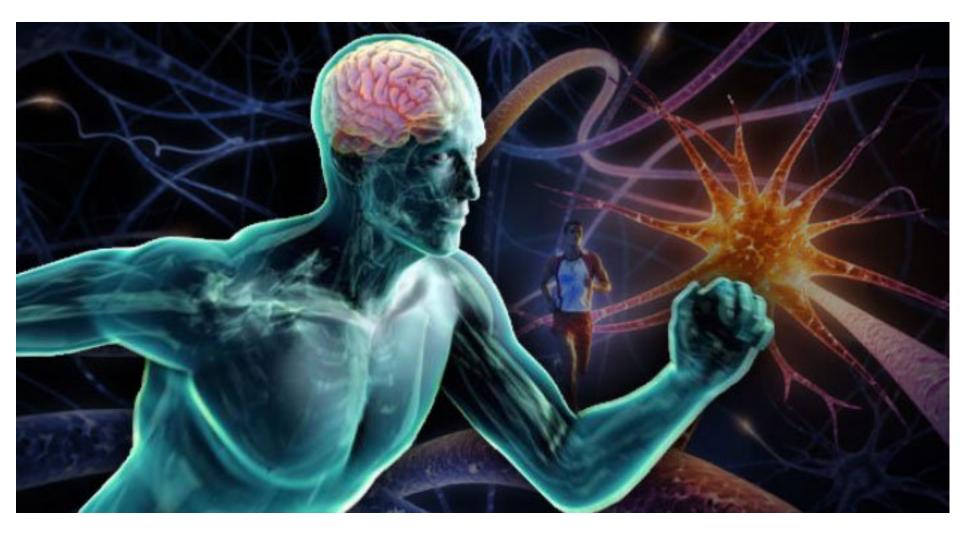
- Exercise influences brain activation to have positive or negative effects on performance & learning
- Physical training improves fitness, circulation, brain metabolism, resistance to stressors, size of brain regions

## Summary of exercise & brain function

- Exercise influences brain activation to have positive or negative effects on performance & learning
- Physical training improves fitness, circulation, brain metabolism, resistance to stressors, size of brain regions
- Combining optimal exercise intensity with CNS activity enhances performance & learning

### **General conclusions**

- Like the rest of the body, the brain responds to stress
  - Favorably to optimal doses
  - Unfavorably to insufficient or excessive doses
- The brain can also be kept in shape by brain fitness exercises
- Sounds like OLLI at Duke should be prescribed to all!



### organismic interaction

Quotation on wall at Columbia U. when I joined the faculty in 1968

"A day of high moral purpose depends on one's circulation as well as one's logical grounds."

Jesse Feiring Williams

• Thank you for your attention

• Slides will be uploaded to the course website: olliatdukefrontiersinmedicine.weebly.com

- Thank you for your attention
- Slides will be uploaded to the course website: olliatdukefrontiersinmedicine.weebly.com

 If you have a question or comment, please stand (if you can) & speak into the microphone