

Conférence scientifique

Jason Neva, Ph. D.

Professeur adjoint et directeur de laboratoire
Spécialiste de la neuroplasticité, de l'AVC et
de la stimulation cérébrale
Université de Montréal – CRIUGM



Jeudi 12 juin 2025 de 12 h 00 à 13 h 00

Understanding and Enhancing the Neural Mechanisms Supporting Motor Learning: Applications to Motor Rehabilitation

CRIR
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du Centre-Sud-
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Harnessing Neuroplasticity to Enhance Motor Learning: *Applications in Rehabilitation*

Jason Neva, PhD

Associate Professor

School of Kinesiology and Physical Activity Sciences

Research Centre of the Montreal Geriatrics Institute (CRIUGM)

✉ jason.neva@umontreal.ca

🎓 Jason L. Neva

🐦 @jasonlneva

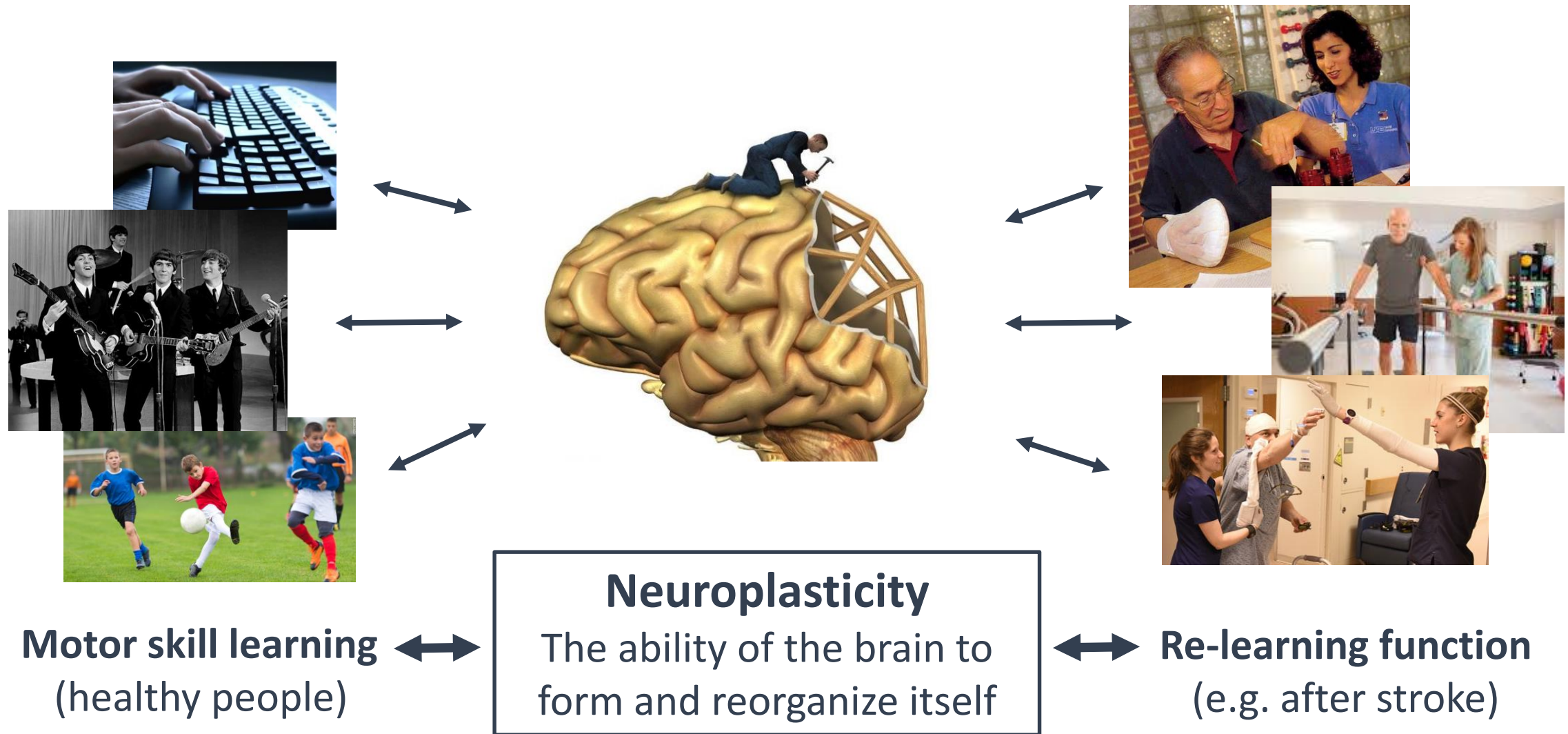
Faculté de médecine
Université  de Montréal **et du monde.**

 Centre de recherche
iugm
Institut universitaire
de gériatrie de Montréal

ELPN lab
Effort Learning Performance Neuroplasticity



Neuroplasticity mechanisms supporting motor learning



My Lab & Research Streams



Fundamental

Applied

1

**Motor Learning &
Motor Control**

2

Acute Exercise, rTMS

3

**Aging,
Parkinson's Disease
& Stroke**

**Transcranial Magnetic Stimulation (TMS):
to *measure* and *modulate* brain excitability**

Adjunct Interventions: Boosting Brain & Behavior



Aerobic exercise



↑ neuroplasticity



Repetitive TMS (rTMS)



↑ motor (re)-learning



1

Aerobic Exercise:
↑ *Motor Learning*
↑ *Neuroplasticity*

2

TMS:
Measure & Modulate
the Brain

3

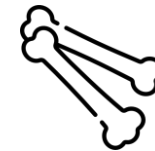
**Clinical Application &
Future Work**

1

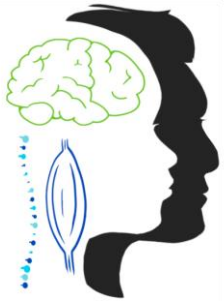
Aerobic Exercise:
↑ *Motor Learning*

Aerobic Exercise: Boosting Brain & Behavior

↑neuroplasticity



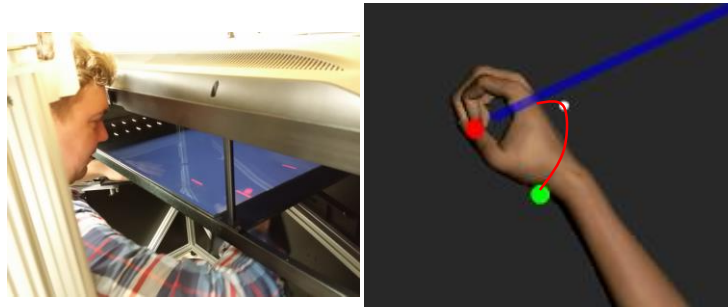
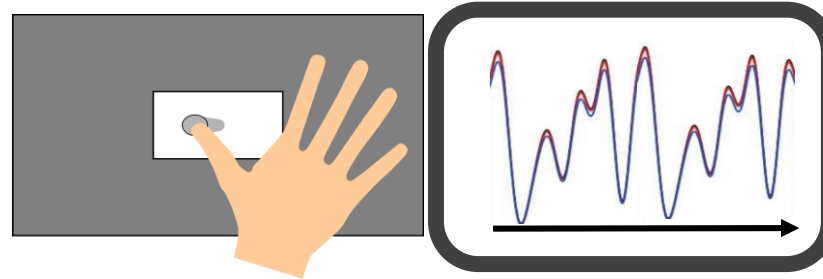
↑motor learning



Exercise enhances motor learning



Acute bout
lower limb cycling exercise
~20 min – moderate-vigorous



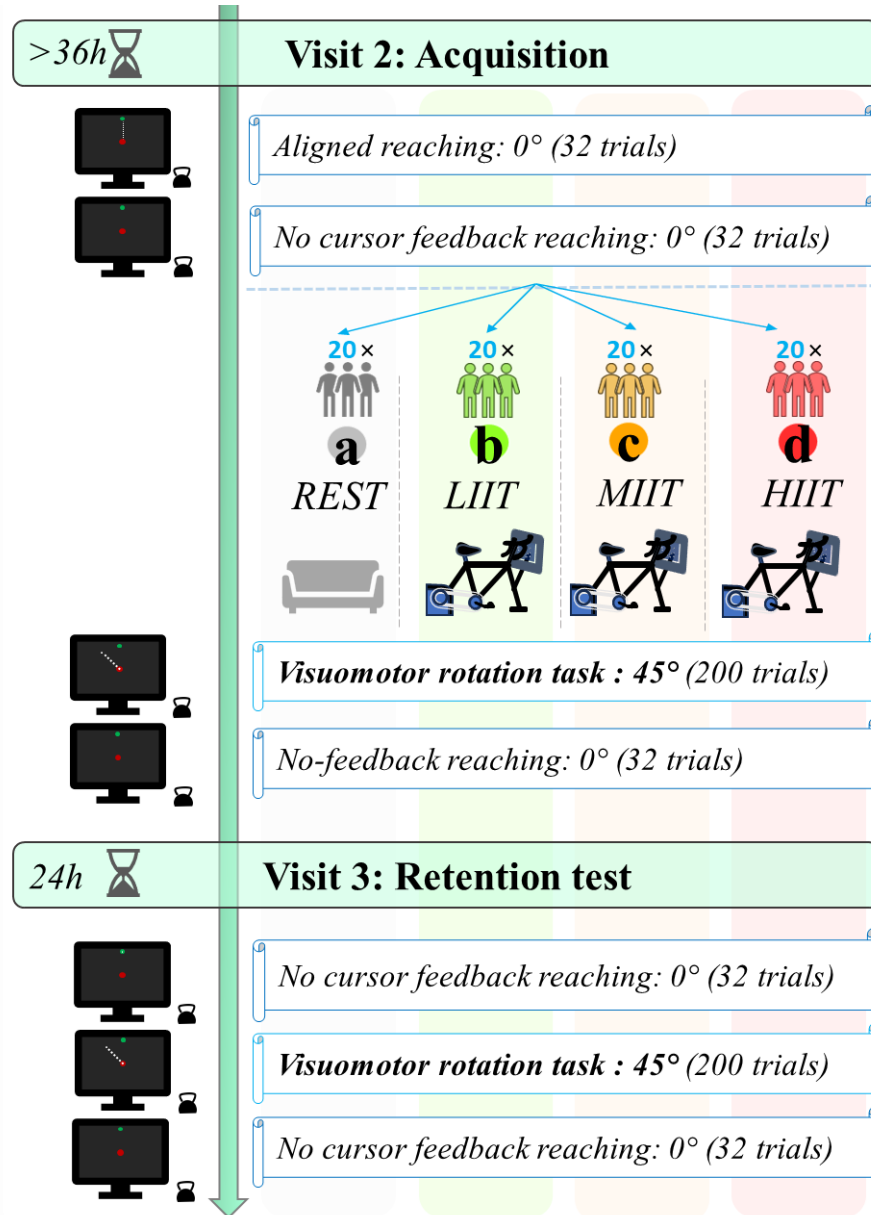
Skilled motor practice
with the *upper limb*

Unanswered questions:

- Exercise intensity??
- Exercise type??

Is there a dose-response effect of acute exercise intensity?

Experimental design



Nesrine Harroum, PhD candidate

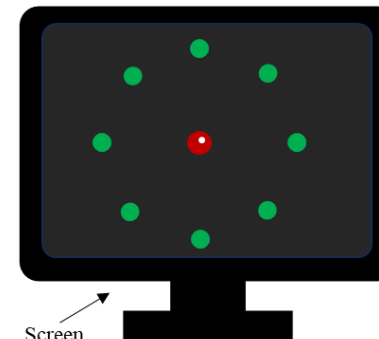
N = 80; young adults, between-subjects design

LIIT: Light-intensity interval training

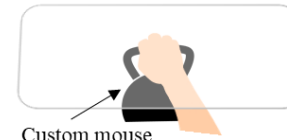
MIIT: Moderate-intensity interval training

HIIT: High-intensity interval training

REST: seated rest

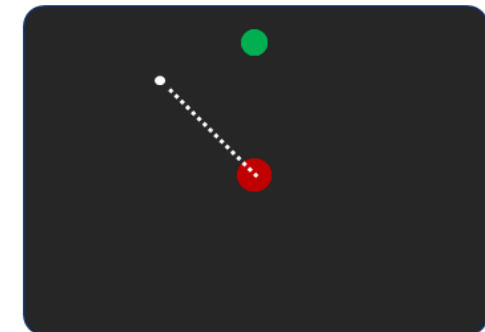


Screen



Custom mouse

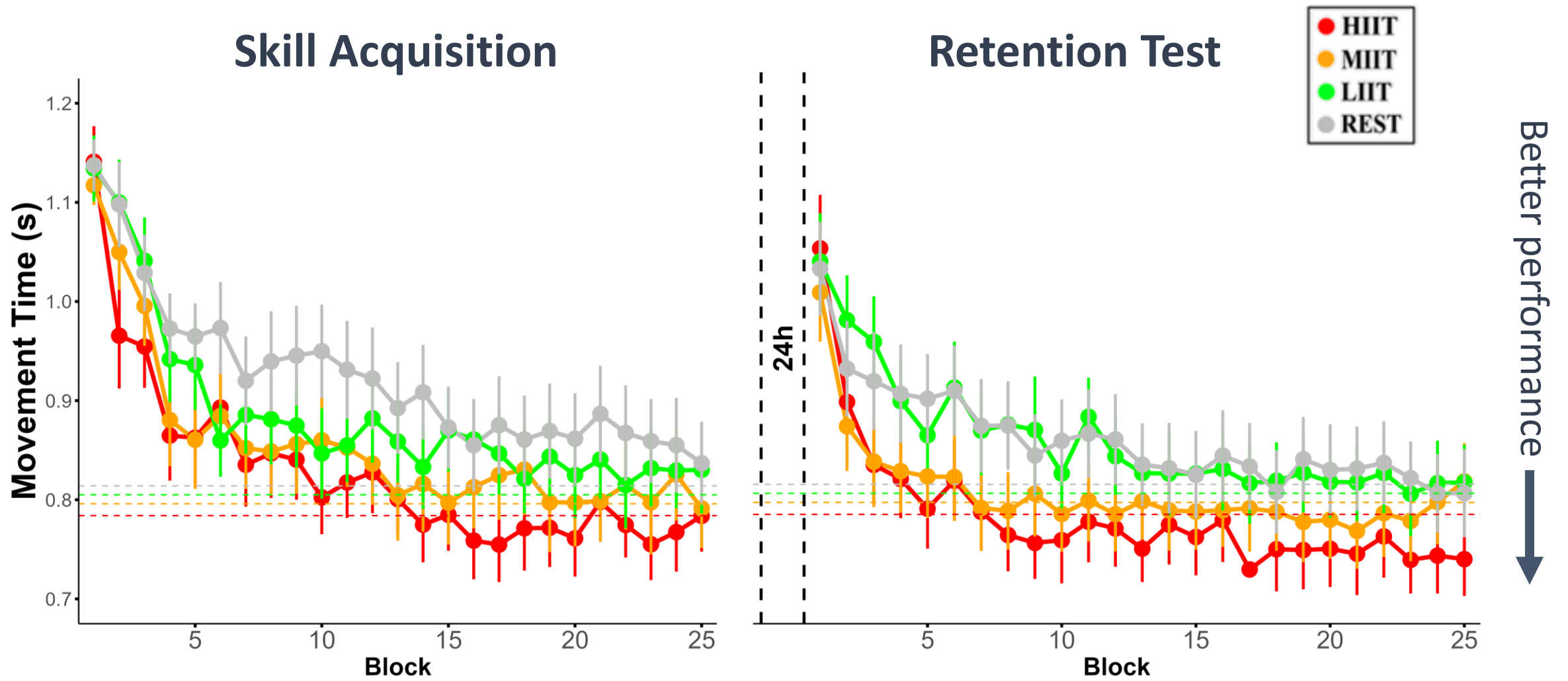
Visuomotor rotation task : 45°



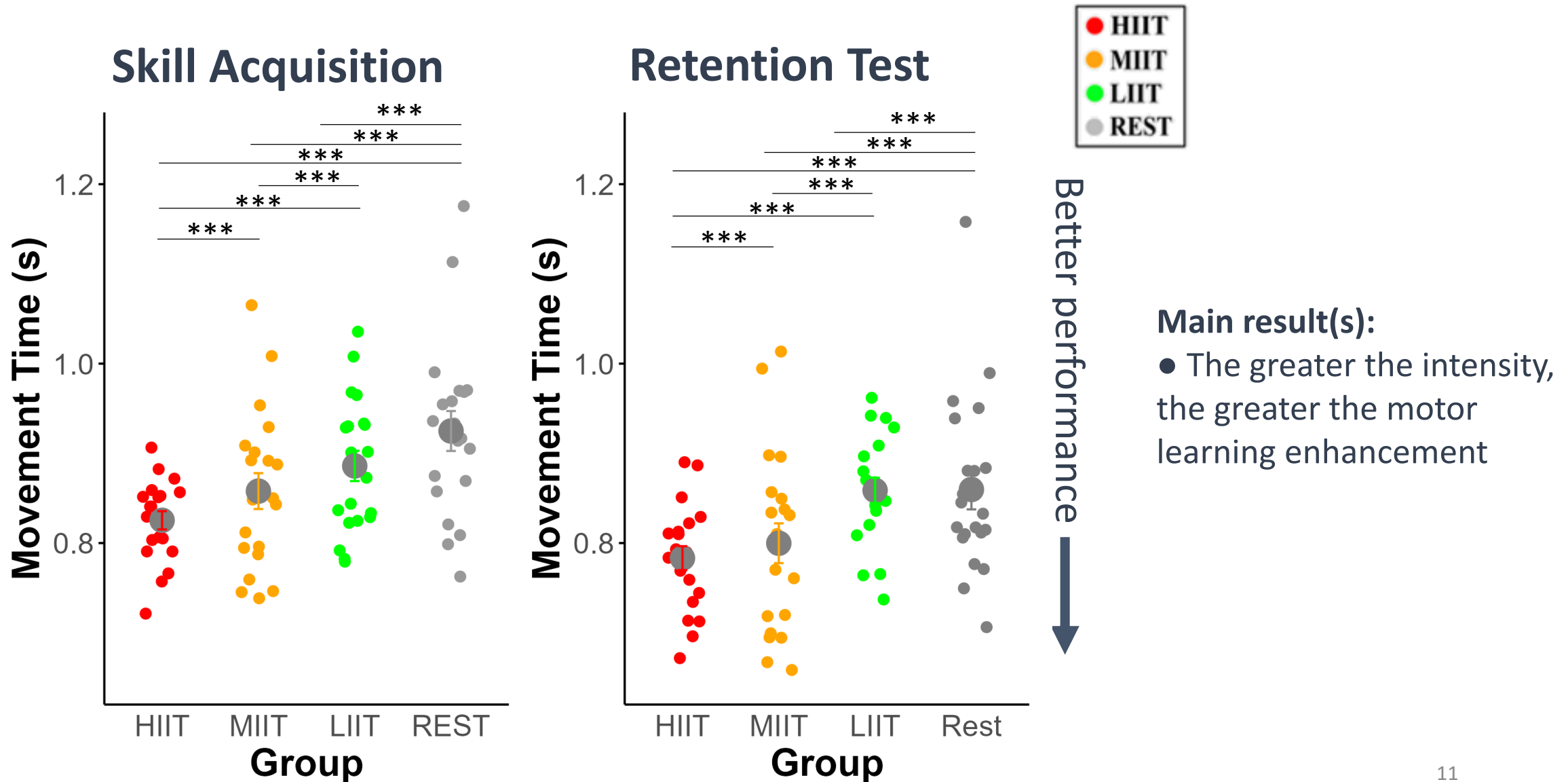
Cursor feedback is rotated **systematically** by 45° about the starting target.



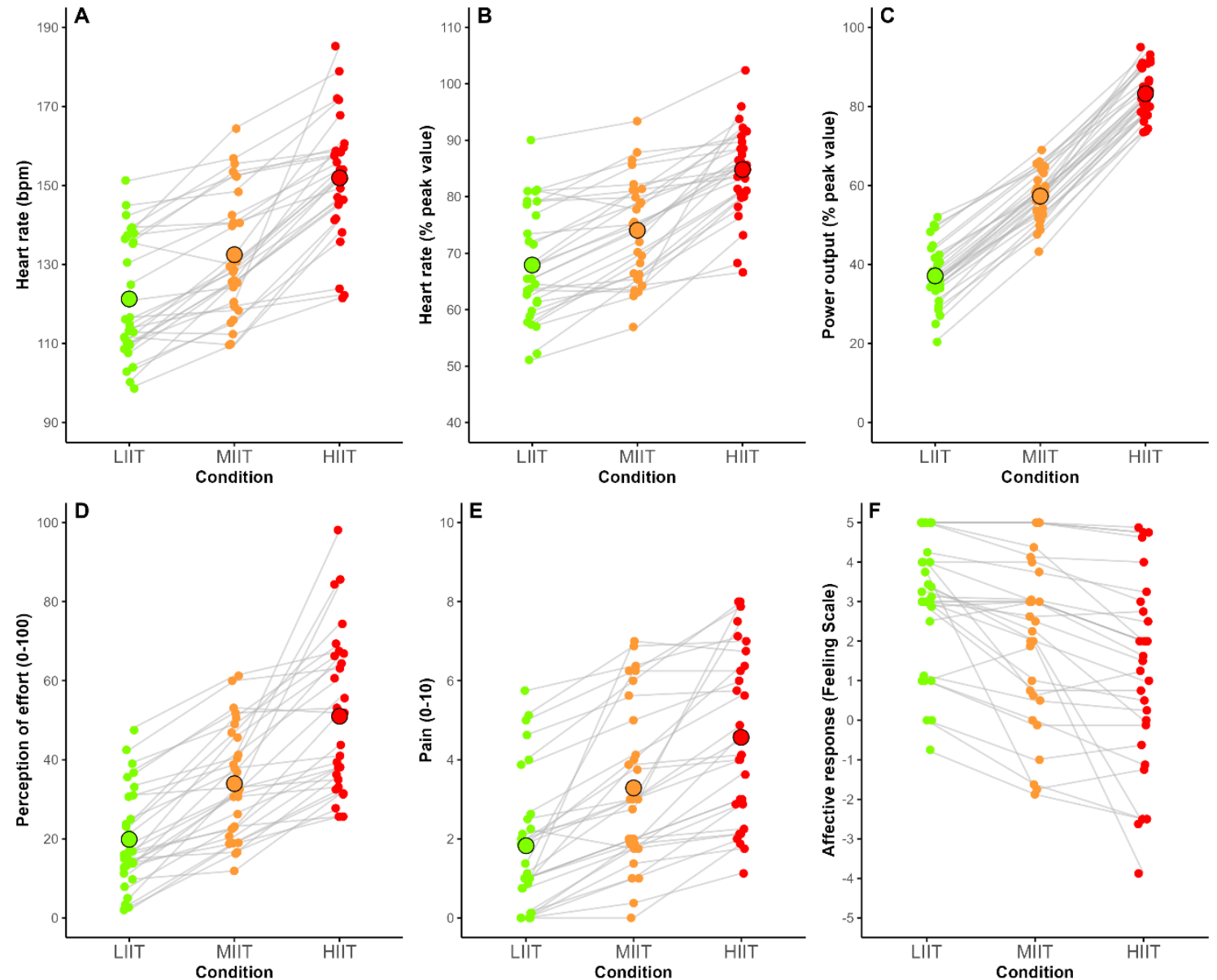
There is a dose-response effect of acute exercise intensity!



There is a dose-response effect of acute exercise intensity!



Dose-response effect of intensity on psycho-physiological measures



With ↑ exercise intensity there is:

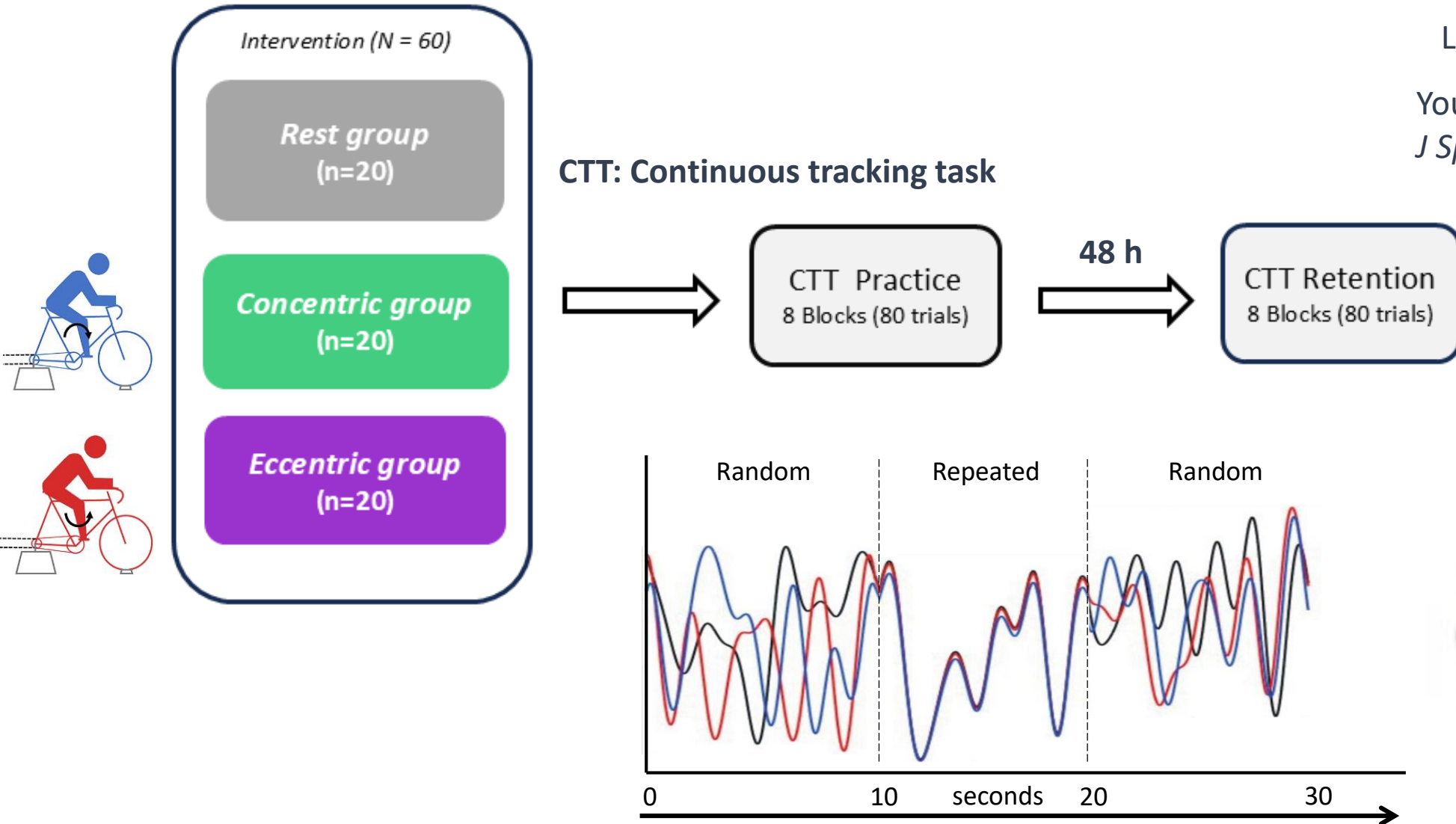
- ↑ perception of effort
- ↑ muscle pain
- ↑ *negative* affect

Is there an effect of acute exercise type?



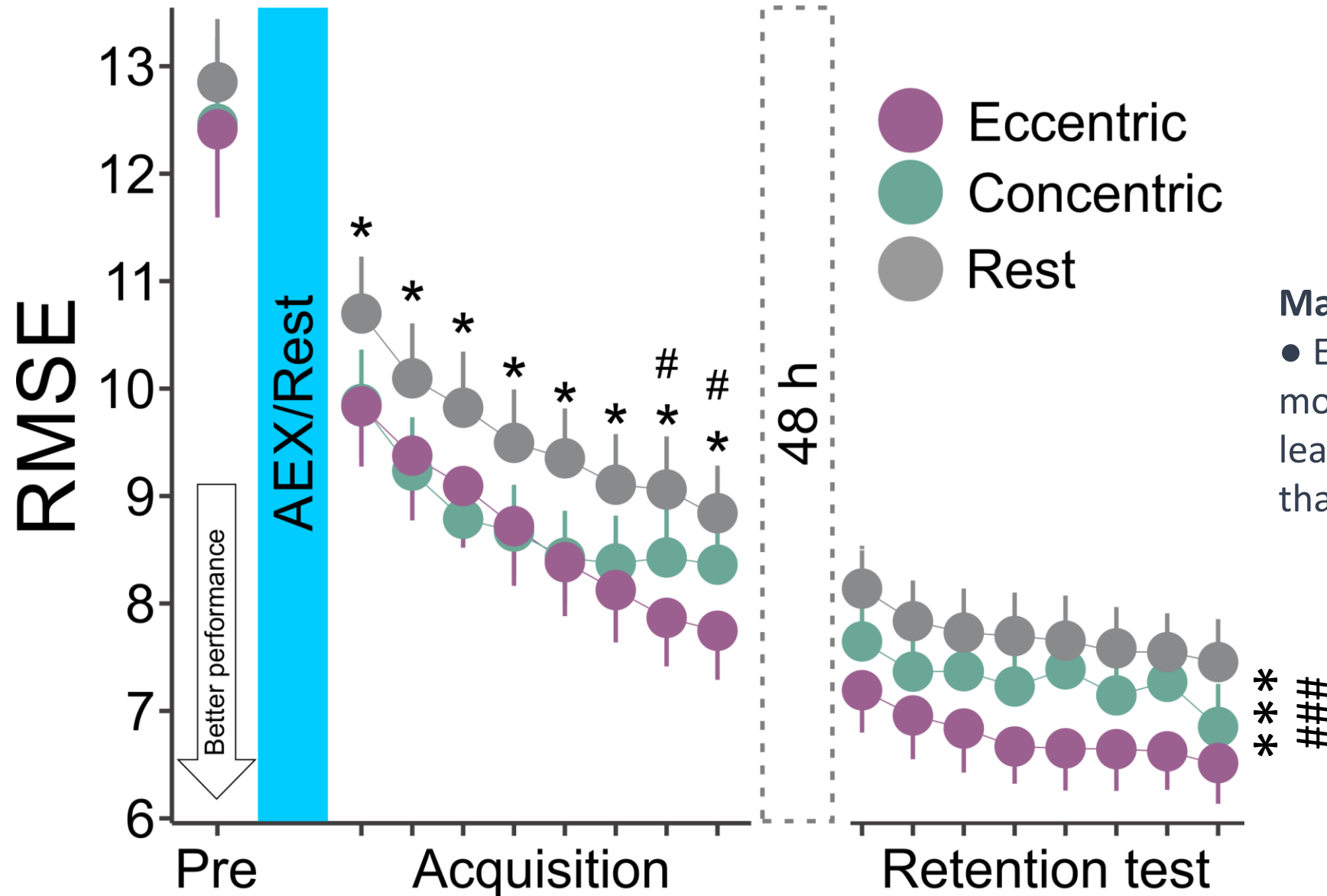
Layale Youssef, PhD student

Youssef et al., 2025
J Sport Health Sci (under review)



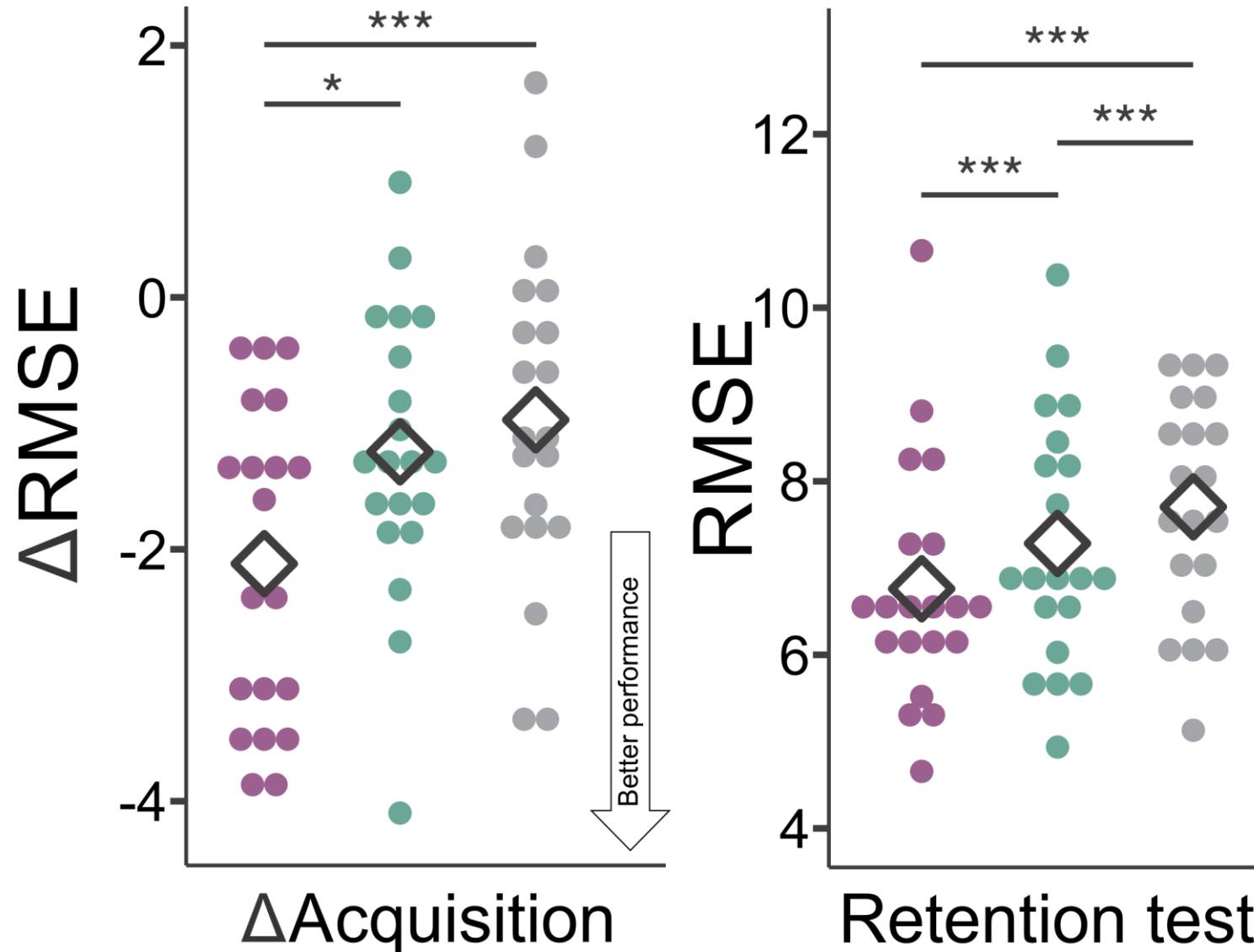
There is an effect of acute exercise type!

Youssef et al., 2025
J Sport Health Sci (under review)



There is an effect of acute exercise type!

Youssef et al., 2025
J Sport Health Sci (under review)



Main result(s):

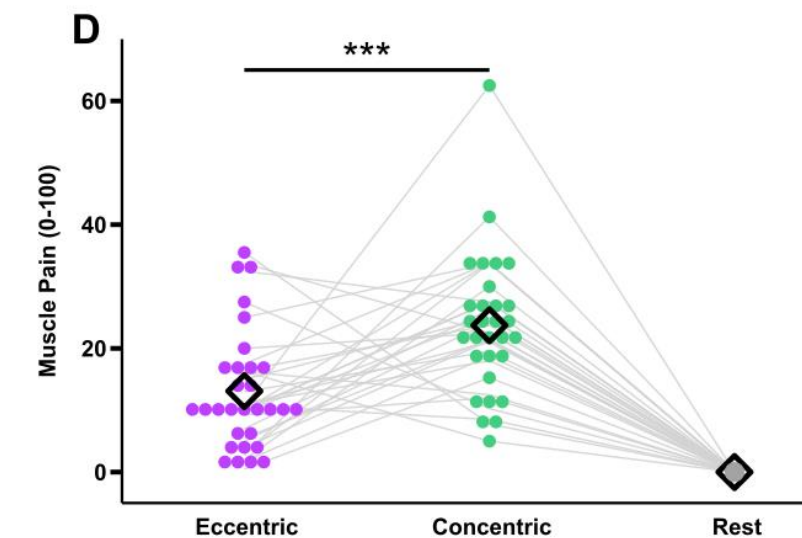
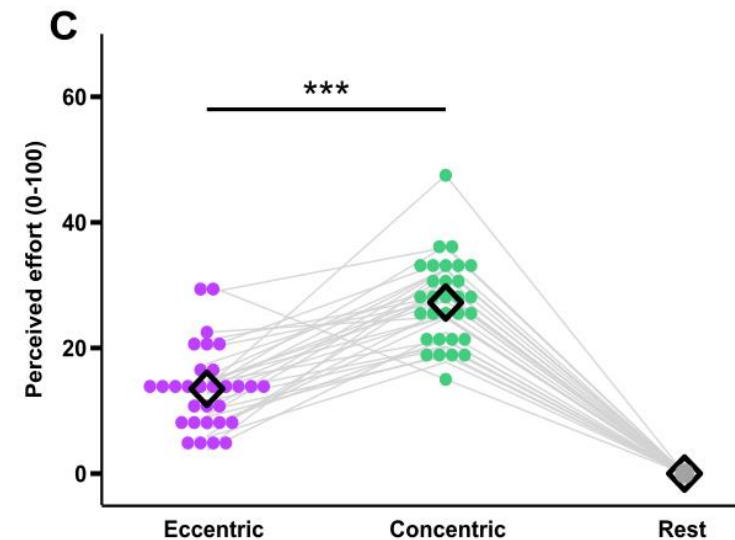
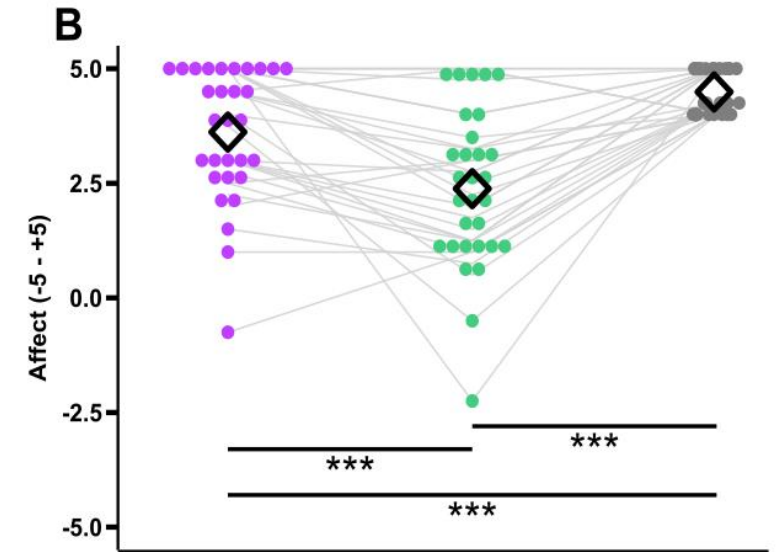
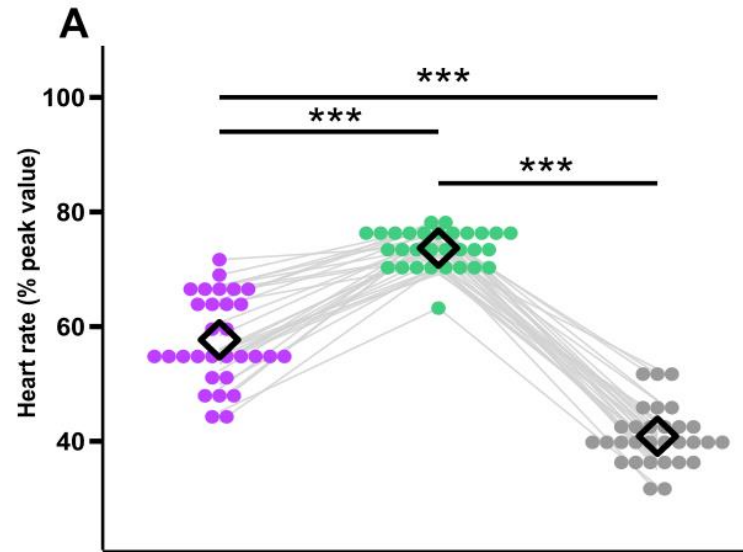
- Eccentric exercise enhances motor skill acquisition and learning to a greater extent than concentric exercise

The effect of exercise type on psycho-physiological measures

Eccentric vs concentric exercise:

- ↓ heart rate response
- ↑ *positive* affect
- ↓ perception of effort
- ↓ muscle pain *during* exercise

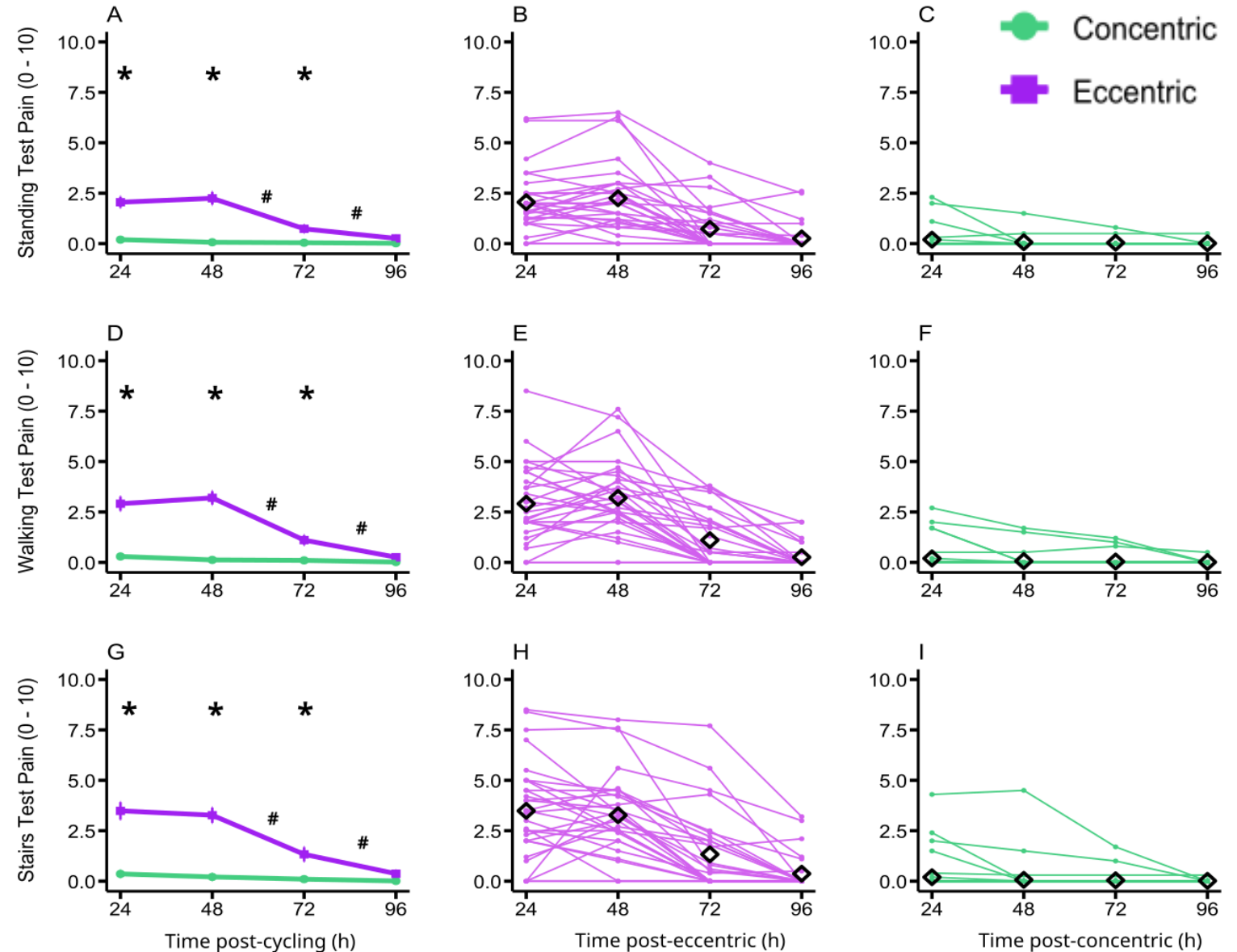
However.....

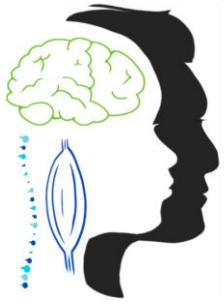


The effect of exercise type on *long-term muscle pain*

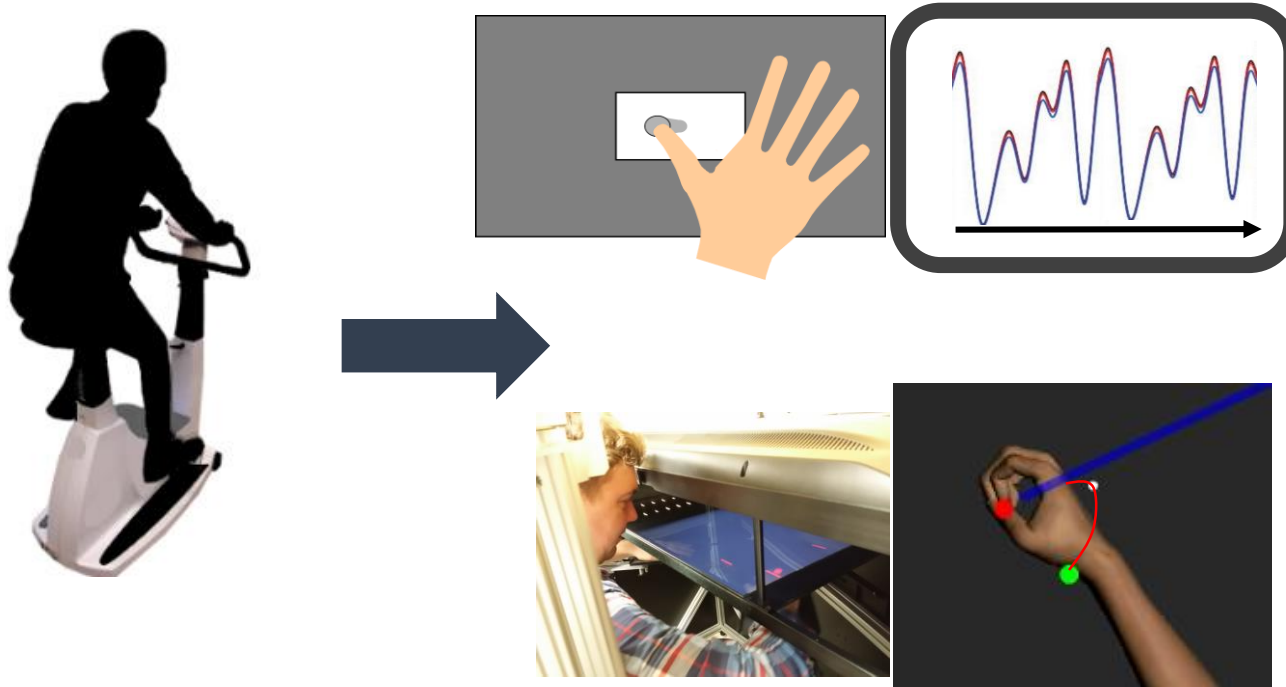
Eccentric vs concentric exercise:

- **↑ muscle pain *after* exercise**
 - 24h, 48h & 72h post
 - peak at ~48h post





Exercise enhances motor learning



Answered questions:

- Exercise intensity??
 - ↑ intensity, ↑ learning
- Exercise type??
 - Eccentric ↑ more than concentric (traditional)

Important considerations:

- *psycho-physiological responses*

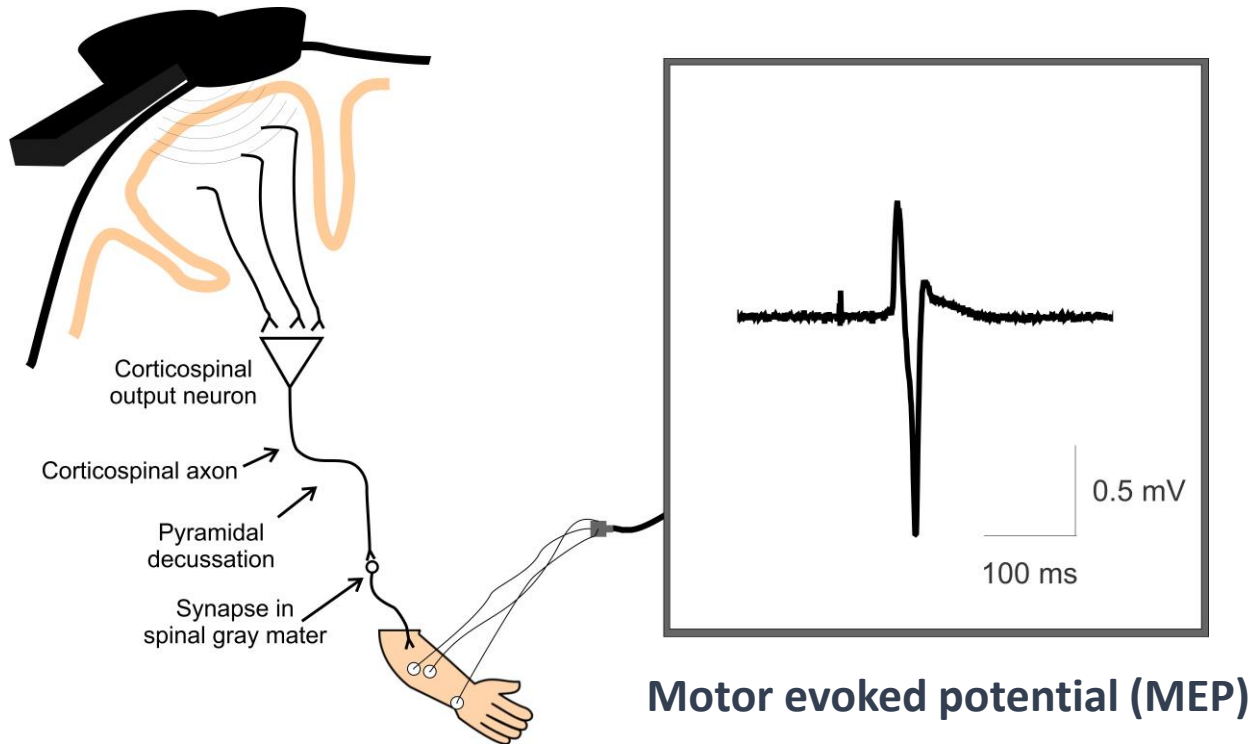


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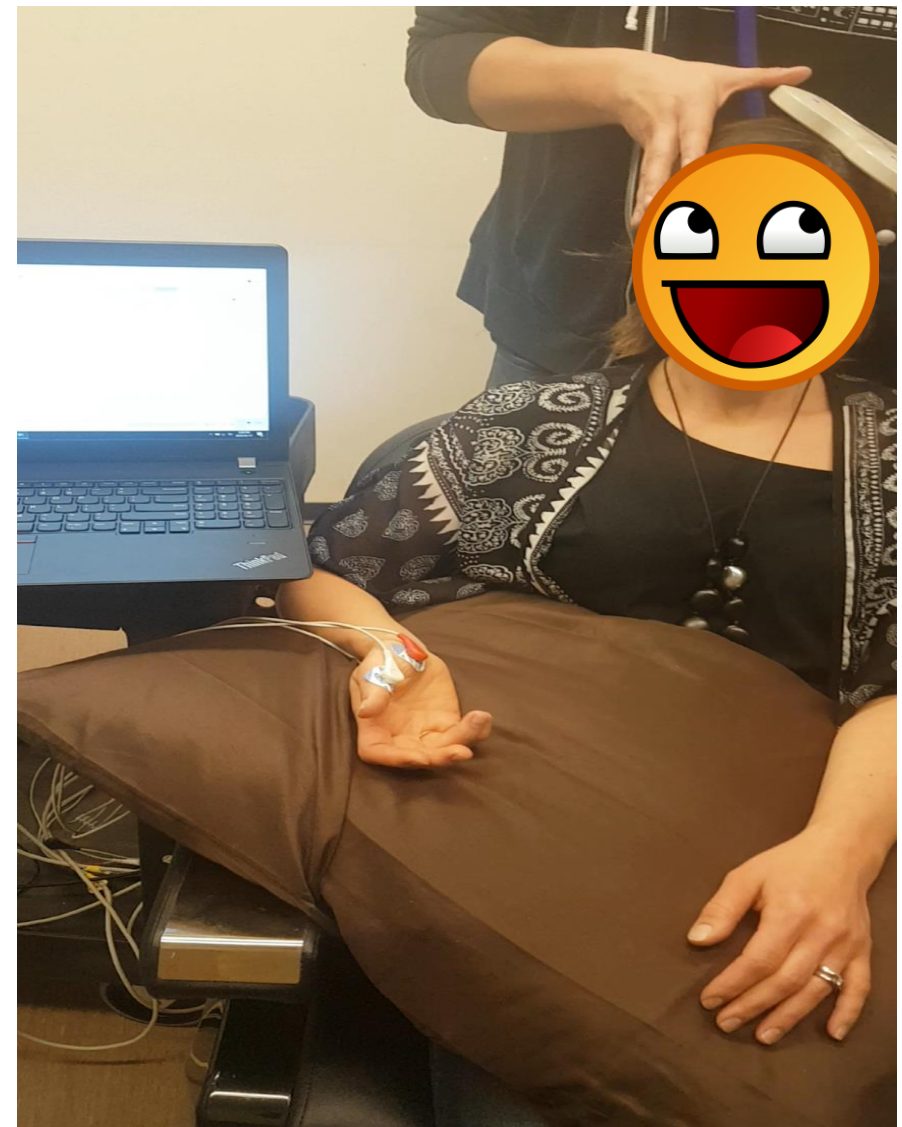
Aerobic Exercise:
↑ *Motor Learning*
↑ *Neuroplasticity*

Measuring neuroplasticity mechanisms

Transcranial magnetic stimulation (TMS)

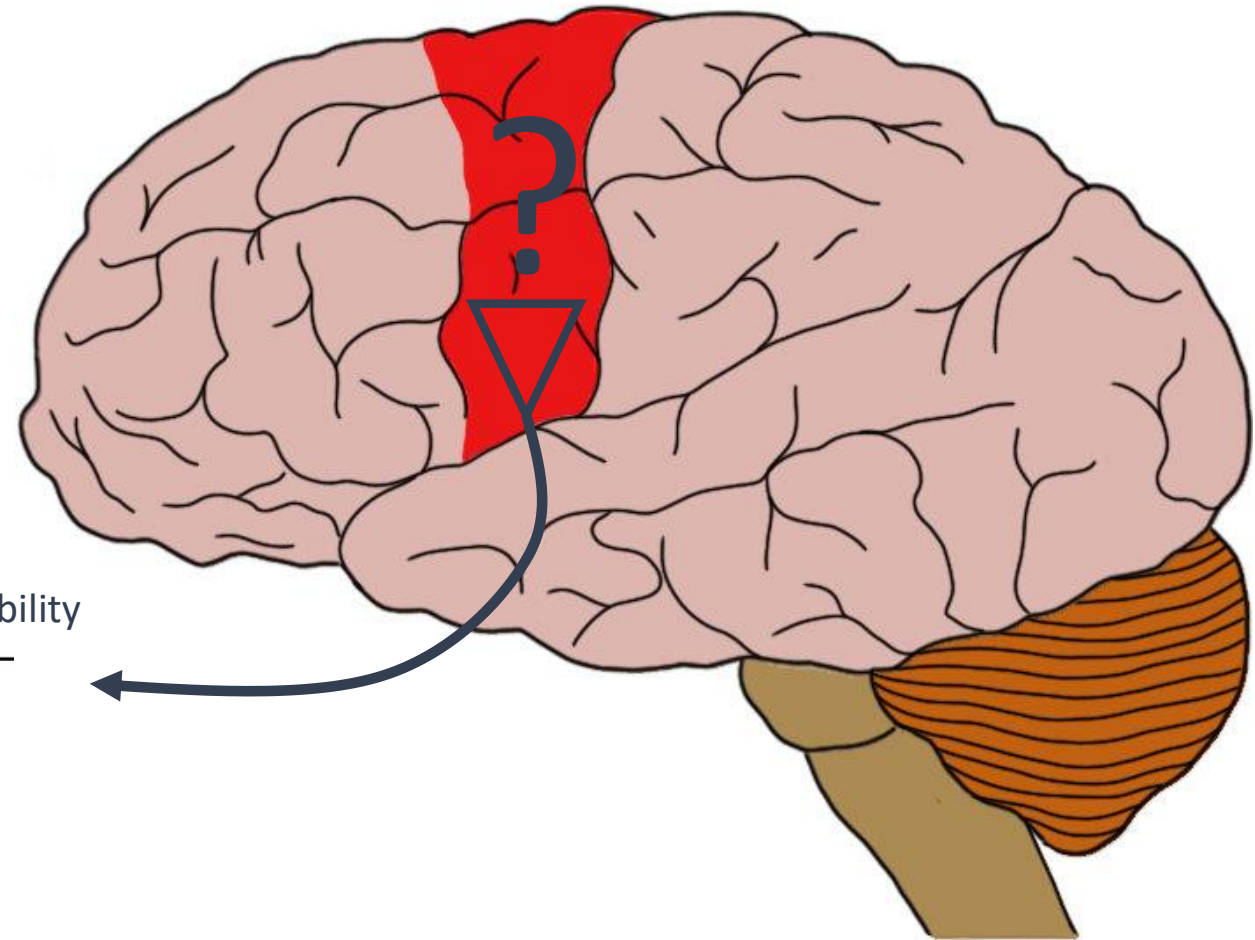
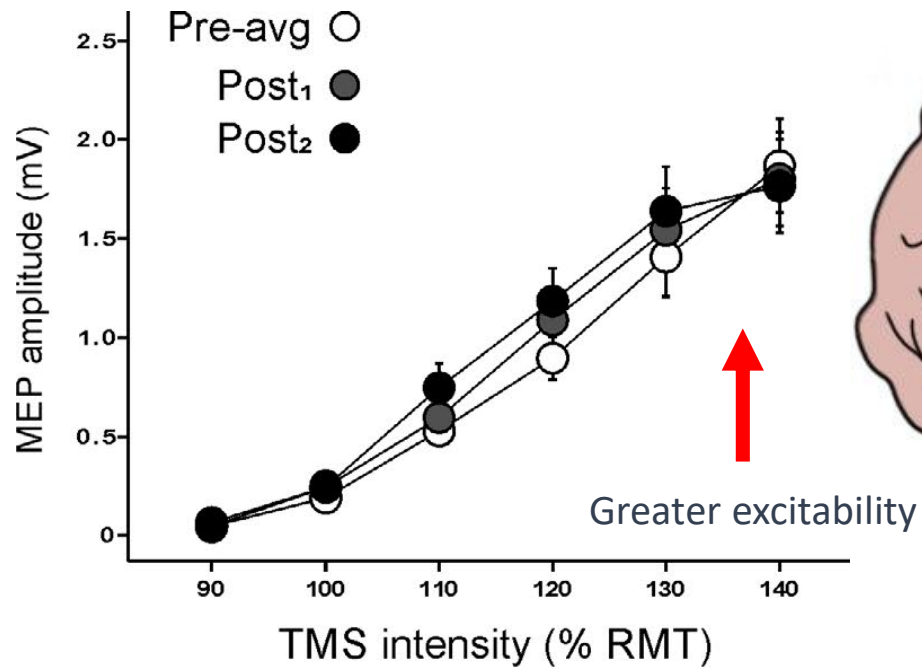
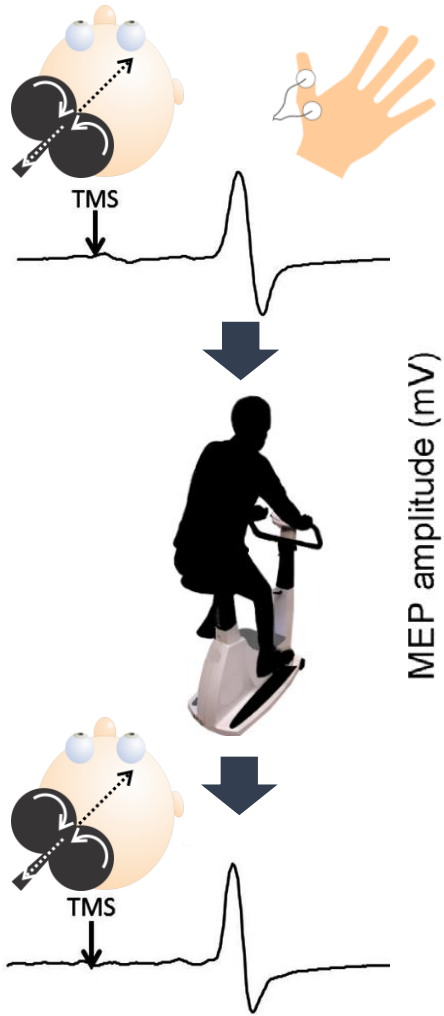


Surface electromyography (EMG)



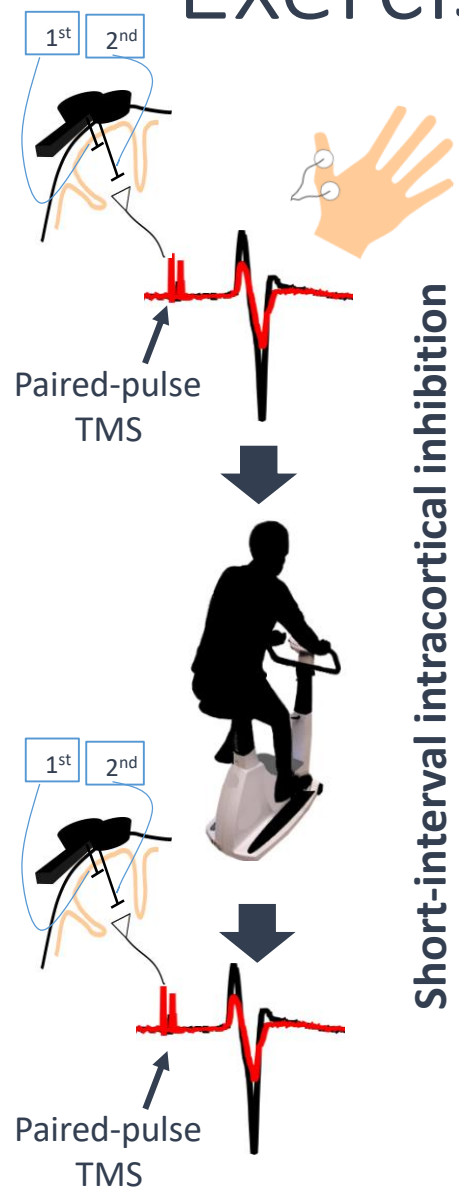
- TMS assesses brain excitability
- Biomarker of **neuroplasticity**

Corticospinal excitability does *not* change

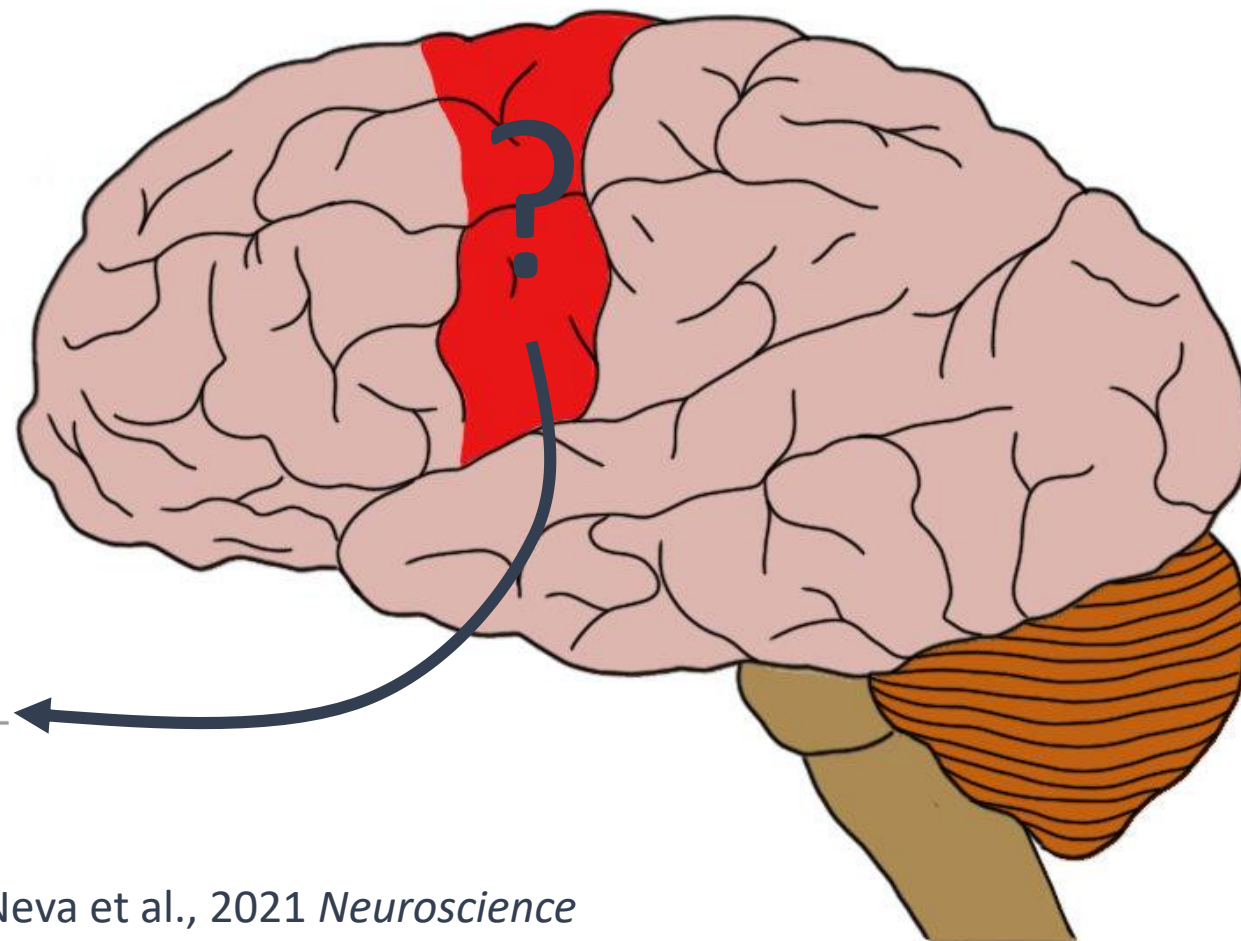
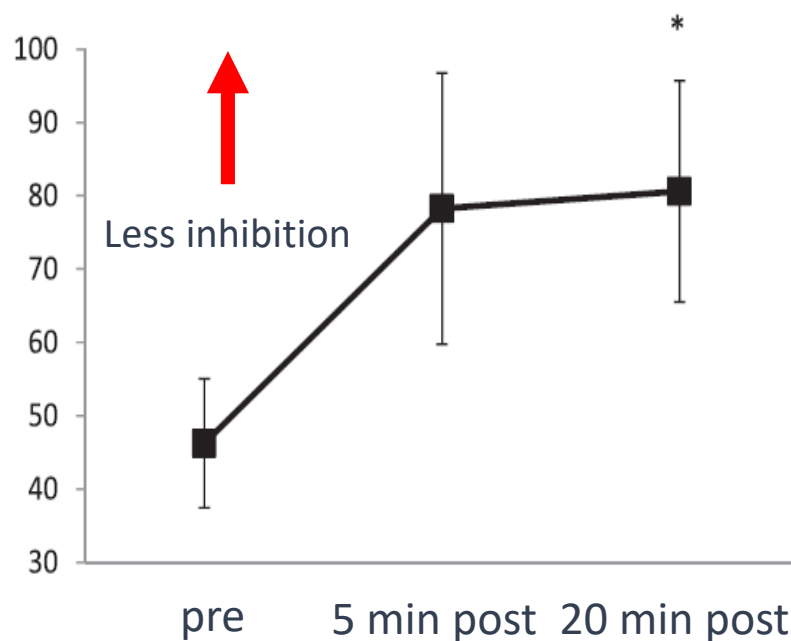




Exercise decreases motor cortex inhibition



Short-interval intracortical inhibition

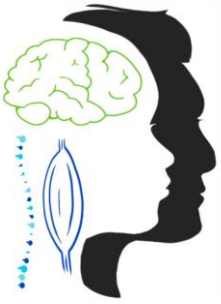


Neva et al., 2021 *Neuroscience*
Neva et al., 2017 *Eur J Neurosci*
Singh, Duncan, Neva et al., 2014 *BMC Sport Sci*

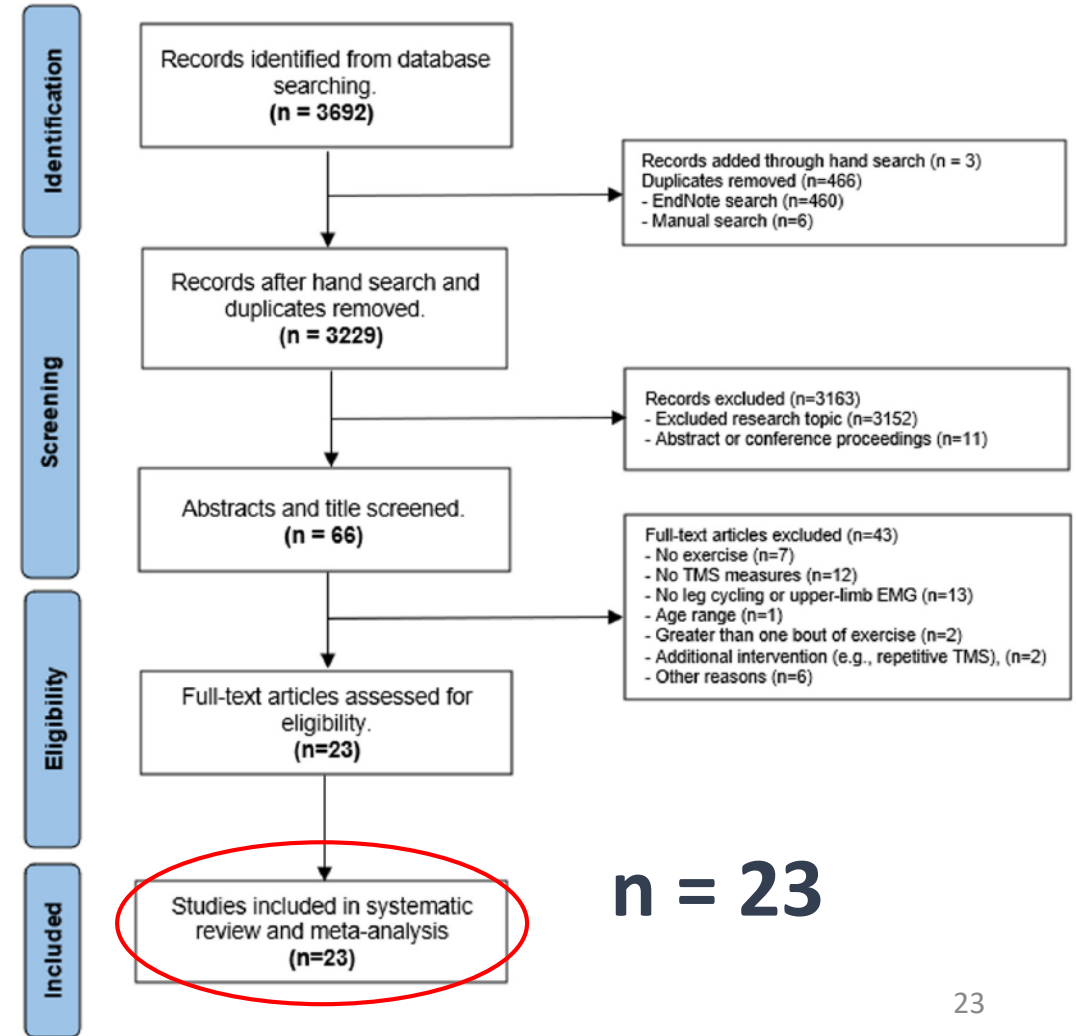
Exercise-induced neuroplasticity (TMS): A meta-analysis



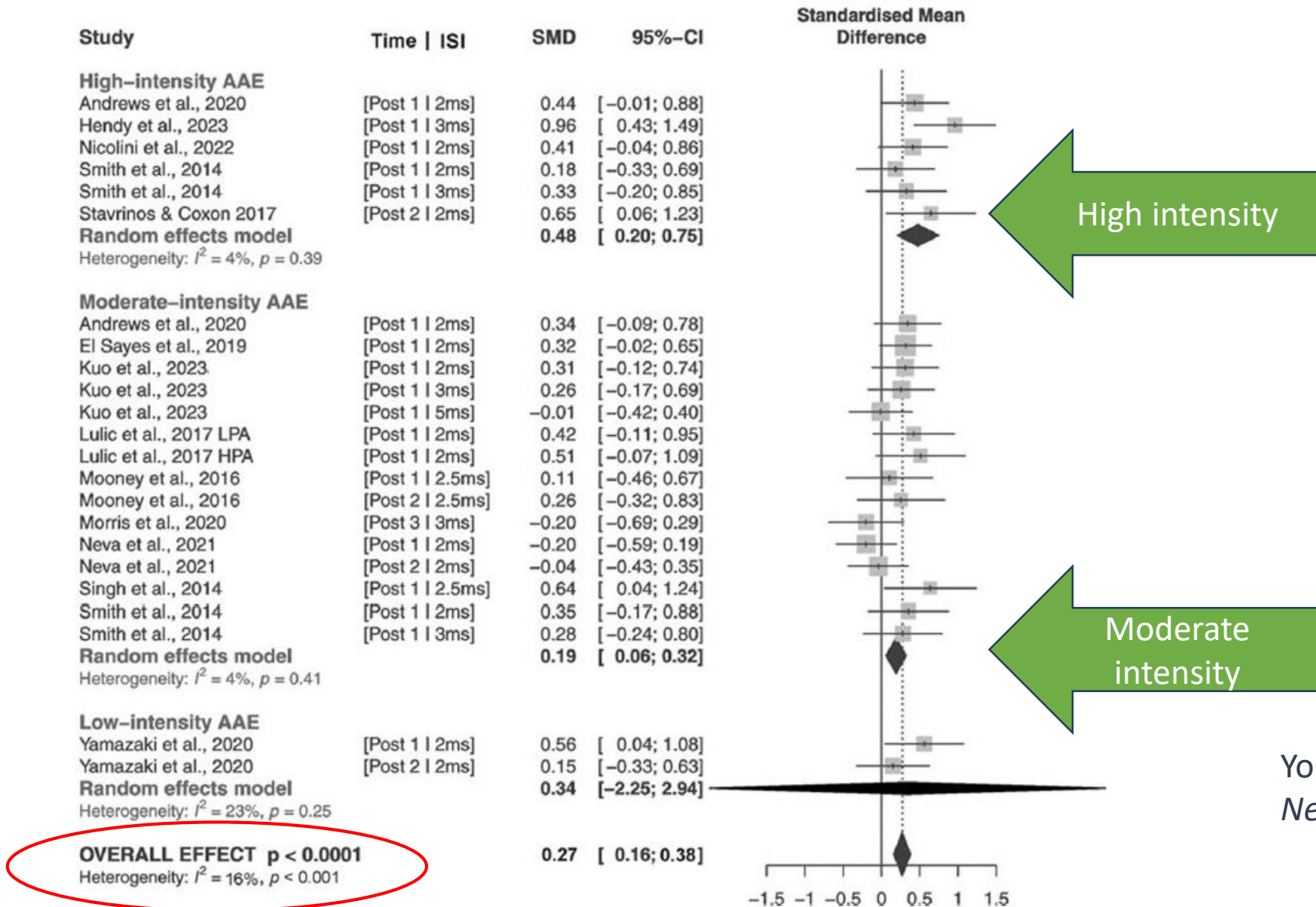
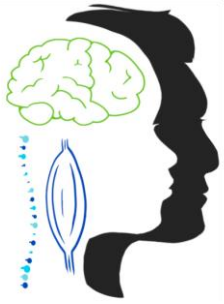
Layale Youssef, PhD candidate



1. What **TMS measure** is most **consistently** impacted by acute exercise?
2. What is the effect of **exercise intensity**?



↓ SICI (cortical inhibition) after exercise



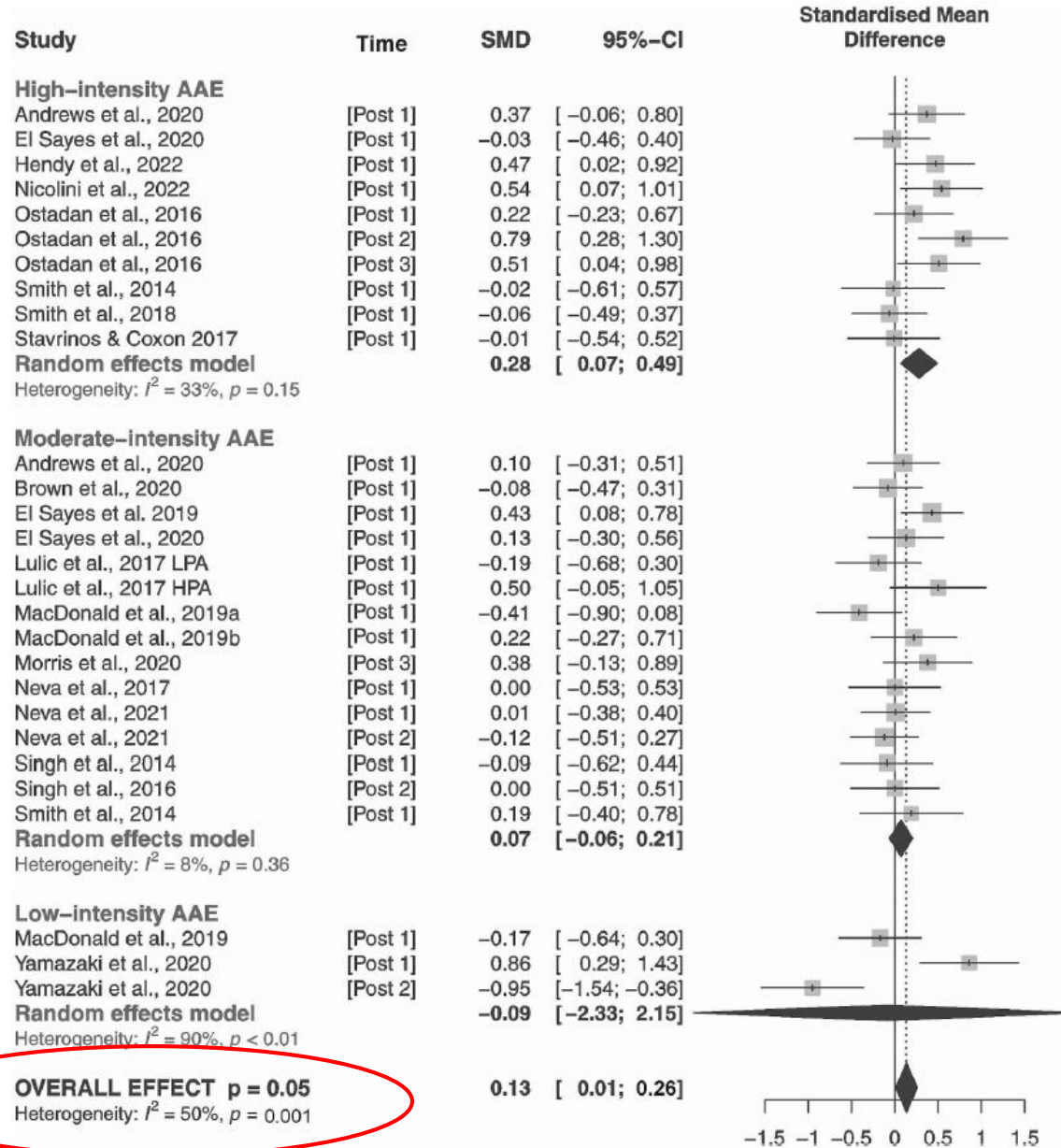
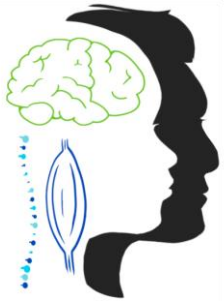
High intensity

Moderate intensity

Youssef et al., 2024
Neurosci Biobehav Rev

↓ inhibition after exercise →

↑ corticospinal excitability after high intensity



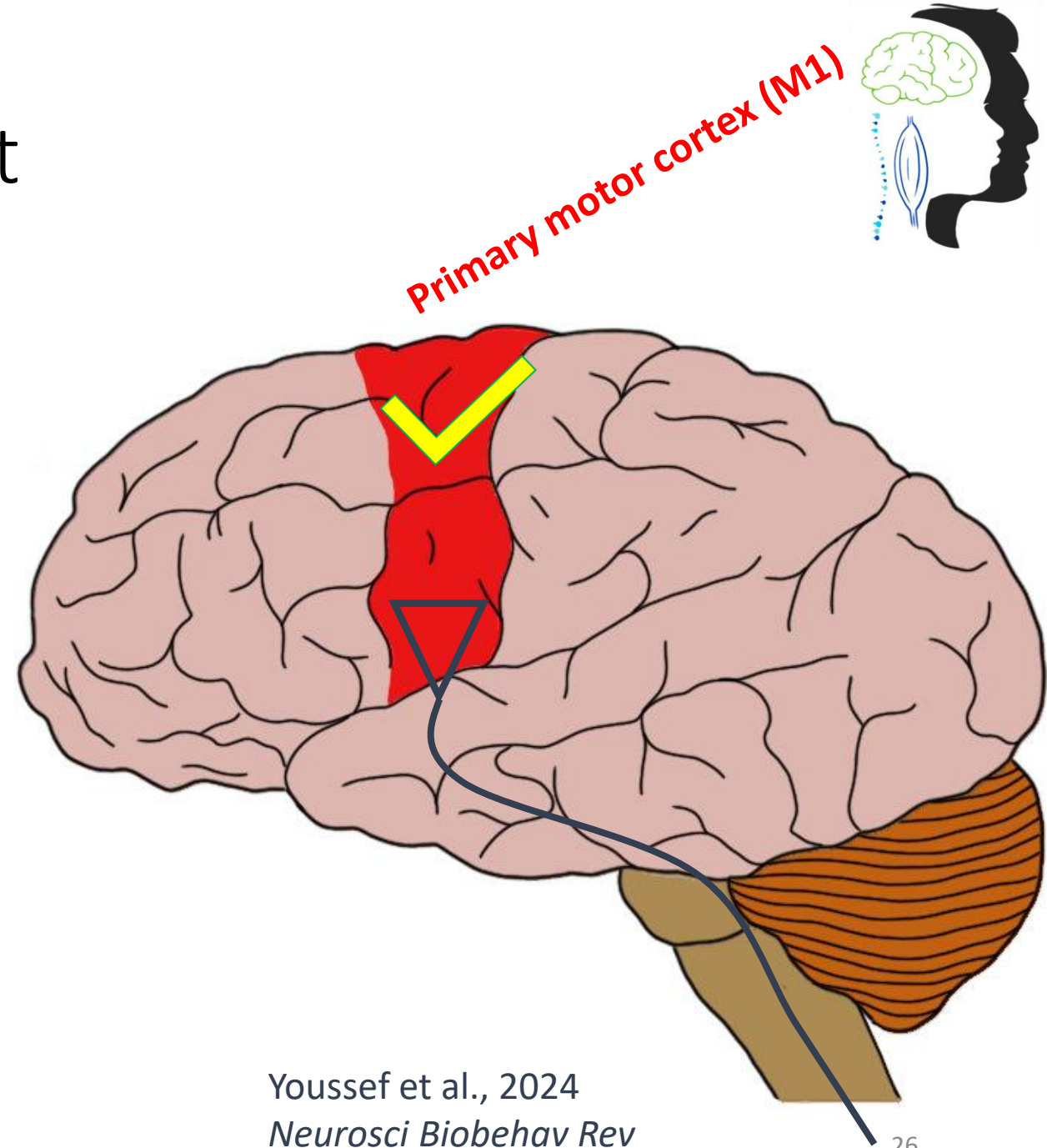
High intensity

Youssef et al., 2024
Neurosci Biobehav Rev

↑ excitability after exercise

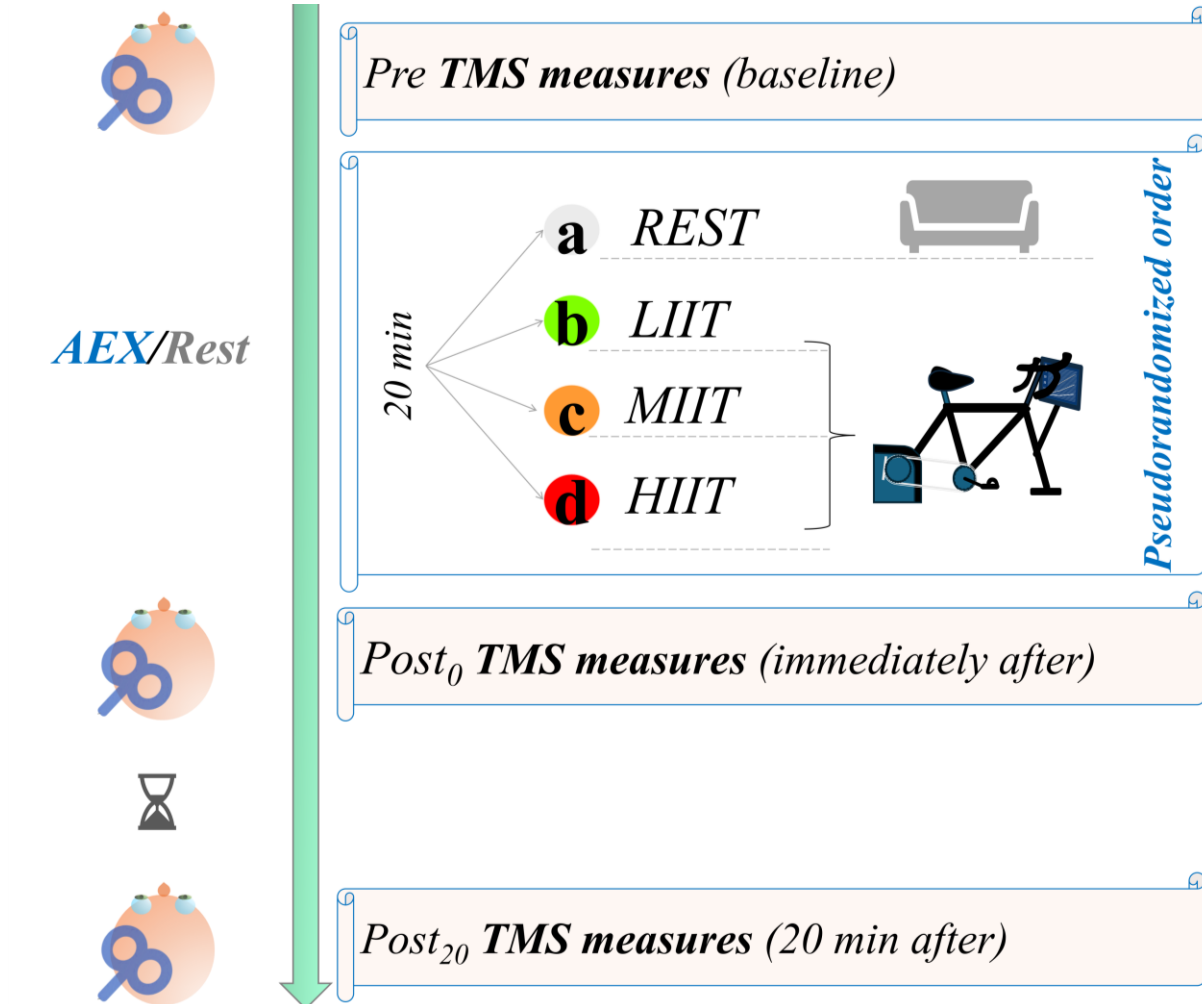
What is the most consistent TMS measure impacted by acute exercise?

- ↓ motor cortex inhibition (SICI) ✓
 - moderate-to-high intensity exercise drives the effect
- What is the effect of exercise intensity?
 - Is there a **dose-response** effect?



Is there a dose-response effect of acute exercise intensity?

Experimental design



Nesrine Harroum, PhD candidate

N = 30; young adults, within-subjects design

LIIT: Light-intensity interval training

MIIT: Moderate-intensity interval training

HIIT: High-intensity interval training

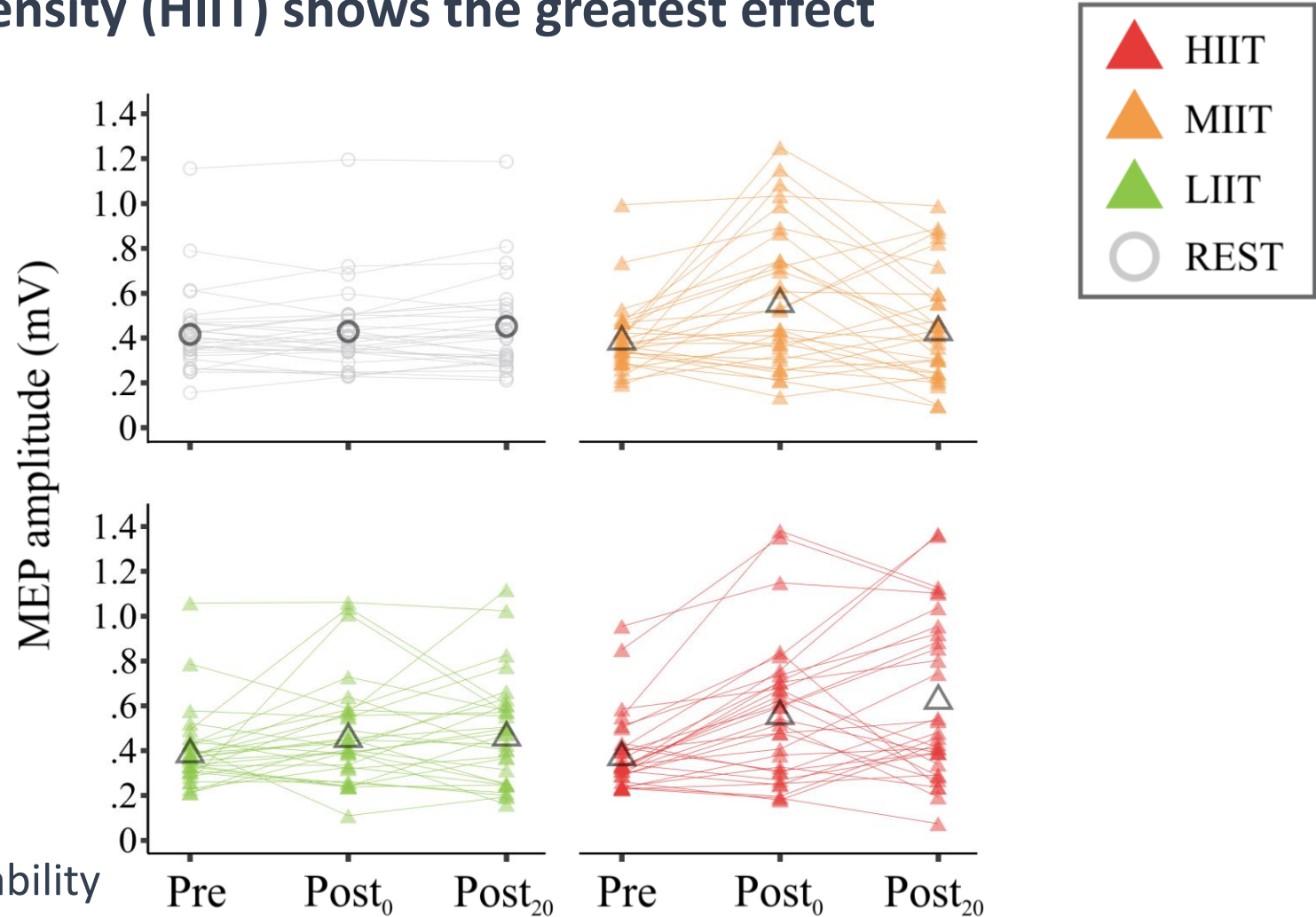
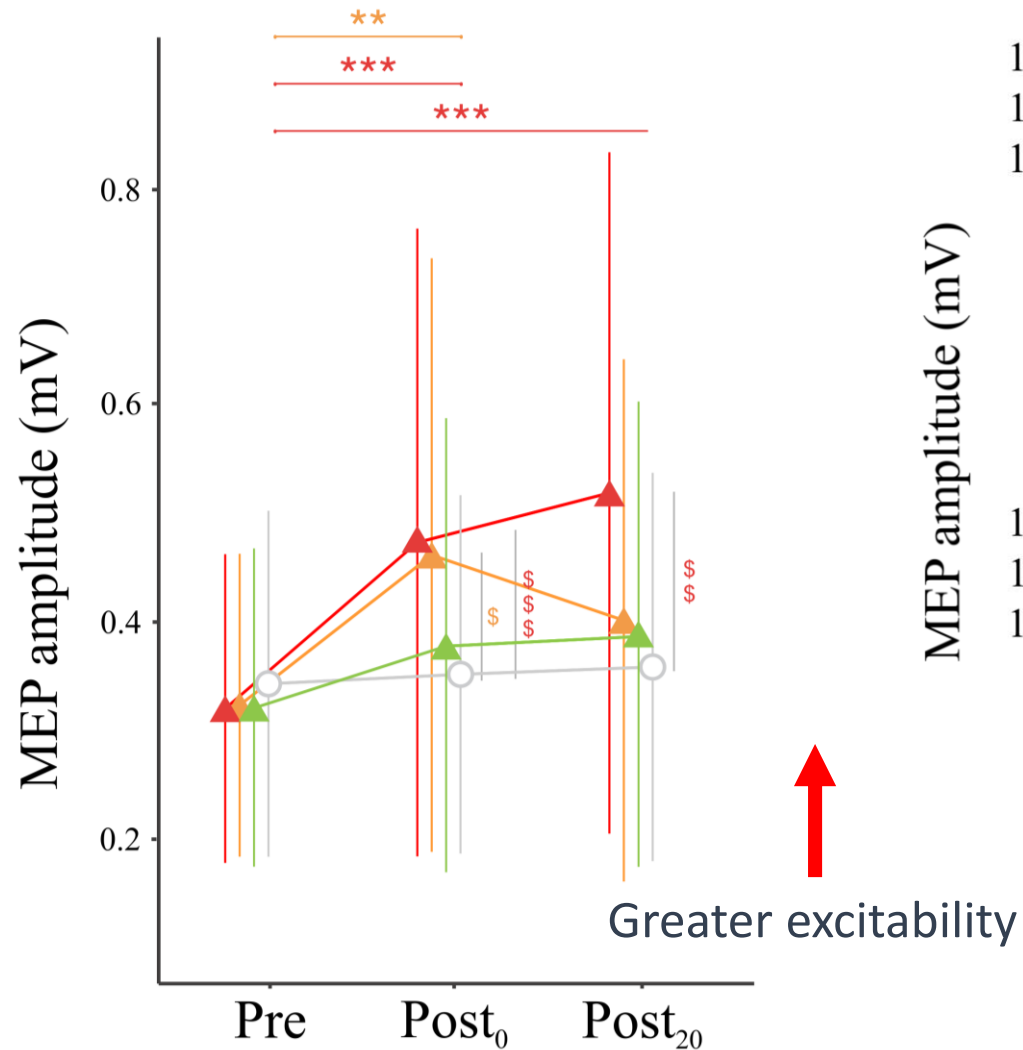
REST: seated rest

Harroum et al., 2025

Cerebral Cortex (revisions requested) 27

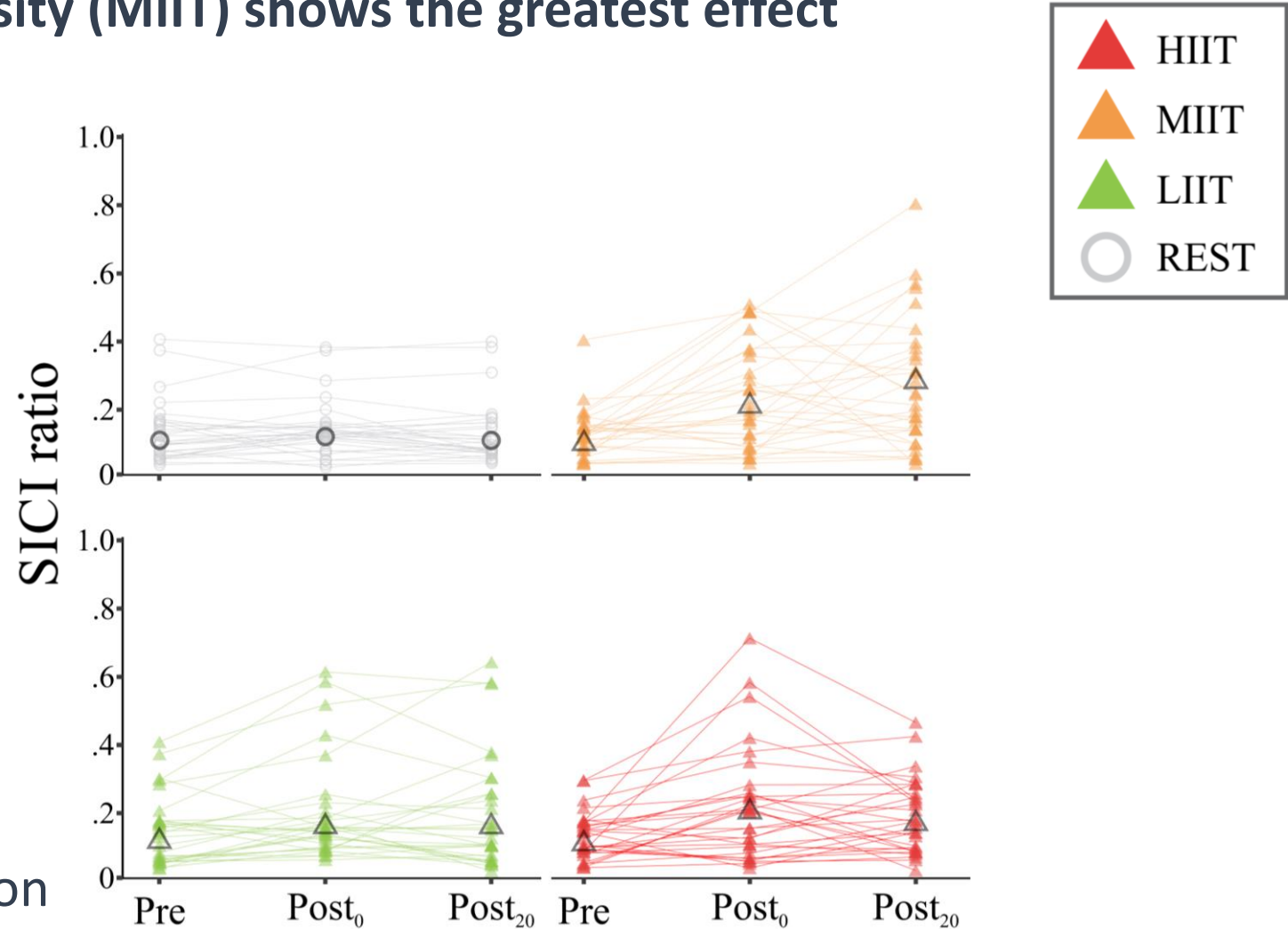
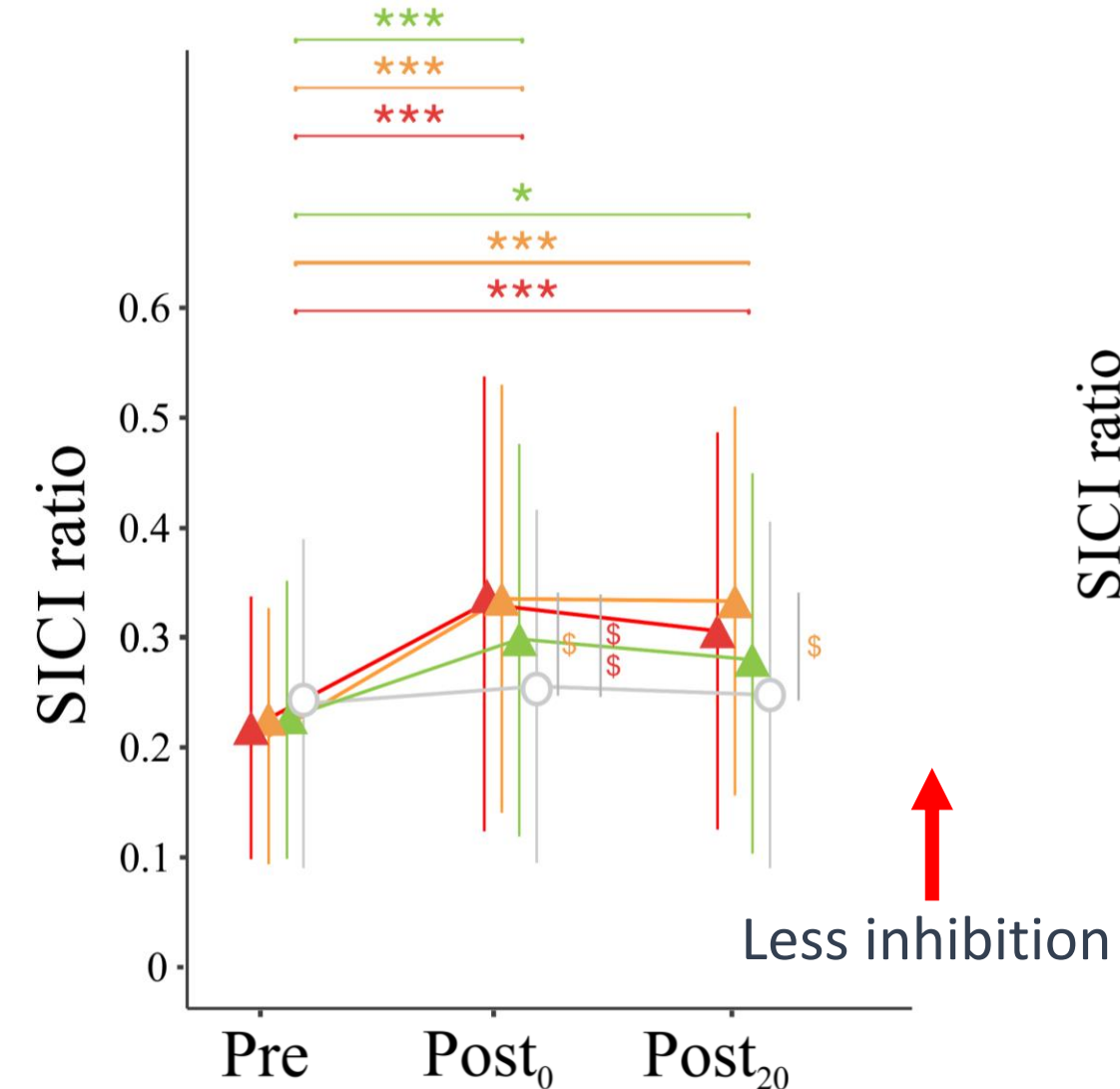
There is a dose-response effect of acute exercise intensity!

Corticospinal excitability → High intensity (HIIT) shows the greatest effect



There is a dose-response effect of acute exercise intensity!

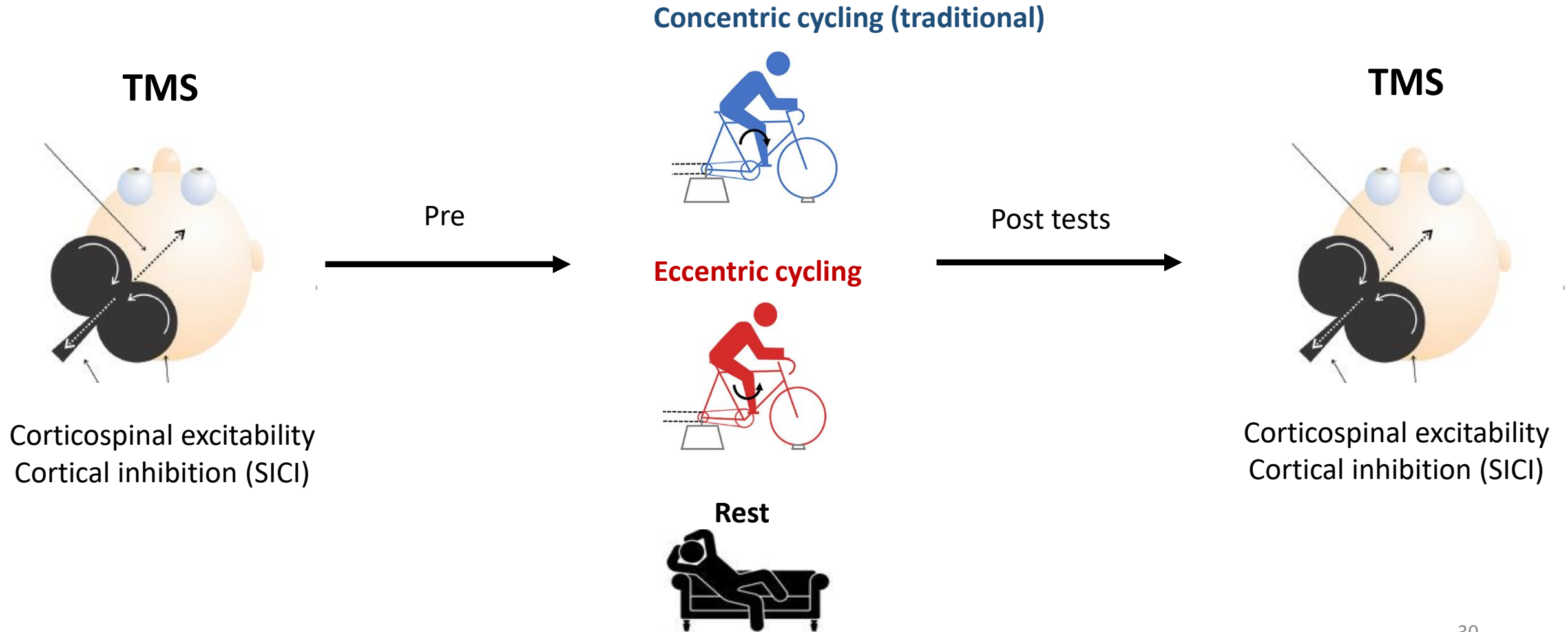
Cortical inhibition → Moderate intensity (MIIT) shows the greatest effect



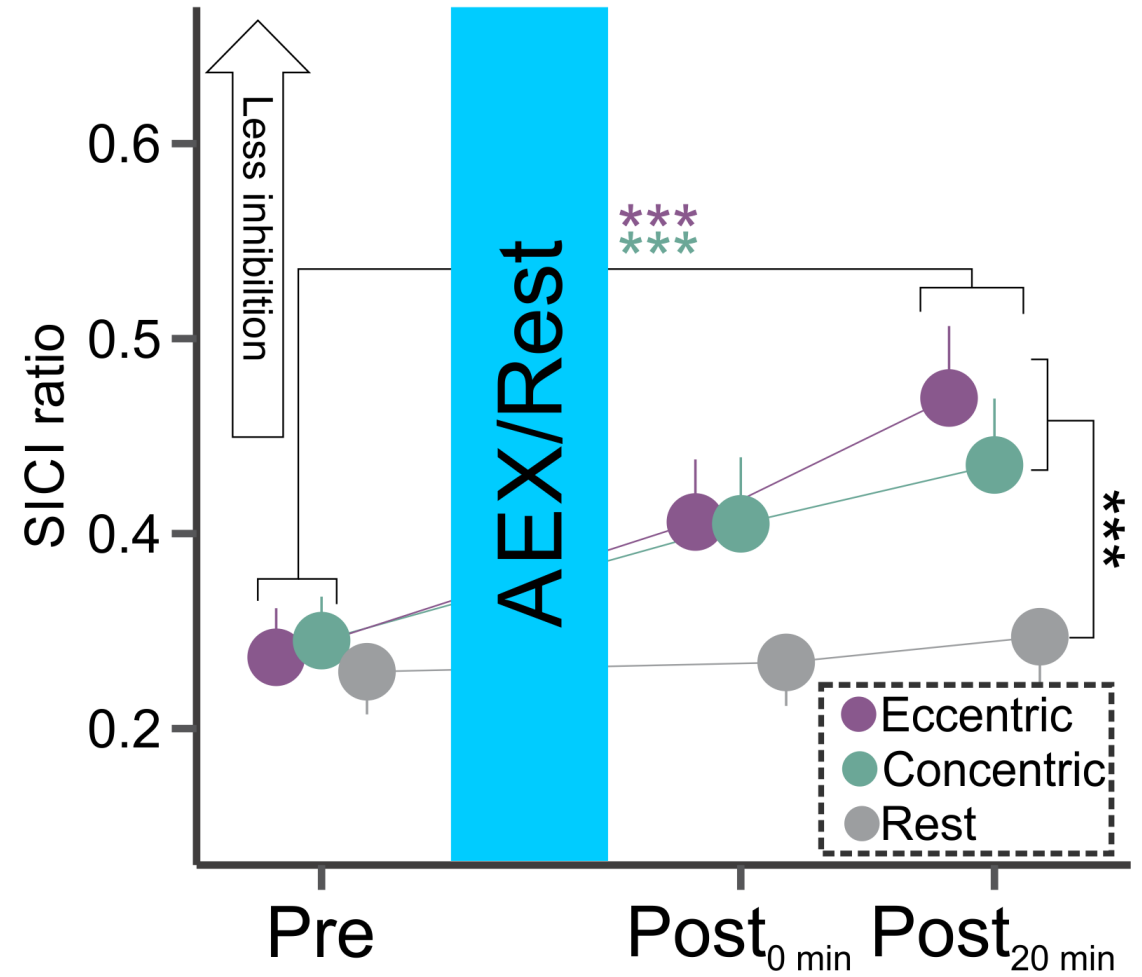
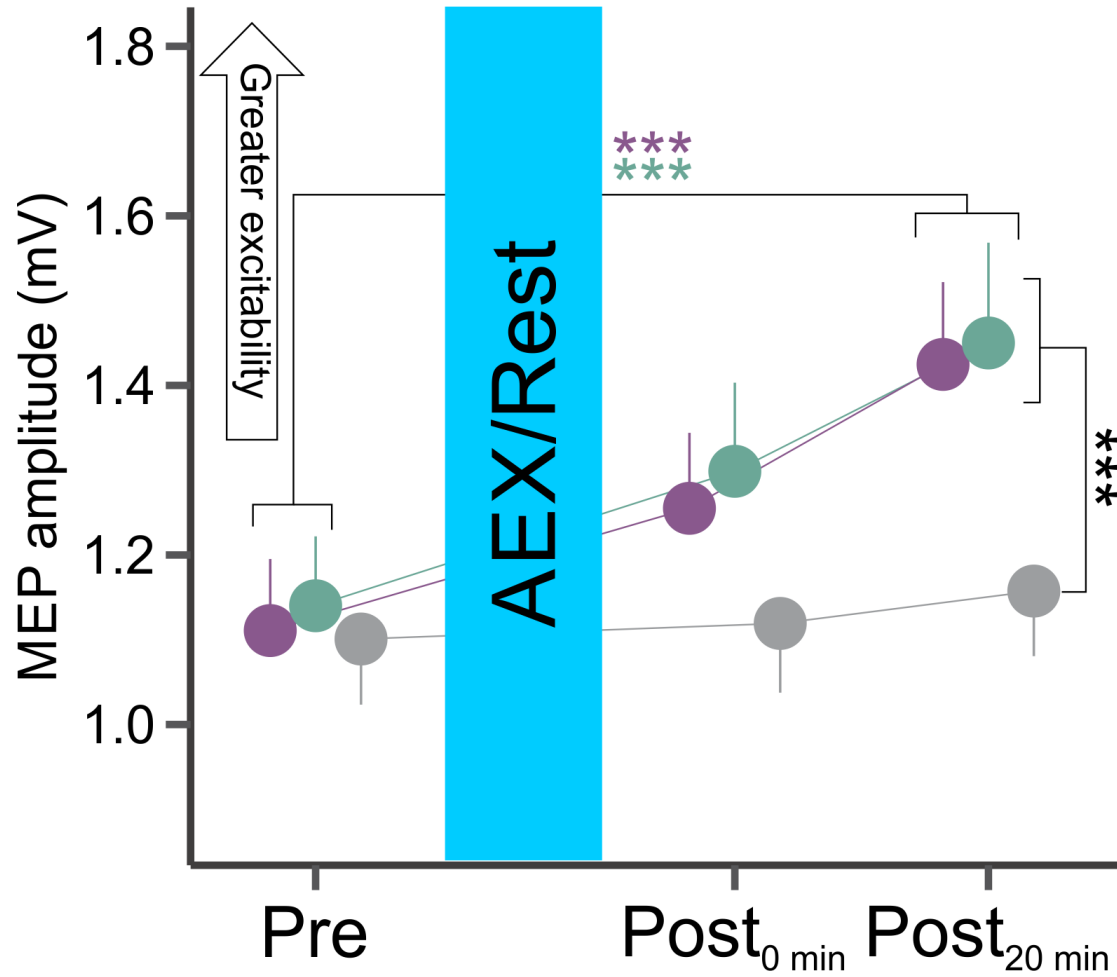
Is there an effect of acute exercise type?



Layale Youssef, PhD student



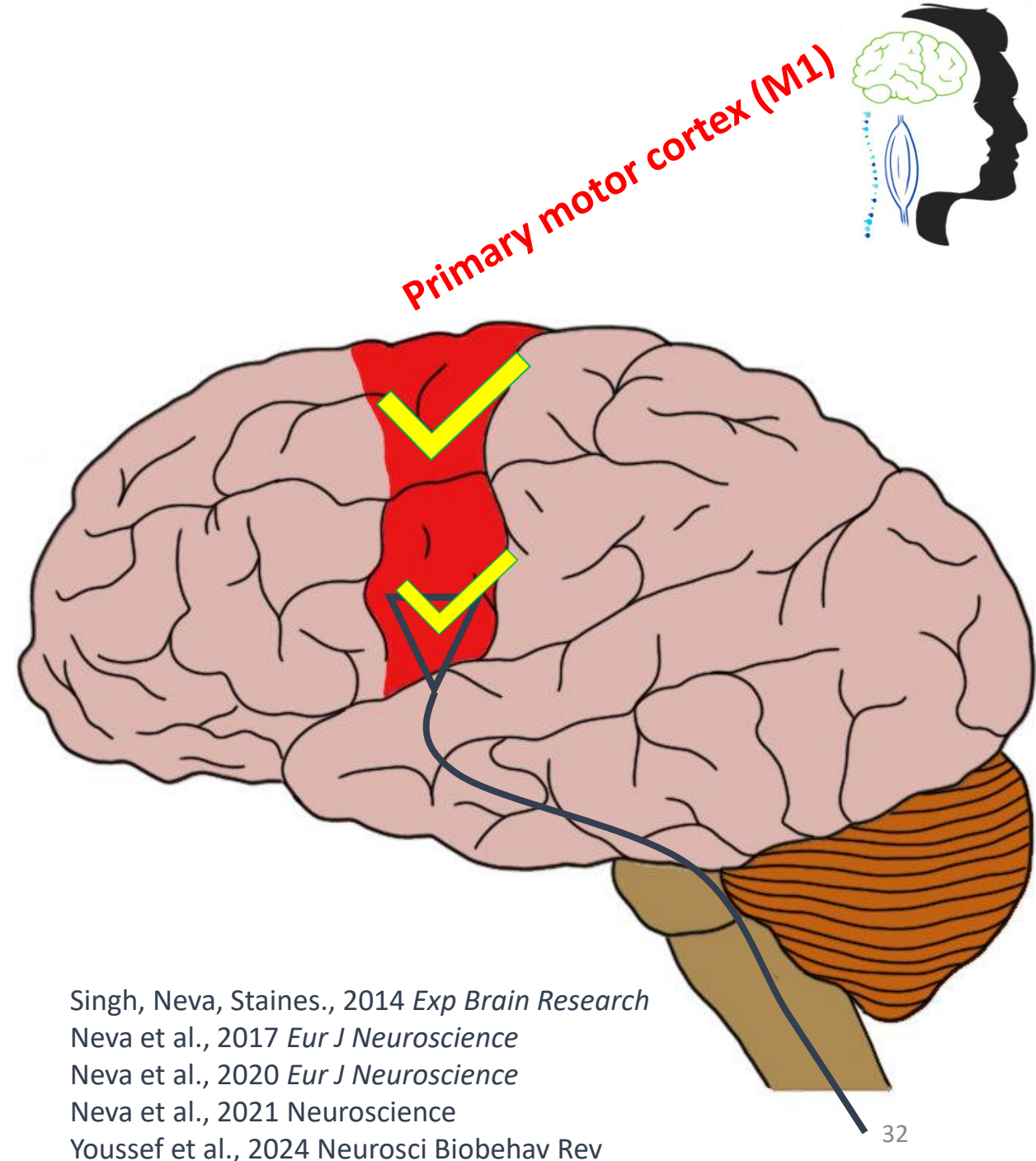
Same effect for Eccentric and Concentric Exercise



*Eccentric exercise ↑ M1 excitability and ↓ inhibition like concentric (traditional) exercise!

How does exercise impact the brain?

- ↓ motor cortex inhibition ✓
- ↑ motor cortex output excitability ✓
 - rapid neuroplasticity
 - early motor learning stages
 - recovery of function after stroke
- Important factors:
 - Aerobic exercise intensity
 - Aerobic exercise type





1

Aerobic Exercise:
↑ *Motor Learning*
↑ *Neuroplasticity*

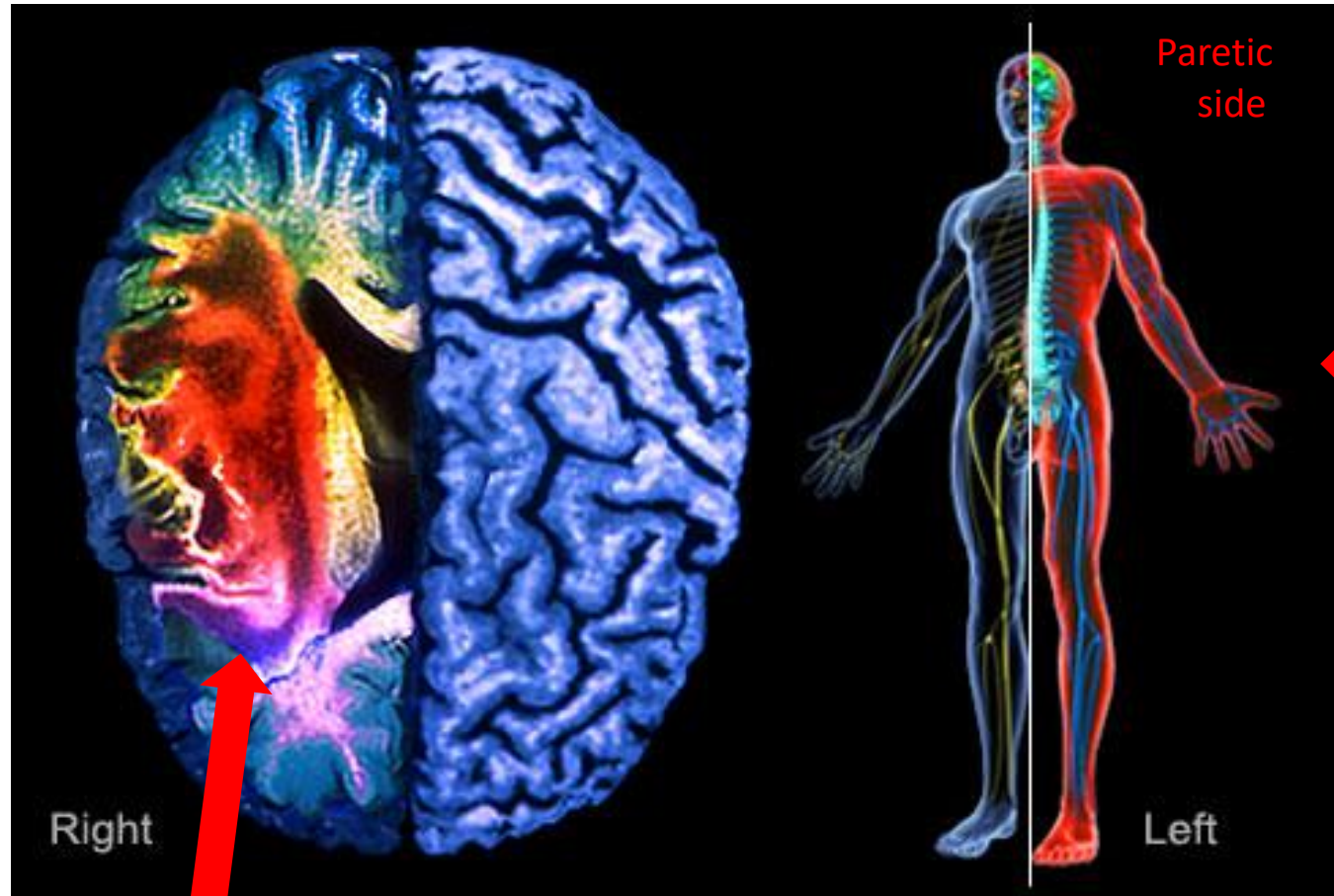
2

TMS:
Measure & Modulate
the Brain

Motor impairment after stroke

Stroke (“brain attack”)

- Loss of blood & oxygen to the brain
- Brain tissue damage



Stroke affected
region

~85% of Canadians live with persistent impairments
into the chronic stage (< 1 year) post-stroke

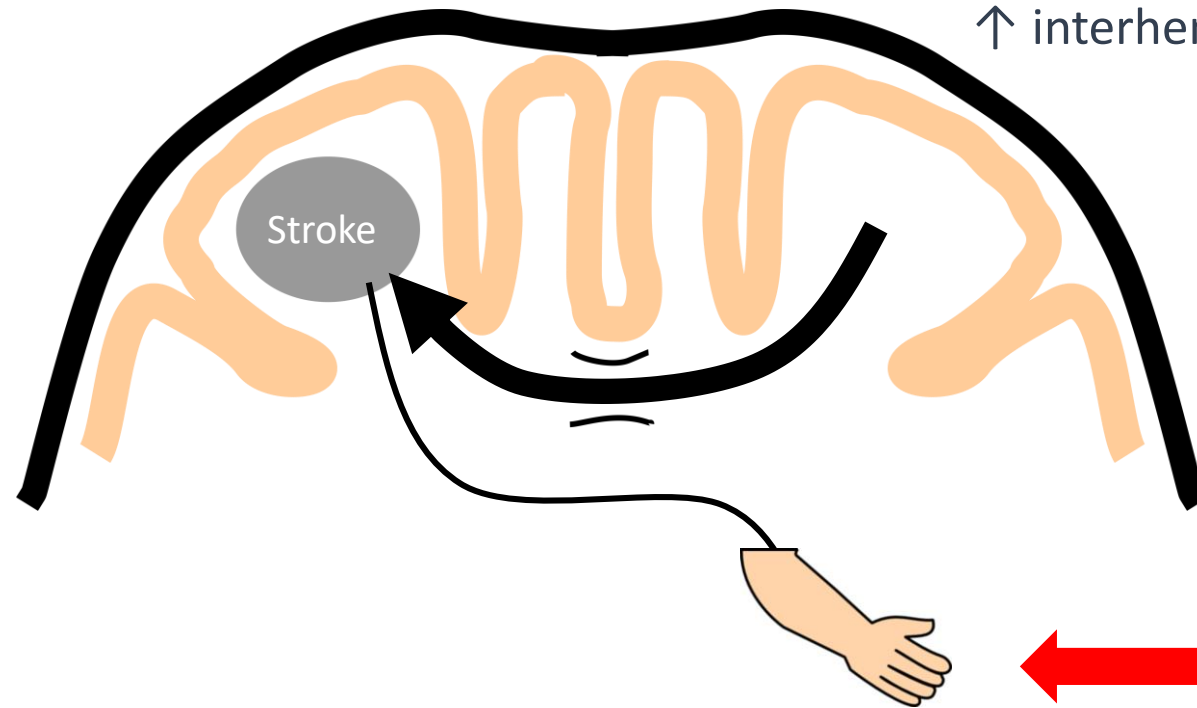
The interhemispheric competition model

↓ motor function on opposite/contralesional side

↓ cortical activity

↑ cortical activity

↑ interhemispheric inhibition

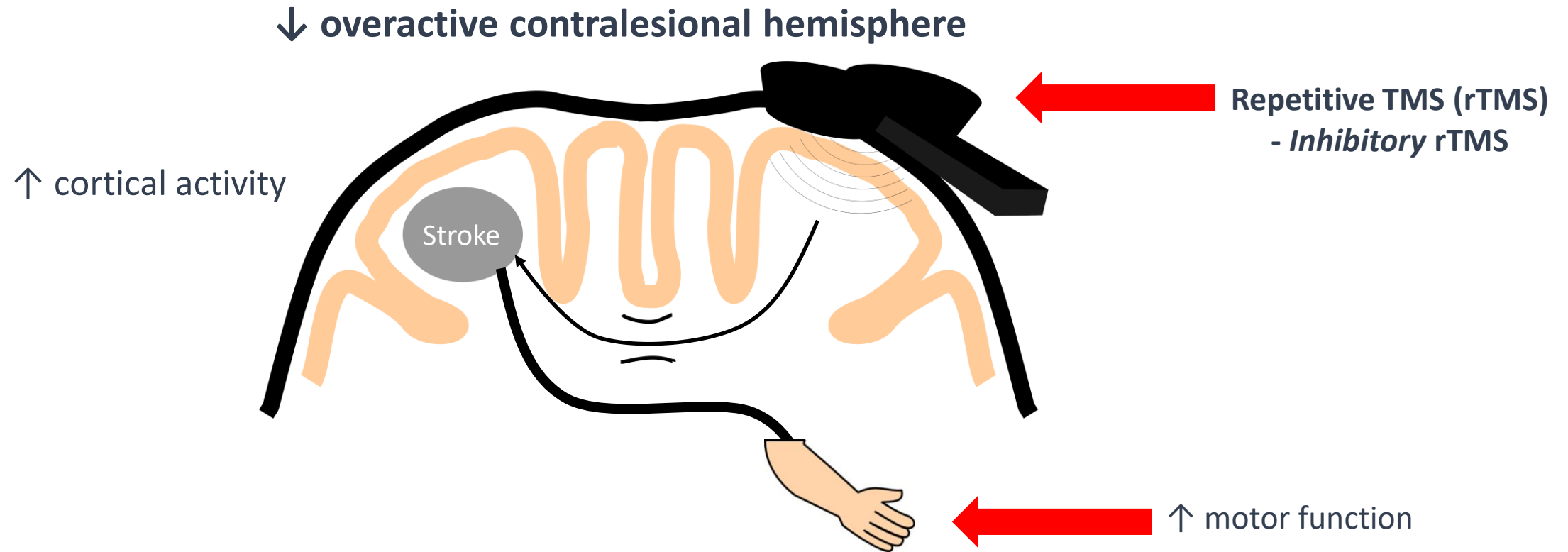


Neva et al., 2019 *Restorative Neurol & Neurosci*

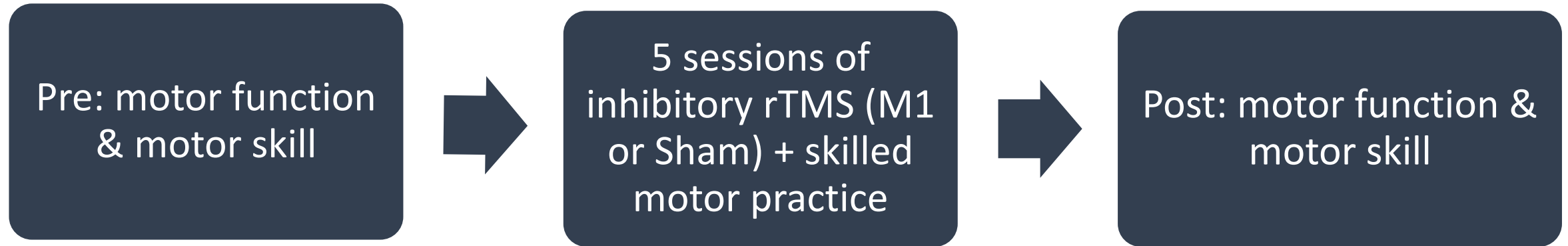
Auriat, Neva et al., 2016 *Front Neurology*

Neva et al., 2020 *The Wiley Encyclopedia of Health Psychology, Volume III*

Counteracting interhemispheric competition

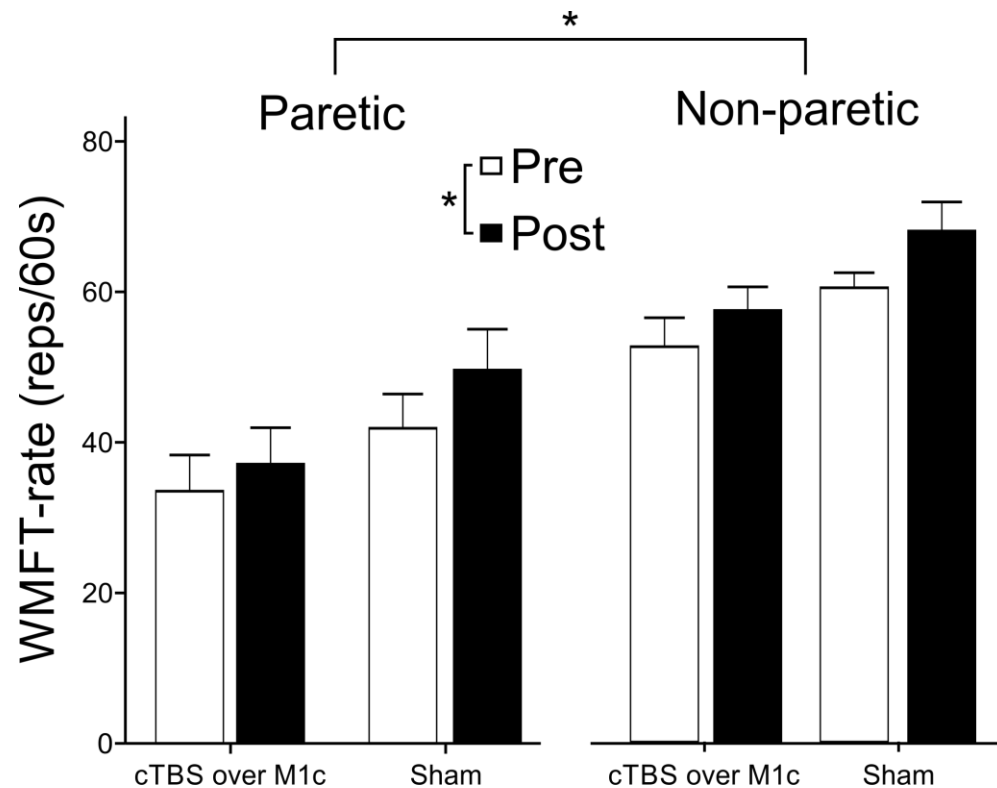


Pairing rTMS to contralesional motor cortex with paretic motor practice

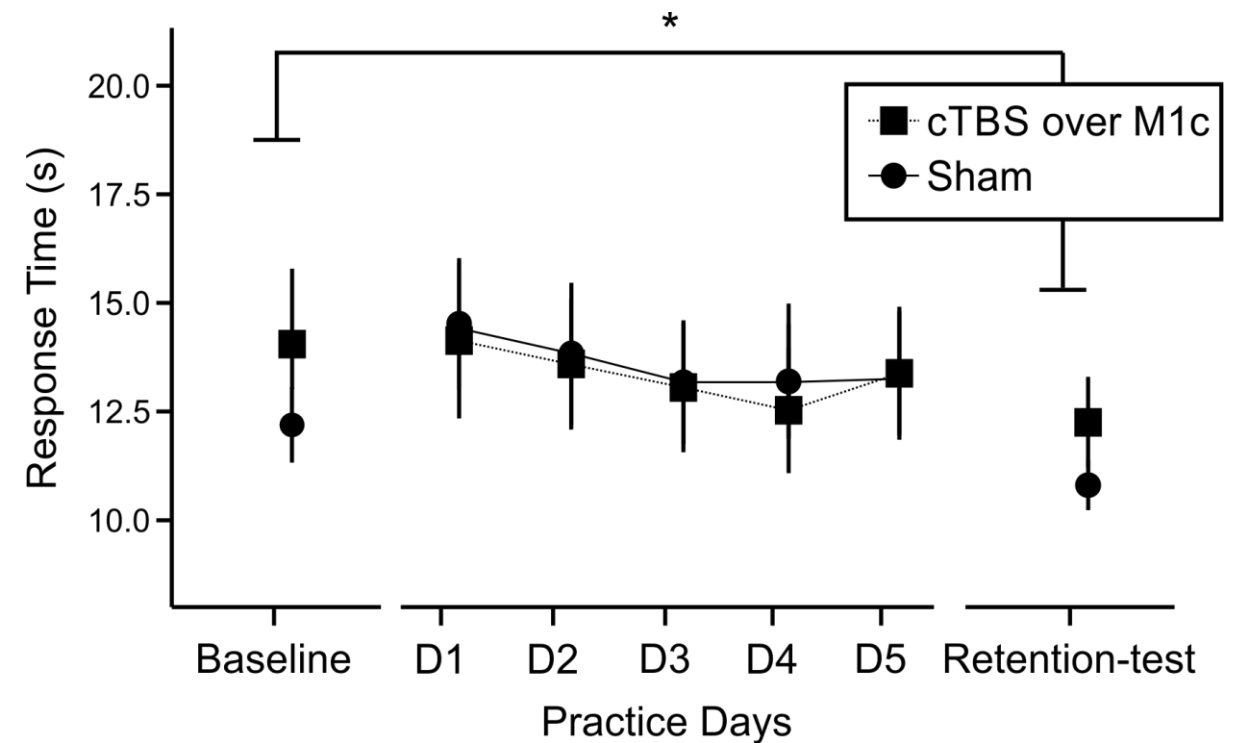


Inhibitory rTMS to contralesional **motor cortex** showed *no improvement*

No additional ↑ to motor function



No additional ↑ to motor learning



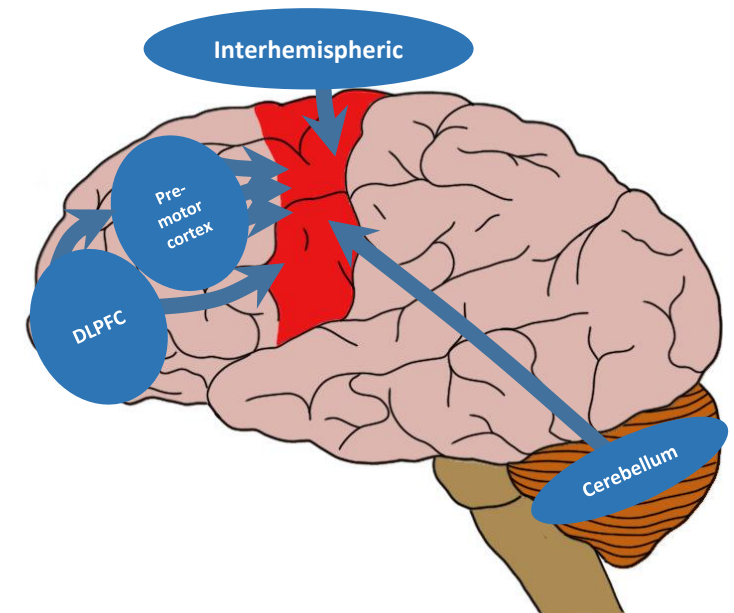
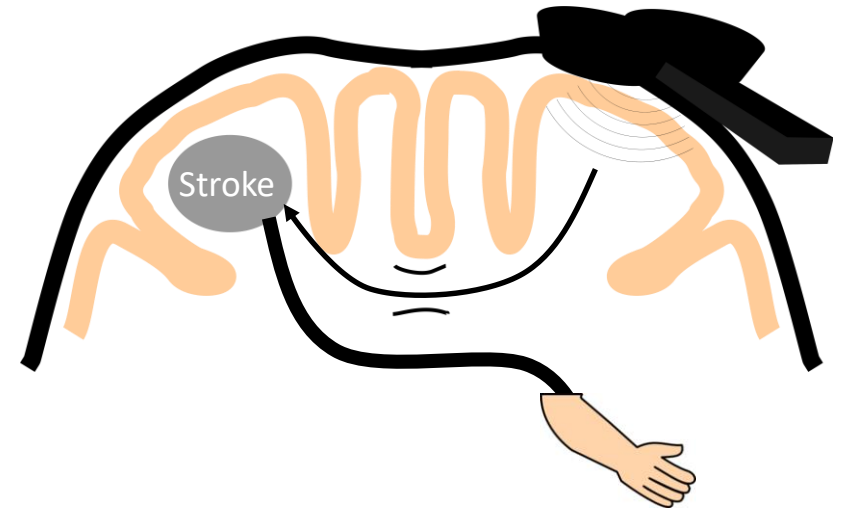
Contralesional *motor* cortex suppression: *may not be the best solution...*

- Meta-analysis shows minimal effect of repetitive transcranial magnetic stimulation over the motor cortex

(Hsu et al., 2012 *Stroke*)

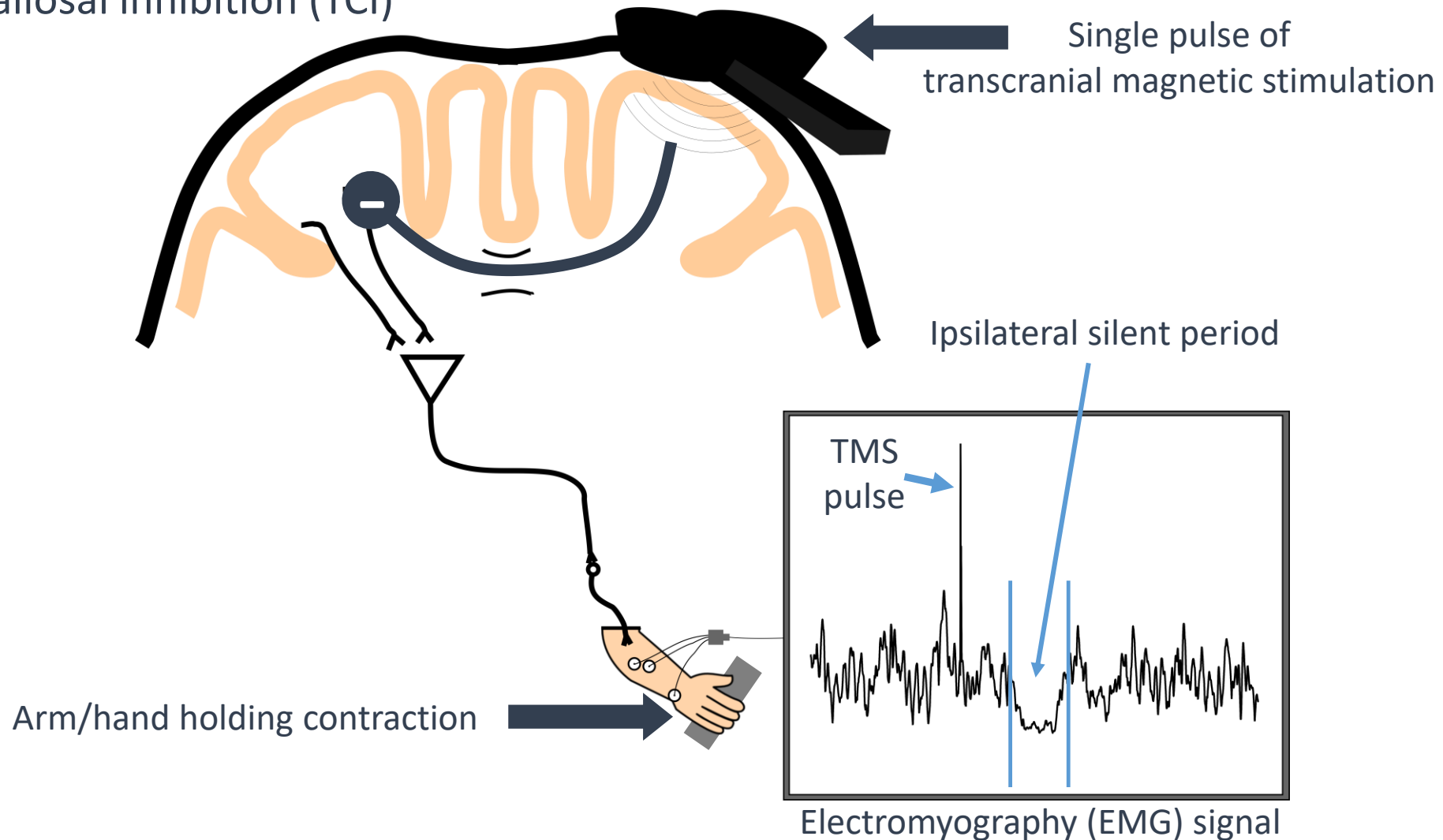
- **Executive function, planning & sensory feedback** cortical regions compensate for stroke-related damage to motor cortex

(Neva et al., 2019 *Wiley Encyclopedia of Health Psychology, Vol III*)

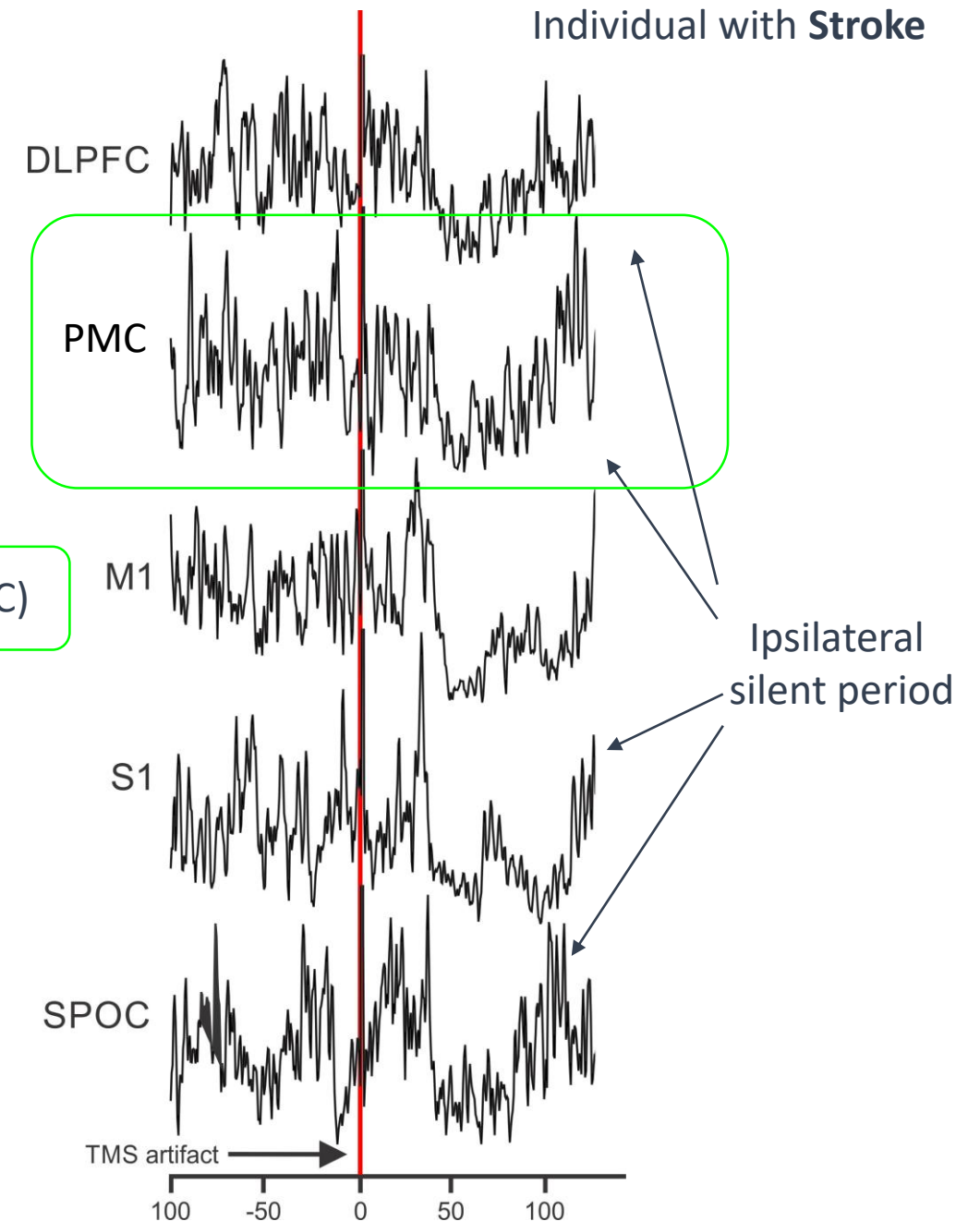
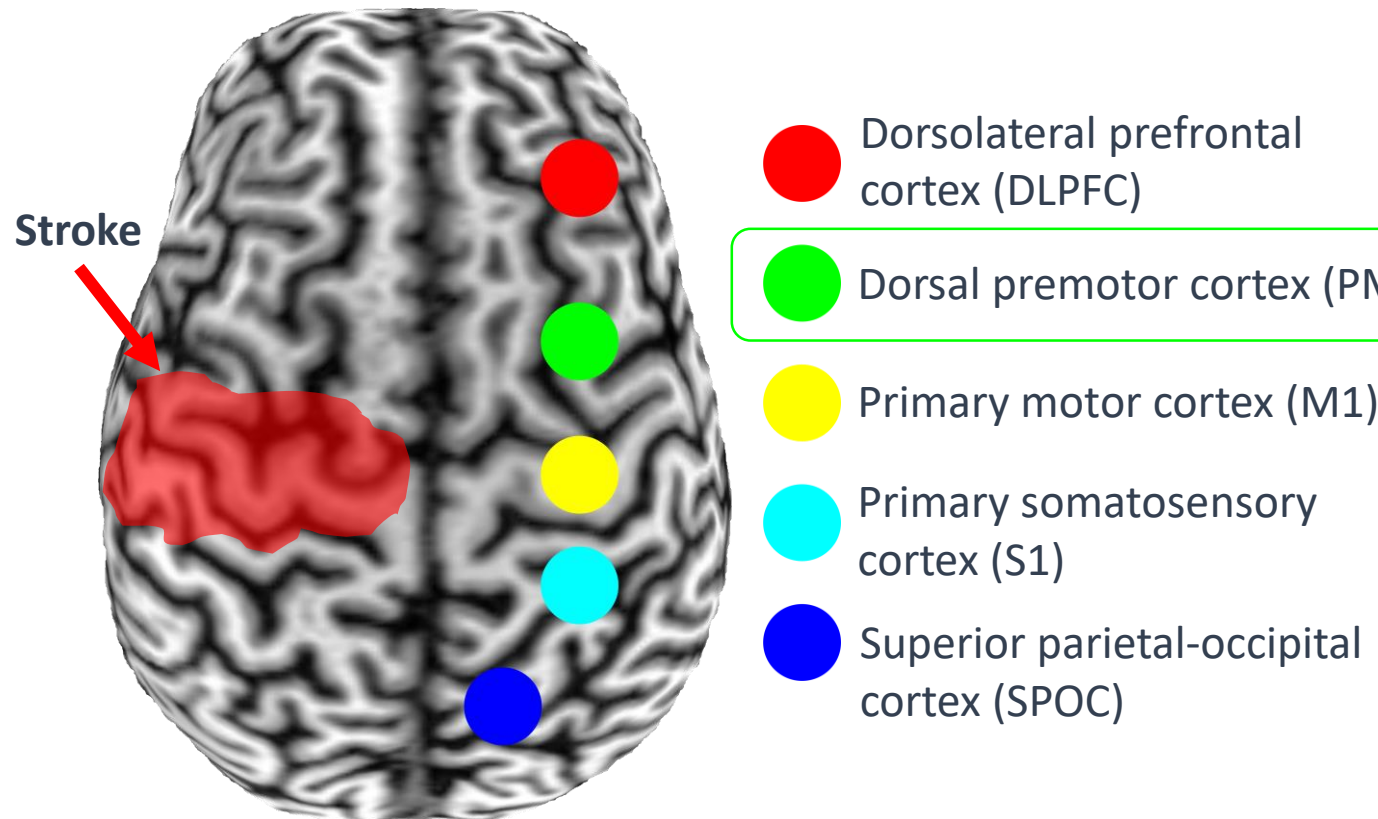


Measuring interhemispheric connectivity

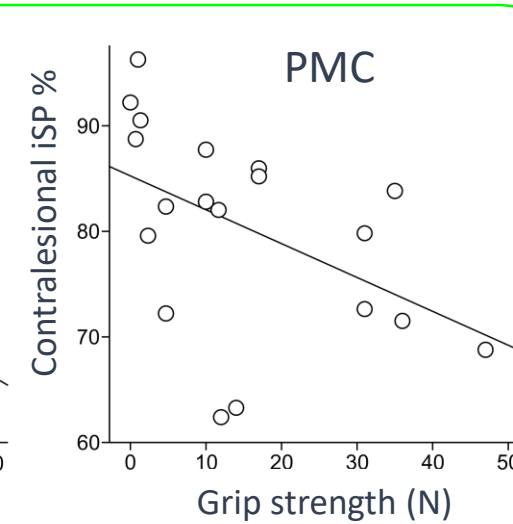
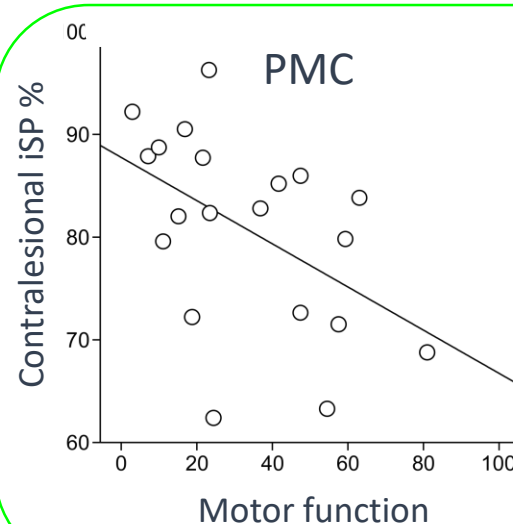
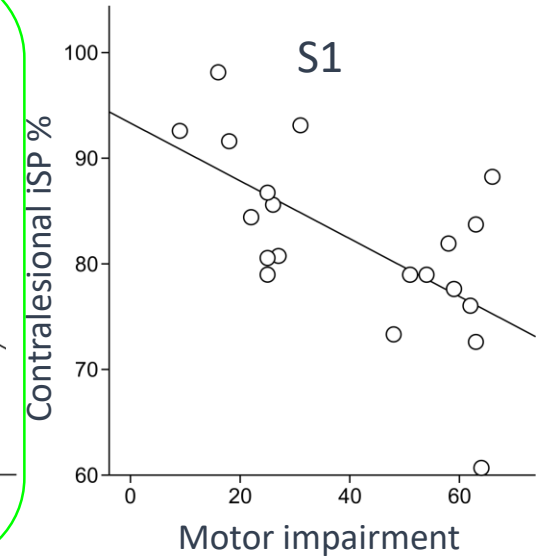
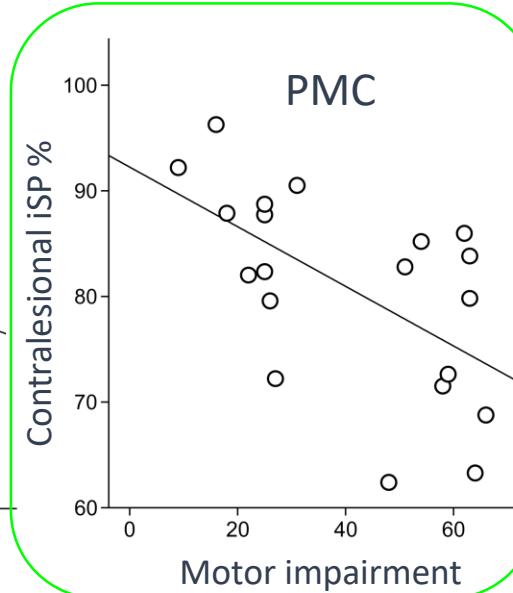
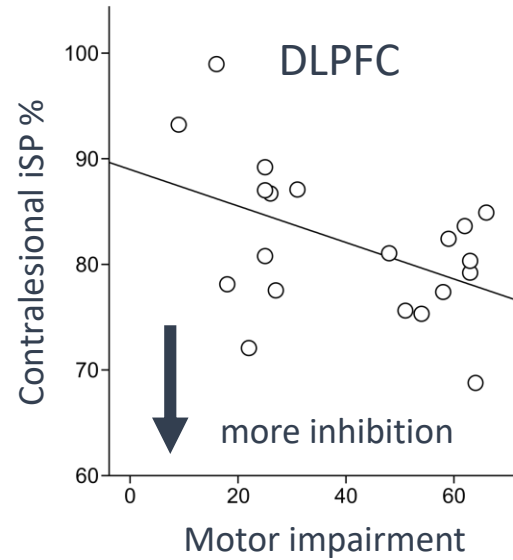
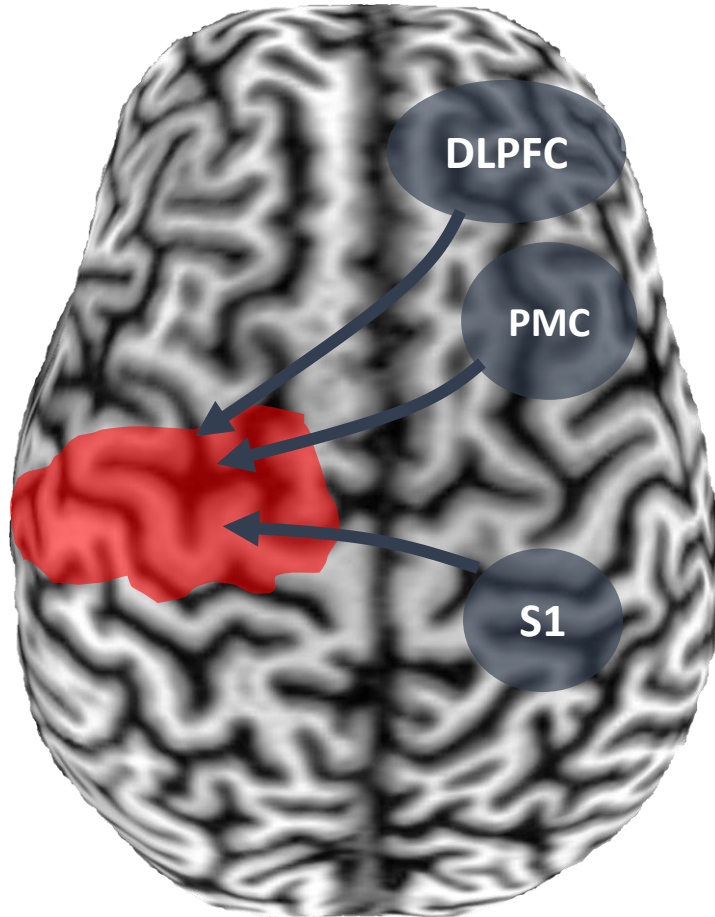
Transcallosal inhibition (TCI)



Transcallosal inhibition elicited from frontal & parietal cortical regions



Frontal & parietal interhemispheric communication is associated with post-stroke function



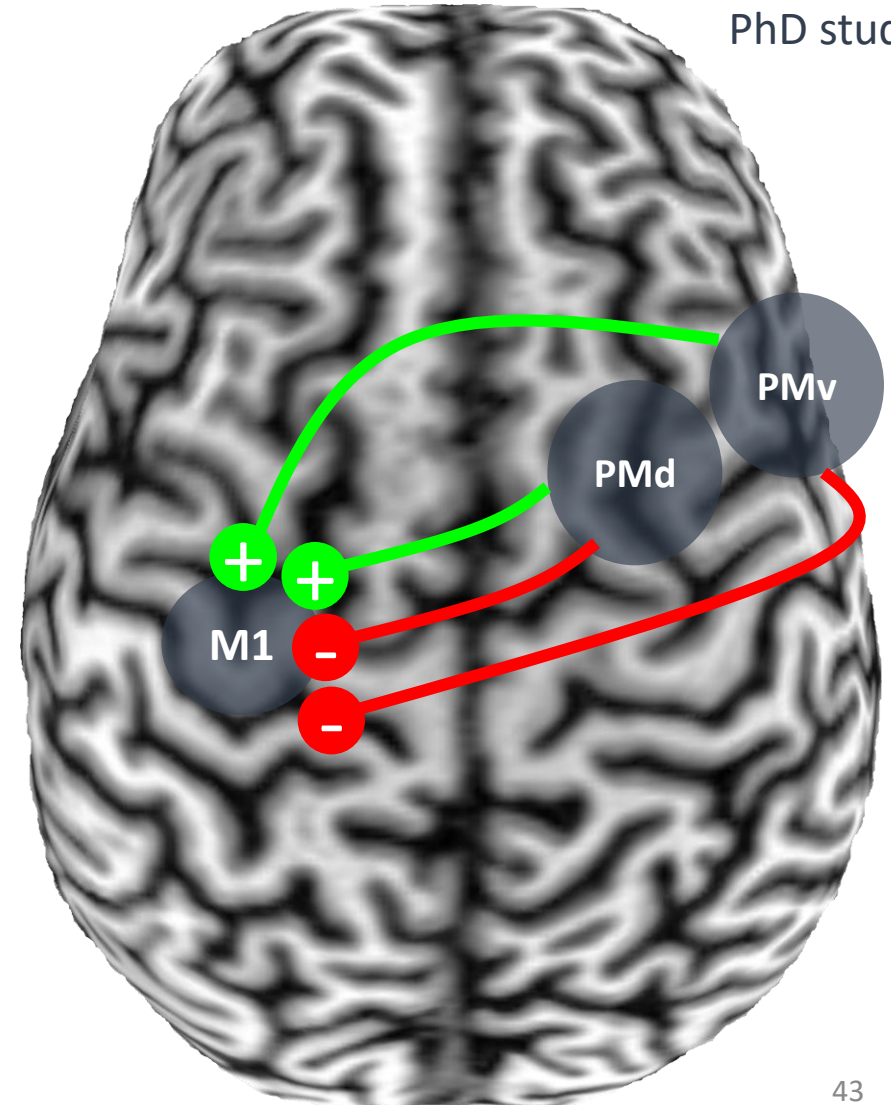
Premotor cortex likely plays an important for recovery after stroke

How does PMC communicate with M1?



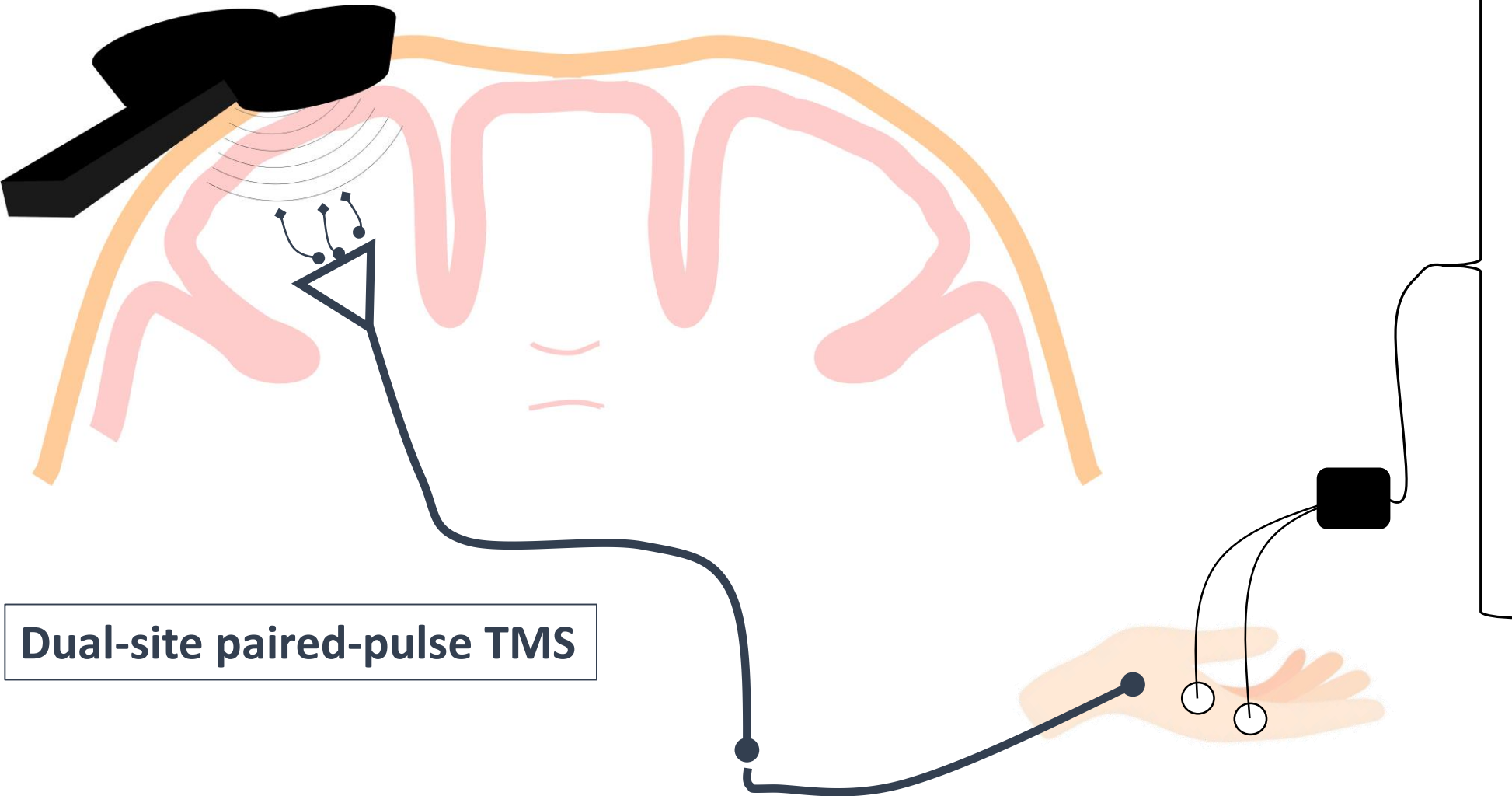
Elnaz Allahverdloo,
PhD student

- Premotor cortex (PMC) regions:
 - Dorsal (PMd) and ventral (PMv) premotor cortices
 - Distinct communication with M1
 - PMd → more interhemispheric inhibition
 - PMv → mix of inhibition & facilitation
 - PMC → *contralateral* M1 communication not well understood
 - **Objective:** *To investigate how PMd/PMv impact contralateral M1 excitability*
 - Examine the different *neurophysiological pathways* of communication with contralateral M1
 - **Highly relevant to stroke-rehabilitation**

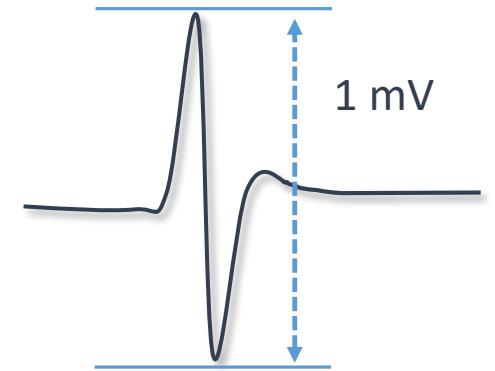


Measuring interhemispheric connectivity

Test stimulus (TS)



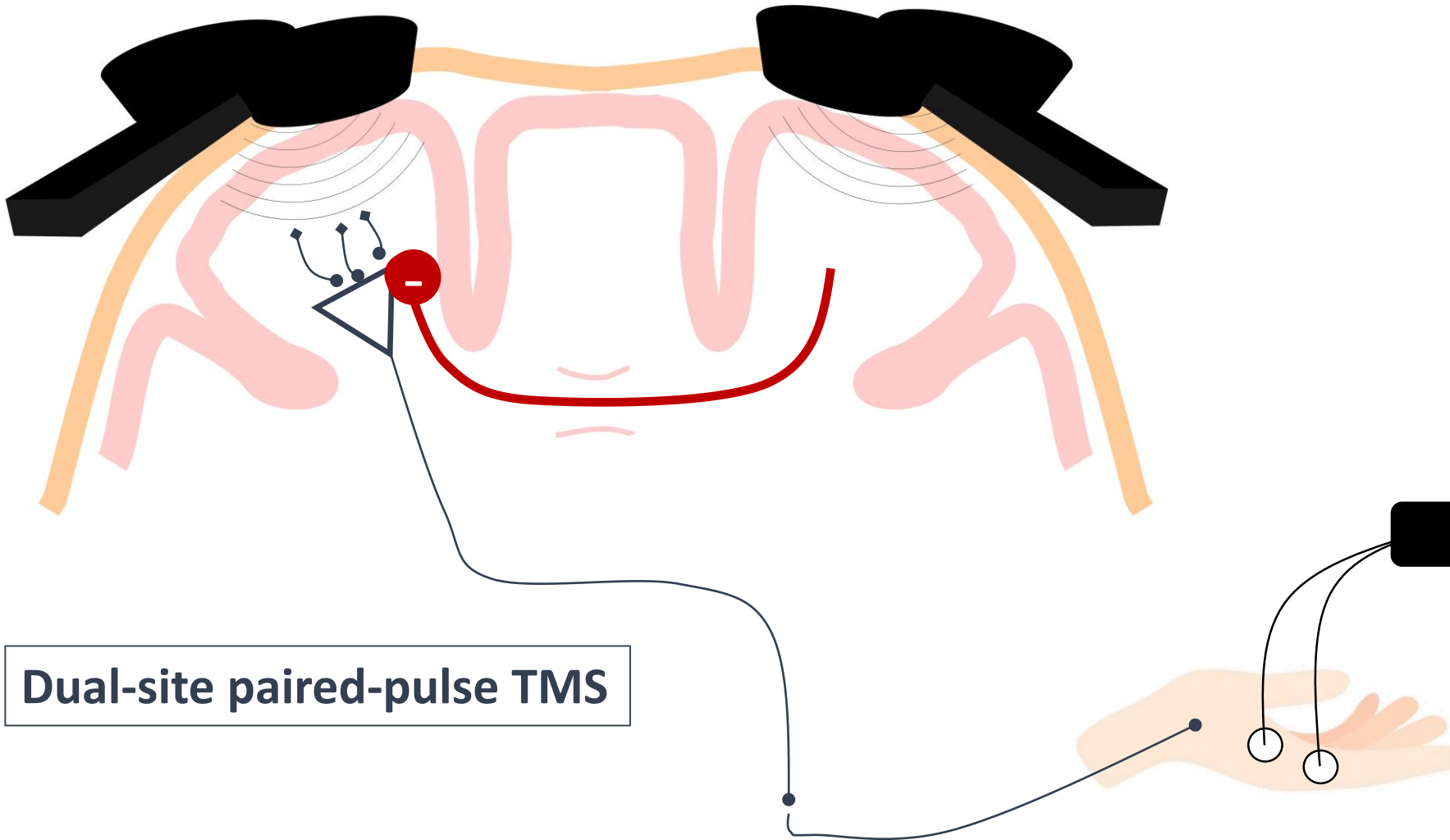
Motor evoked potential
from the TS



Measuring interhemispheric connectivity

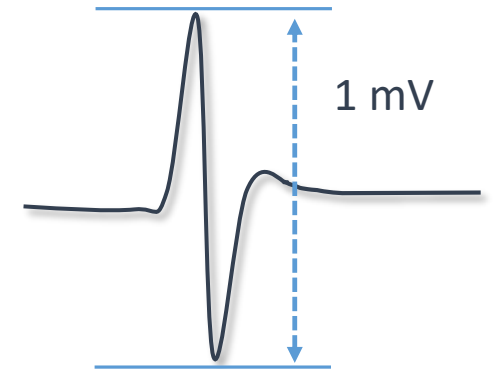
Test stimulus (TS)

Conditioning stimulus (CS)
e.g., 10 ms before the TS

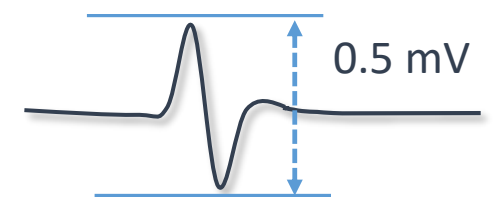


Dual-site paired-pulse TMS

Motor evoked potential
from the TS



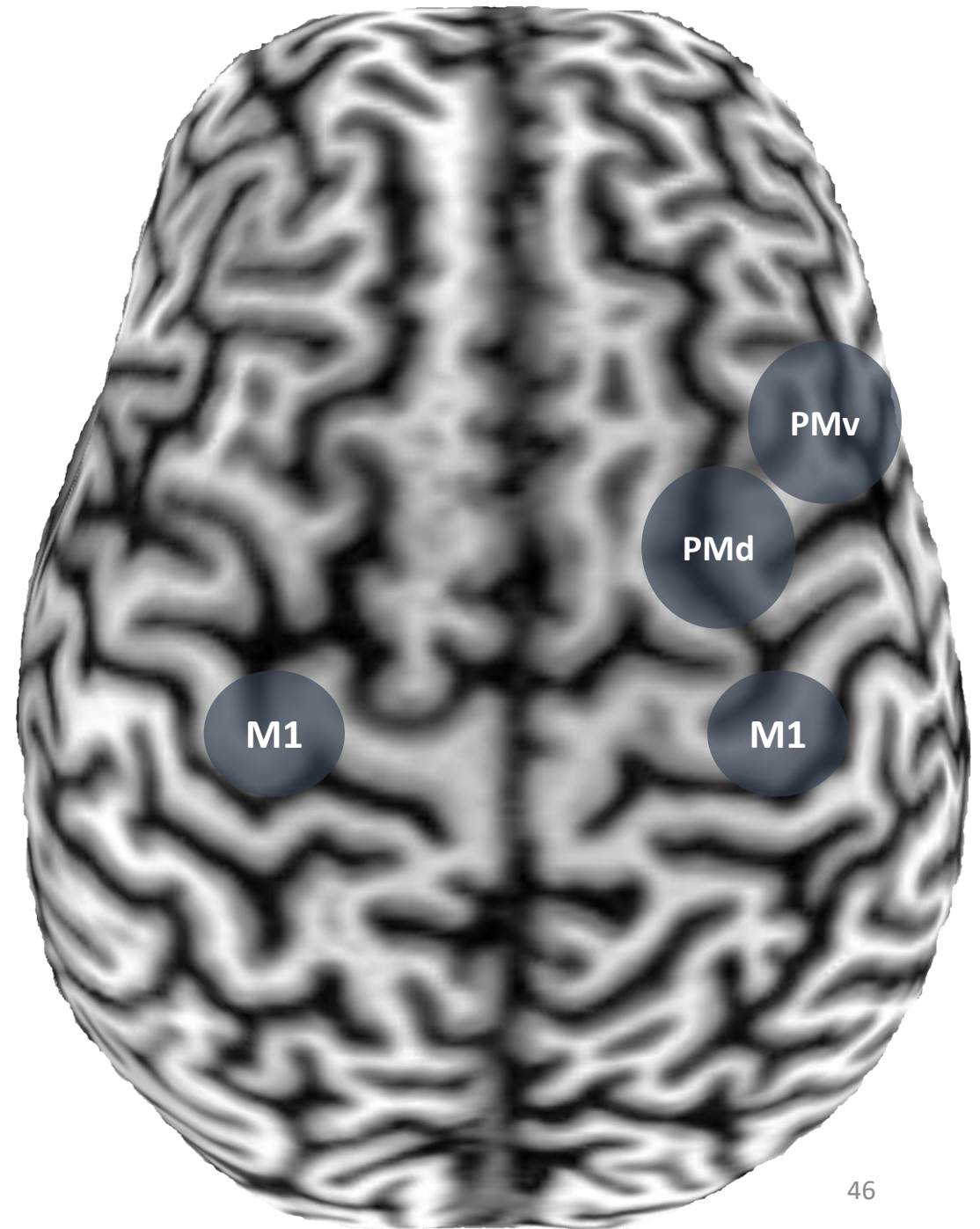
Motor evoked potential
from the CS + TS



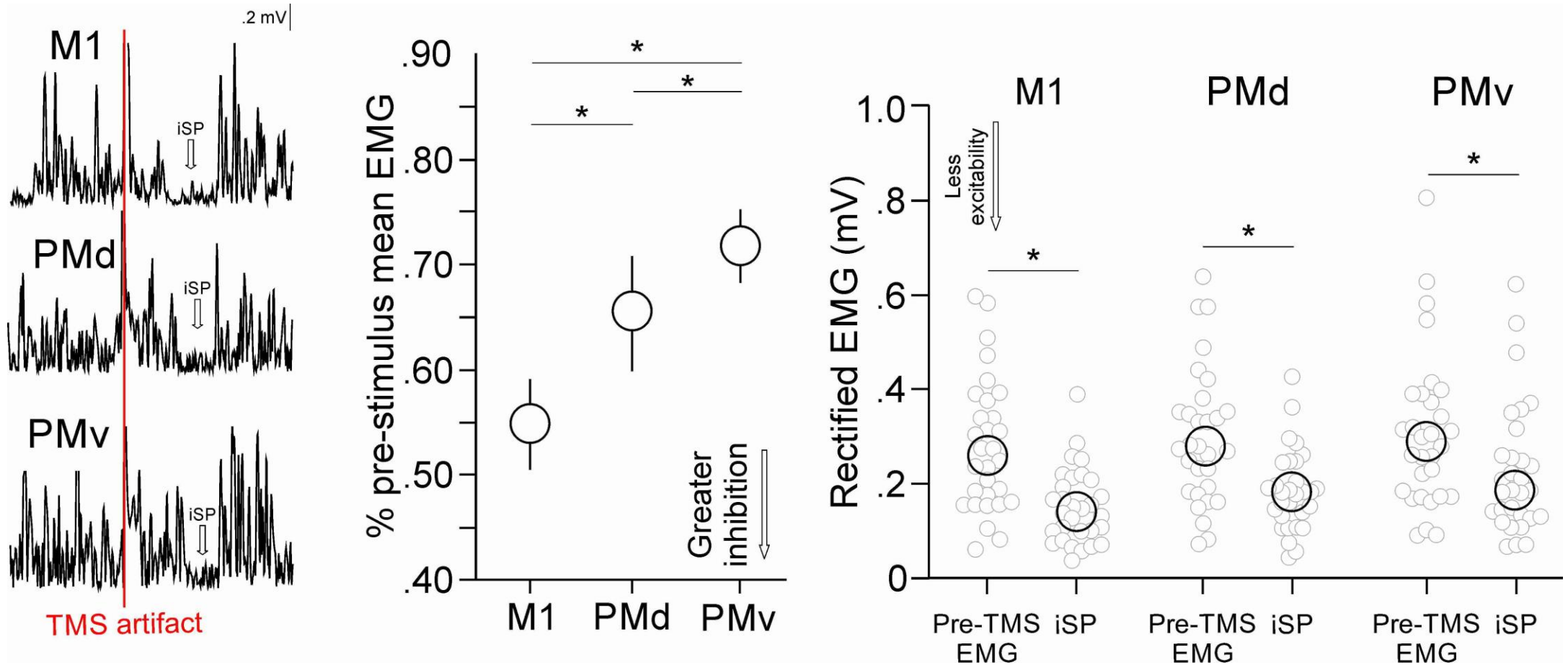
$$\frac{\text{CS + TS}}{\text{TS}} = 0.5 \rightarrow 50\% \text{ inhibition}$$

Methods

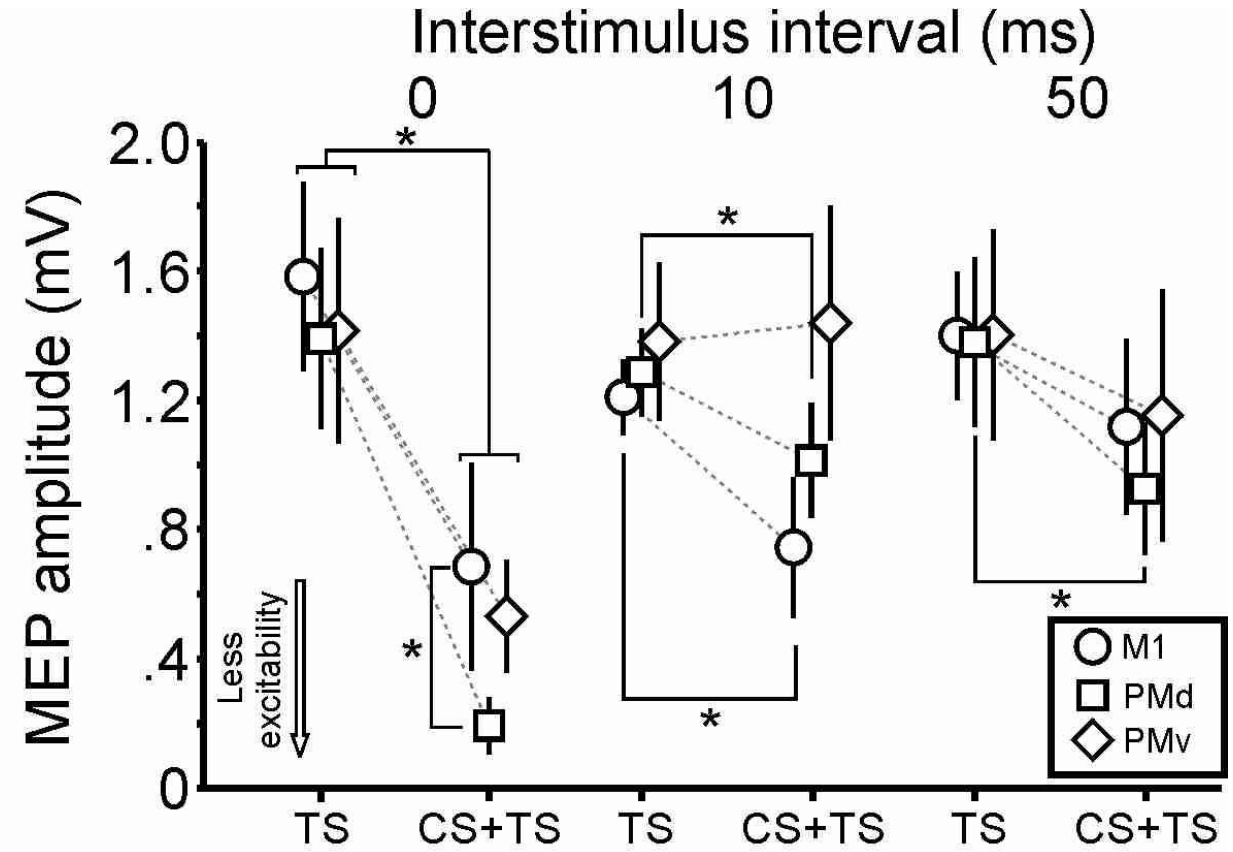
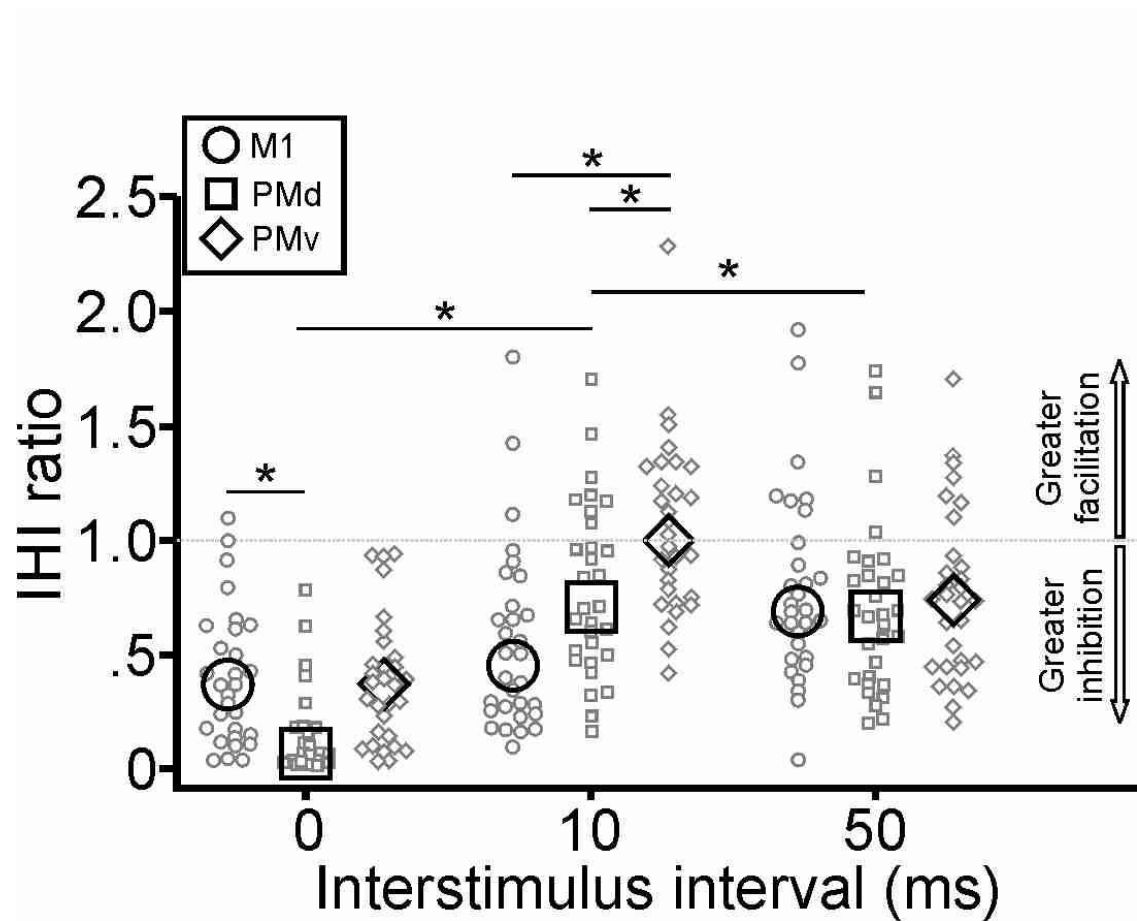
- 30 healthy young adults
- 3 sessions
 - 1st: MRI
 - 2nd: PMC→M1 connectivity
 - 3rd: M1→M1 connectivity (control)
- Neurophysiological pathways of PMd/PMv → M1 communication
 - Single-pulse TMS: ipsilateral silent period (iSP)
 - Dual-site TMS: Interstimulus intervals:
 - 0 ms (subcortical pathway)
 - 10 ms (short transcallosal pathway)
 - 50 ms (long transcallosal pathway)



iSP: PMd & PMv *inhibit* contralateral M1



Dual-site: PMd *inhibits* contralateral M1 the most!



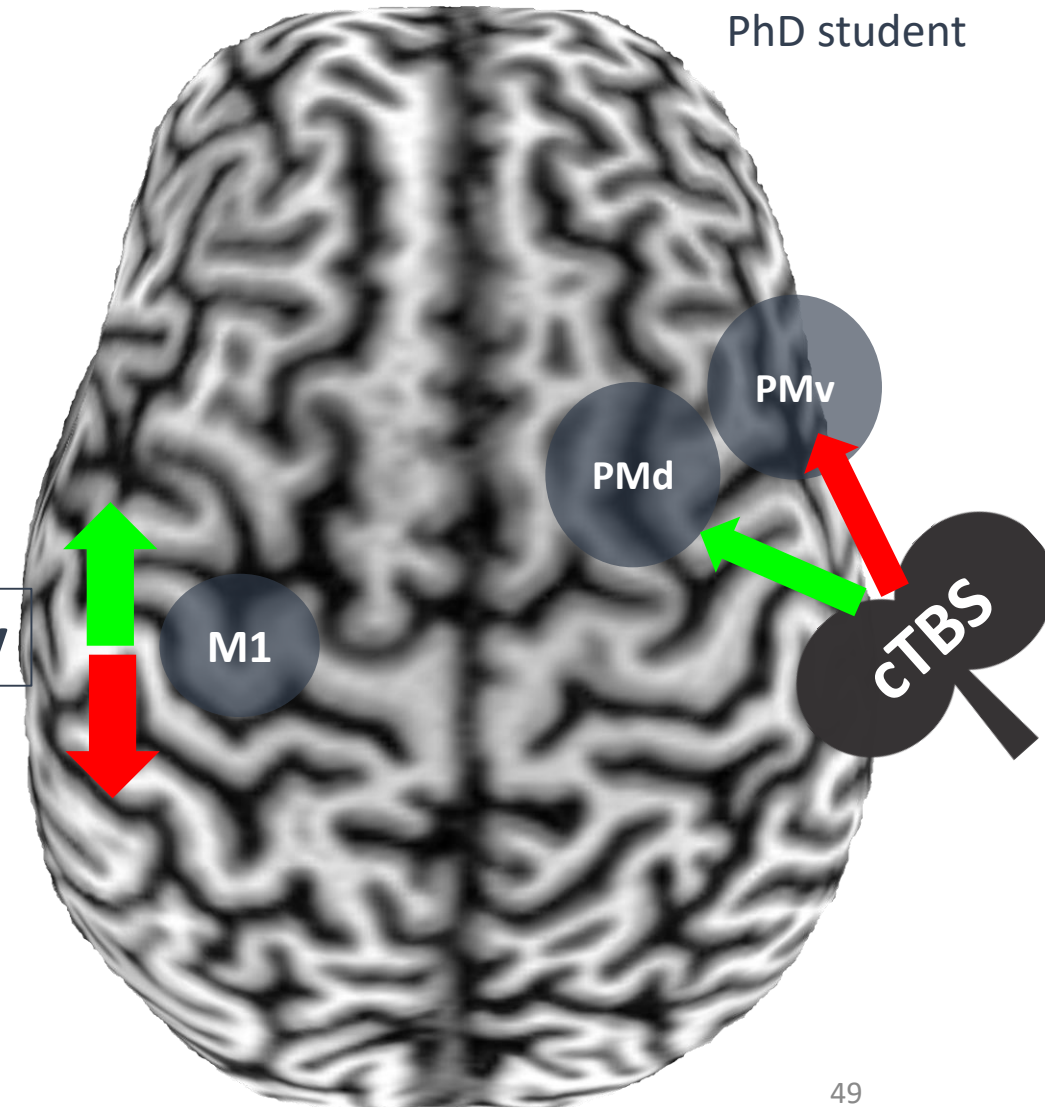
Can we modulate PMC → M1 connectivity?



Elnaz Allahverdloo,
PhD student

- Can we remotely modulate contralateral M1 excitability via theta burst stimulation (TBS) over PMd/PMv?
- Can we modulate *interhemispheric communication* between PMd/PMv → M1?
- Conditions:
 1. Continuous TBS over PMd
 - Suppress cortical excitability
 2. Intermittent TBS over PMd
 - Increases cortical excitability
 3. Continuous TBS over PMv
 4. Intermittent TBS over PMv
 5. Sham
- Measures:
 - Bilateral M1 corticospinal excitability
 - PMC → M1 interhemispheric inhibition

M1 excitability





1

Aerobic Exercise:
↑ *Motor Learning*
↑ *Neuroplasticity*

2

TMS:
Measure & Modulate
the Brain

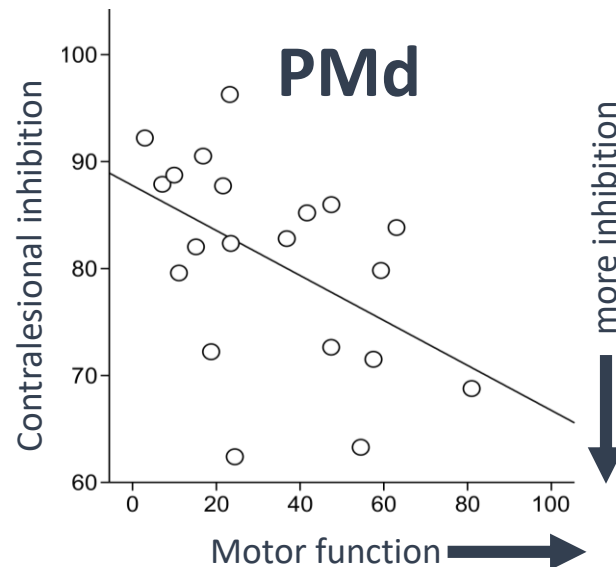
3

**Clinical Application &
Future Work**

The Role of Premotor Cortex (PMC) in Stroke Recovery

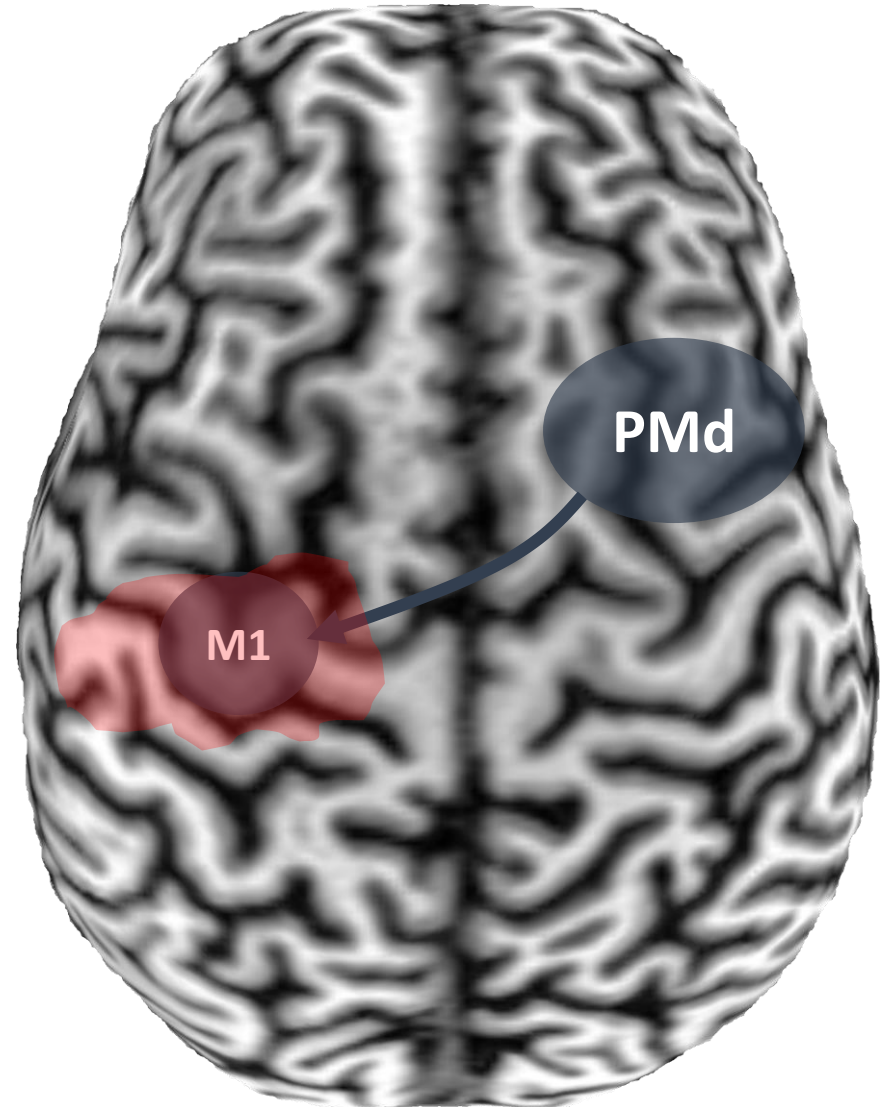
- Increasing contralesional PMC excitability can \uparrow motor function
- *Increased inhibition* from contralesional PMC is associated with *better* motor function
- PMd demonstrates *strongest* connectivity with contralateral M1 (*healthy adults*)

Contralesional PMd may play an important role in recovery & is a viable target for rTMS!



Ipsilesional

Contralesional



Methods: Participants & Pilot Design

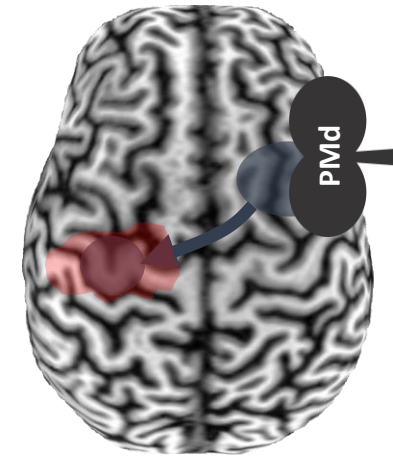
- **Participants:**

- Recruit 30 individuals, subacute phase of stroke from IUGM Intensive Rehabilitation Unit
- 50% F, aged 50-85 yo
- Subacute stage (1-3 mo) after first-time middle cerebral artery stroke
- Fugl-Meyer 15-55 (motor impairment)
- No contraindications to TMS

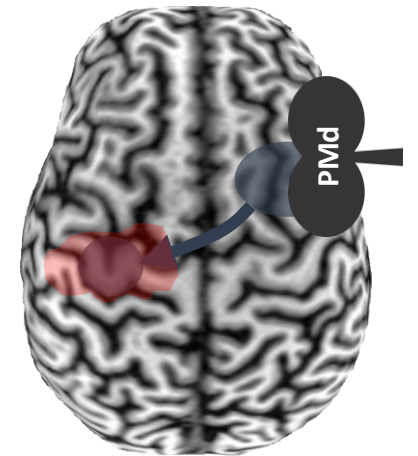
- **3 Intervention Groups (n=10/group)**

1. Continuous Theta Burst Stimulation (cTBS) to contralesional dorsal premotor cortex (cPMd)
 - *Inhibition* of contralesional cortex
2. Intermittent TBS (iTBS) to cPMd
 - *Facilitation* of contralesional cortex
3. Sham TBS (control)
 - No active stimulation

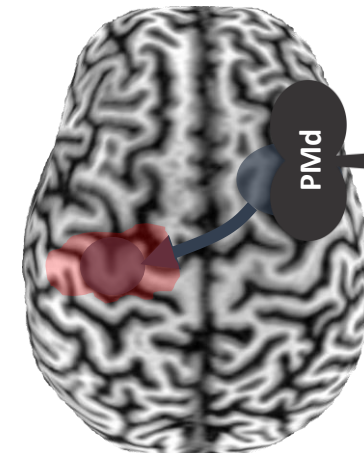
Group 1: cTBS to cPMd




Group 2: iTBS to cPMd

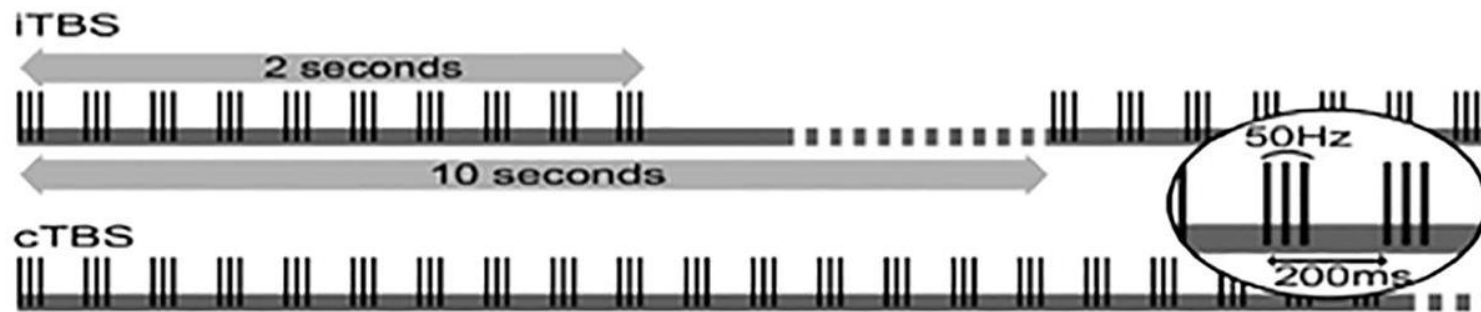


Group 3: Sham TBS

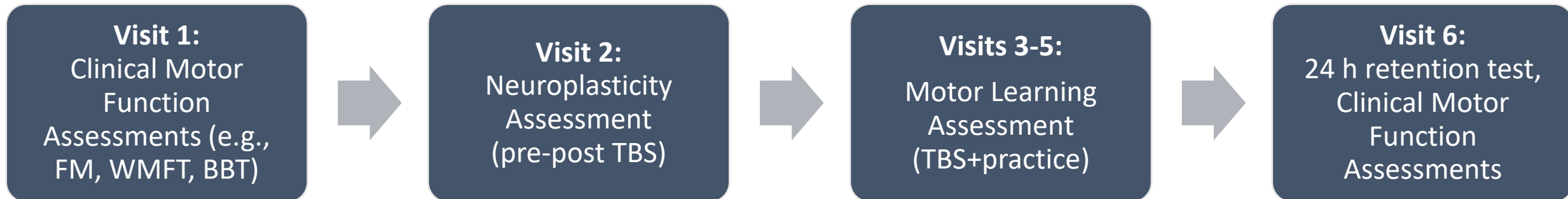


Methods: Interventions & Visits

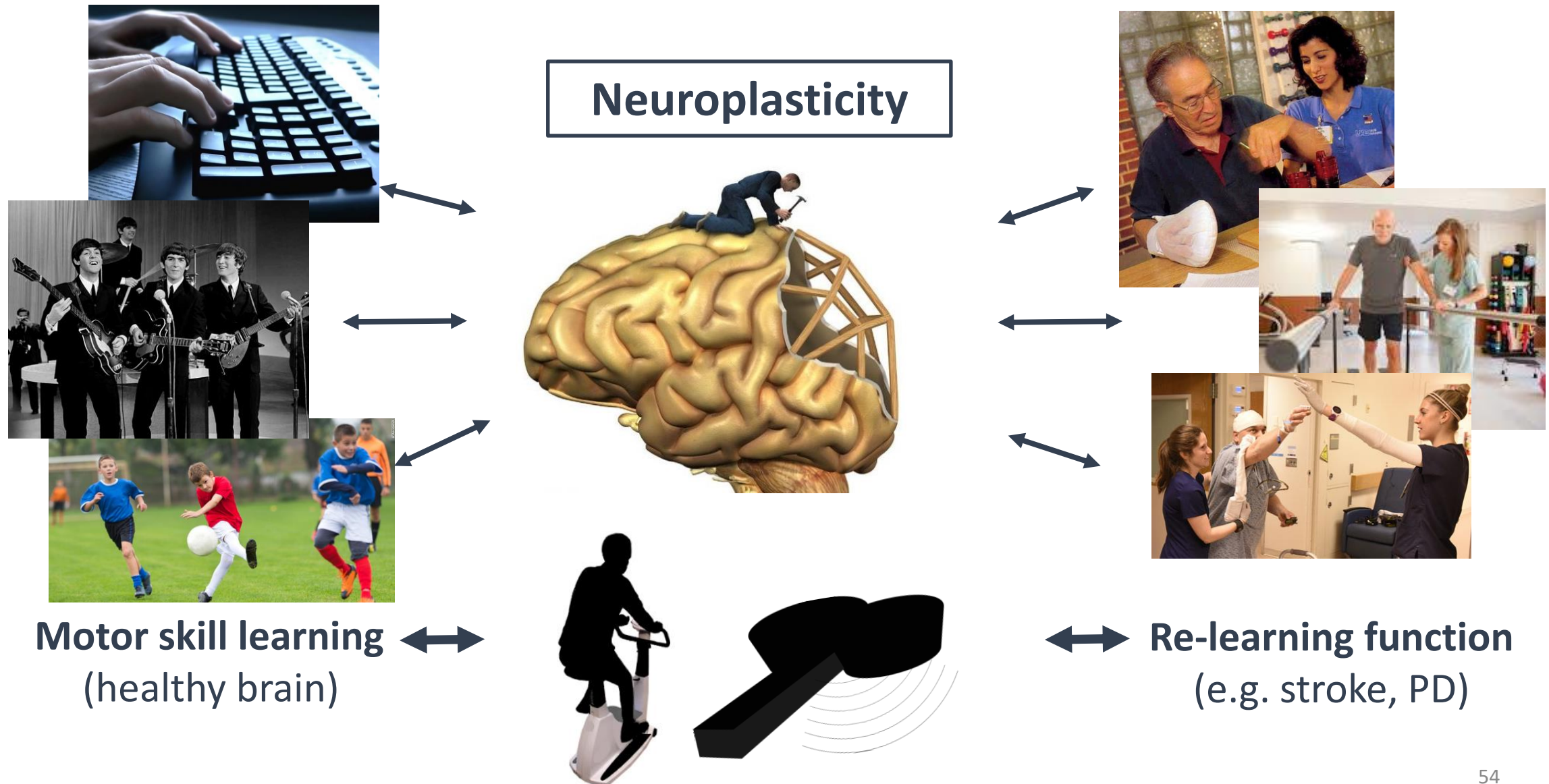
- Theta Burst Stimulation (TBS) 
 - Continuous theta burst stimulation (cTBS) – ↓ excitability
 - Intermittent theta burst stimulation (iTBS) – ↑ excitability



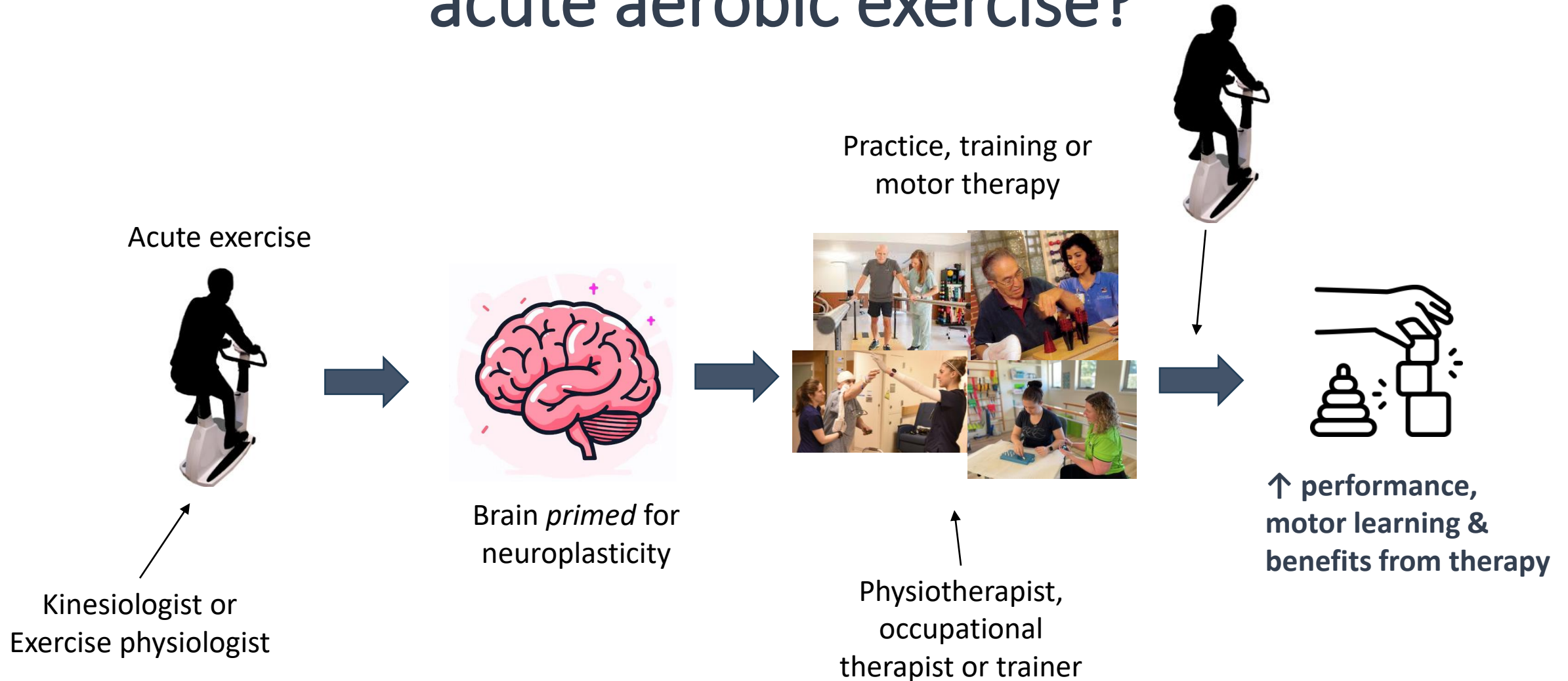
• Visits



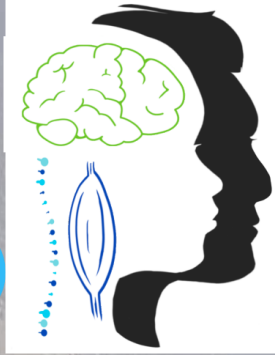
Neuroplasticity mechanisms supporting motor learning



How to capitalize on the beneficial effects of acute aerobic exercise?



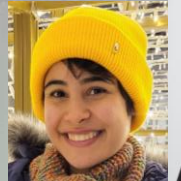
ELPN lab



Thank you!

Collaborators

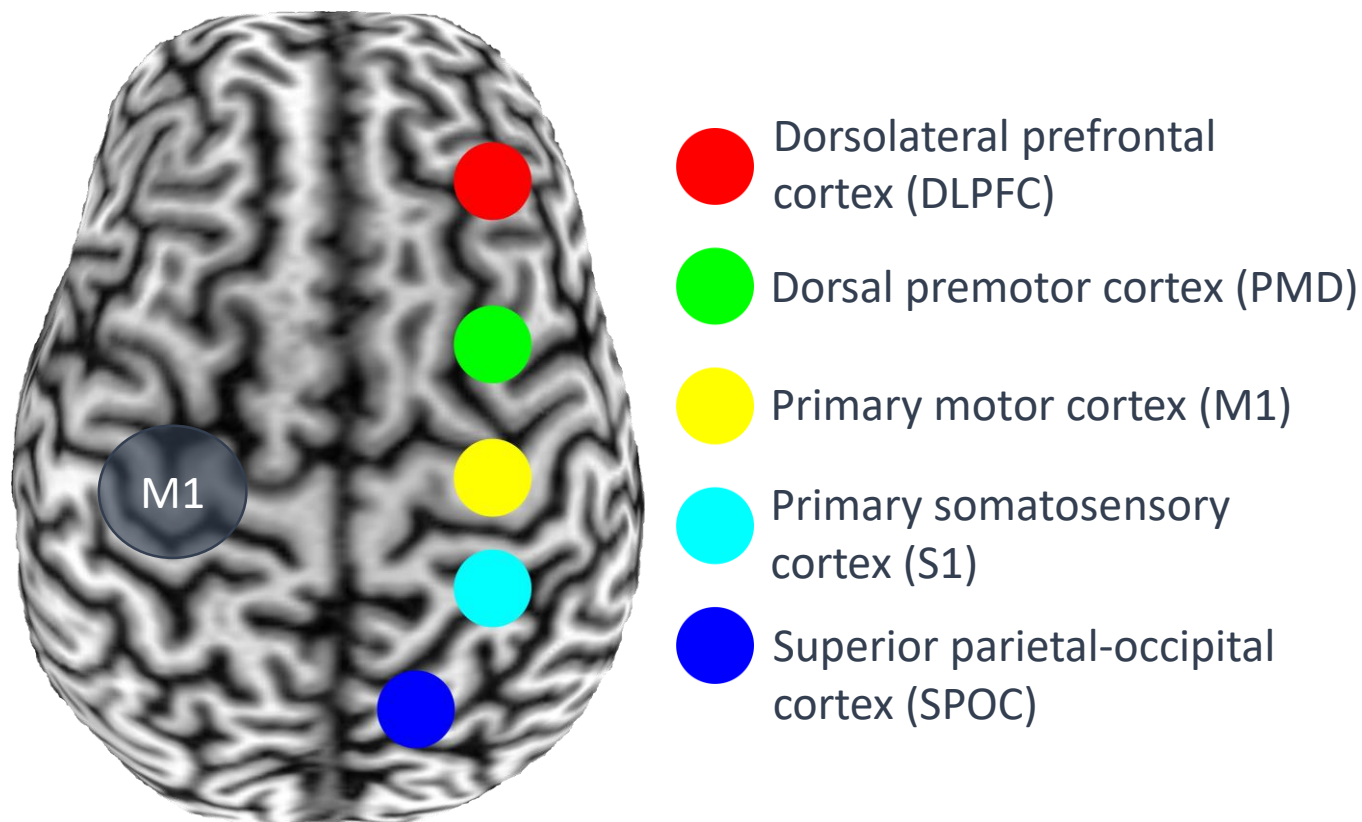
- Dr. Benjamin Pageaux (Kinesiology, UdeM; CRIUGM)
- Dr. Numa Dancause (Neuroscience, UdeM; CRIUGM)
- Dr. Alexandru Hanganu (Psychology, UdeM; CRIUGM)
- Dr. Dorothy Barthélemy (Rehabilitation, UdeM; CRIR)
- Dr. Julie Messier (Kinesiology, UdeM; CRIUGM)
- Dr. Ana Ines Ansaldo (Language Pathology, UdeM; CRIUGM)
- Dr. Daniel Gagnon (Kinesiology, UdeM; EPIC)
- Dr. Lara Boyd (University of British Columbia)
- Dr. Cameron Mang (University of Regina)
- Dr. Richard Staines (University of Waterloo)
- Dr. Doris Doudet (University of British Columbia)
- The CanStim working group
- Dr. Michael Vesia (USA)
- Dr. Kate Hayward (AUS)



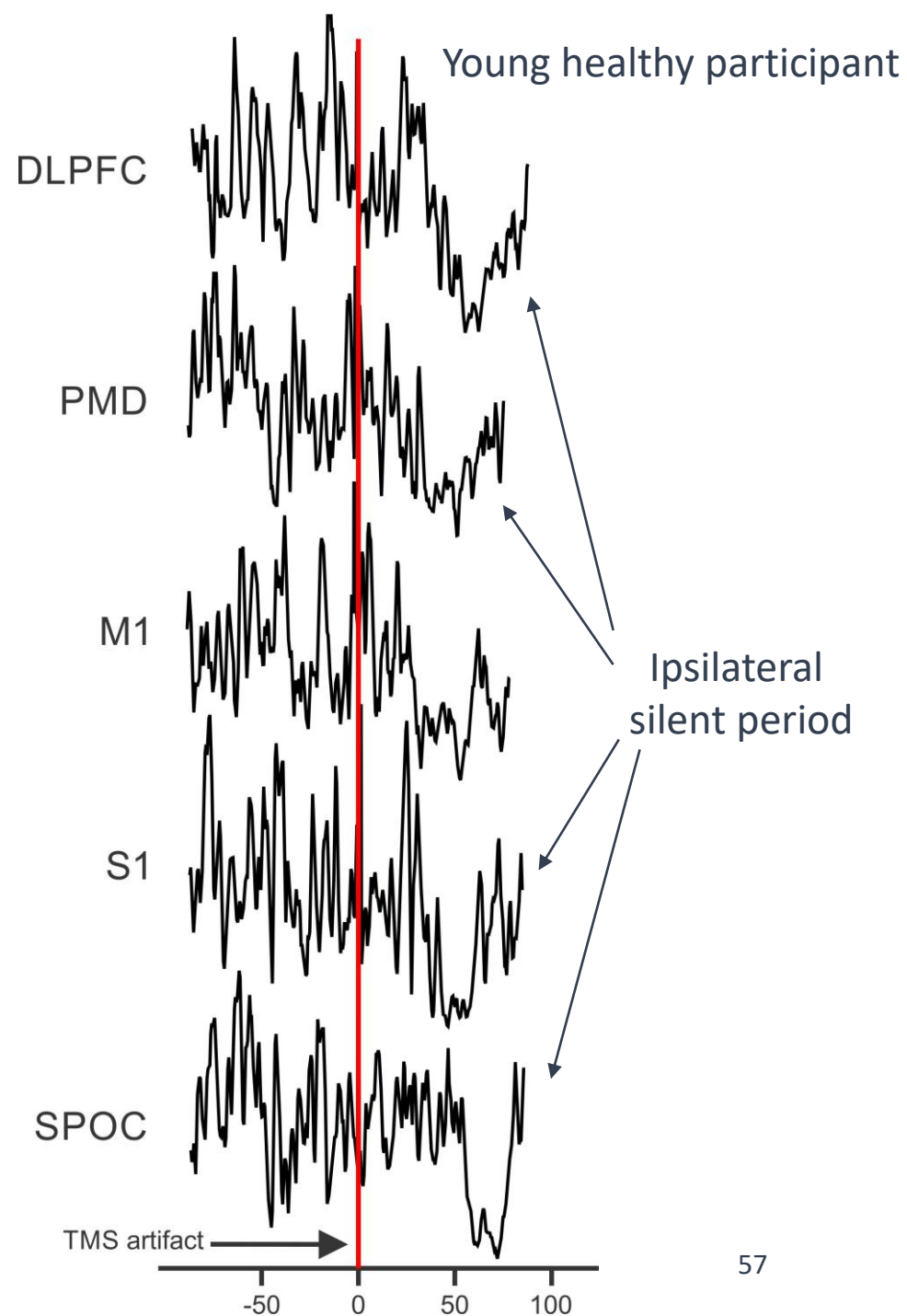
Funding



Transcallosal inhibition elicited from frontal & parietal cortical regions



Neva et al., 2020d (in preparation)





1

Exercise and Learning (↑ *motor learning*)

- ↑ skill acquisition
- ↑ motor learning

2

The Brain on Exercise (↑ *neuroplasticity*)

- ↑ output excitability from motor cortex
- ↓ cortical inhibition
- ↑ prefrontal contribution to motor cortex plasticity

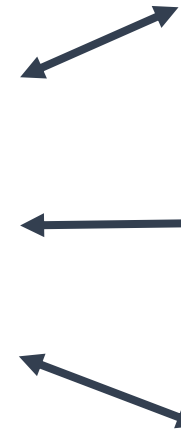
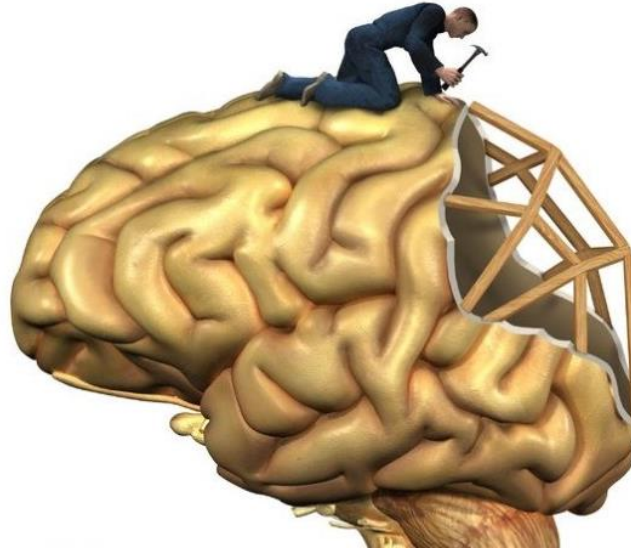
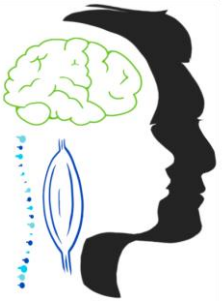
3

Key Takeaways and Clinical Application

- Positive effects of acute exercise
- Eccentric exercise promising avenue for future research and clinical application

Exercise *intensity* and *type* are very important factors to consider

The beneficial impact of acute exercise



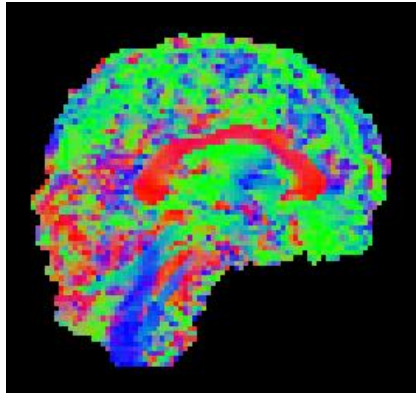
Acute aerobic exercise

↑ Neuroplasticity

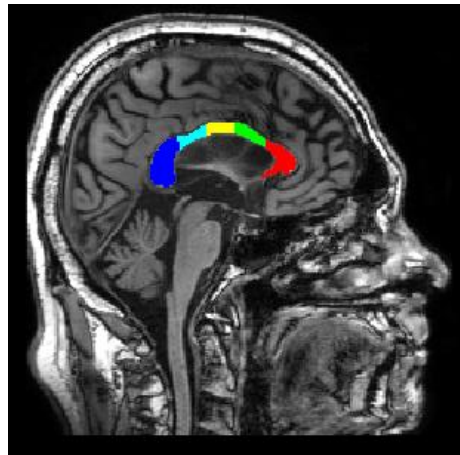
- ↑ Blood flow, dopamine, BDNF
- ↓ Inhibition within brain regions
- ↑ Prefrontal-motor cortex connectivity

**↑ re-learning,
rehabilitation
(e.g., aging, stroke)**

Frontal white matter structural integrity is vital for motor function after stroke

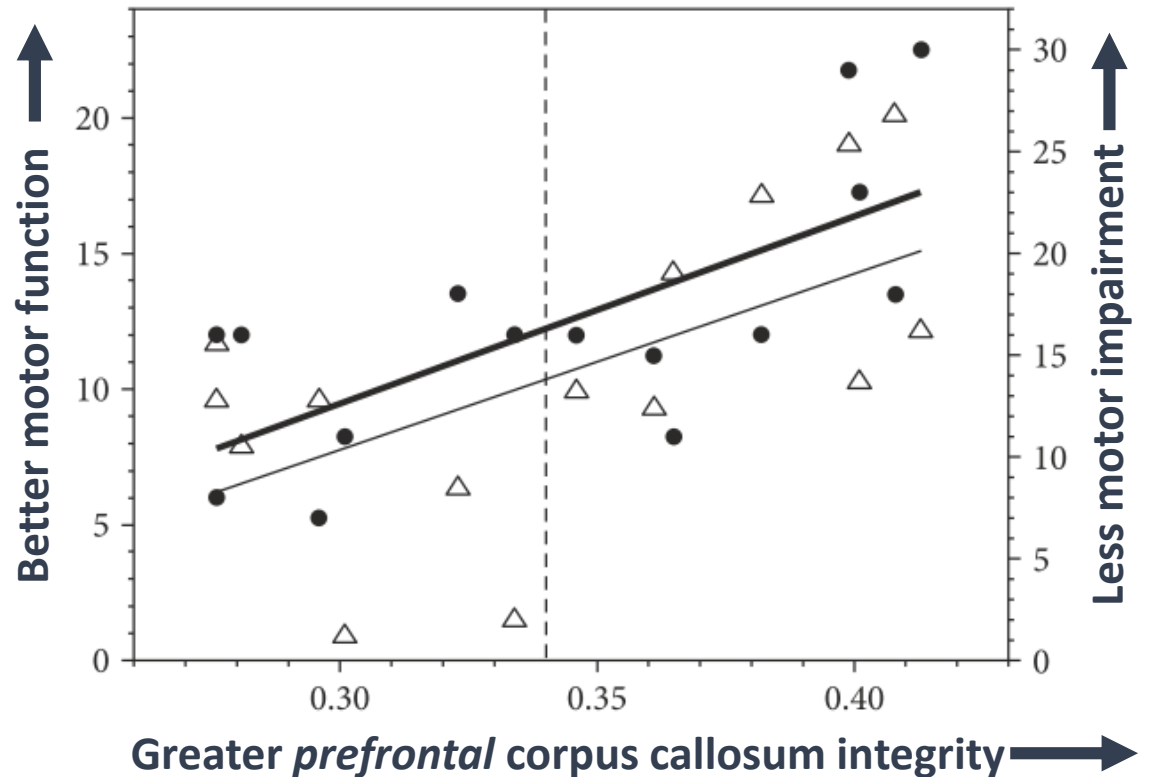


Diffusion tensor imaging (DTI)



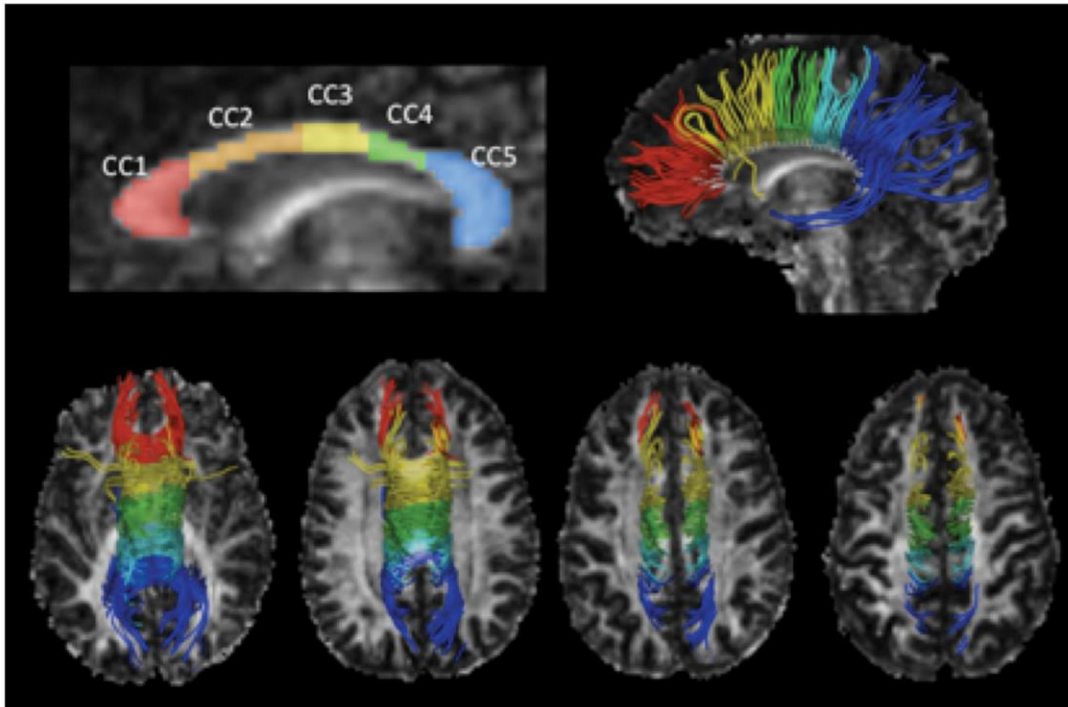
Fractional anisotropy
of frontal corpus callosum regions

- Prefrontal
- Premotor
- Motor



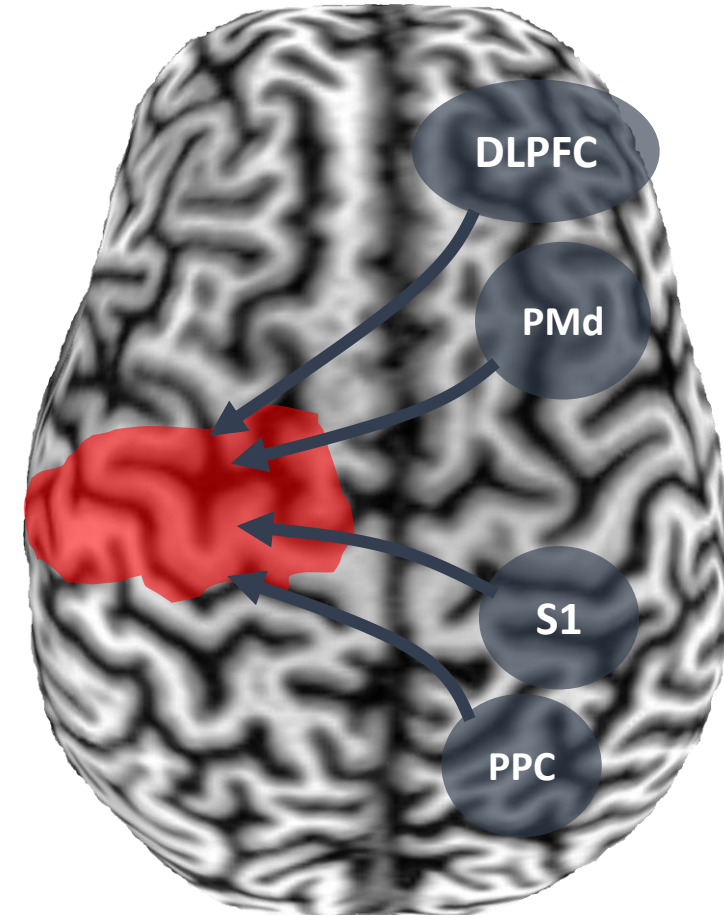
Frontal & parietal brain regions in stroke

Brain *structure*



Hayward, Neva et al., 2017 *Neural Plasticity*

Brain *function*



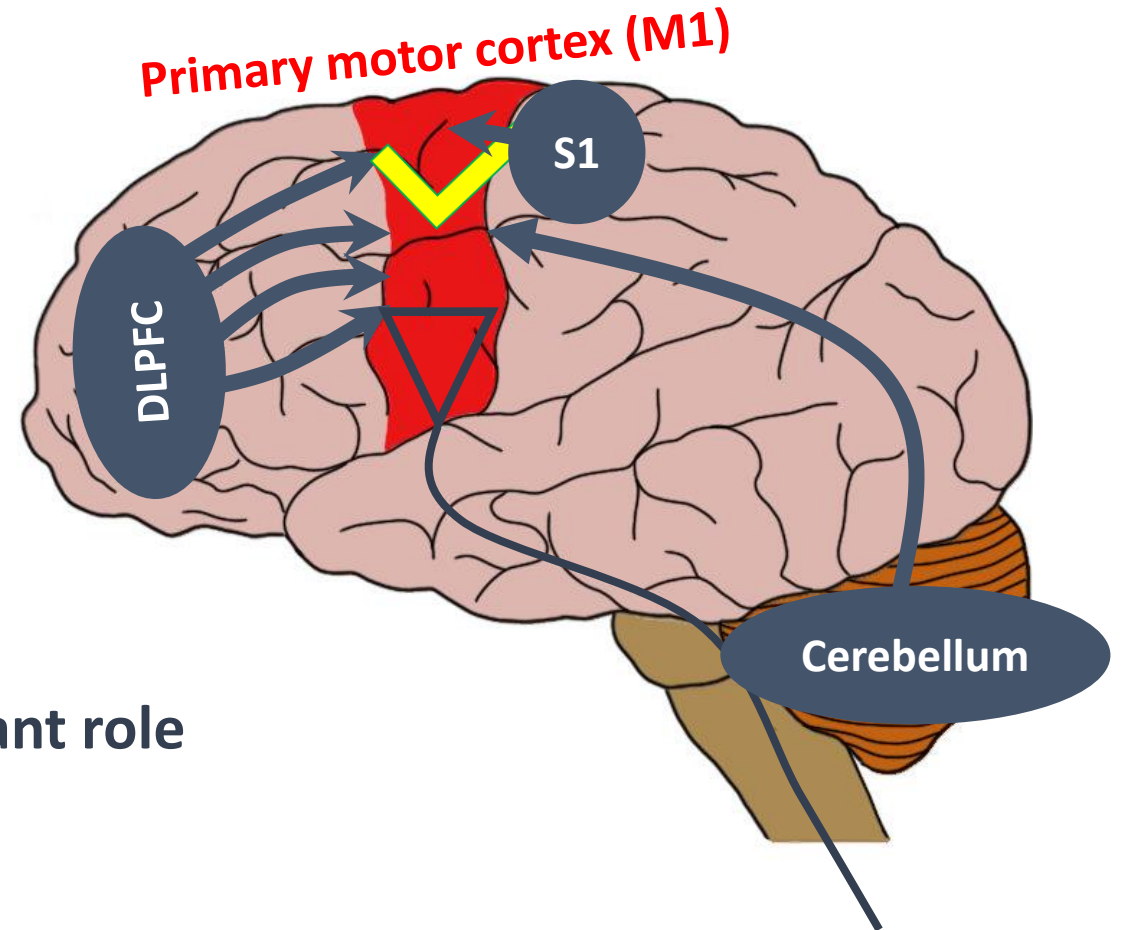
Neva et al., 2020d (in preparation)

Brain circuits contribute to exercise-induced motor cortex plasticity?

Acute exercise impact on brain excitability & neuroplasticity

Summary of findings

- ↓ motor cortex inhibition ✓
- ↑ motor cortex output excitability ✓
- several other brain circuits are impacted
 - sensorimotor integration
 - cerebellar inhibition & plasticity
 - unique motor cortex interneurons
- Prefrontal cortical circuits may play an important role in exercise-induced motor cortex neuroplasticity

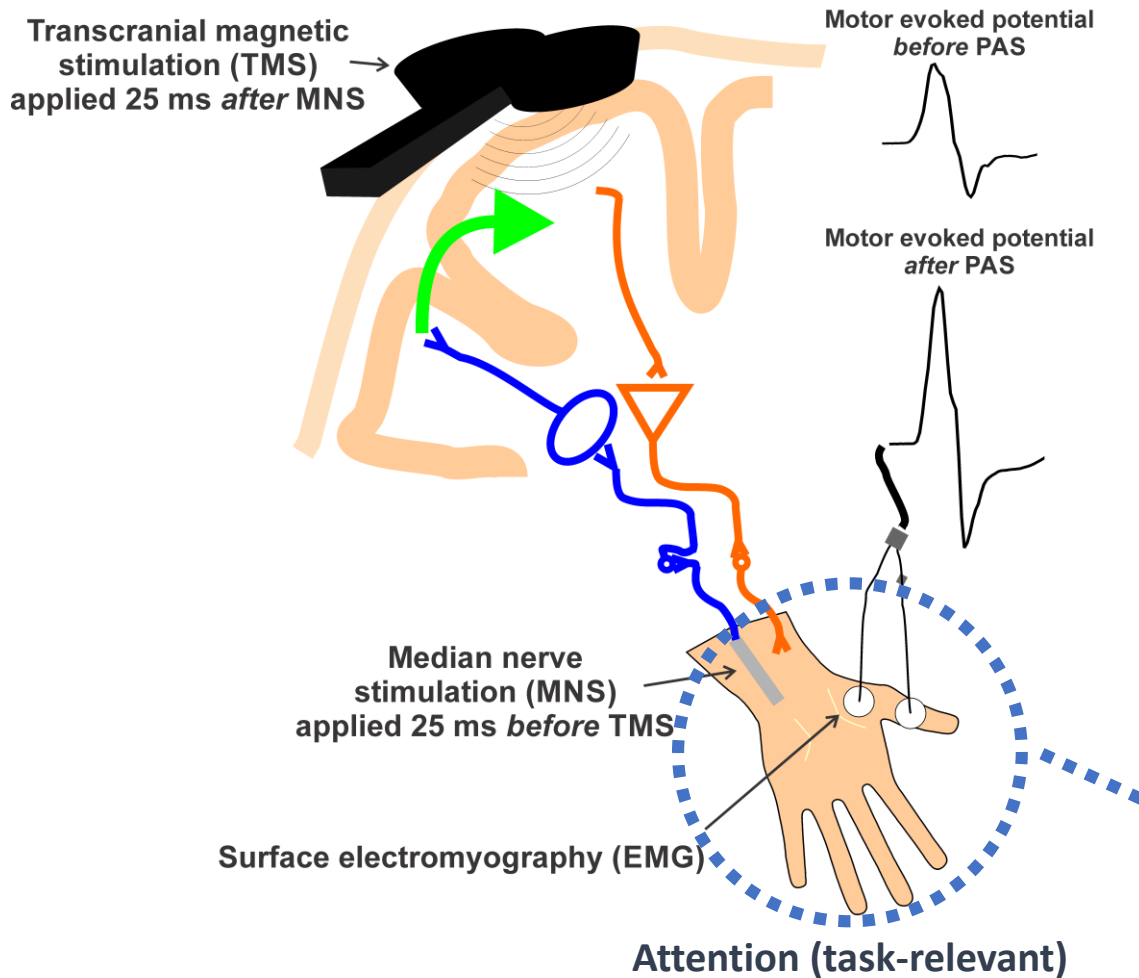


Prefrontal circuits play a role in exercise-induced motor cortex plasticity?

Paired Associative Stimulation (PAS) – Motor cortex neuroplasticity



Amanda O'Farrell,
PhD candidate



Acute exercise



PAS response

Singh, Neva, Staines 2014 *Exp Brain Res*
Mang et al., 2014 *J App Phys*

PAS response

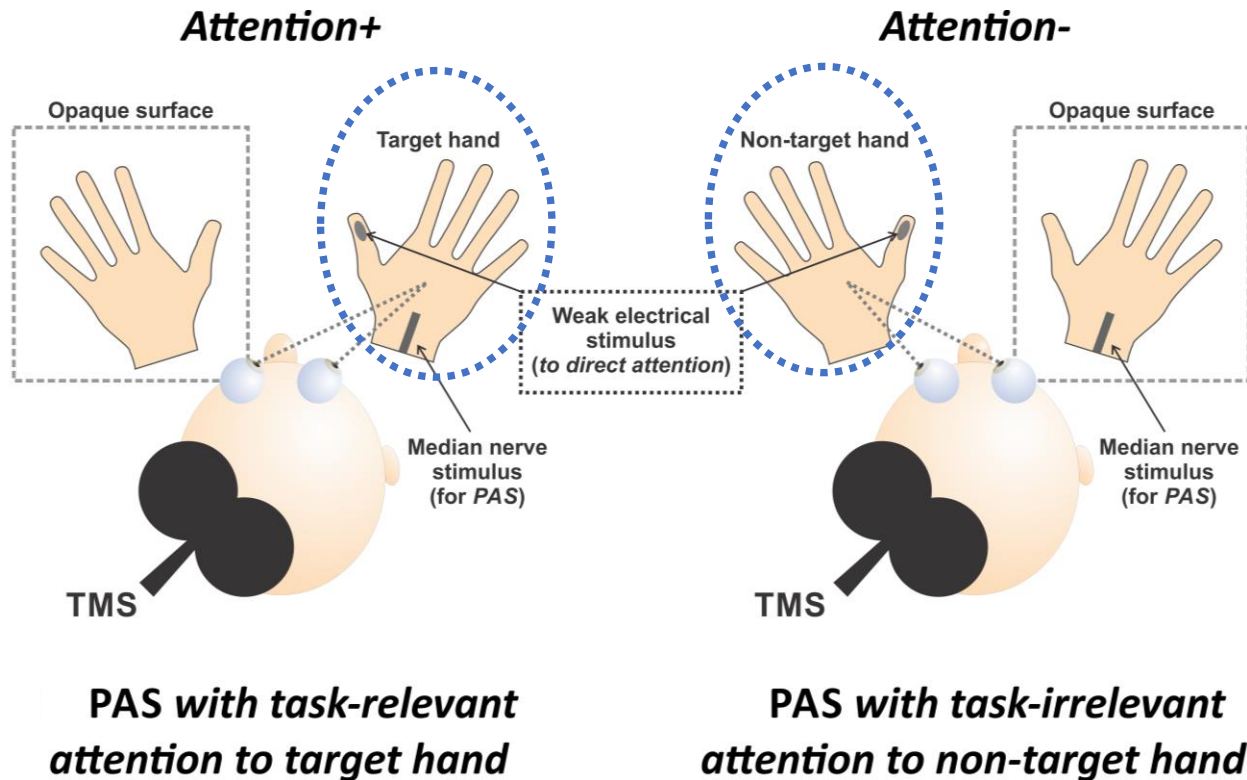
Stefan et al., 2004
J Neurophys

Previous studies did not control for the contribution of attention during PAS.

Thus, the contribution of attention-related brain circuits to motor cortex neuroplasticity remains unknown.

Prefrontal circuits play a role in exercise-induced motor cortex plasticity?

Paired Associative Stimulation (PAS) – Attention conditions



Amanda O'Farrell,
PhD candidate

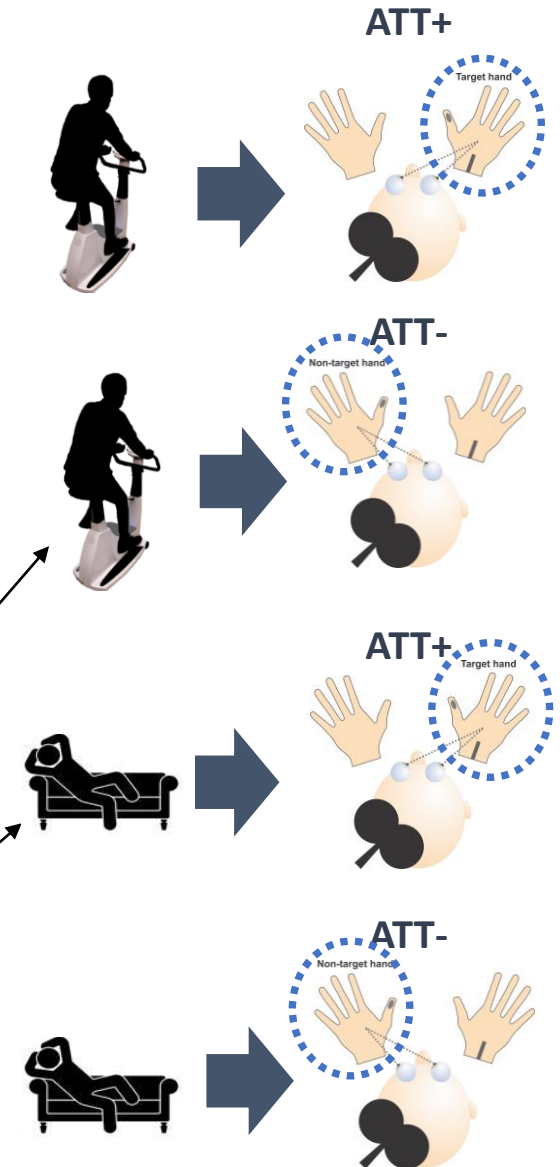
Experimental design

4 conditions:

- 1) Exercise + PAS_{ATT+}
- 2) Exercise + PAS_{ATT-}
- 3) Rest + PAS_{ATT+}
- 4) Rest + PAS_{ATT-}

Acute moderate
intensity exercise

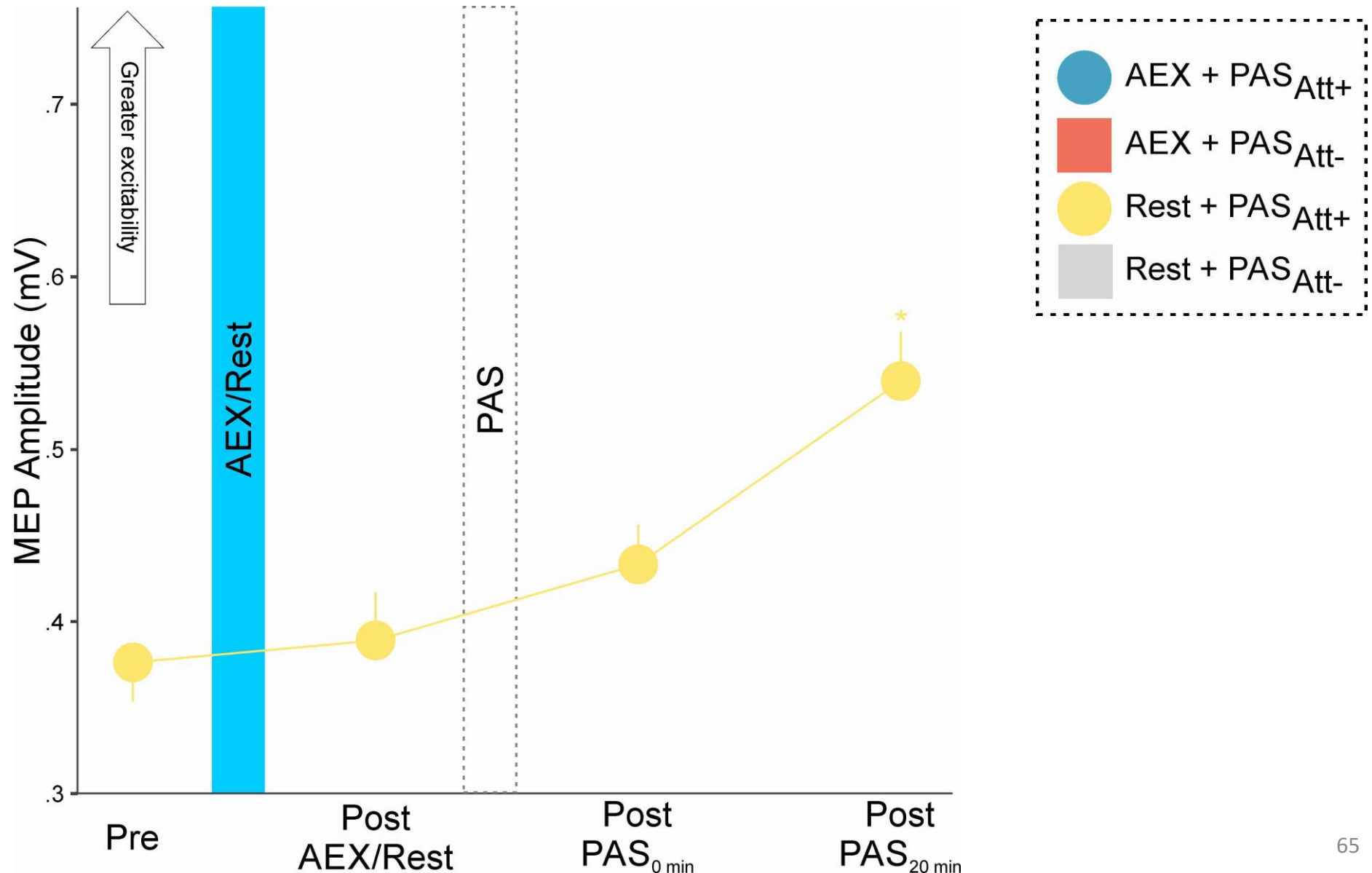
Rest



Prefrontal circuits play an essential role in exercise-induced M1 plasticity!



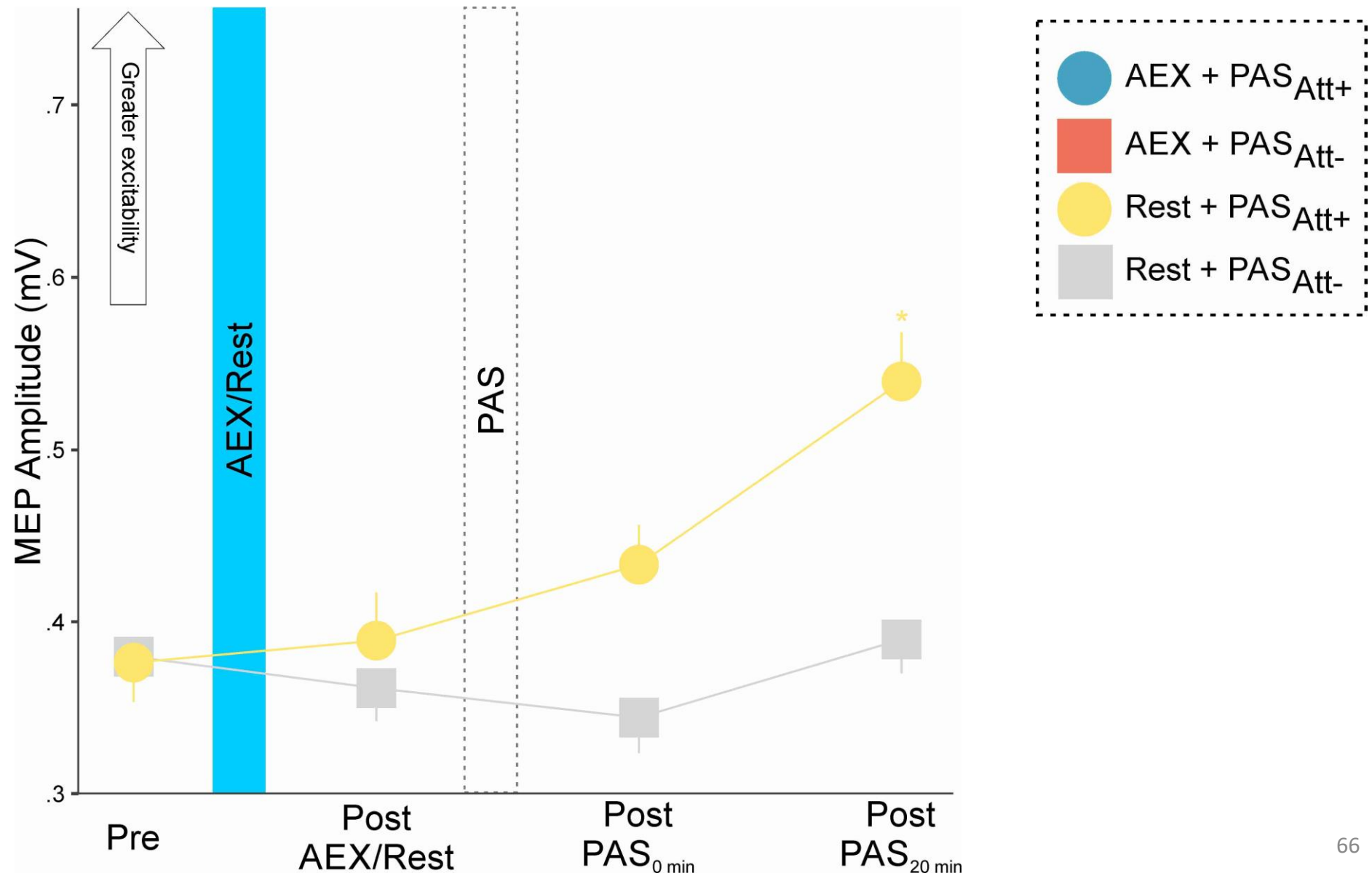
Amanda O'Farrell,
PhD candidate



Prefrontal circuits play an essential role in exercise-induced M1 plasticity!



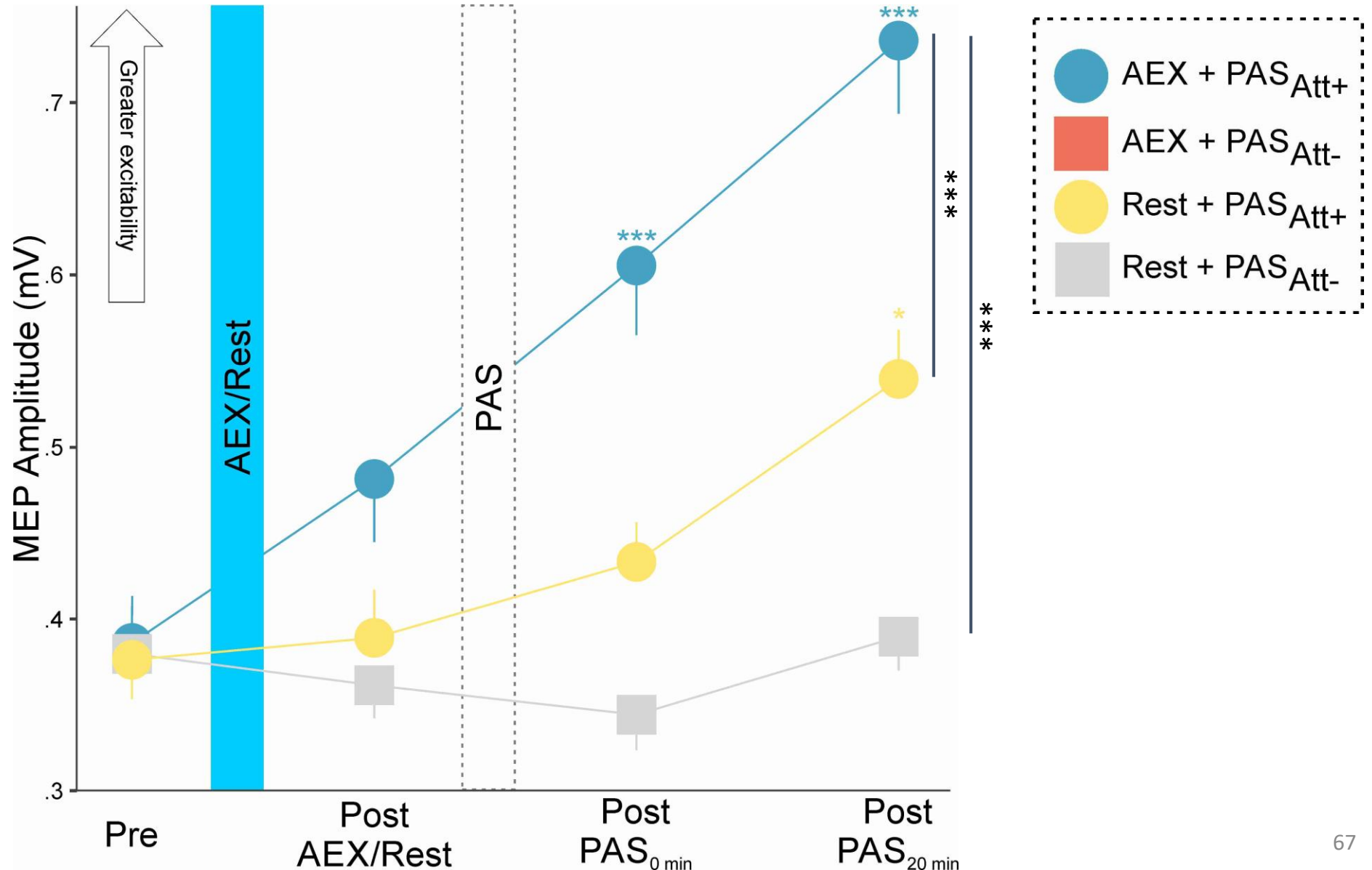
Amanda O'Farrell,
PhD candidate



Prefrontal circuits play an essential role in exercise-induced M1 plasticity!



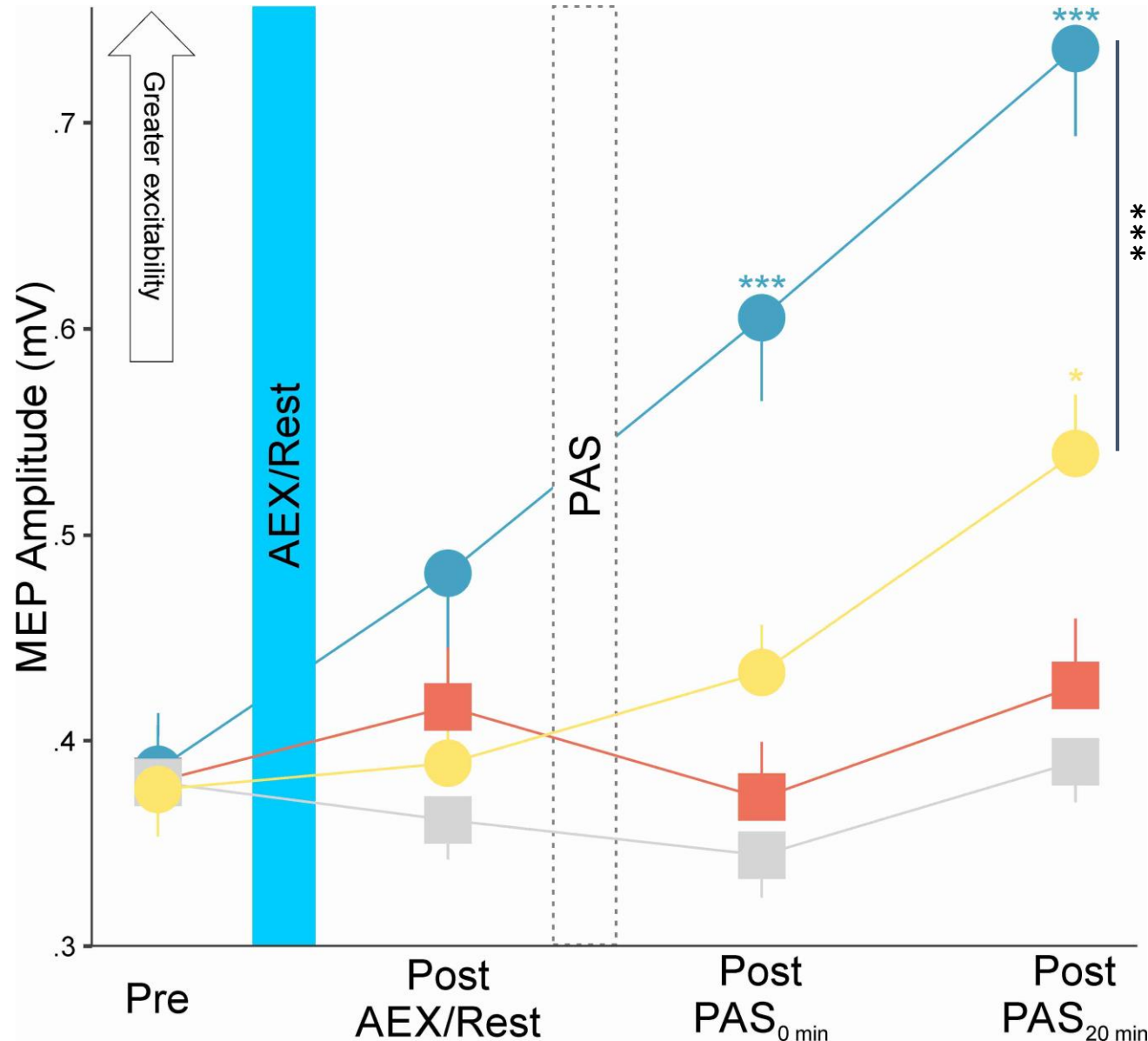
Amanda O'Farrell,
PhD candidate



Prefrontal circuits play an essential role in exercise-induced M1 plasticity!

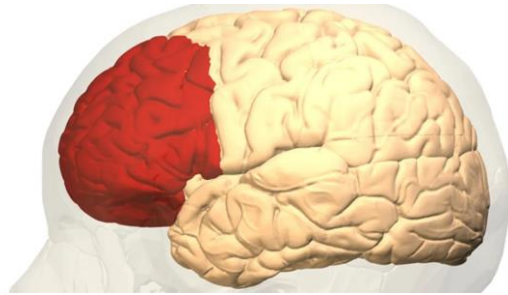


Amanda O'Farrell,
PhD candidate

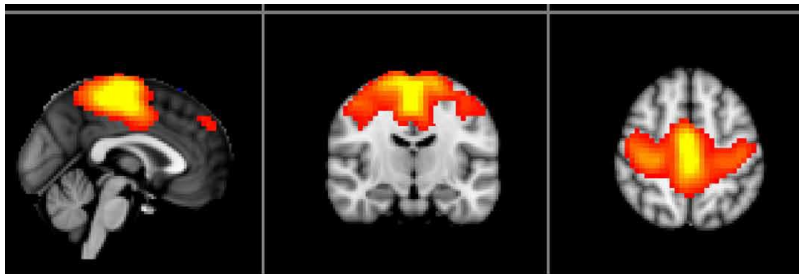
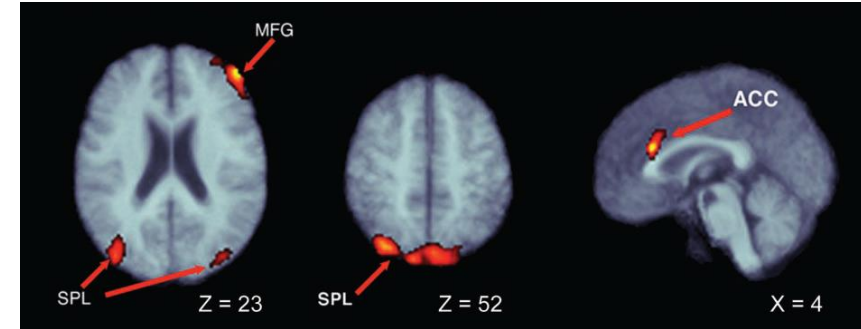


***Attention-related
prefrontal brain circuits
play an important role in
acute exercise-induced primary
motor cortex (M1) neuroplasticity!***

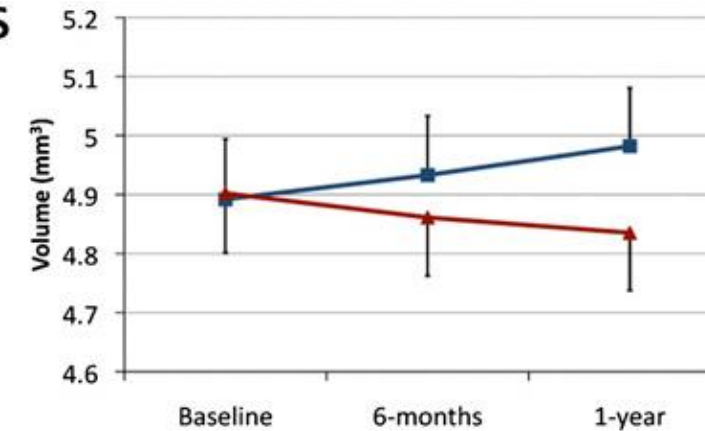
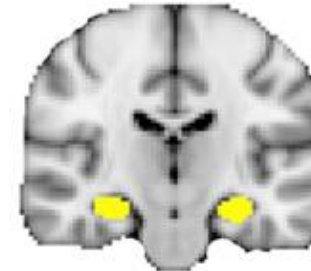
Aerobic Exercise Enhances Brain Function & Plasticity



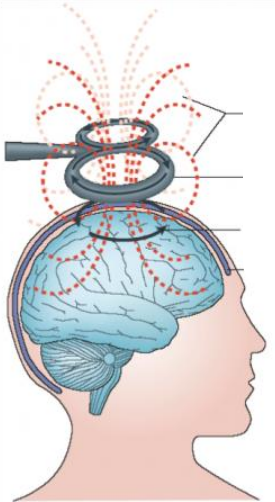
↑frontal blood flow



Hippocampus



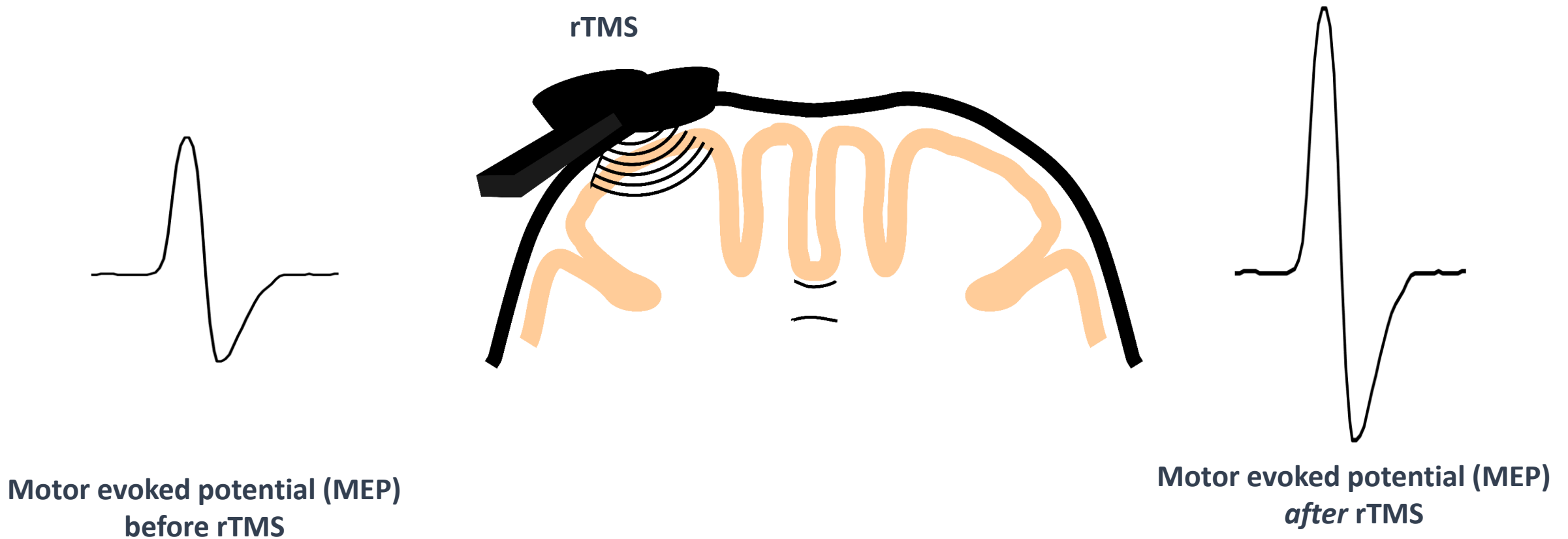
Transcranial Magnetic Stimulation
(TMS)



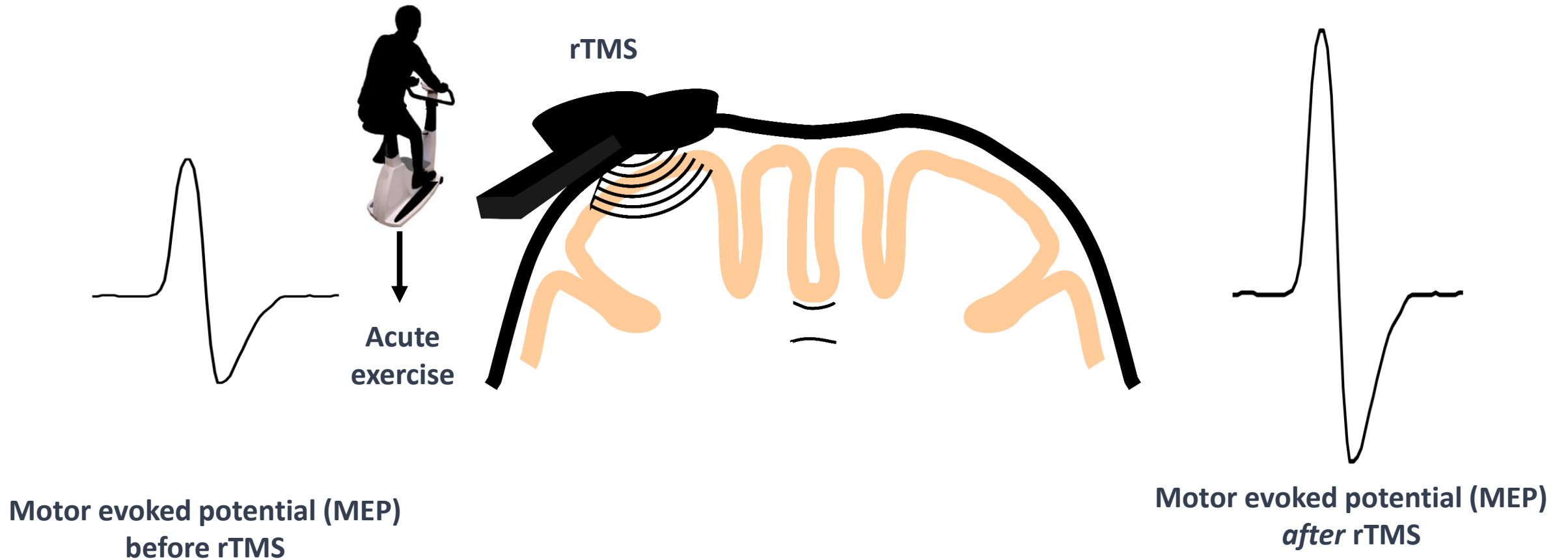
Modulating neuroplasticity mechanisms

Repetitive Transcranial Magnetic Stimulation (rTMS)

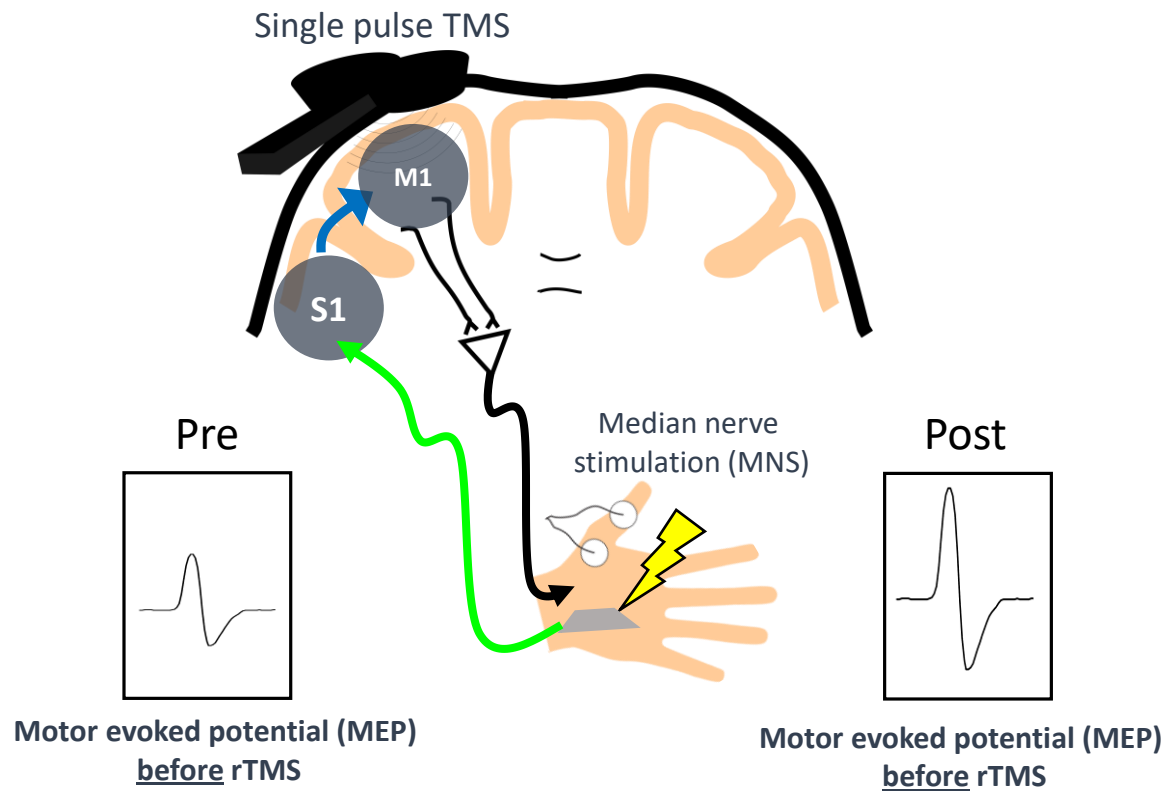
- \uparrow or \downarrow cortical excitability transiently after stimulation



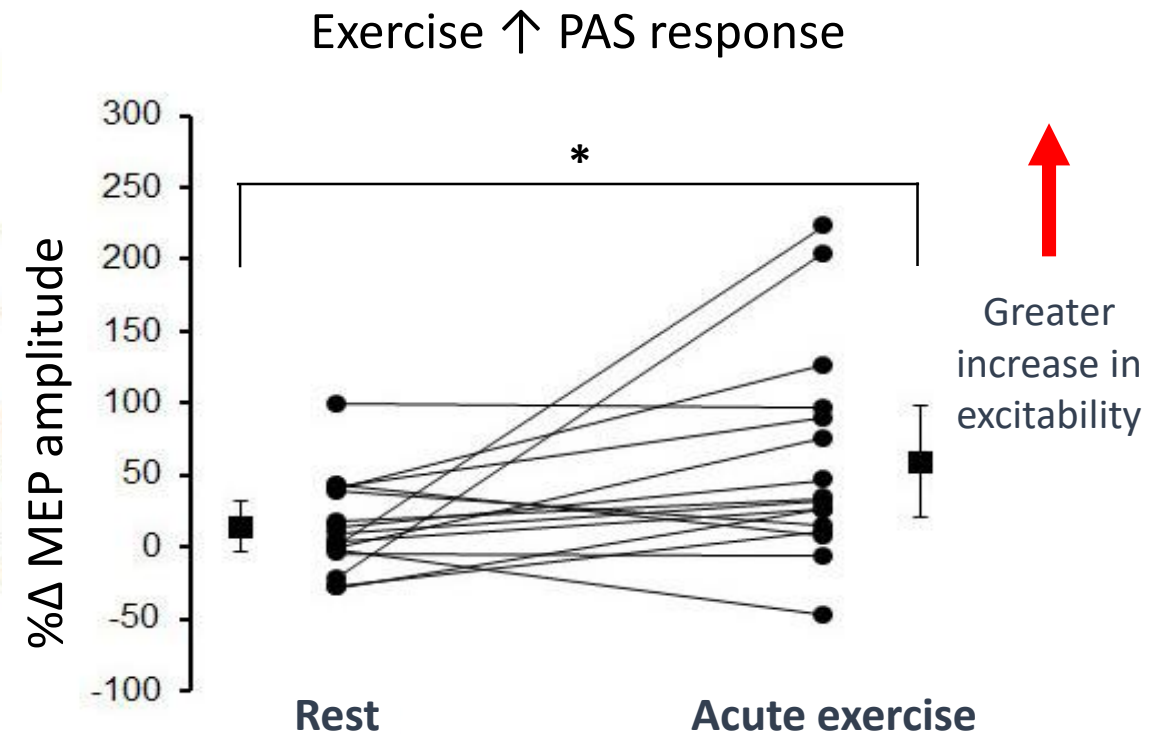
Acute exercise 'primes' neuroplasticity induction



Acute exercise ↑ response to Paired-Associative Stimulation (PAS)

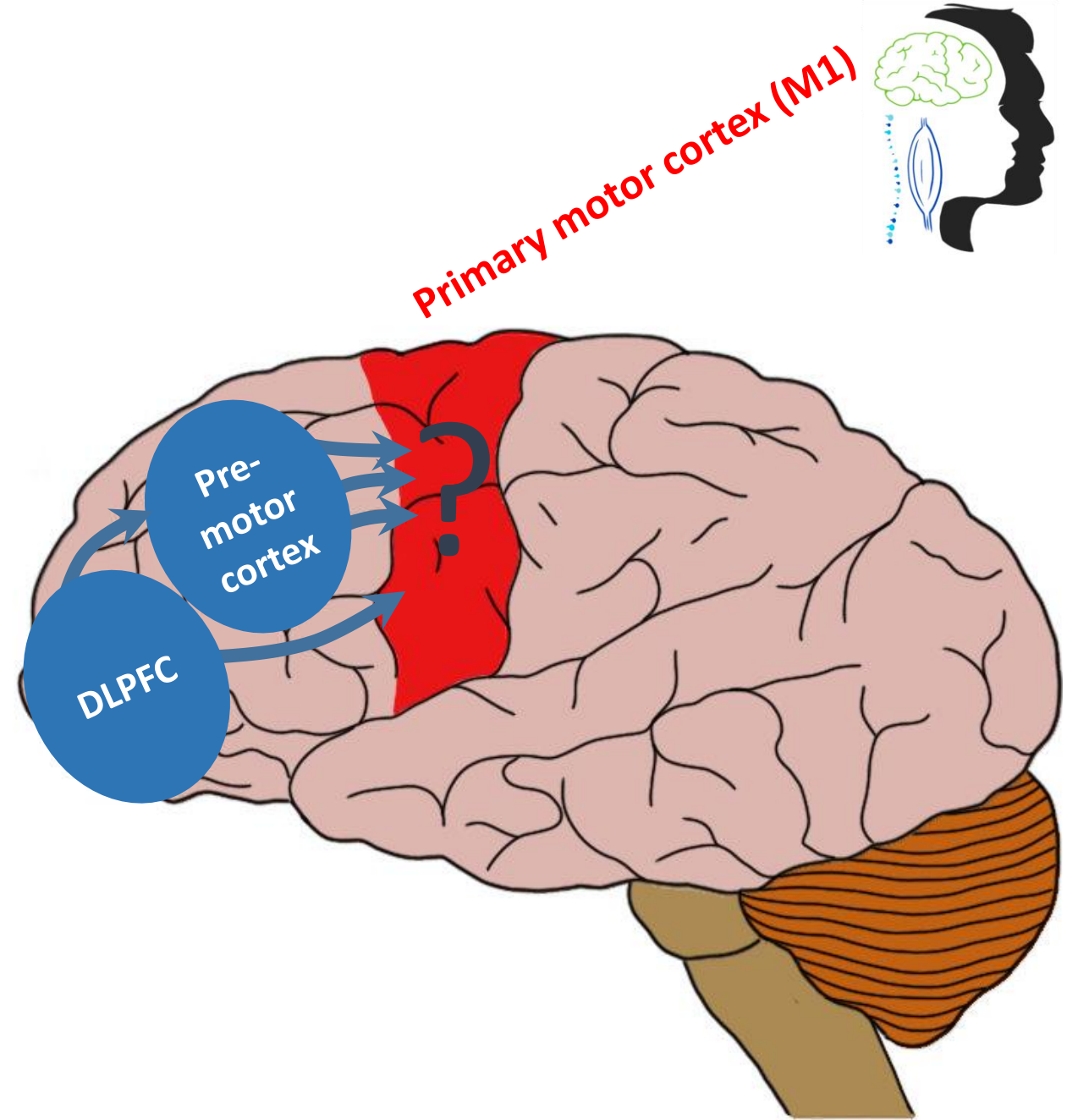


Paired-Associative Stimulation (PAS)
(25 ms interval between SNM + TMS, total of
200 paired stimuli)



Acute exercise increases neuropalsticity

How does
exercise improve
motor learning?



Aerobic Exercise Enhances Neuroplasticity



Add image of TMS and brain

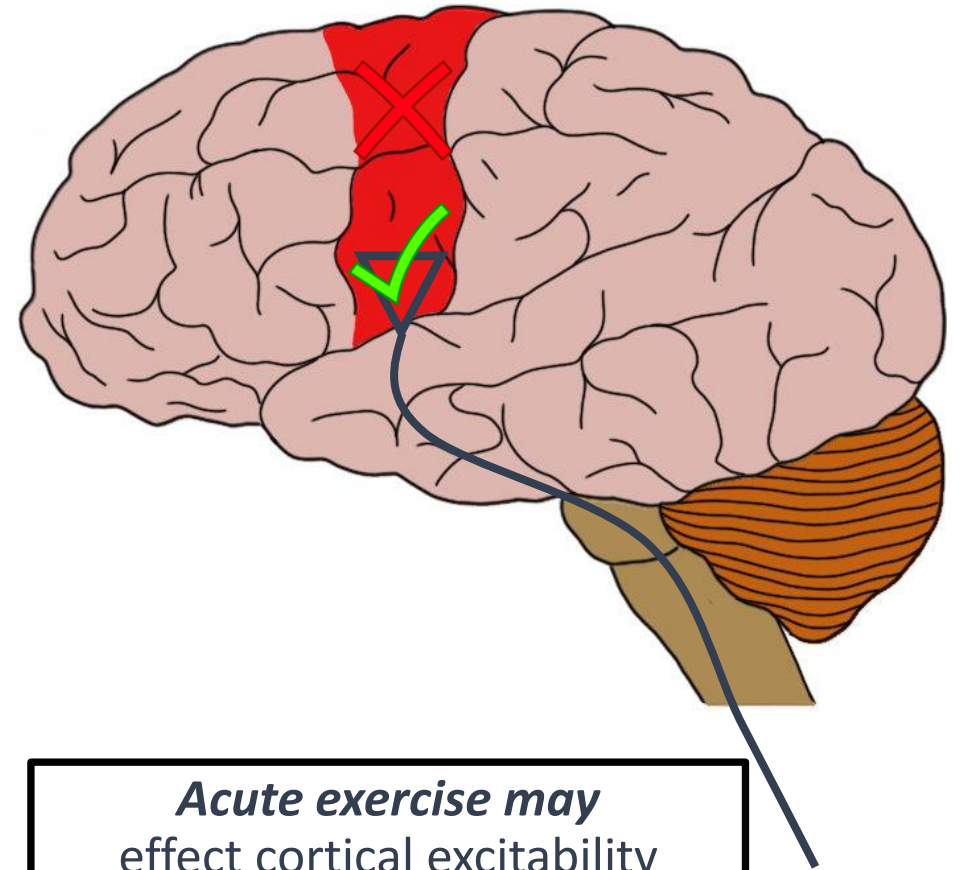
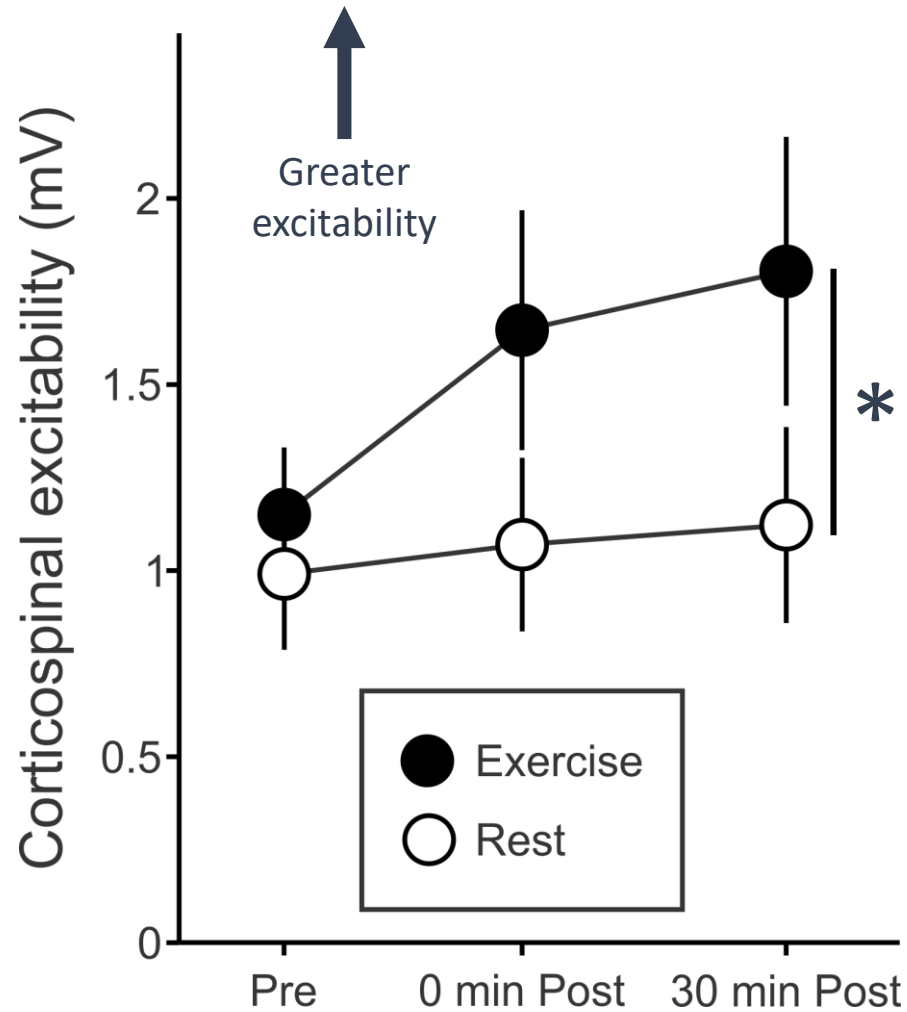
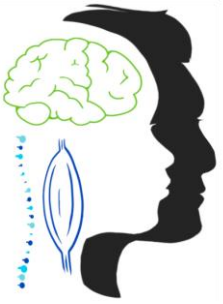
rTMS (make it look like rTMS and
Single pulse too....

Transition right to typical TMS slide



Add image of MEPs, arm and EMG

Healthy **older** people: Exercise ↑ corticospinal excitability



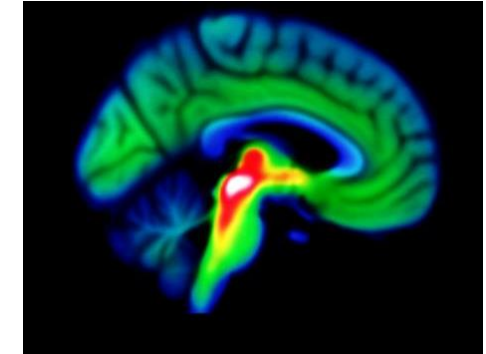
Acute exercise may
effect cortical excitability
differently ***across the lifespan***

Parkinson's disease (PD)

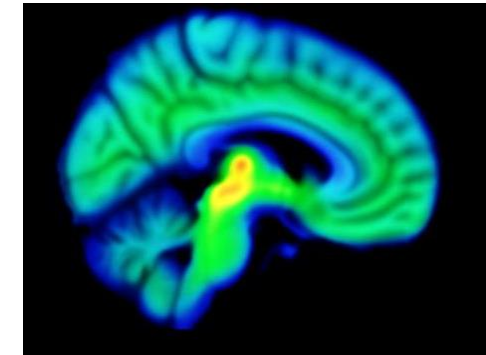
- Neurodegenerative disorder
- Bradykinesia, instability, tremor and rigidity
- ↓ motor cortex neuroplasticity
- ↓ motor learning on tasks requiring **cognitive strategy** and **attention**



Individual with PD



Healthy individual

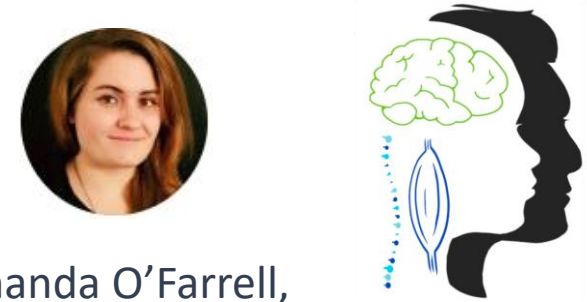


Person with PD

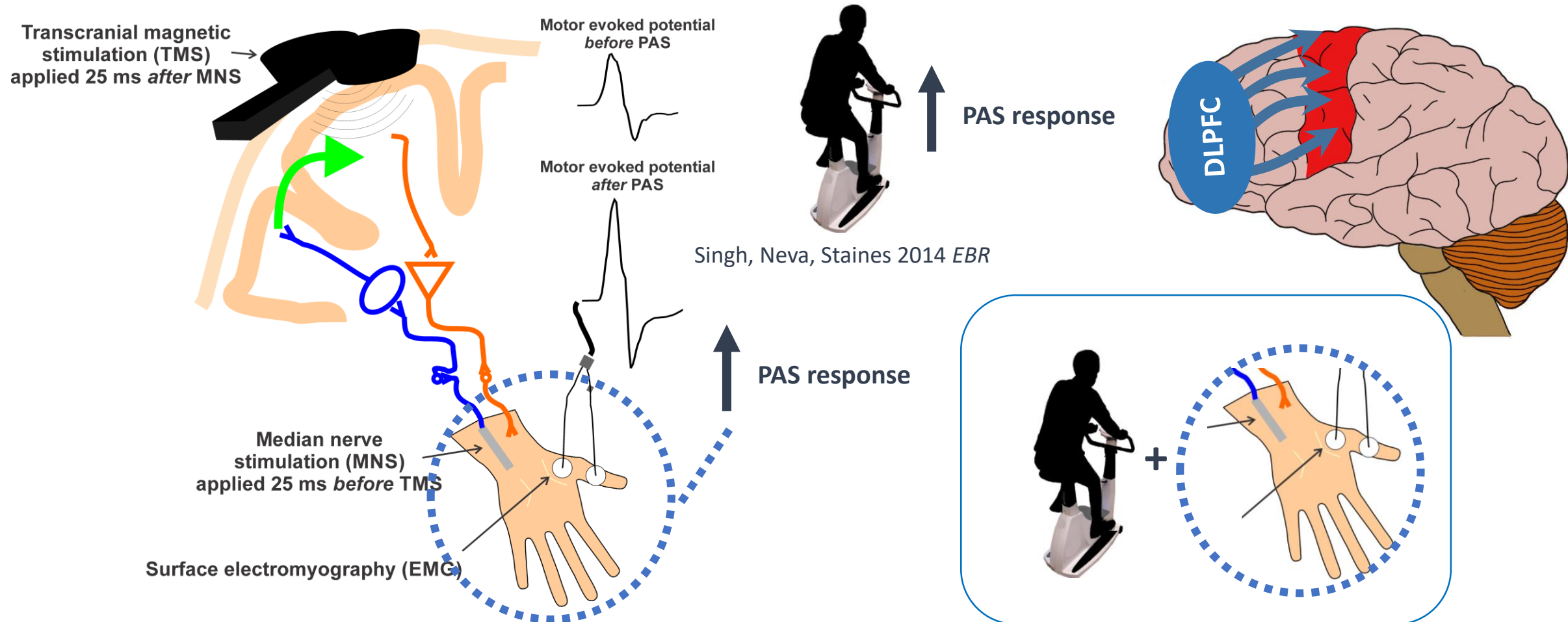
Basal ganglia affected

Aerobic exercise may improve PD-related symptoms

Parkinson's disease & attention: Exercise-induced neuroplasticity



Amanda O'Farrell,
PhD student

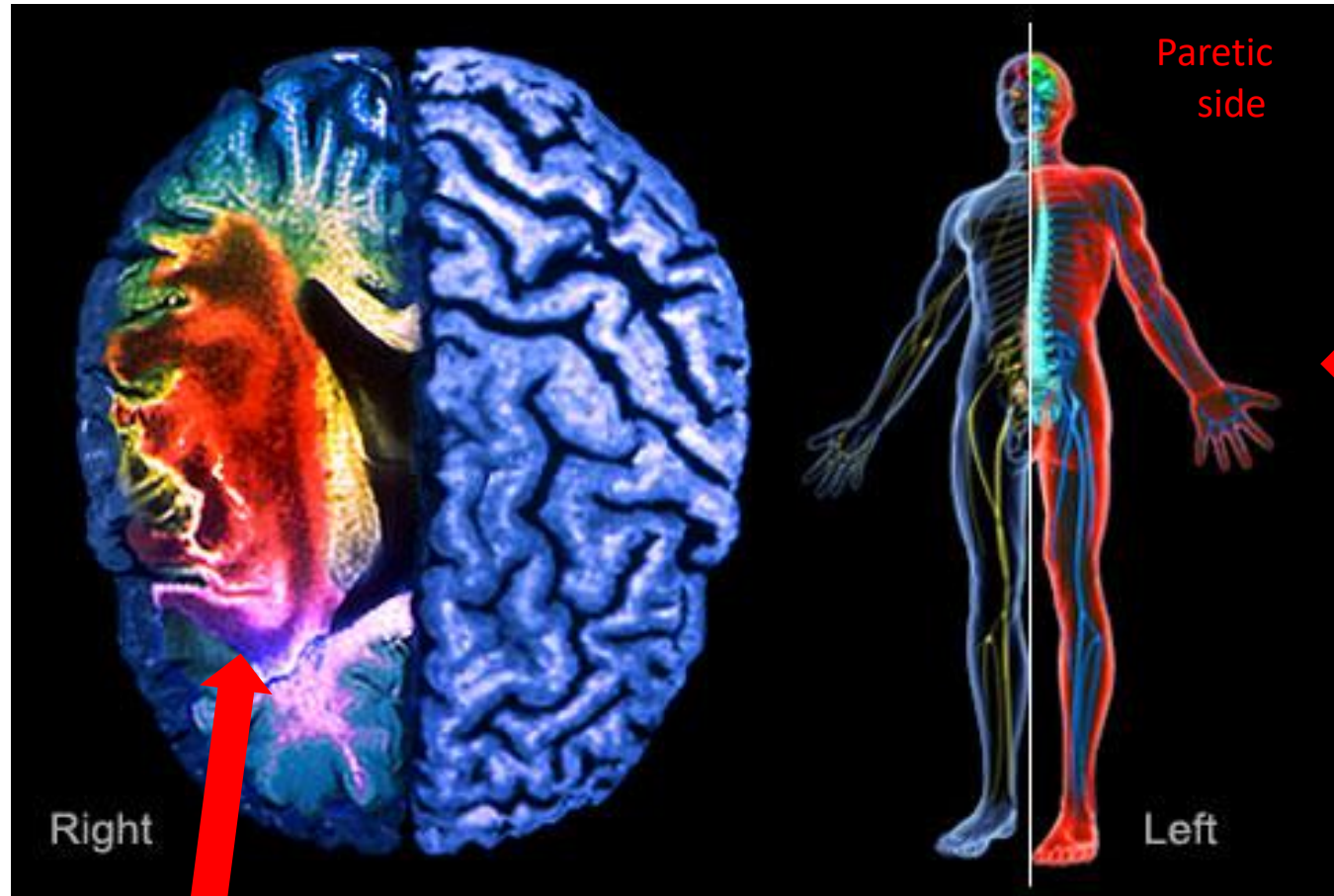


A. Paired-associative stimulation (PAS)

Stroke

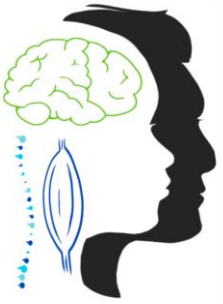
“Brain attack”

- Loss of blood & oxygen to the brain
- Brain tissue damage



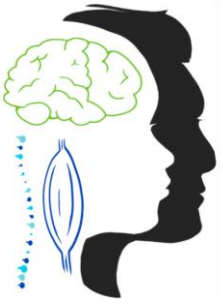
Stroke affected
region

~85% of Canadians live with persistent impairments
into the chronic (< 1 year) post-stroke

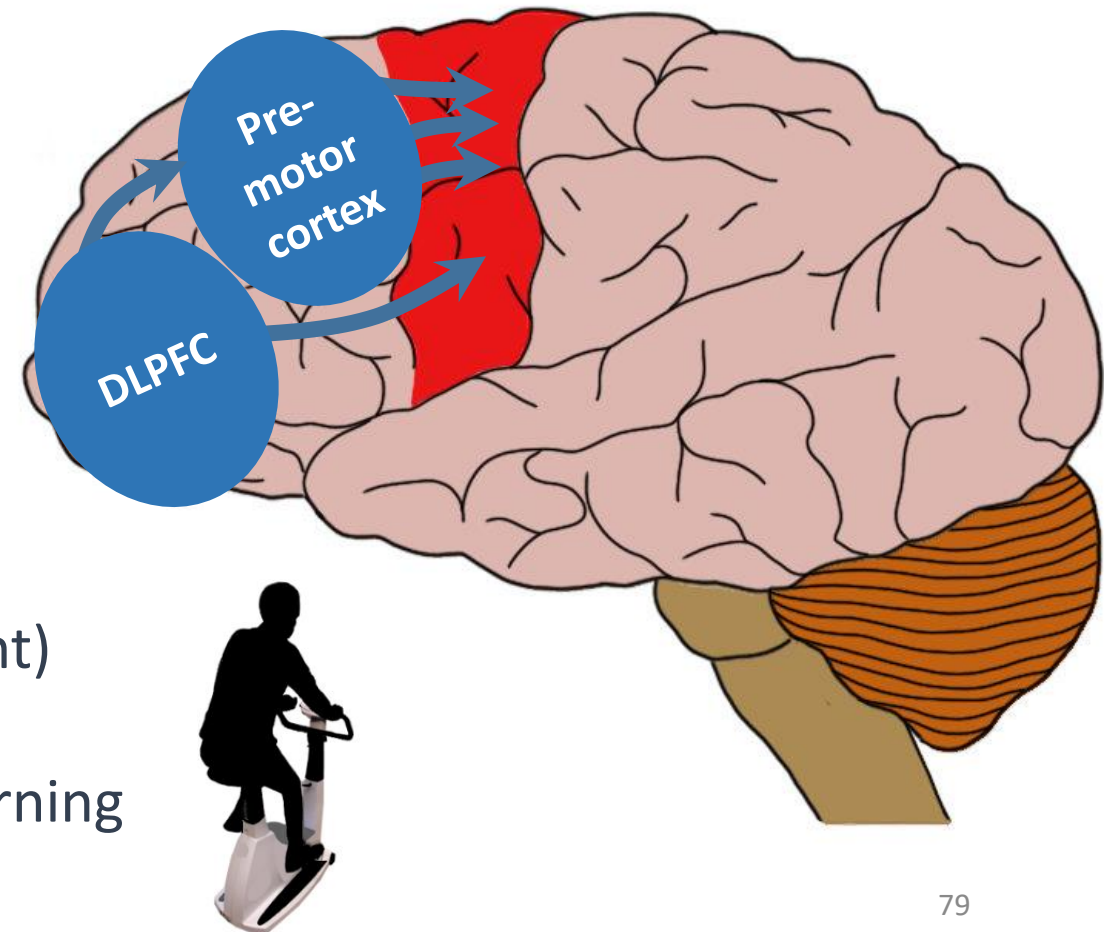


Stroke

Neva et al., 2019, Restorative Neurology & Neuroscience;
Neva et al., 2020 *Wiley Encyclopedia of Health Psychology*, Vol III



- Cortical resources associated with **planning** and **cognitive strategy** contribute to recovery of function following stroke
- Specifically, how these regions interact with the motor cortex after middle cerebral artery **stroke** (motor-related damage/impairment)
- Acute exercise: ↑ neuroplasticity + ↑ motor learning



Stroke & attention:

Exercise-induced neuroplasticity

Future work

