

# *Neuroplasticity and Parkinson Disease*

**Lara Boyd, PT, PhD**

Professor & Wall Scholar

[lara.boyd@ubc.ca](mailto:lara.boyd@ubc.ca)



Djavad Mowafaghian  
CENTRE FOR BRAIN HEALTH



# Conflicts of interest



- I have no personal financial conflicts of interest to disclose



# Part I.

# The Neuroplastic Brain

# Neuroplasticity



- All learning of new facts and skills as well as re-learning to support recovery from brain damage is represented neurologically by plasticity or structural change in the brain
- Both mature and developing brains are constantly reorganizing
- You are doing it right now

# Neuroplasticity



- Brain plasticity supports learning
- Brain plasticity after neurological insults contributes to recovery
- Specific interventions can facilitate positive plasticity throughout life

# Neuroplasticity is Experience-Dependent



- The adaptive capacity of the brain is highly influenced by behaviour
  - There is no drug that promotes neuroplasticity
  - Neuroplastic patterns can be highly variable from person to person
- Neuroplasticity can be both **positive** (learning) and **negative** (addiction)

➤ **What limits and what facilitates neuroplasticity?**

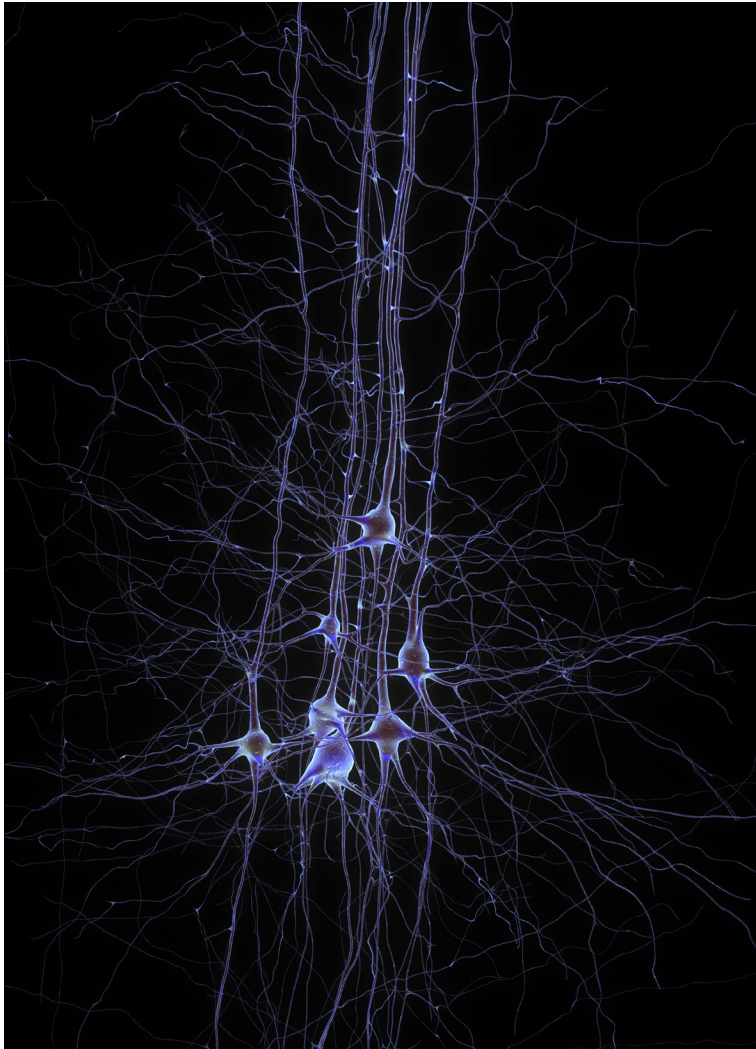
# Neuroplastic Change



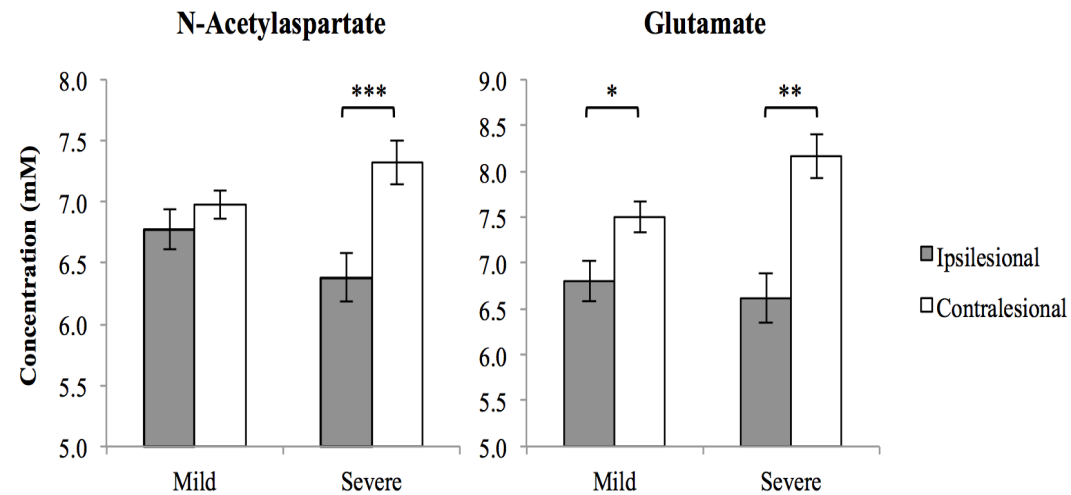
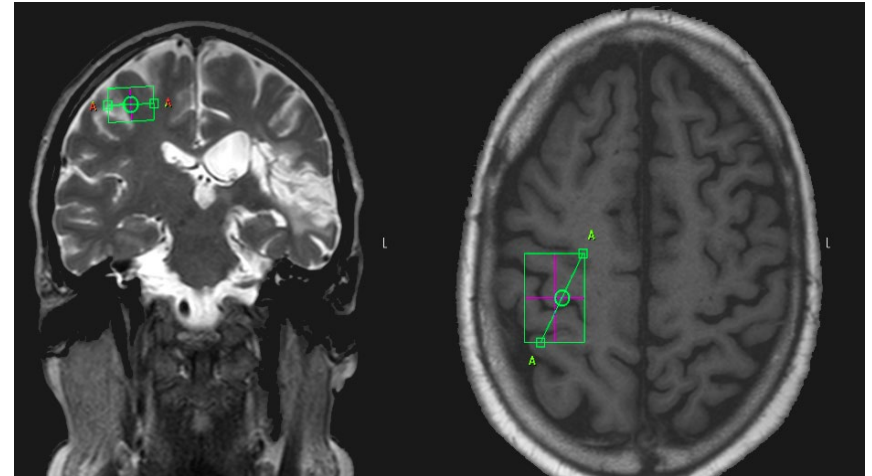
Neuroplasticity is driven by change in:

1. Brain Chemistry
2. Brain structure
3. Brain Function
4. All of the above

# Brain Chemistry



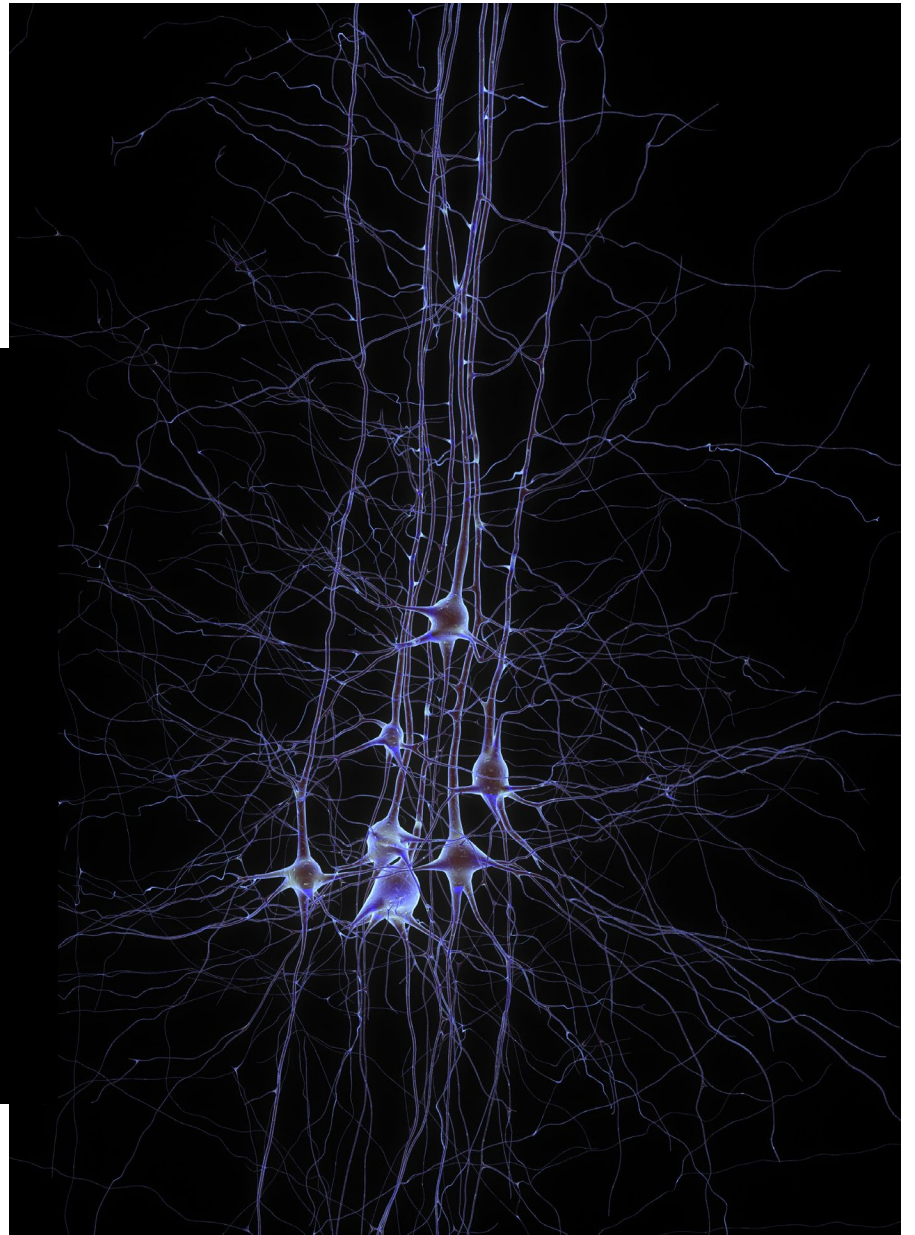
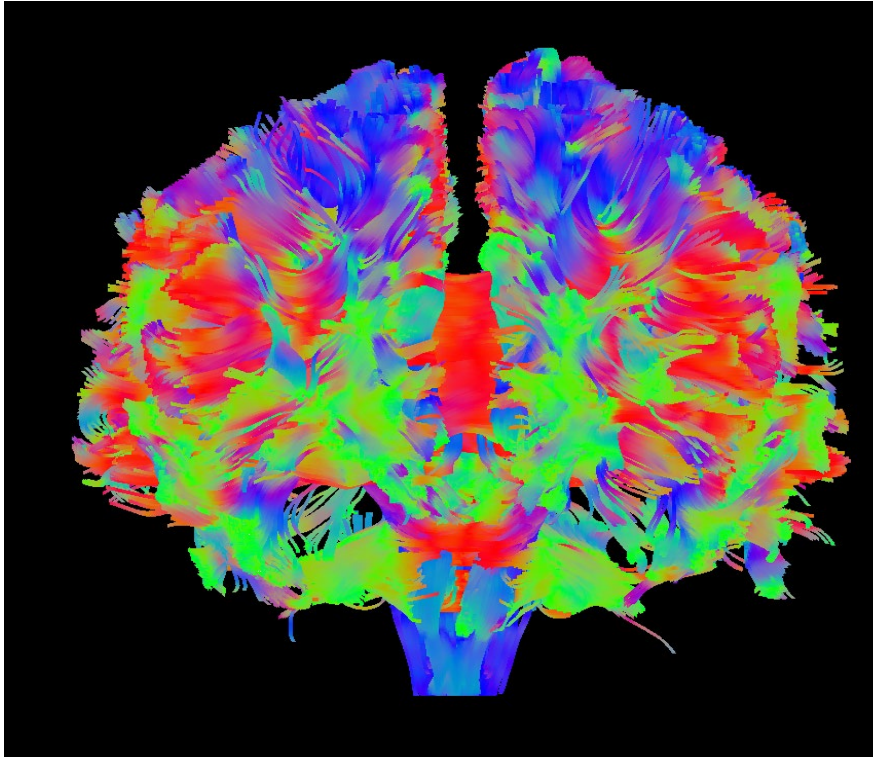
adapted from Kandel, 2013



Ferris et al, 2016

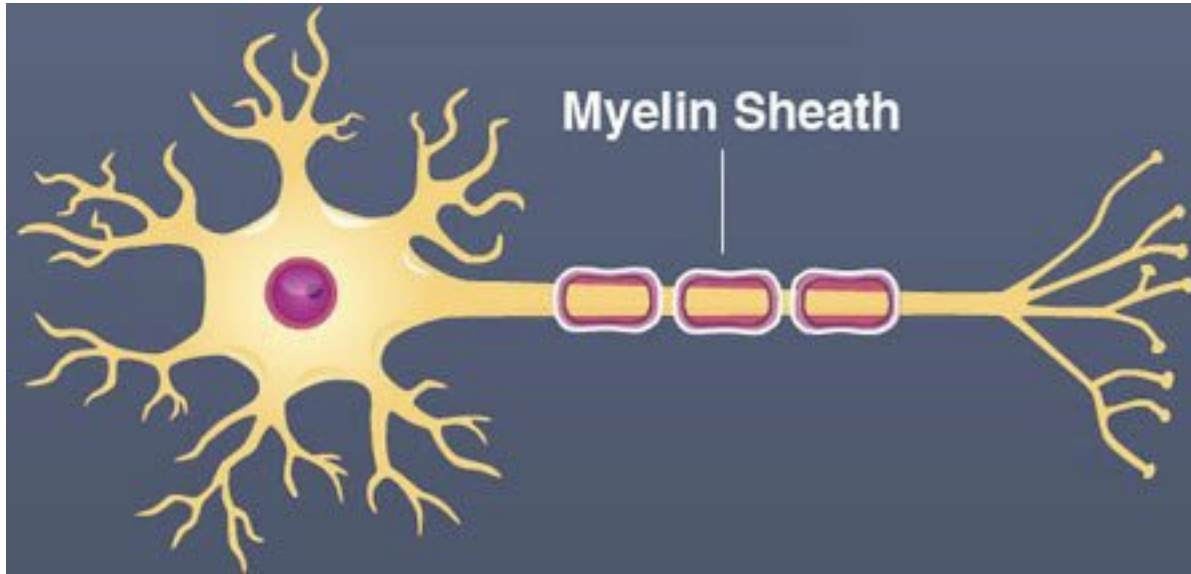


# Brain Structure

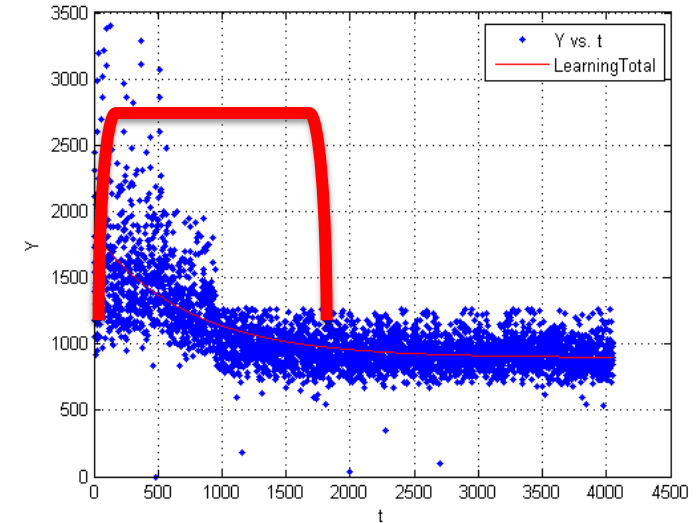
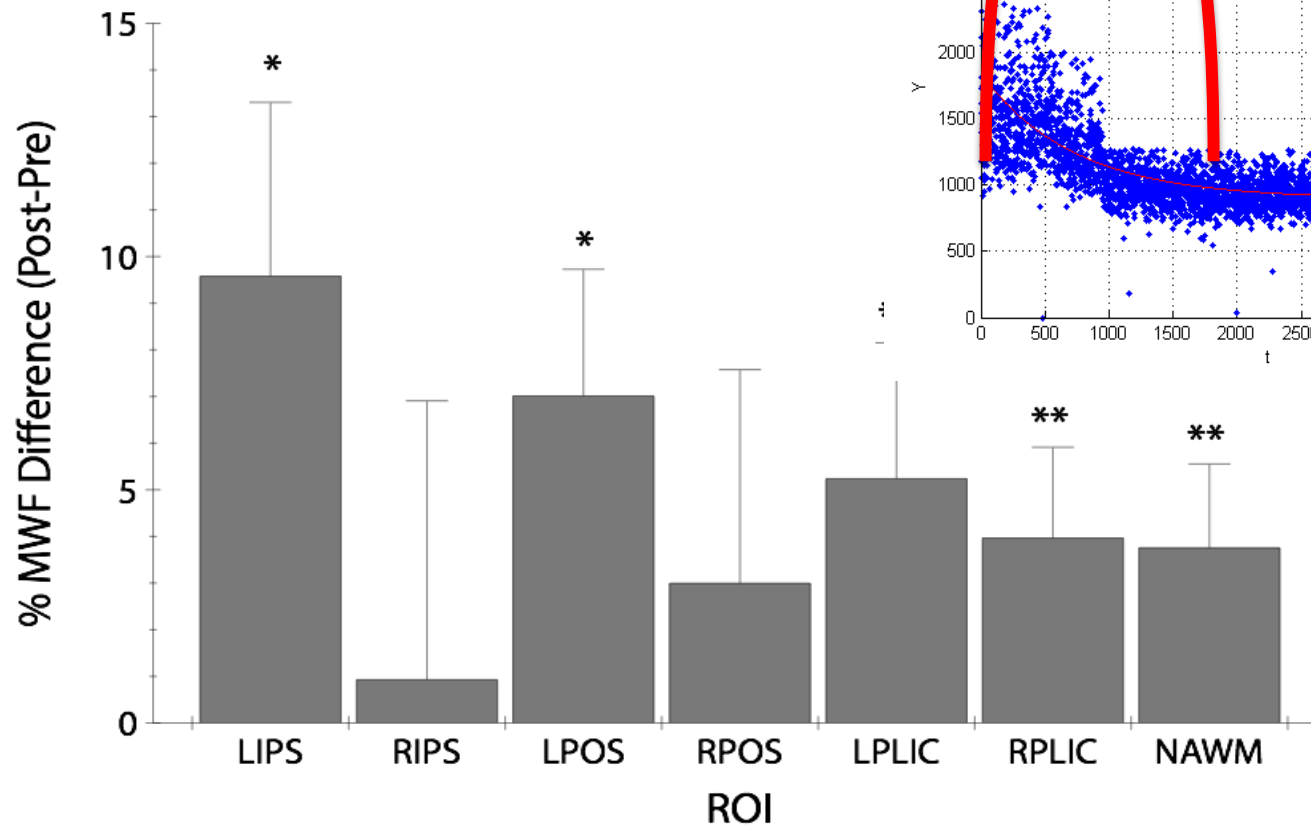
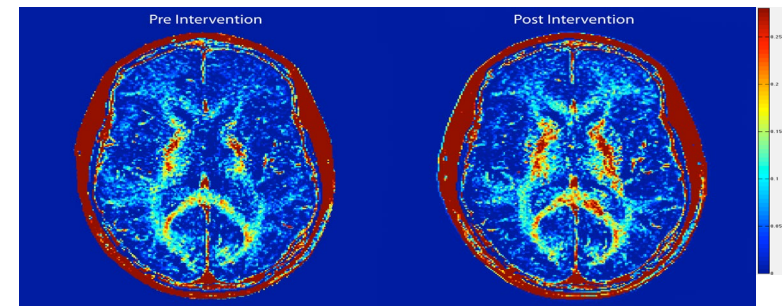


adapted from Kandel, 2013

# Myelin



# Learning Increases Myelin in the Healthy Human Brain



# Struggle During Learning is Good

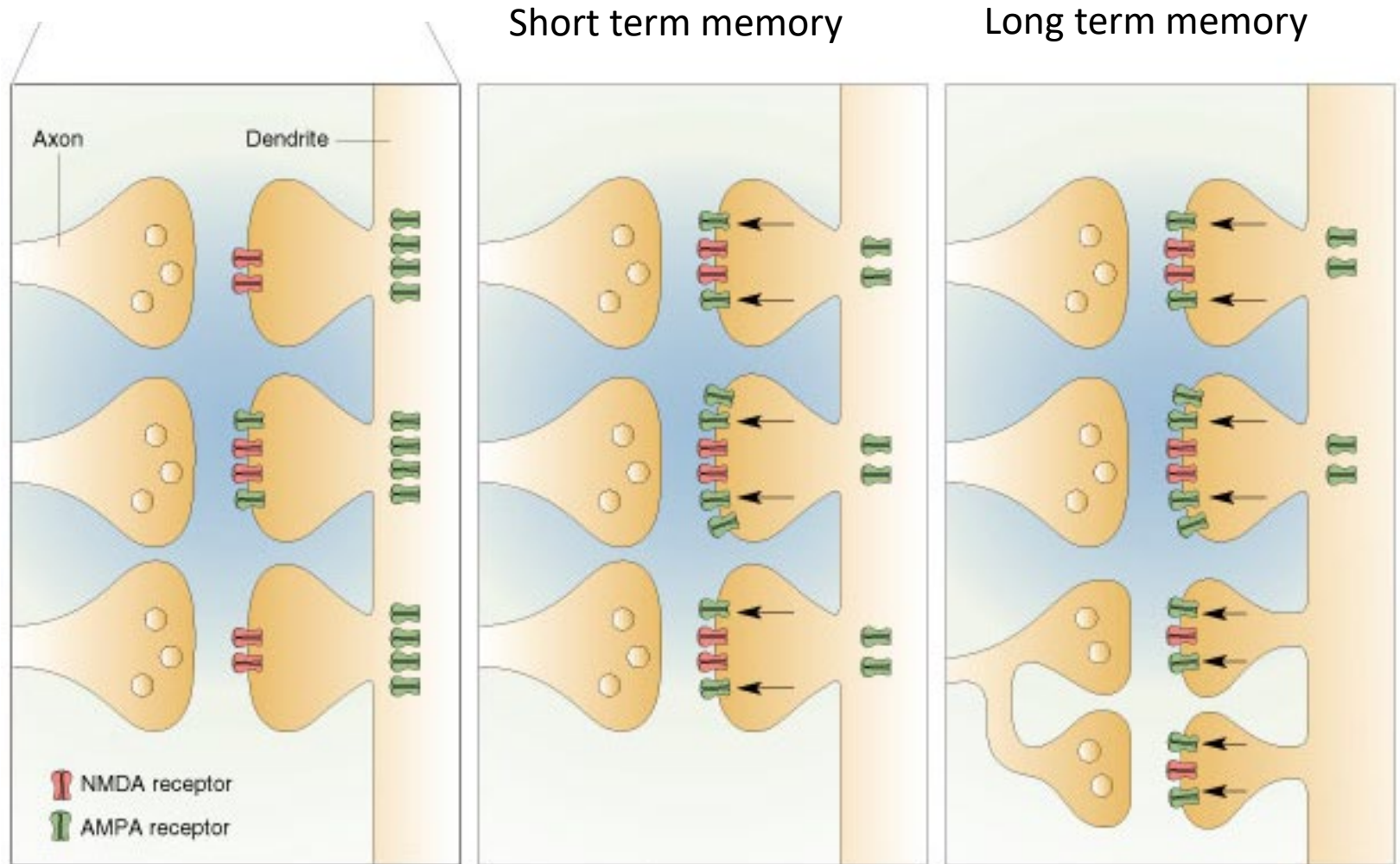


We find relationships between the amount of time in early learning

- **Slower change in behaviour leads to larger neuroplastic change in myelin**



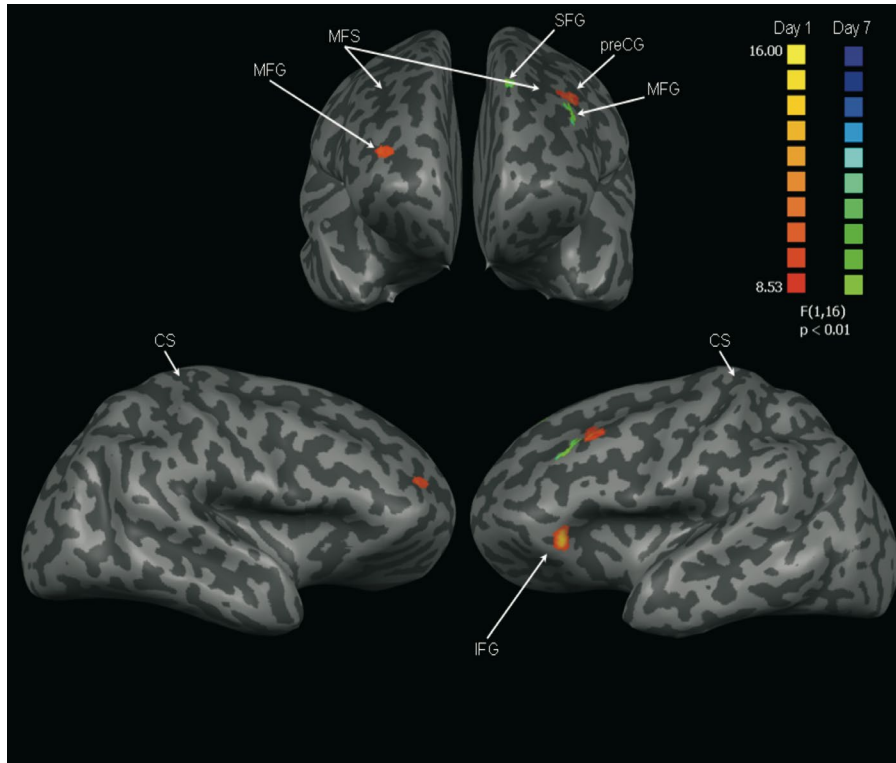
# Brain Chemistry and Structure interact to create Long-term Memories



adapted from Kandel, 2013

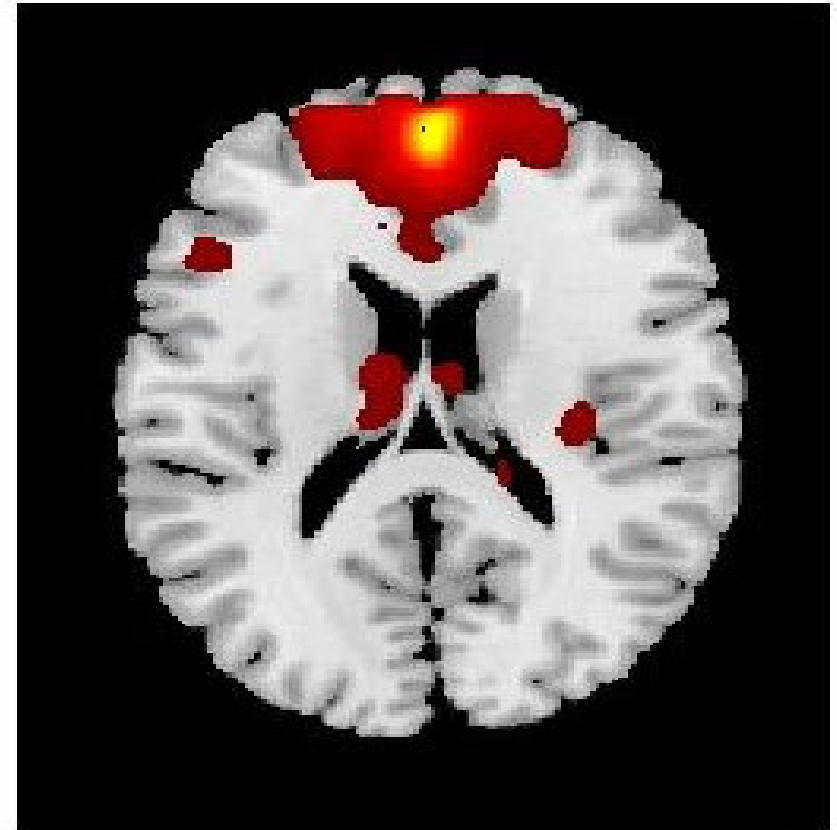
# Brain Function

## Task based



Meehan & Boyd, 2011

## Resting



Kraeutner et al, 2021

# Summary: The Neuroplastic Brain



- All brains are neuroplastic
- Neuroplasticity occurs at the chemical, structural and functional level
- The brain is never at “rest”
- Neuroplasticity supports change in behaviour and learning



# **Part II.**

# **Neuroplasticity:**

# **Promise and Peril**





- Why can't we learn anything we choose to with ease?
- Why do kids fail in school?
- Why don't people recover fully after brain damage?

**What limits and what facilitates neuroplasticity?**

# Not all neuroplastic change is positive

- Repetitive Use injuries
- Chronic pain
- Drug and/or Alcohol use
- Stress / Anxiety

# Back Pain Alters the Sensory Cortex

Chronic back pain leads to:

- Increased cortical reactivity to painful stimuli
- Increased cortical reactivity to non-painful stimuli
- Increased cortical reactivity when body parts other than the back are touched





# Stress Response - Cortisol

The hormone **Cortisol** is secreted by the adrenal glands.

Cortisol is key for:

- Glucose Metabolism
- Regulation of blood pressure
- Insulin release for blood sugar maintenance
- Immune function
- Inflammatory response
- Arousal

And cortisol release can **positively affect memory**, immunity, pain sensitivity...



# Stress Response - Cortisol

Higher and prolonged levels of cortisol in the bloodstream (with chronic stress) has negative effects:

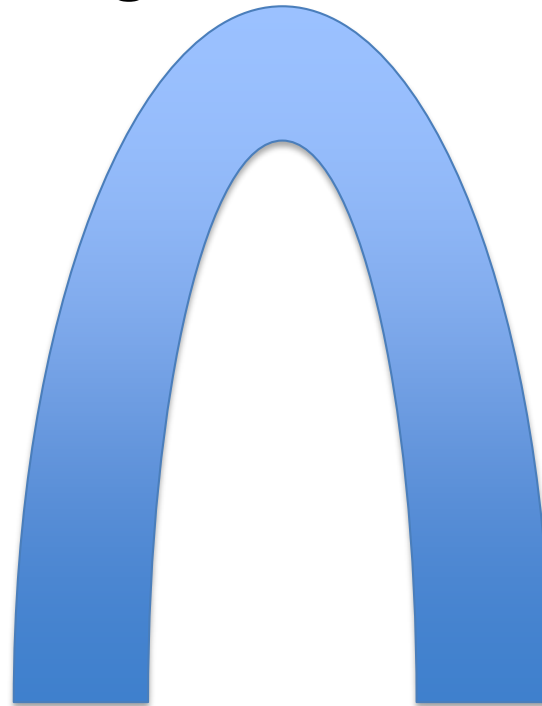
- **Impaired cognitive performance**
- Suppressed thyroid function
- Blood sugar imbalances (hyperglycemia)
- Decreased bone density
- Decrease in muscle tissue
- High Blood pressure
- Low immunity but high inflammatory responses in the body
- Increased abdominal fat
- Higher levels of “bad” cholesterol (LDL) and lower levels of “good” cholesterol (HDL)

# Stress Response and Cortisol



- An inverted “U” relationship with health

## Just the Right Amount of Cortisol



**Positive effects on  
memory, immunity,  
pain sensitivity**

### **Too little Cortisol**

Low Motivation  
Low Arousal

### **Too Much Cortisol**

Anxiety  
Memory impairments  
Health Issues – weight gain

# Stress, depression and neuroplasticity



- Persistent exposure to stress leads to less brain derived neurotrophic factor (BDNF) and atrophy in key memory structures (hippocampus) of the brain
- Stress can impair the formation of new memories and limit learning

# Managing Stress (and Cortisol)



- Adults who practiced Buddhist meditation significantly decreased cortisol and blood pressure in 6-weeks.
- Six hours of sleep vs. eight increases cortisol in the bloodstream by 50% in adults.
- Exercise: if intense increases cortisol but rebounds to lower levels
  - moderate intensity exercise reduces cortisol
- Children who engage in mindfulness (Mind Up Program) show higher empathy, more optimism & less depression



# The Dose Problem

The dose of practice required to change the brain can be very large

- 9,600 retrievals over 4 weeks (Nudo et al., 1996)
- 10,000 repetitions of skilled movement (myelin; Borich, et al 2013; Lakhani et al., 2016)
- 31,500 repetitions of a sequence (Karni et al., 1995)

# Summary: Neuroplasticity, Promise and Peril



- Not all neuroplastic change is beneficial to function or health
- Changing behaviour means changing brain
- Behaviour can remediate negative neuroplastic change
- The dose of practice required to change the brain is large



## **Part III.**

# **Exploiting Neuroplasticity**

# Priming the Brain to Learn



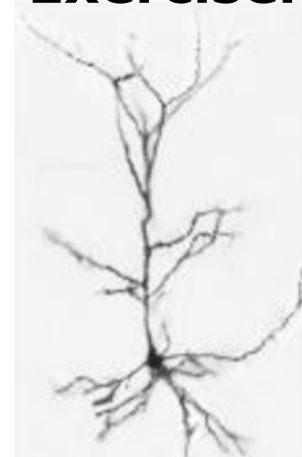
**3 X 3 minutes 90%  $\text{VO}_2$  max Cycling**

# Exercise and Brain Plasticity

## Exercise Enhances...

- Blood Flow
- Blood Vessel Formation
- Cerebral White and Grey Matter
- Neuron and Synapse Growth
- Neural Growth Factors
- Neurotransmitters

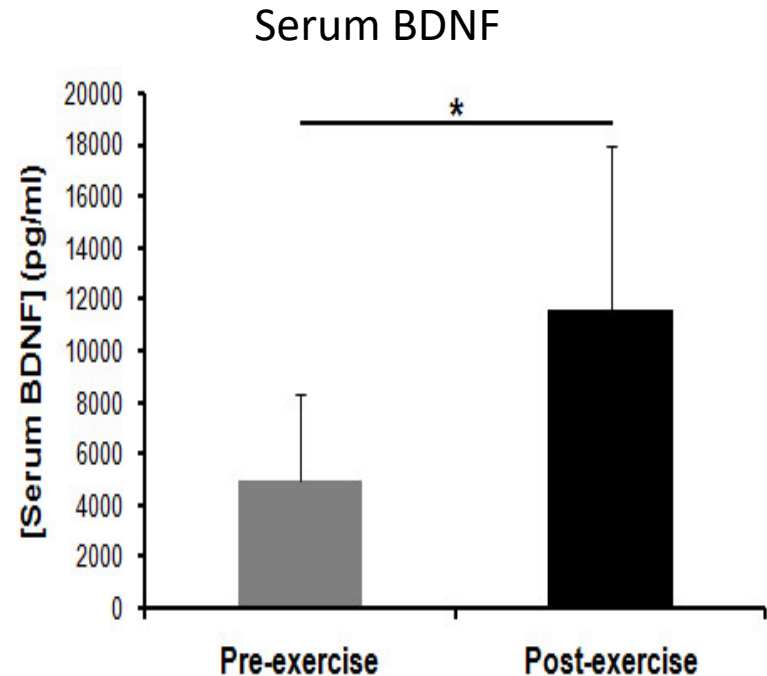
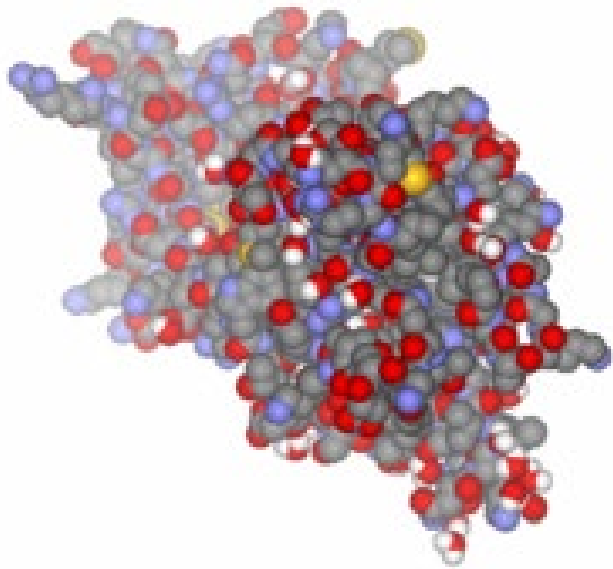
**Non-  
Exerciser**



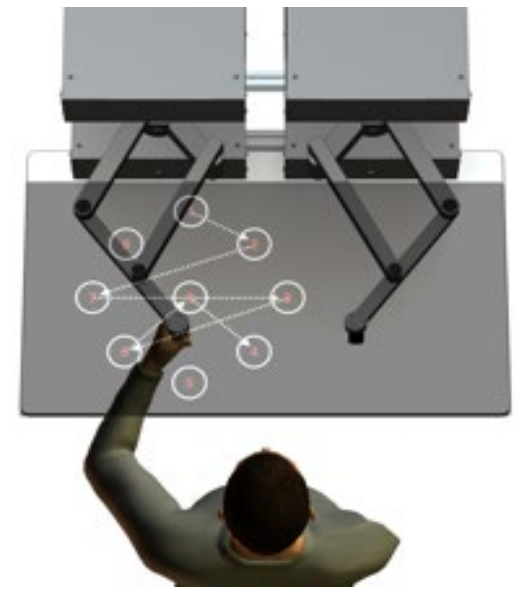
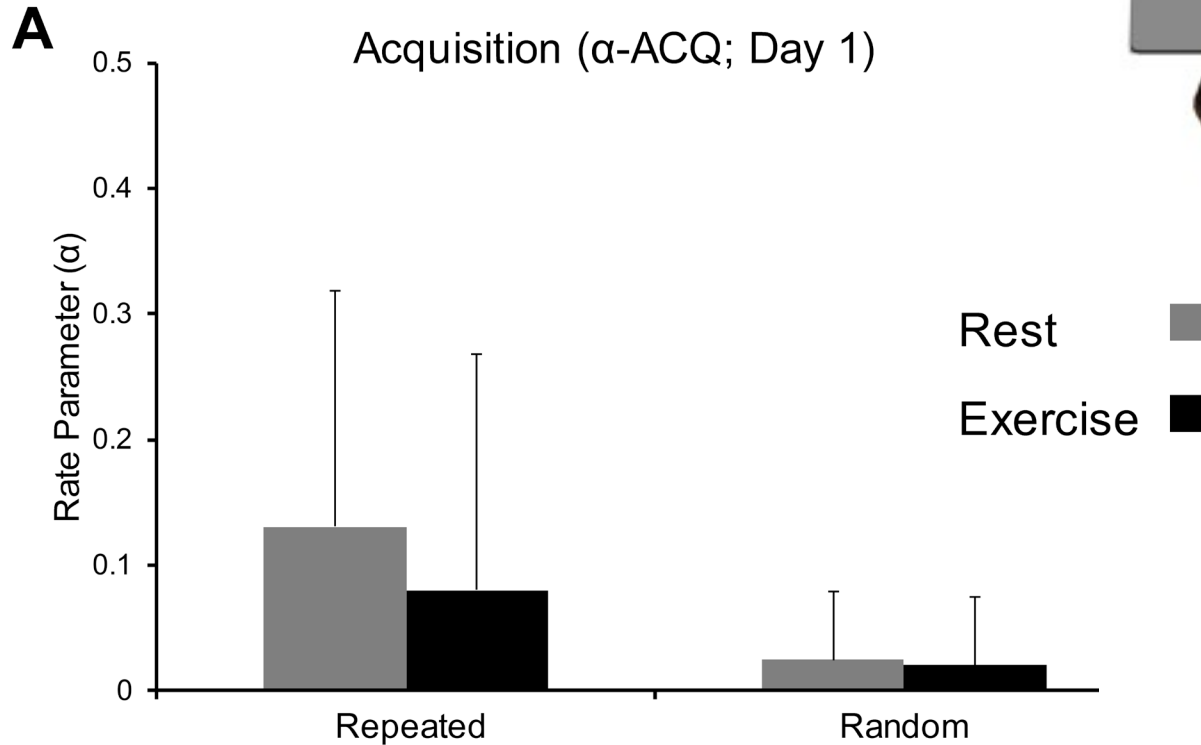
**Exerciser**



# A single session of aerobic exercise enhances brain derived neurotrophic factor



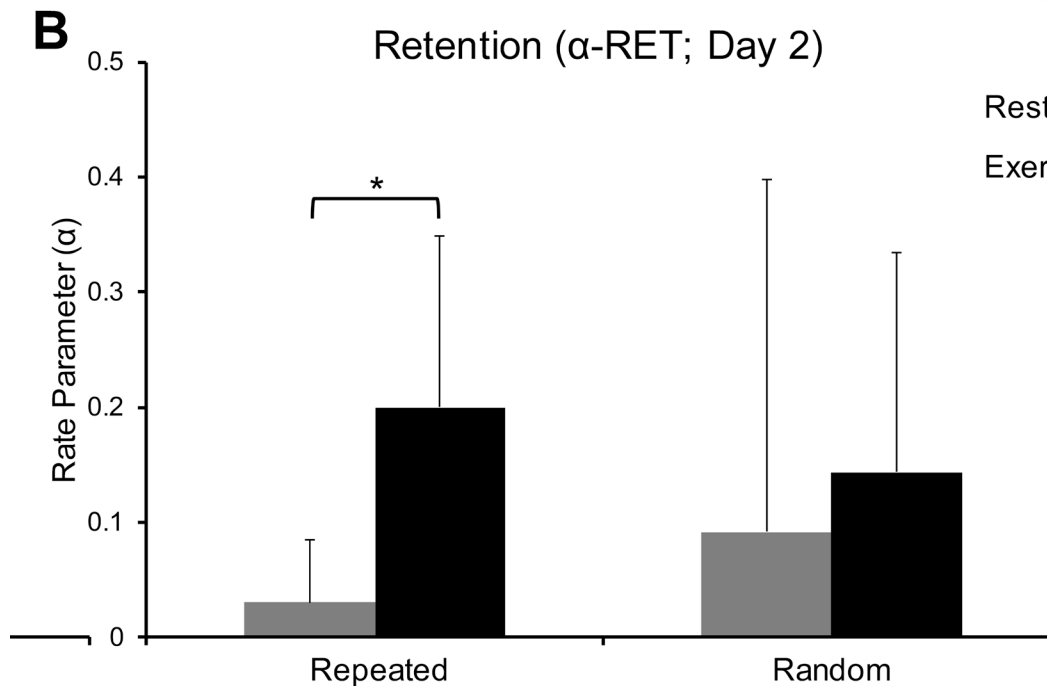
# A single bout of exercise has little impact on motor performance



Mang et al, MSSE, 2017

Mang et al, Journal of Applied Physiology, 2014

# A single bout of exercise facilitates learning through motor memory consolidation



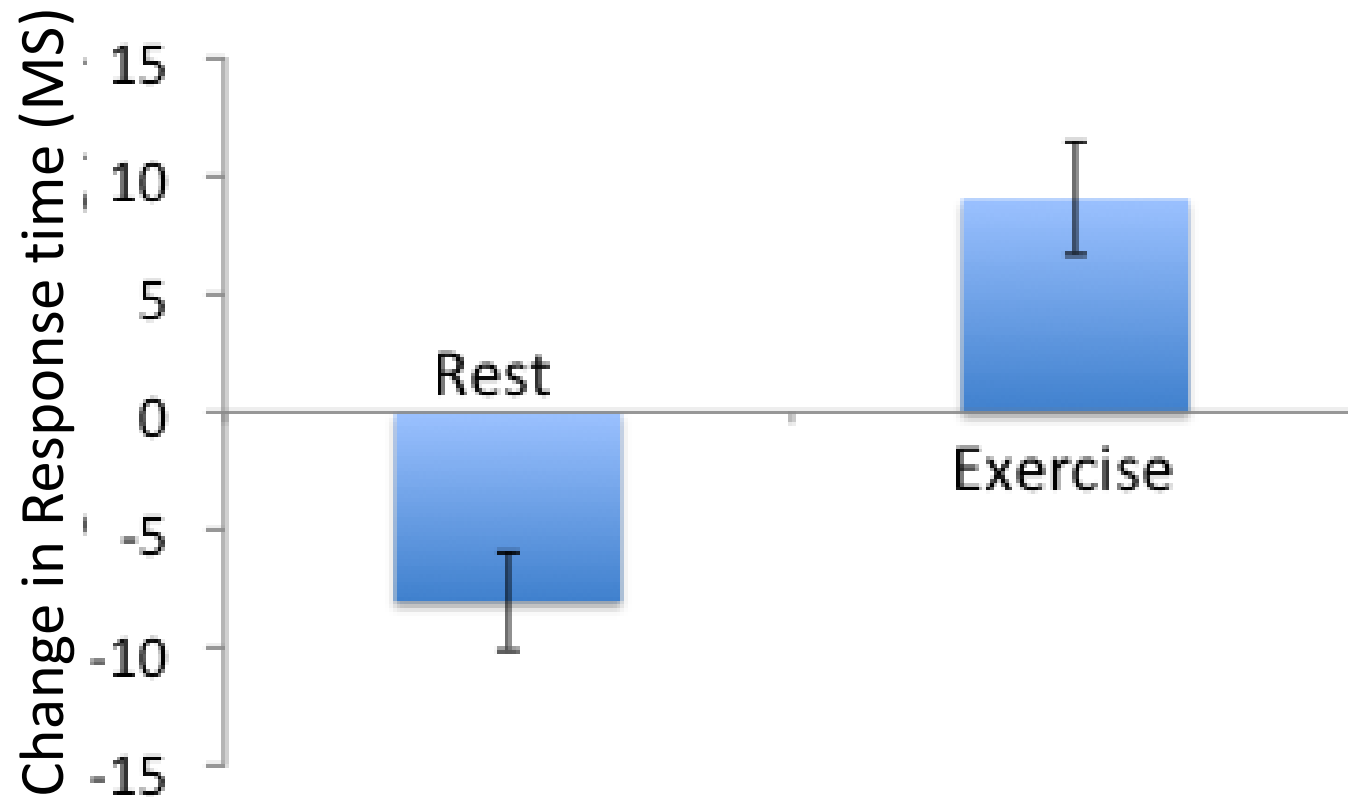
Learning effects are only evident after a 24-hour delay.

Mang et al, MSSE, 2017

Mang et al, Journal of Applied Physiology, 2014



# Priming Exercise may facilitate motor learning in individuals with stroke (multiple sessions)





# Impact of exercise in individuals with PD



## RESEARCH ARTICLE

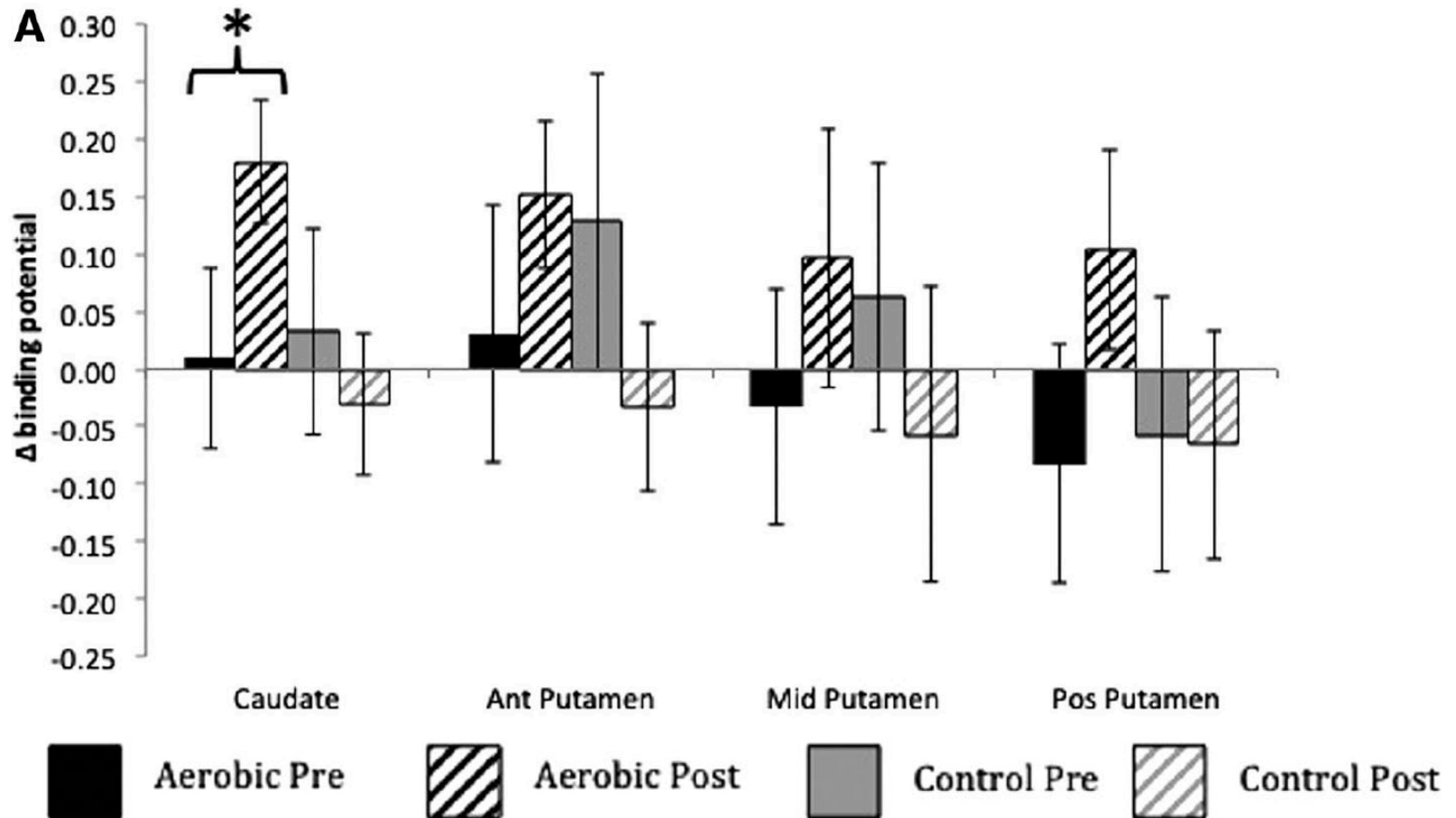
### Exercise Increases Caudate Dopamine Release and Ventral Striatal Activation in Parkinson's Disease

Matthew A. Sacheli, MSc,<sup>1\*</sup>  Jason L. Neva, PhD,<sup>2</sup> Bimal Lakhani, PhD,<sup>2</sup> Danielle K. Murray, MSc, MD,<sup>1,3</sup> Nasim Vafai, MSc,<sup>4</sup> Elham Shahinfard, PhD,<sup>4</sup> Carolyn English,<sup>4</sup> Siobhan McCormick, MSc,<sup>4</sup> Katie Dinelle, MSc,<sup>4</sup> Nicole Neilson, RN,<sup>1</sup> Jessamyn McKenzie, LPN,<sup>1</sup> Michael Schulzer, PhD,<sup>1</sup> Don C. McKenzie, MD, PhD,<sup>5</sup> Silke Appel-Cresswell, MD,<sup>1,3</sup> Martin J. McKeown, MD, BEng,<sup>1,3</sup> Lara A. Boyd, PT, PhD,<sup>2</sup> Vesna Sossi, PhD,<sup>4</sup> and A. Jon Stoessl, MD<sup>1,3</sup> 

40-60 minutes cycling, 3X week for 36 weeks  
Hoehn & Yahr I-III

# Impact of exercise

Exercise increases evoked dopamine release in the caudate in individuals with PD



# Many forms of Exercise promote brain health

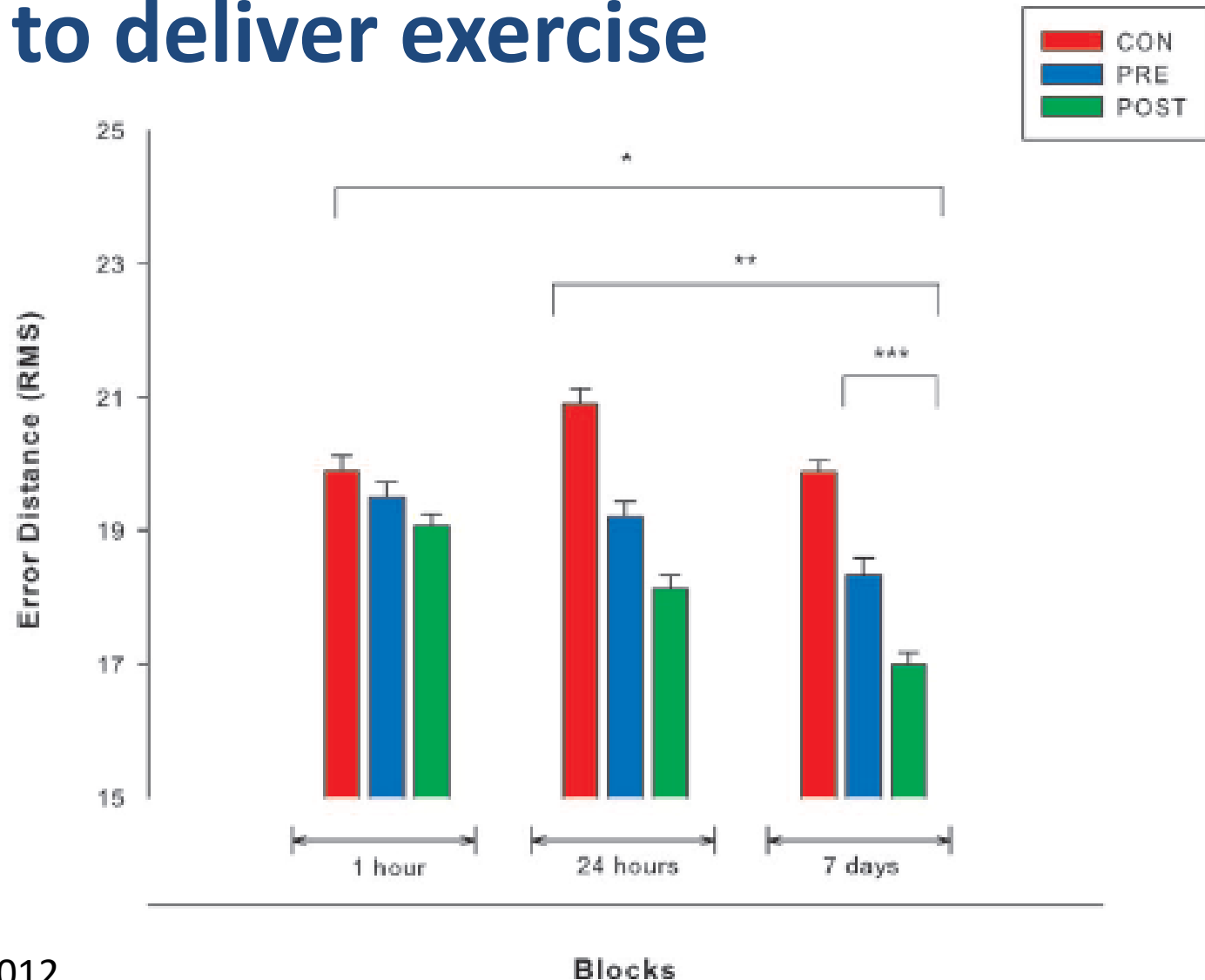


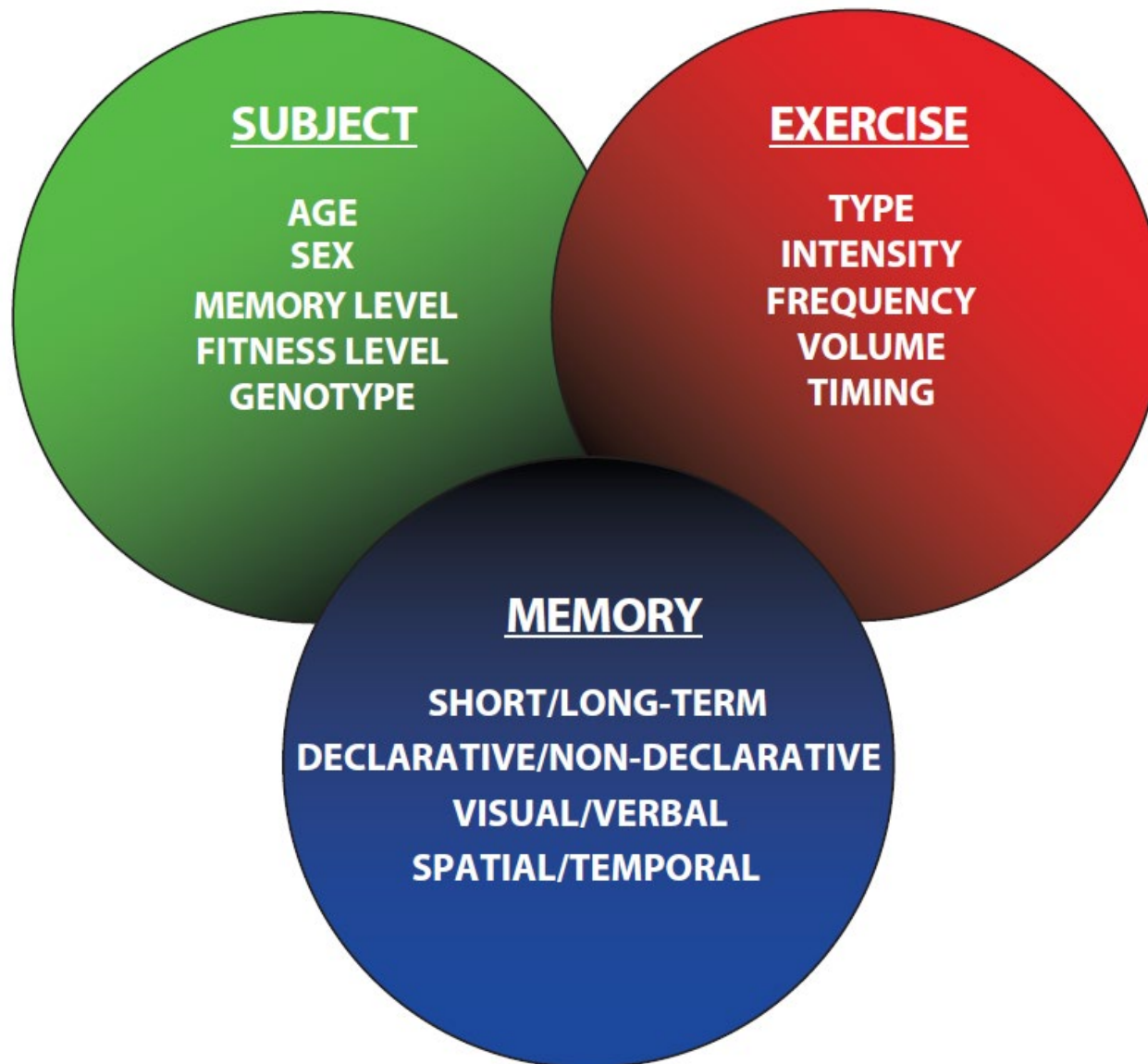
Weight lifting, regular walks and gardening all have been shown to promote improved cognition and reduce dementia rates.



# Exercise Parameters:

## When to deliver exercise





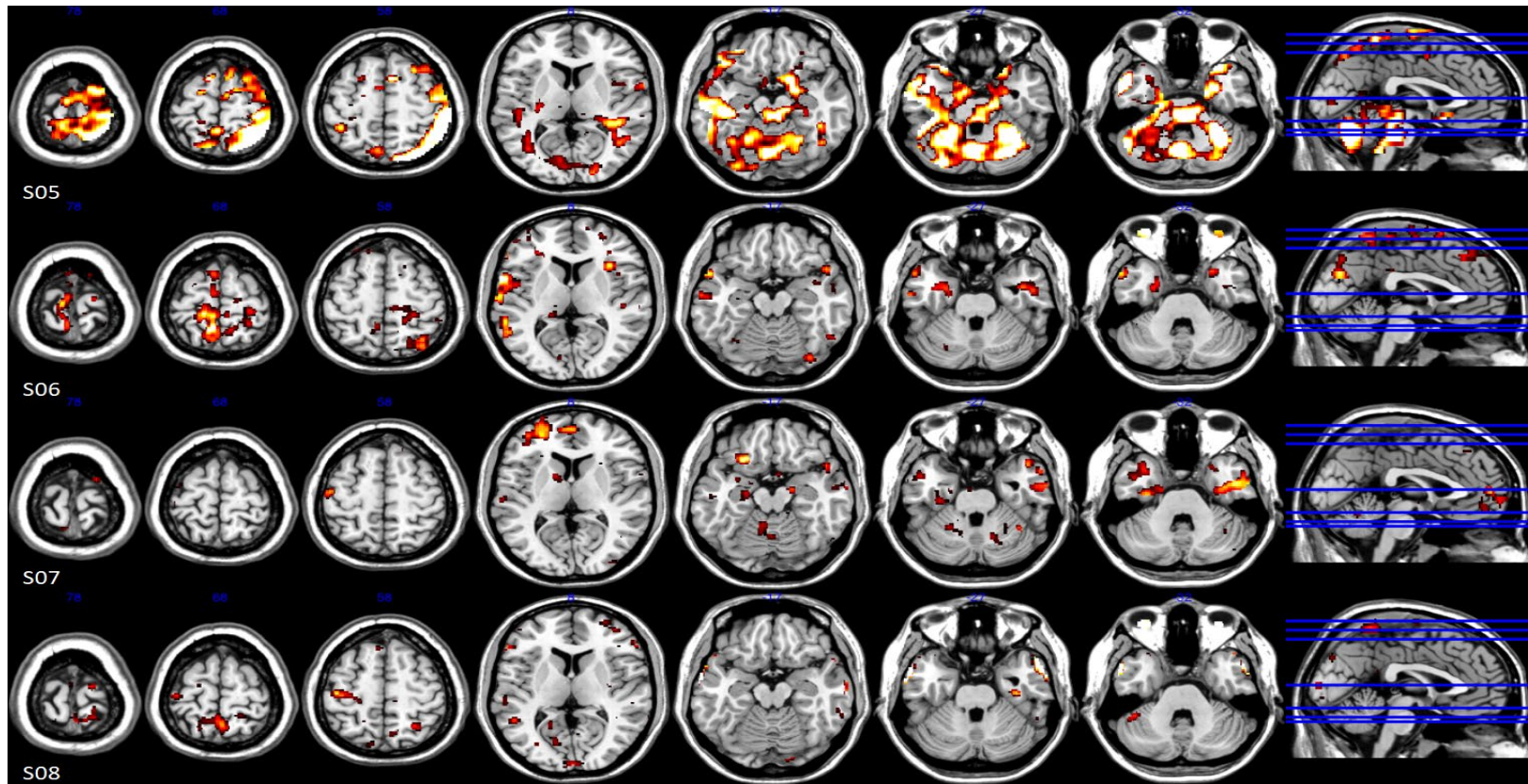


# One size does not fit all:

## Variability in response after stroke



- After stroke individuals employ unique networks to support motor learning



# Personalized Medicine & Learning



The uniqueness of your brain affects you as both teacher and learner

- Research challenge is to decipher patterns of variability in neuroplasticity and learning

Understanding these differences between individuals will enable the next great advance in neuroscience



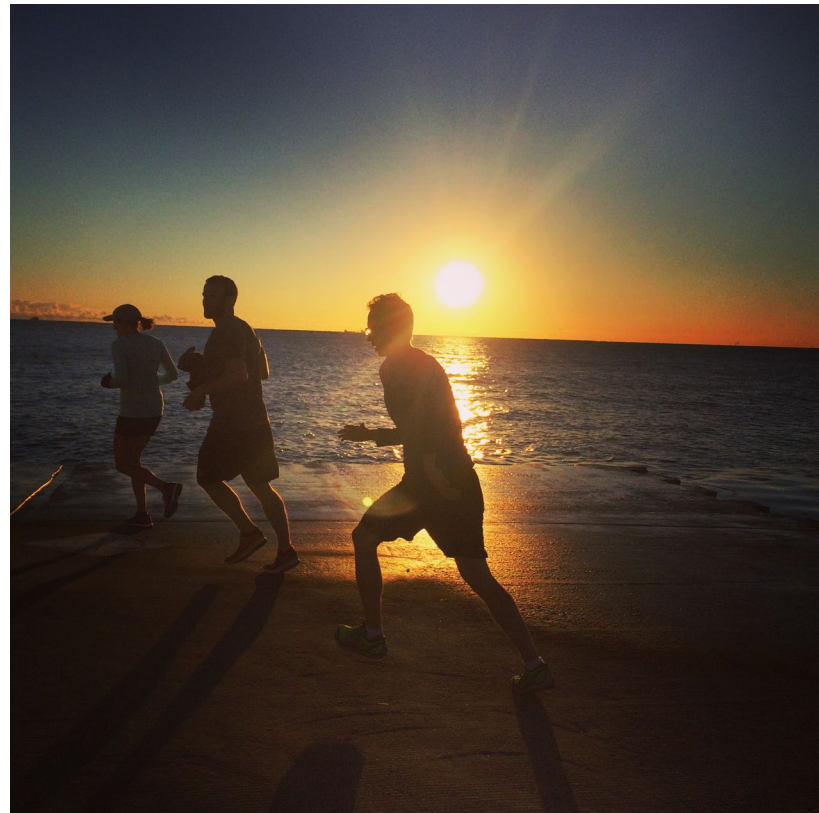
# Summary: Exploiting Neuroplasticity



Behaviour is the largest stimulant of neuroplastic change

- Exercise primes the brain to learn
  - Exercise affects memory in both the short- and long-term
  - Positively alters neurophysiology
  - Facilitates an overall environment of excitability in the brain that favors plasticity

# Brain Health and Repair



Brain Behaviour lab @UBC\_BrainLab  
Practice what we preach



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