Transcranial Stimulation: From Cortical Mapping to Clinical Implications

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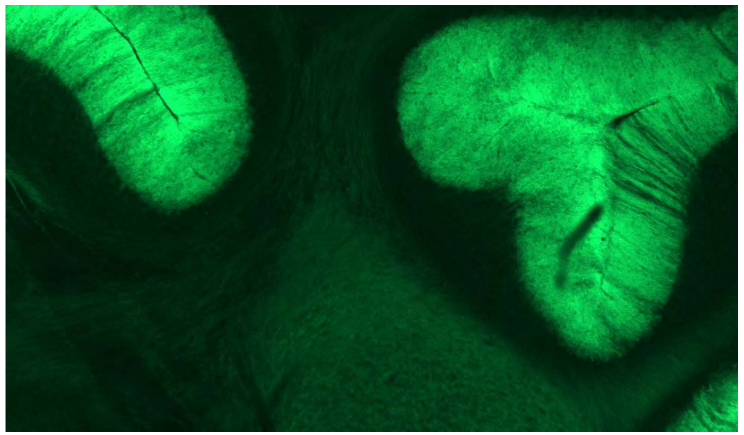
Education

- Ithaca College
- University of Tennessee Health Science Center

Clinical

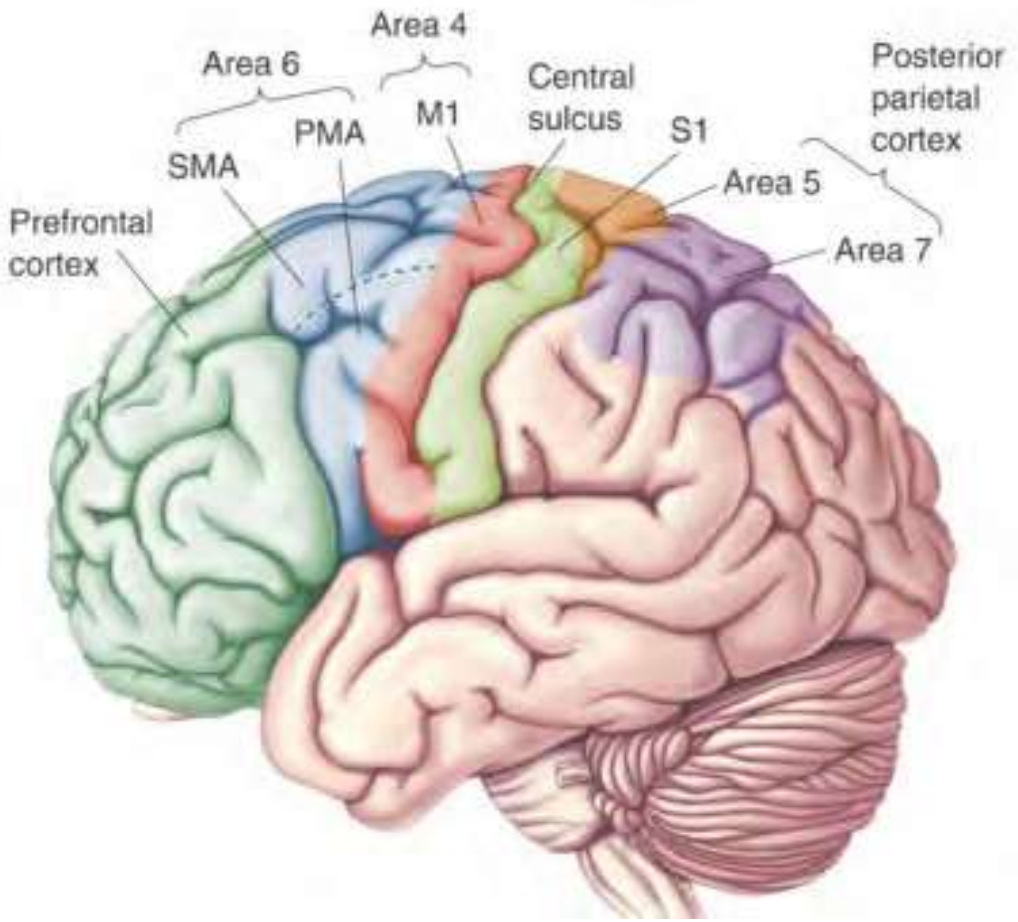
- HealthPro Heritage: Pediatrics/ Outpatient Orthopedics
- Roam Yoga & Physio, LLC
- Memphis Rox Climbing + Community



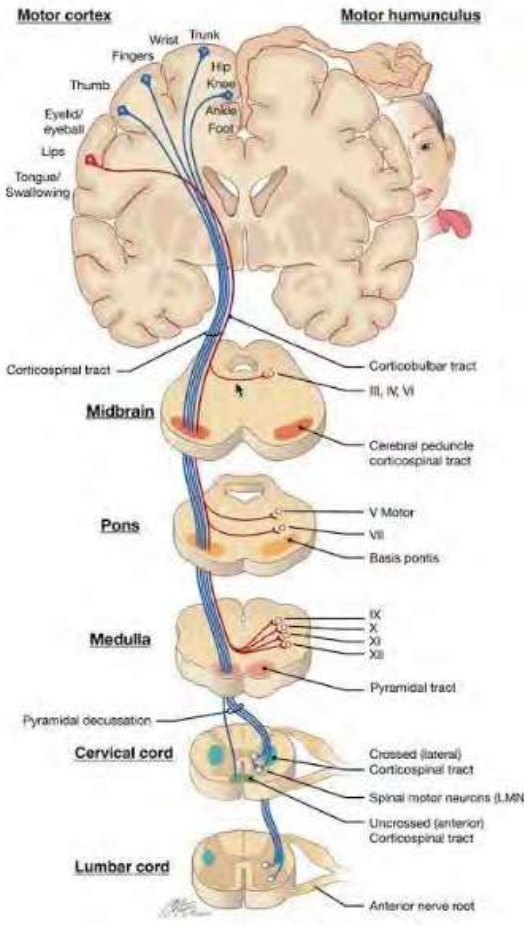
Overview

- Review Neuroanatomy
- Transcranial Magnetic Stimulation
- Cortical Oscillations/ Synchrony/ Coherence
- TMS + Peripheral Nerve Stimulation and Cortico-muscular Coherence

Cortical Centers



Corticospinal tracts



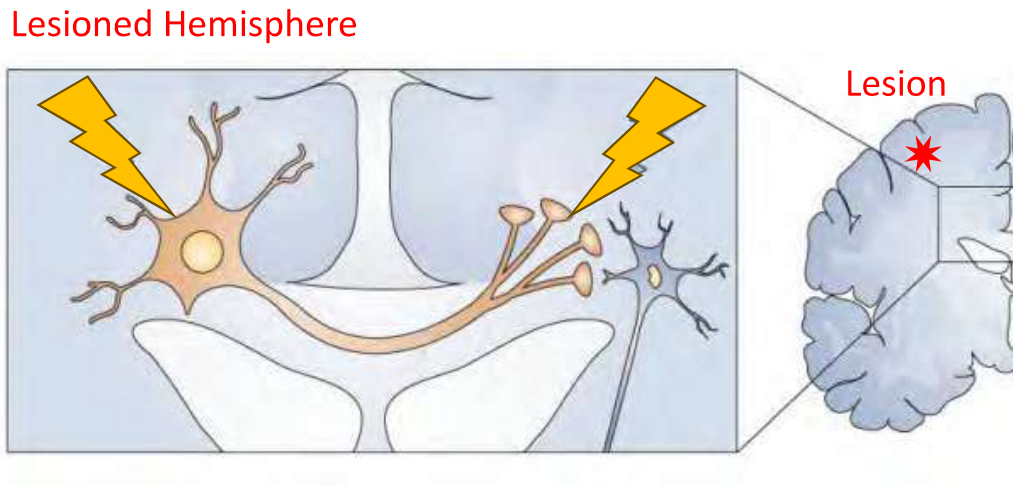
Interhemispheric Inhibition (IHI)

Inhibition between L/ R hemisphere unbalanced:

- lesioned hemisphere ↓ inhibition of unaffected hemisphere

- ↑ excitability of unaffected hemisphere

- excessive inhibition of lesioned hemisphere from unaffected hemisphere



Inhibition between L/ R hemisphere equal

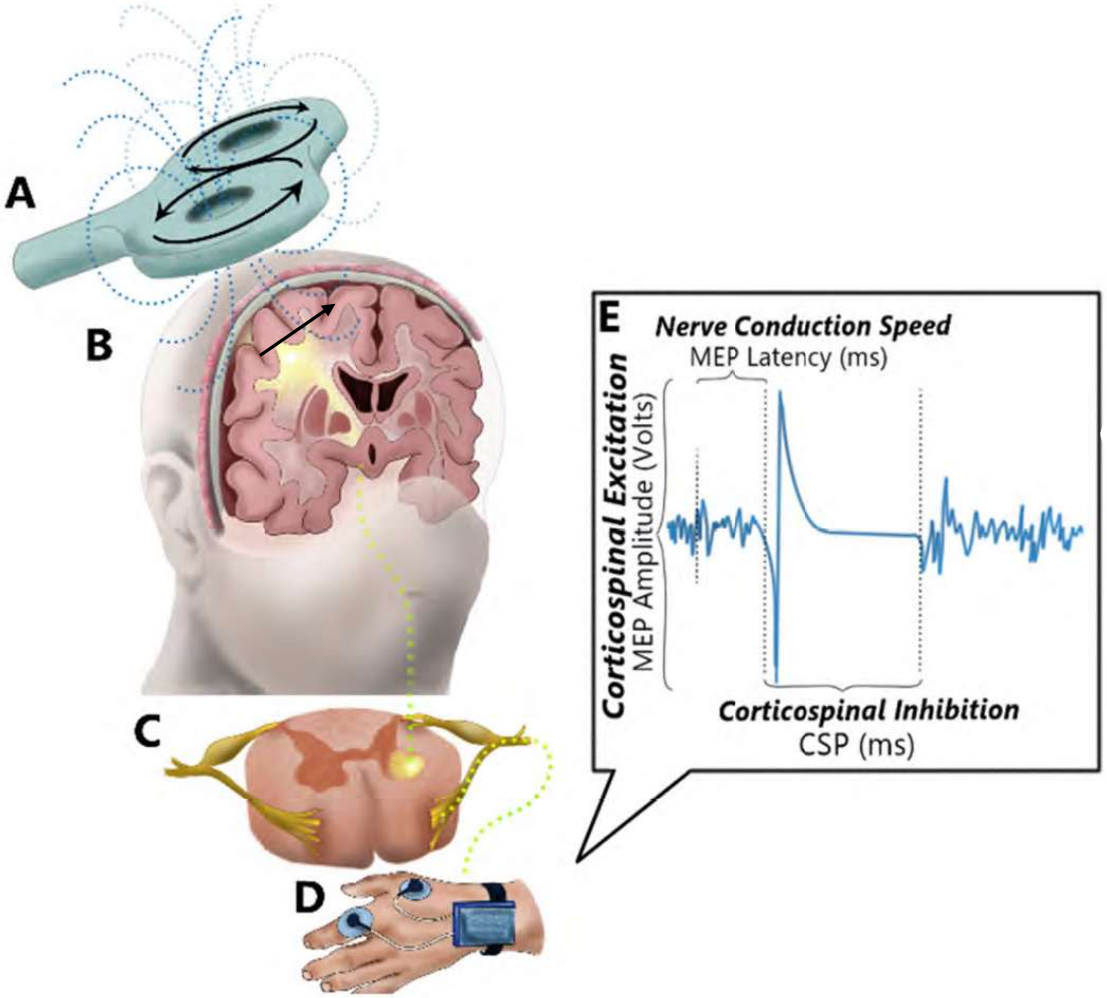
- baseline inhibition bilaterally

- ↑ inhibition of the ipsilateral hemisphere during unimanual movements

Result:
- Impede neuroplasticity
- limit motor recovery of lesioned hemisphere

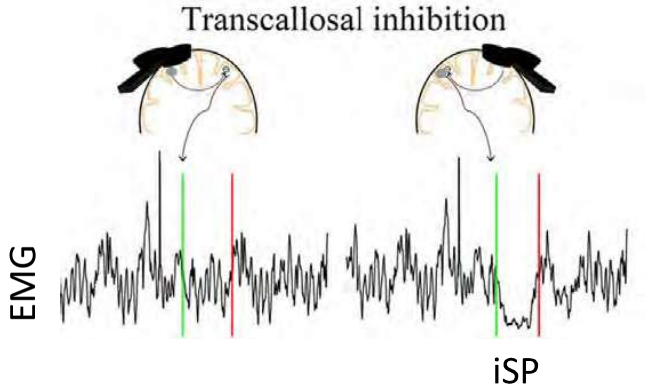
Result:
- Suppress “mirrored” movements

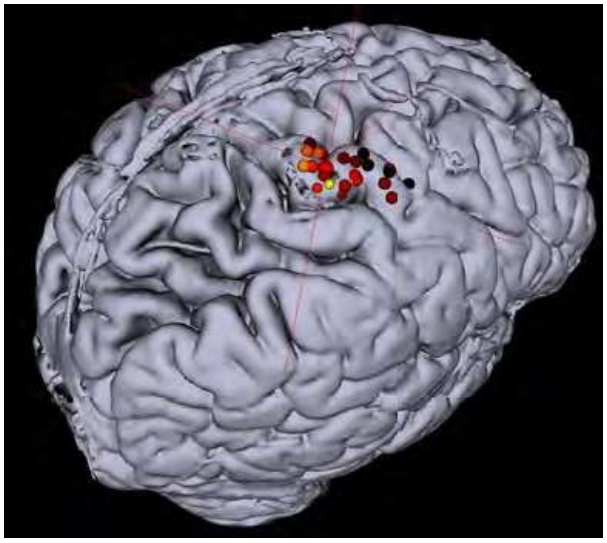
Mechanism of Transcranial Magnetic Stimulation (TMS)



Neurophysiological measurements of TMS

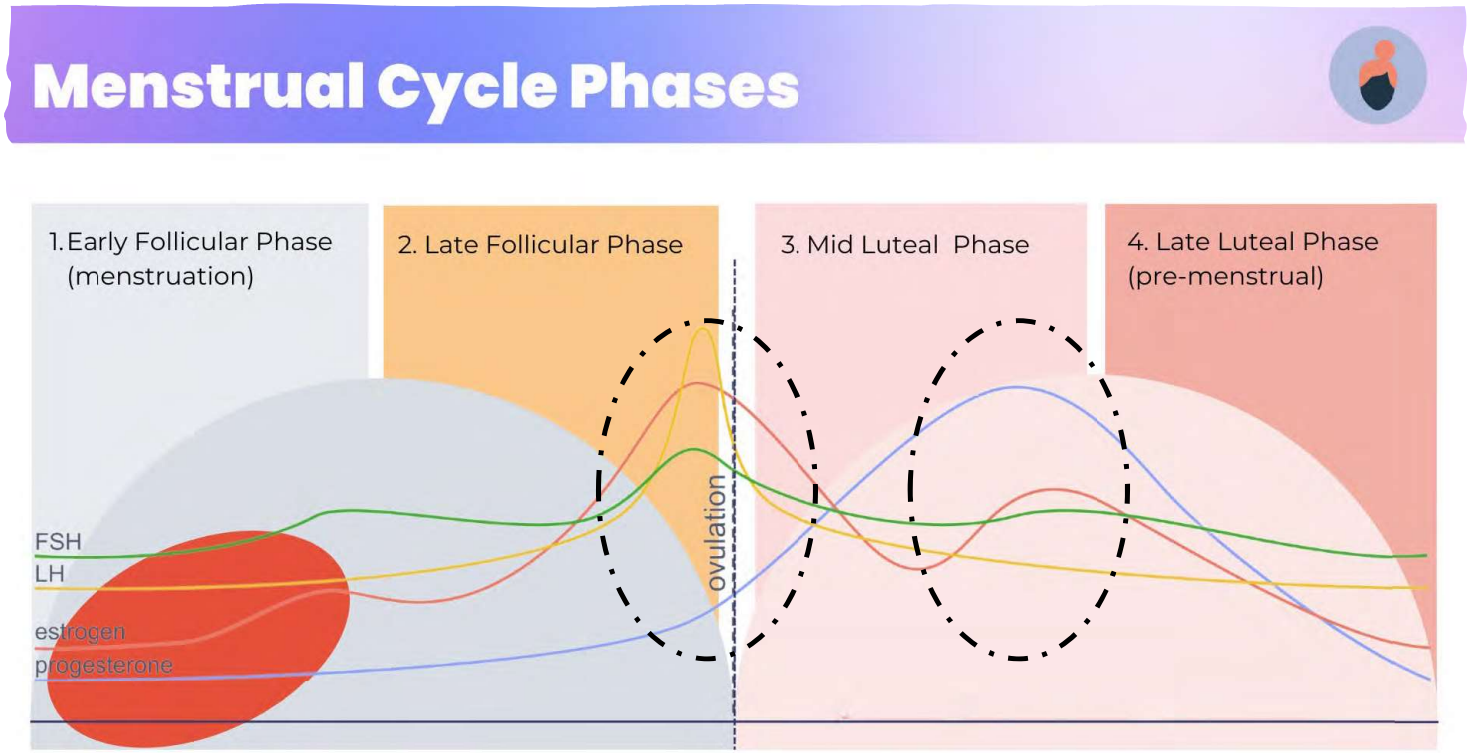
- Cortical excitability
  - Measured by the electrical field required to evoke a MEP (V/m)
- Inhibitory balance
  - Transcollosal inhibition (or IHI): Visible ipsilateral silent period (iSP) with stimulation of the ipsilateral hemisphere or isometric m contraction of the contralateral extremity
  - Measured by SICI/ LICI
- Nerve conduction velocity
  - Latency of MEP
- Motor mapping
  - Presented as center of gravity value for each muscle tested





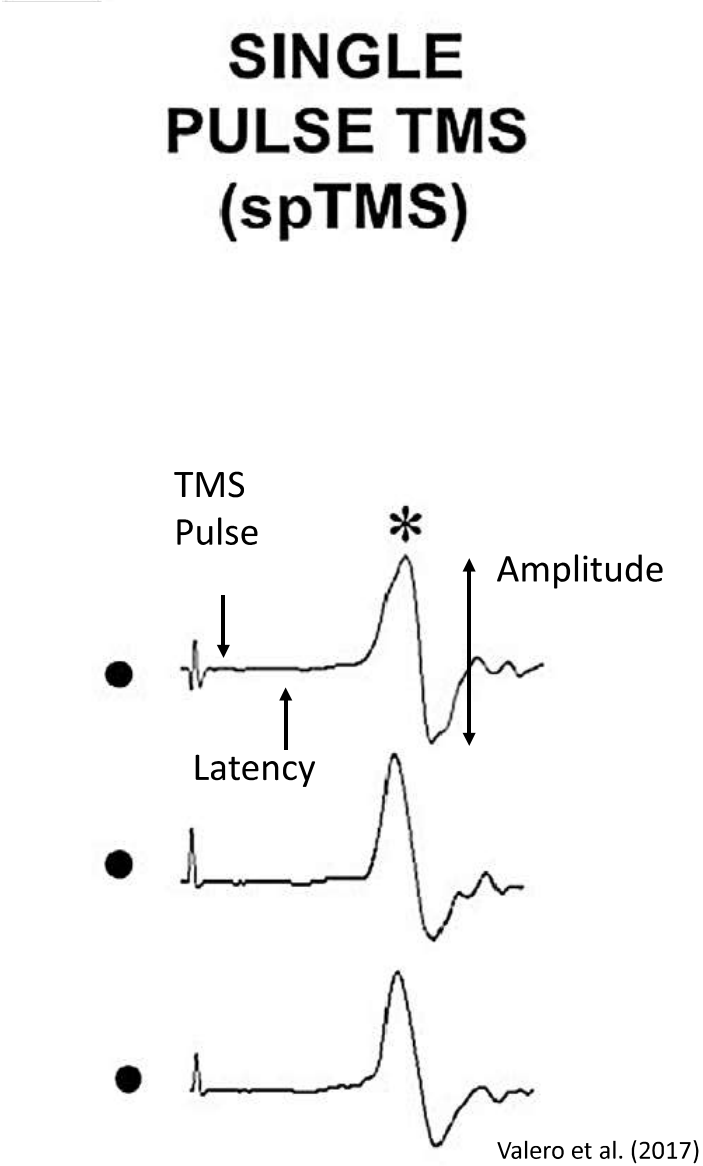
Considerations for Cortical Excitability

- Caffeine/Nicotine intake
- Sleep / Circadian cycle
- Age
- Medications (i.e. Antiepileptic Meds, Birth Control)
- Menstrual Cycle Phase



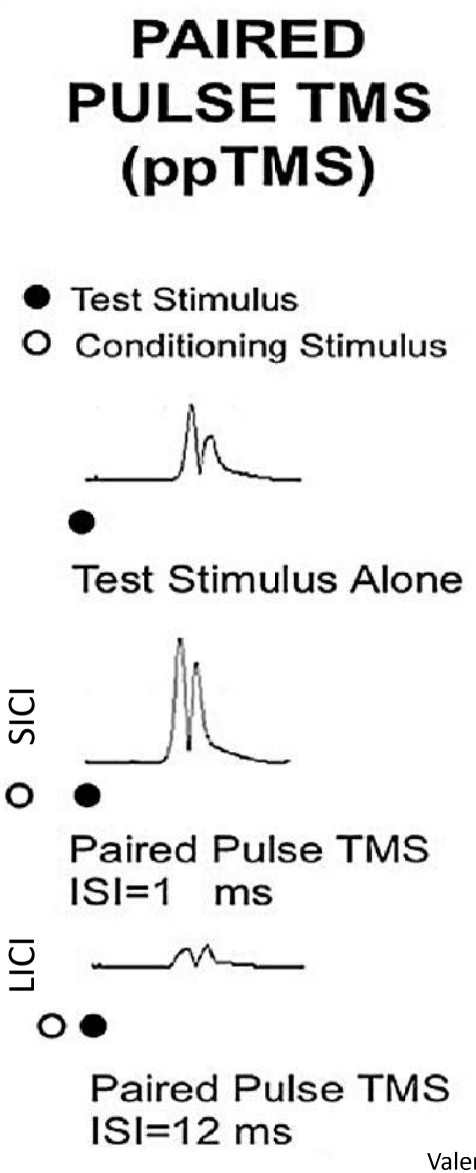
Types of TMS

- Single Pulse (spTMS)



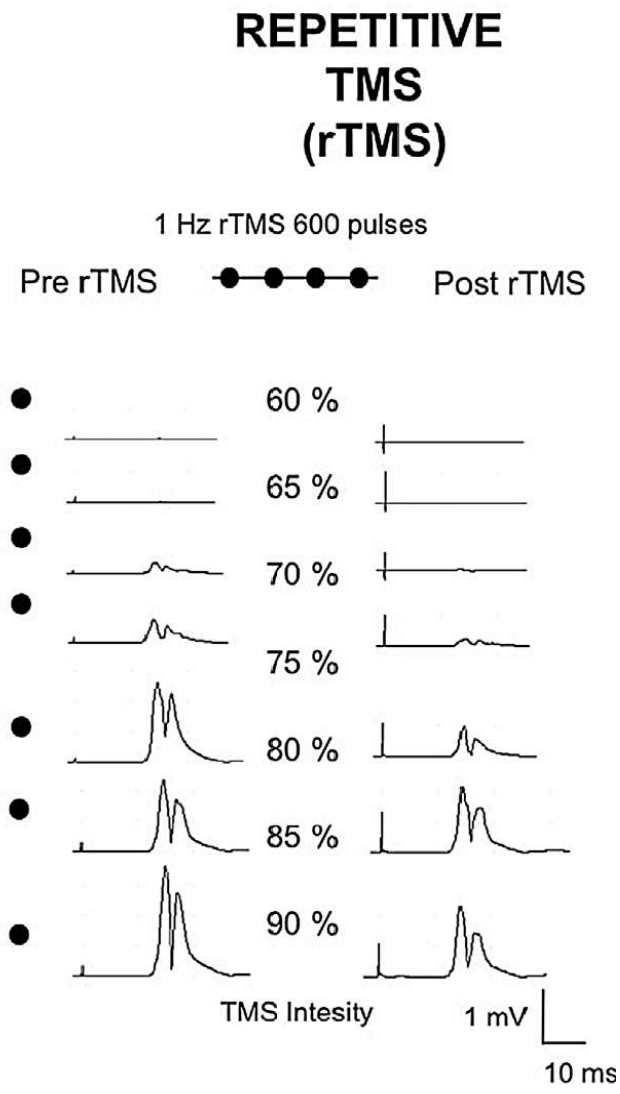
Types of TMS

- Paired Pulse (ppTMS)
  - Short ISI (1 - 6 ms)
    - Short interval intracortical inhibition (SICI) → Subthreshold CS + Suprathreshold TS
    - Short interval intracortical facilitation (SICF)→ Suprathreshold CS + Subthreshold TS
  - Moderate ISI (10 - 15 ms)
    - Intracortical facilitation → Subthreshold CS + Suprathreshold TS
  - Long ISI (50 - 200 ms)
    - Long Interval intracortical inhibition (LICI) → Suprathreshold CS + TS
    - Long Interval intracortical inhibition (LICF) → Subthreshold CS + Suprathreshold TS



Valero et al. (2017)

Types of TMS



- Repetitive (rTMS)
  - Slow trains (≤ 1 Hz) → decreases excitability
  - Fast trains (>1 Hz) → increases excitability

Valero et al. (2017)

Transcranial Magnetic Stimulation (TMS) Contraindications

- Contraindications
  - Metallic objects implanted in head
  - Deep brain stimulators
  - Vagus Nerve Stimulators

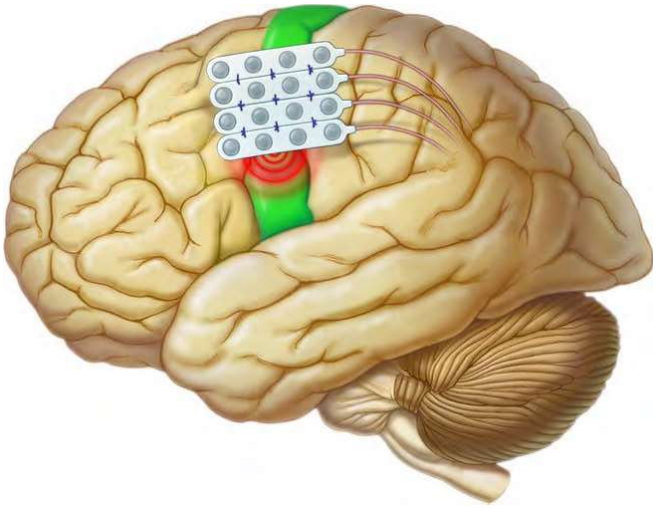
- Adverse Effects
  - Seizures (atypical)
  - Irritation from the sensation of stimulation
    - Feels like a tapping sensation – similar to nerve conduction study/ NMES

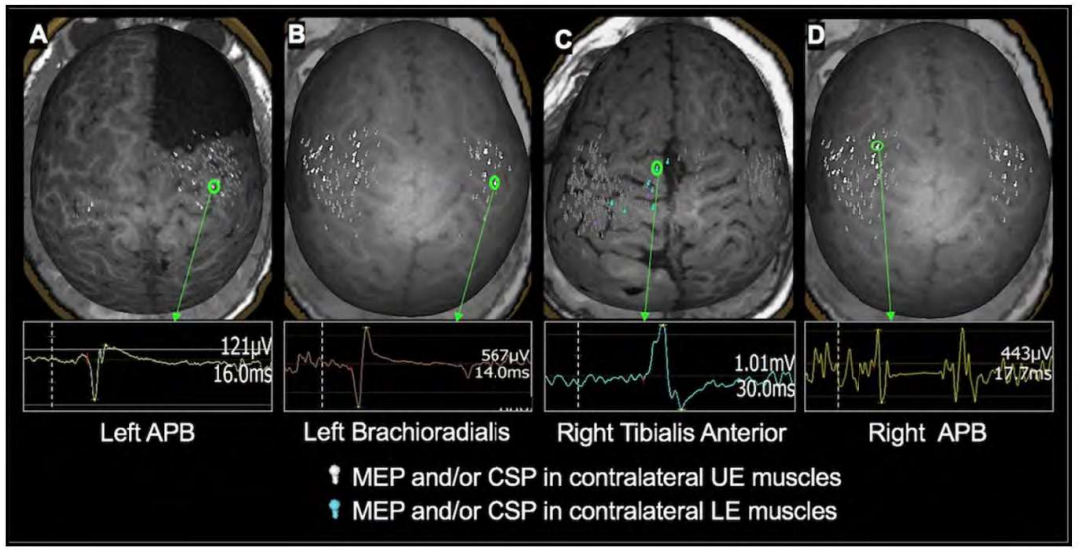
TMS Uses

- FDA approved
  - Major Depressive Disorder (2008)
  - Migraines (2013)
  - Obsessive Compulsive Disorder (2018)
  - Smoking Cessation (2020)
  - Anxious Depression (2021)
  - PTSD (2023)

- Presurgical Mapping of Motor + Speech Areas
  - Alternatives: Cortical stimulation (invasive), fMRI, and MEG

- Current Research
  - UE/ LE motor function after CVA
  - Gait training for PD
  - Fatigue for fibromyalgia
  - Cortico-muscular Coherence





TMS Motor Mapping

TMS Language Mapping

Semantic Error

Performance Error

Speech Arrest

rTMS effects on rehabilitation from CVA

- Lesioned hemisphere
  - Most studies used high-frequency rTMS (3 – 20 Hz) with variable results
    - Dependent on white matter volume and subcortical lesion presence

- Unaffected hemisphere
  - Goal: reduce inhibitory control of the unaffected hemisphere on lesioned hemisphere thus making it more excitable

  - Low-frequency rTMS (<1 Hz) or Theta Burst Stimulation
    - Improved hand function/ reach-to-grasp movements
    - Associated with reduced inhibition to lesioned M1

  - High-frequency rTMS
    - Improved motor performance of paretic hand
    - Decreased unaffected hemisphere activity during affected UE movement
    - Improved connectivity between SMA/ M1 in the lesioned hemisphere

TMS promotes gait training in patients with PD

	1 Hz rTMS (n = 17)	25 Hz rTMS (n = 17)	Sham rTMS (n = 16)
Intervention	• 600 pulses in 10 minutes	• 600 pulses in 4 second trains with ISI 50 sec	• Disconnected coil on head + connected coil making sounds

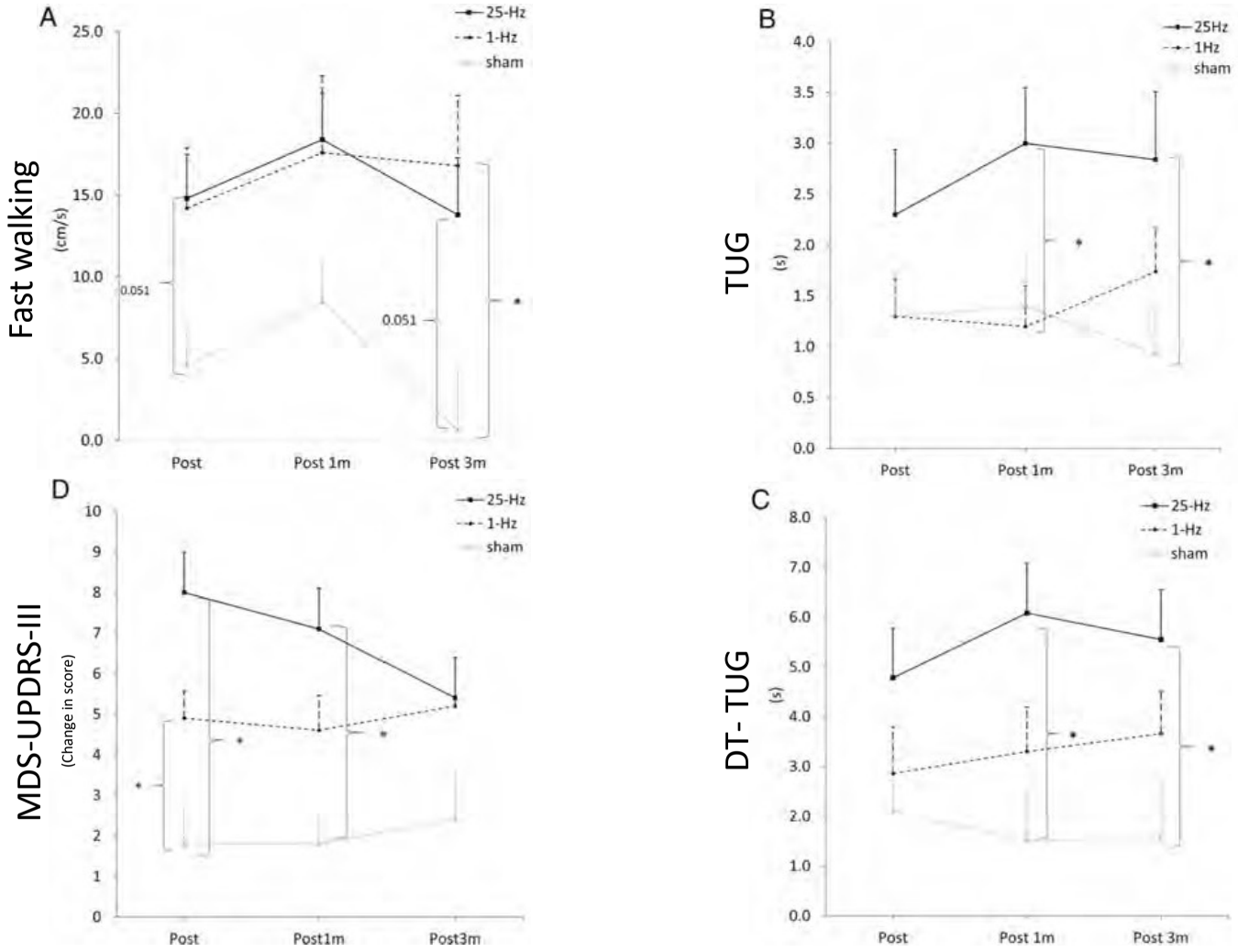
Intervention	• TMS + 30-min Treadmill training (4x/week x 3 weeks)
	  • ↑ speed by 0.2 km/hr every 5 minutes
	  • Maintained max speed until end of session		

Assessment	• Assessments at 1-day, 1-month[#], and 3-months[+] after intervention
	  • Max walking speed, total distance, Borg perceived exertion scale, MDS-UPDRS-III
	  • Excitability (slope of recruitment, cortical silent period, SICI values)		

Results	• ↑ fast walking speed • Improved TUG[+] and DT-TUG • ↓ MDS-UPDRS-III	• ↑ fast walking speed[+] • Improved TUG [# +] and DT-TUG [# +] • ↓ MDS-UPDRS-III [# +]	• ↑ fast walking speed

Lau-Ha Chung et al. (2020)

TMS promotes gait training in patients with PD



High-frequency TMS + exercise for Women with Fibromyalgia

Physical Exercise Group - PEG (n=16)	TMS Group - TMSG (n=17)	Control group - CG (n = 16)
• 2 x 60 min low-intensity exercise/ week x 8 weeks	• 5 x 20 min high-frequency TMS/ week x 2 weeks	• No intervention

Izquierdo-Alventosa et al. (2021)

High-frequency TMS + exercise for Women with Fibromyalgia

- Perceived Pain
  - 10 cm VAS at rest
- Average Pressure pain Threshold
  - Algometer at 18 different points on body (used to dx FM)
- QOL
  - Revised Fibromyalgia Impact Questionnaire (FIQR) – subsections include physical function, overall impact, and severity of symptoms
- Endurance
  - 6-Minute Walking test (heart rate, SpO_2, Borg rate of perceived fatigue)
- Induced Fatigue
  - CR-10 Borg Scale (after 6MWT)
- Gait Velocity
  - 4-meter gait speed test
- Sit-up power
  - 5 repetitions sit-to-stand
- Anxiety
  - Hospital Anxiety and depression Scale (7-item anxiety subscale)
- Depression
  - Beck Depression Inventory-Second Edition
- Stress
  - Perceived Stress Scale-10

Izquierdo-Alventosa et al. (2021)

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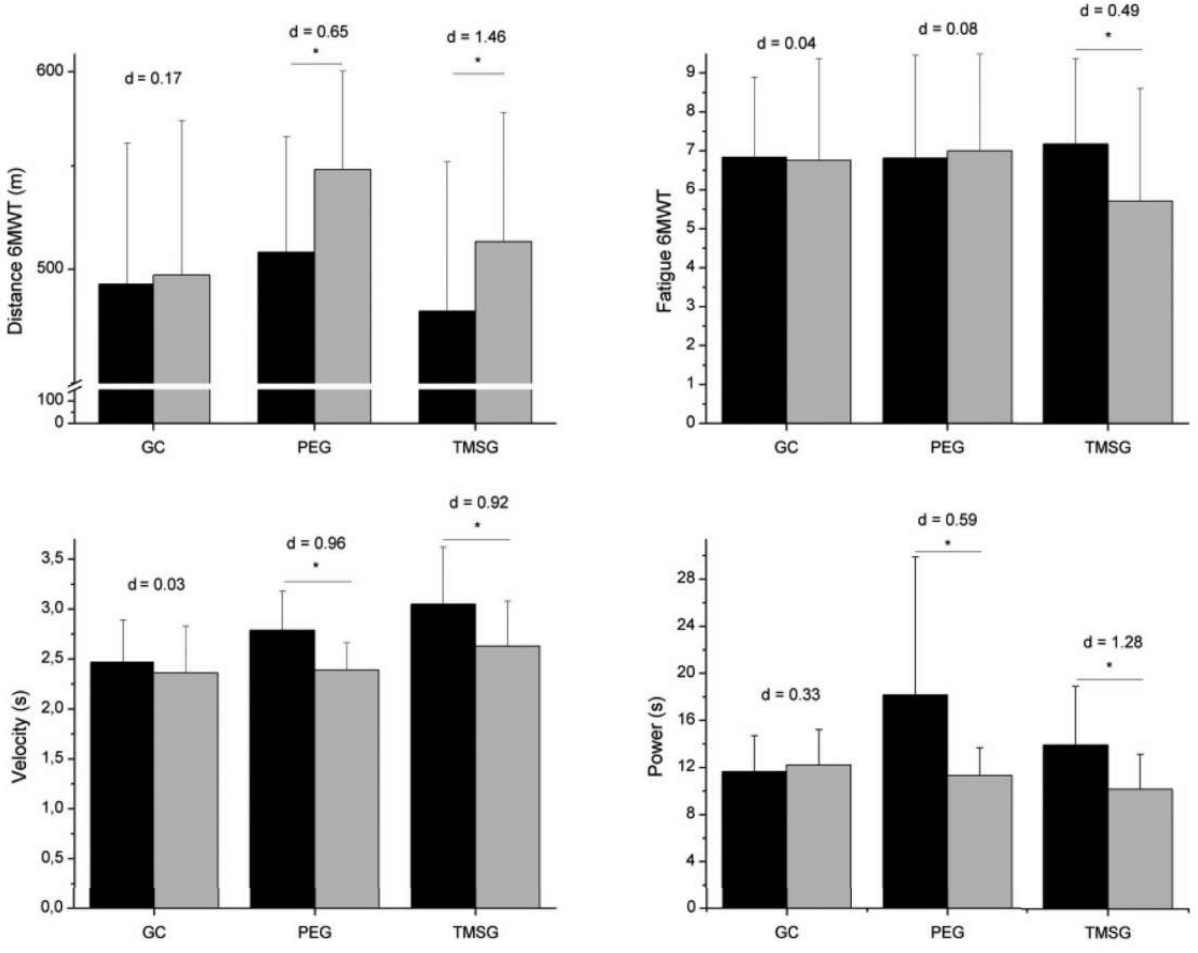
• 2 x 60 min low-intensity exercise/ week x 8 weeks	• 5 x 20 min high-frequency TMS/ week x 2 weeks	• No intervention
• ↑ pressure pain threshold • ↑ QOL (FIQR) - in overall impact only • ↑ distance in 6MWT • ↓ anxiety, depression, + stress	• ↓ perceived pain • ↑ pressure pain threshold • ↑ QOL (FIQR)* - in physical function, overall impact, severity of sx • ↑ distance + ↓ fatigue in 6MWT • ↓ anxiety, depression*, + stress*	• No significant changes in all measures tested

Izquierdo-Alventosa et al. (2021)

High-frequency TMS + exercise for Women with Fibromyalgia



Izquierdo-Alventosa et al. (2021)

Behavioral/Cognitive

Gait-Phase Modulates Alpha and Beta Oscillations in the Pedunculopontine Nucleus

Shenghong He,[1,2] Alceste Deli,[3] Petra Fischer,[1,2] Christoph Wiest,[1,2] Yongzhi Huang,[4] Sean Martin,[3] Saed Khawaldeh,[1,2,5] Tipu Z. Aziz,[2,3] Alexander L. Green,[2,3] Peter Brown,[1,2] and Huiling Tan[1,2]

[1]MRC Brain Network Dynamics Unit, University of Oxford, Oxford OX1 3TH, United Kingdom, [2]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford OX3 9DU, United Kingdom, [3]Nuffield Department of Surgical Sciences, University of Oxford, Oxford OX3 9DU, United Kingdom, [4]Academy of Medical Engineering and Translational Medicine, Tianjin University, Tianjin 300072, People's Republic of China, and [5]Oxford Centre for Human Brain Activity, Wellcome Centre for Integrative Neuroimaging, University of Oxford, Oxford OX3 7JX, United Kingdom

Brain Network Oscillations During Gait in Parkinson's Disease

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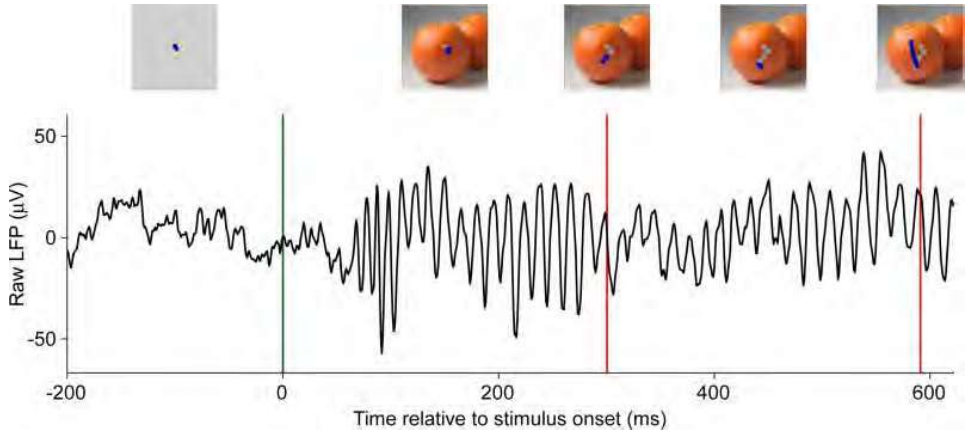
[2] Department of Applied Physiology and Kinesiology, University of Florida, Gainesville, FL, United States

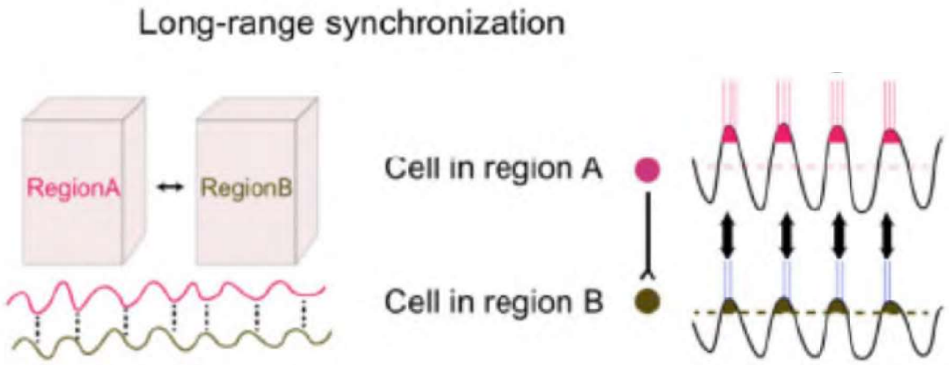
Enhancement of long-range EEG coherence by synchronous bifocal transcranial magnetic stimulation

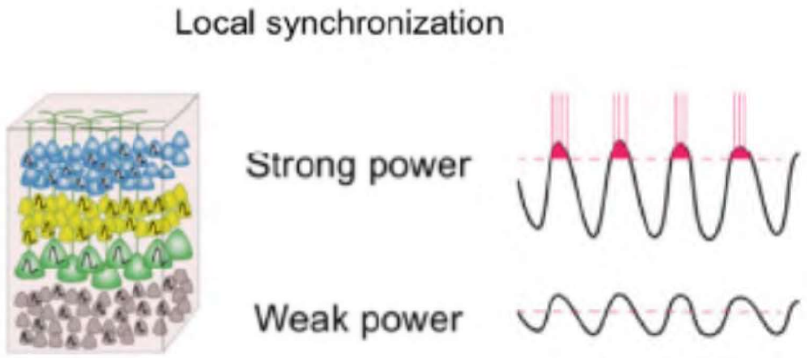
Christian Plewnia, Albrecht J. Rilk, Surjo R. Soekadar, Carola Arfeller, Heiko S. Huber, Paul Sauseng, Friedhelm Hummel, Christian Gerloff

Connectivity Terms

- Oscillations
- Synchrony
- Frequency (Hertz)





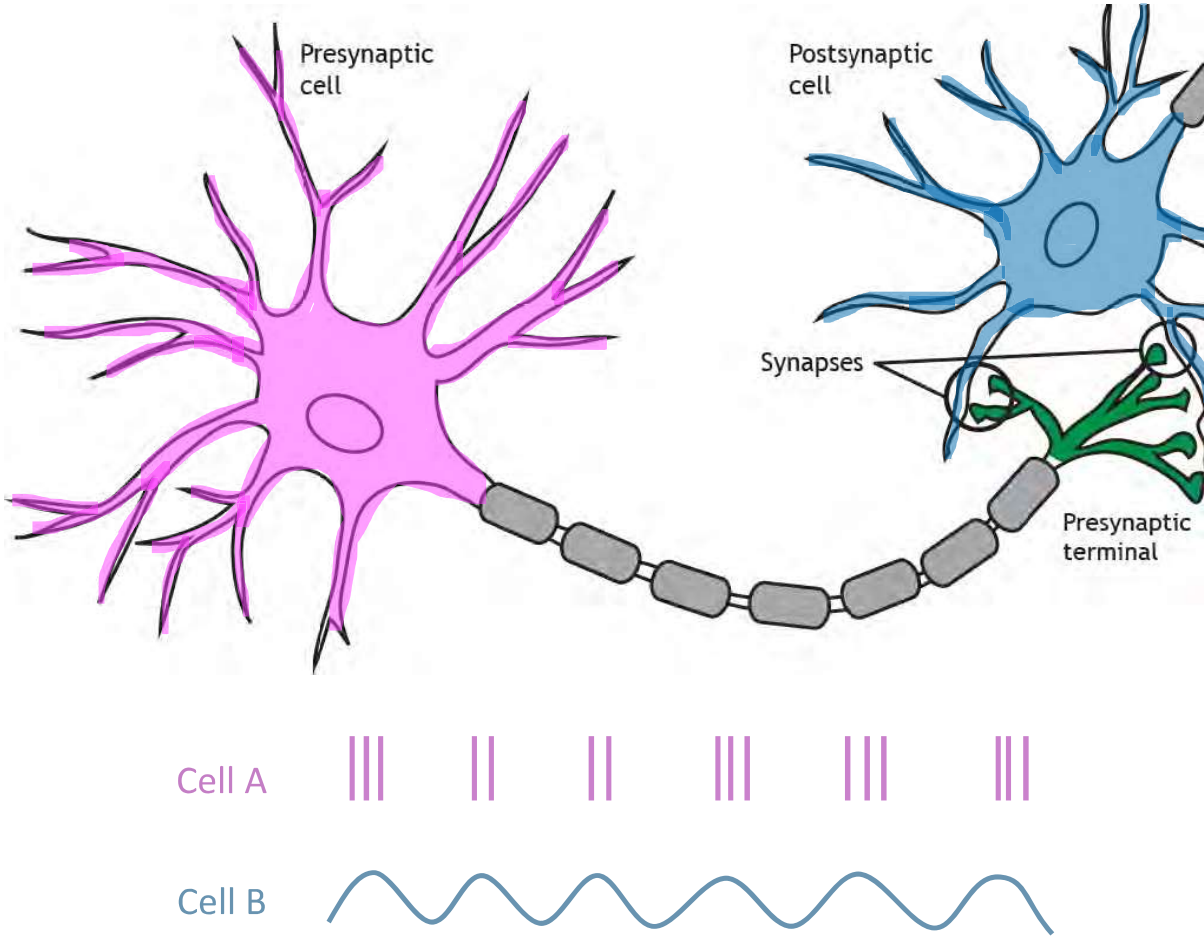


Behavioral States are Represented in Frequency Bands

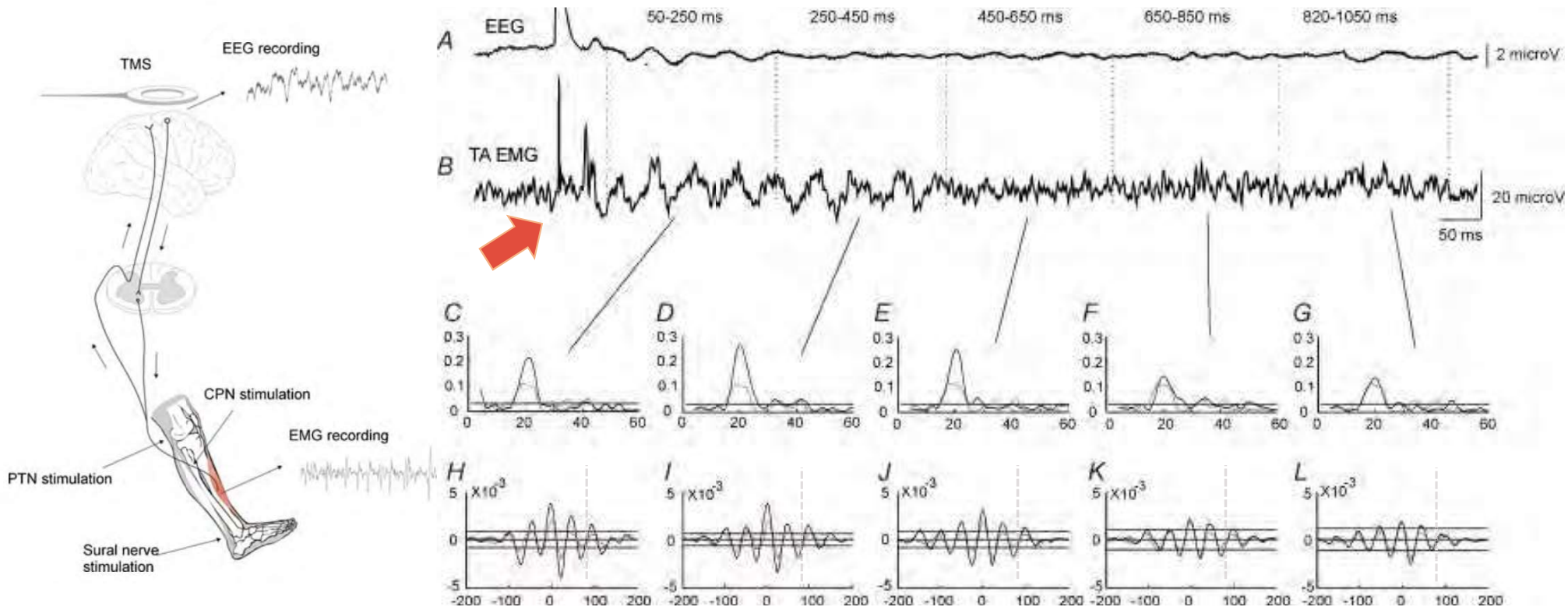
Cortical Oscillation	**Brain/ Behavioral State**
Delta (1-4 Hz)	Slow Wave Sleep
Theta (4-8 Hz)	Meditation, Drowsiness, **Navigation**
Alpha / Mu (8-12 Hz)	Wakeful rest, **Movement Intention**
Beta (12-32 Hz)	Wakeful Consciousness, **Motor Processing**
Gamma(25-140 Hz)	REM Sleep, **Sensory Perception,** Cognition/ Decision Making

Communication Through Coherence

- Synchronous firing of neurons entrained by presynaptic cell
- Stable relationship between presynaptic cell AP transmission and postsynaptic cell excitable
- Frequency of oscillations encodes information about signal input

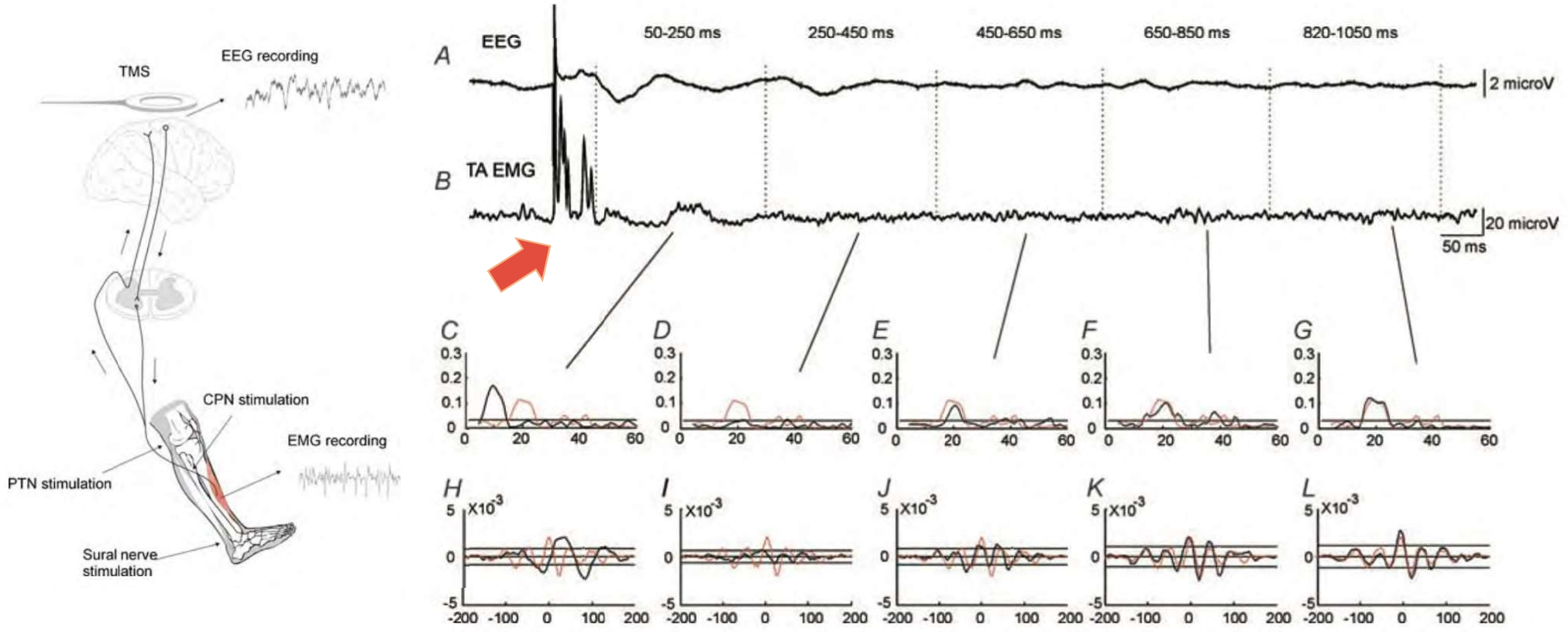


TMS + Peripheral Nerve Stimulation on Cortico-muscular Coherence



(Hansen and Nielsen, 2004)

TMS + Peripheral Nerve Stimulation on Cortico-muscular Coherence



(Hansen and Nielsen, 2004)

Thank you

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