Using Paired Associative Stimulation to Evoke Plasticity as Effective Motor Recovery

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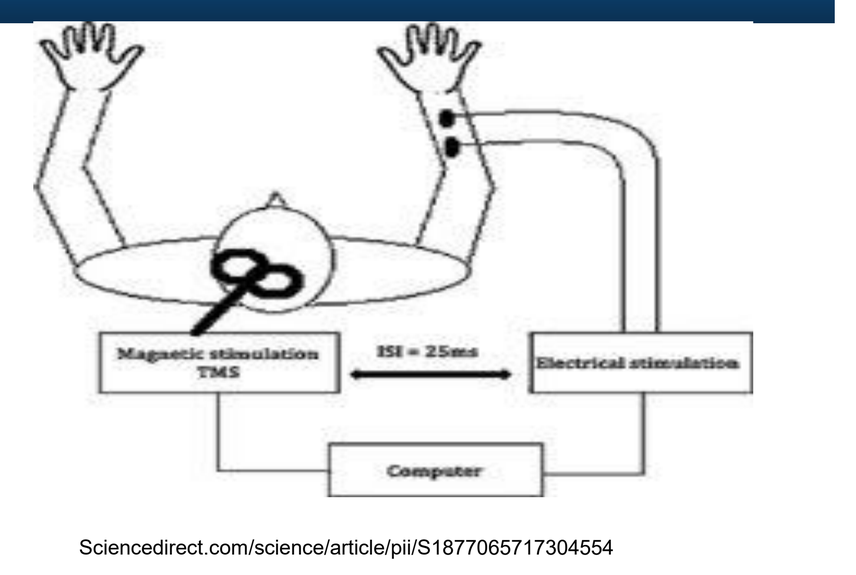
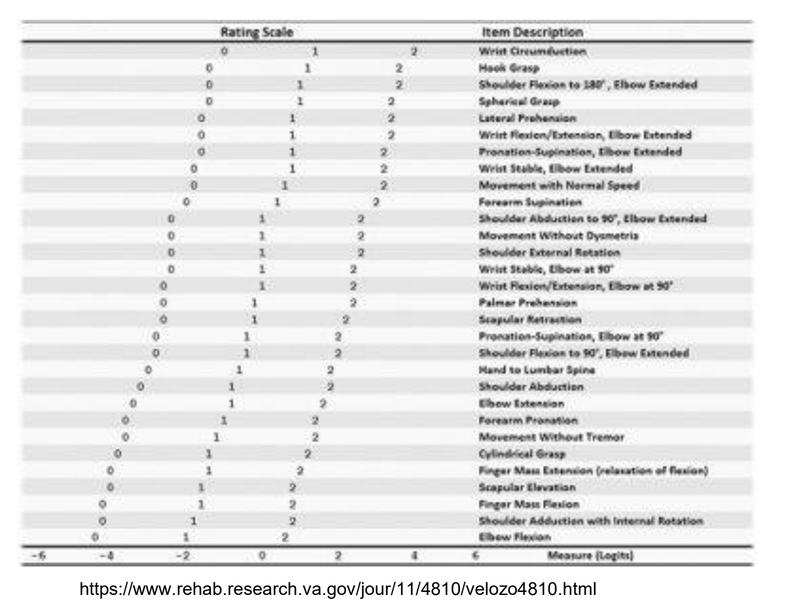
Burke Neurological Institute — The science hope demands

Introduction

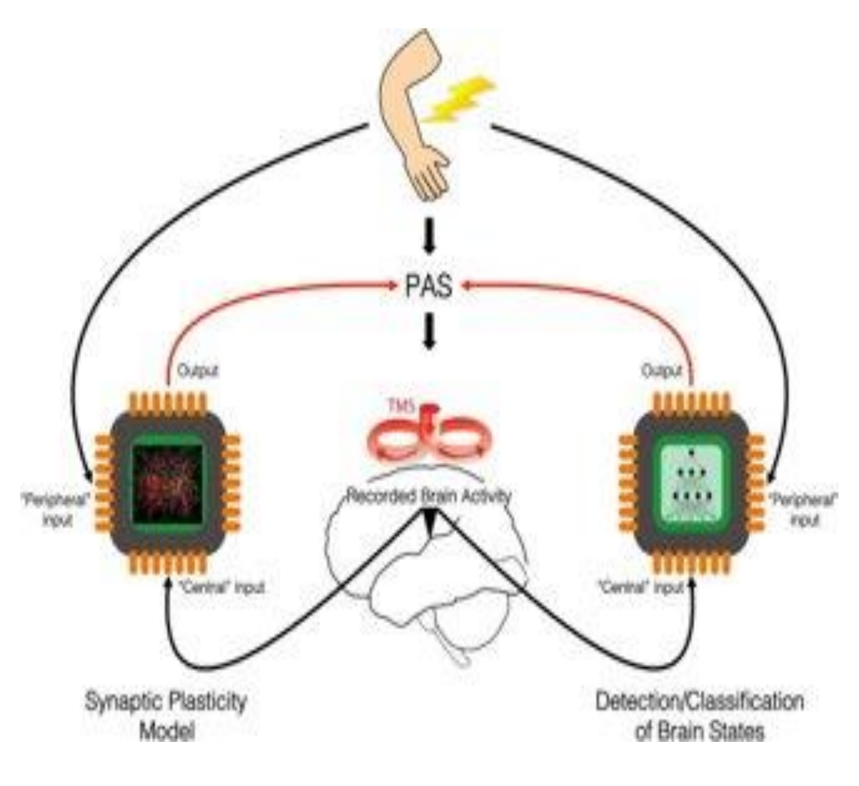
- Strokes are a neurological condition caused by reduced blood flow (1)
- Neurorehabilitation to ameliorate effects (1)
  - Motor control
  - Behavior
- Cognition
- Neurorehabilitation (1,3,4)
  - Not standardized
  - Techniques depend on severity/type
- Motor Learning (1)
- Skill learning (new techniques learned)
- Adaptation (perturbations inducing feedback)
- Paired Associative Stimulation (PAS) (6)
  - Often used with transcranial magnetic stimulation (TMS)
- Fugl-Meyer Assessment (7)
  - Quantitative measure





Literature Review

- Strokes vary patient to patients making uniformity difficult
  - Gladstone et al, 2019
- Stroke recovery is associated with interhemispheric inhibition (IHI)
  - Xu et al, 2019
- Secondary systems are involved with specific regions' recovery (Ex. Finger strength)
  - Kitago and Krakauer, 2013
- Skill learning requires behavioral restitution and compensation
  - Kwakkel et al, 2019
- 3D kinematic analysis and transfer learning is optimal for interpretation of motor function
  - Arac et al, 2019
- Fugl-Meyer Assessment is ideal for motor recovery measurements
  - Gladstone et al, 2019
- PAS combined with TMS is effective in inducing excitability
  - Classen et al, 2004
- PAS and TMS can induce plasticity through use on afferent median nerve
  - Classen et al, 2004



Gap in the Research

- Lack of consistency in motor recovery techniques
- Lack of individualized rehabilitation methods
- Need for ways to increase skill learning for recovery with PAS

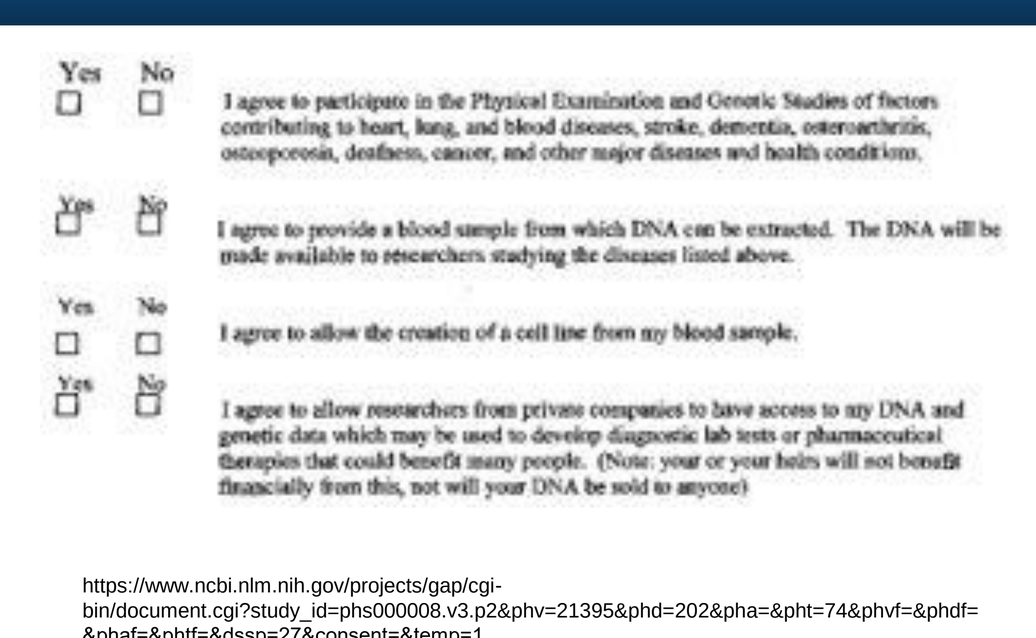
Purpose of Research

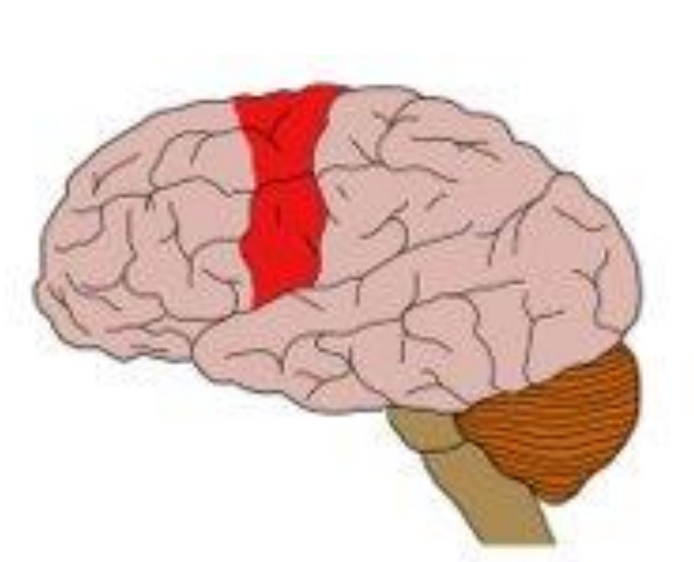
➢ Create effective methods of neurorehabilitation for stroke patients in lower limb

➢ Increase the ability to learn new skills with methods

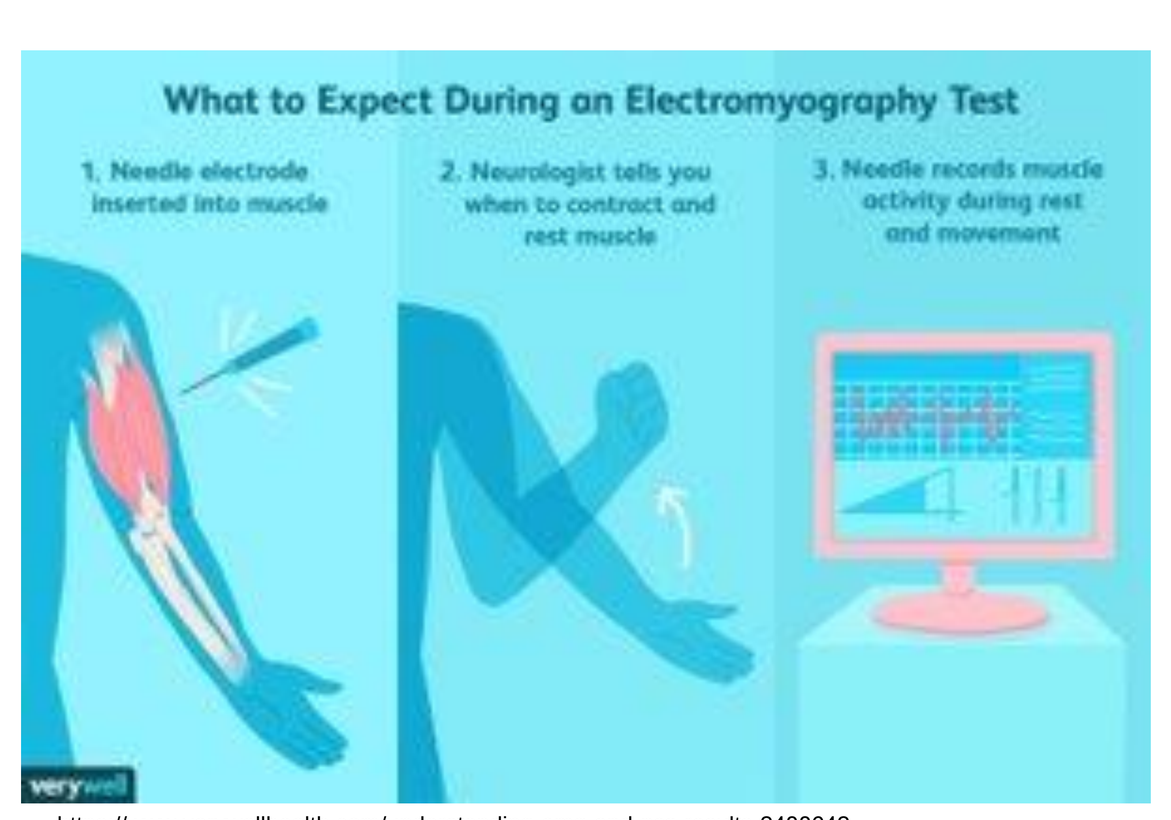
Materials And Methods

- Hemiplegic or ischemic stroke patients (7,11)
  - Recruited through Burke Neurological Institute
  - Controls also needed
- Chosen through severity of symptoms (8)
  - Fugl-Meyer motor scale
- Consent Form (1-14)
  - Approved by Institutional Human Studies Committee
  - Use patients with limited aphasia or hypoesthesia (8)
- Patients perform light tasks (8)
  - Ex. walk on treadmill for 15 minutes
- Patients perform light arm exercise (9)
  - Ex. Squeezing foam ball
- Paired Associative Stimulation (inhibitory) (8,9,10)
  - Applied to affected hemisphere
  - Motor Cortex
  - 0.25 Hz for 10 seconds
- Transcranial Magnetic Stimulation (8,9,10)
  - Wait 10 minutes
  - Motor Cortex
  - 0.25 Hz for 10 seconds
- During treatments MEP amplitudes recorded before and during
- Measurements taken every 5 minutes for 15 minutes following PAS and TMS
  - Patients hone in on sensations in affected extremity
- Electromyography (EMG)
  - Electrodes placed over measured area
- Experiment taken over period of 52 weeks (9)
  - Evaluations at 1 week, 35 weeks, and 52 weeks
- Student t-test administered (8)
  - Compared time periods for each muscle
- 3-Way ANOVA (8)
  - Calculated based post-PAS MEP amplitudes
  - Statistically significant if 0.05





https://www.neuroscientificallychallenged.com/blog/know-your-brain-motor-cortex



https://www.verywellhealth.com/understanding-emg-and-ncs-results-2488642

Anticipated/Past Results

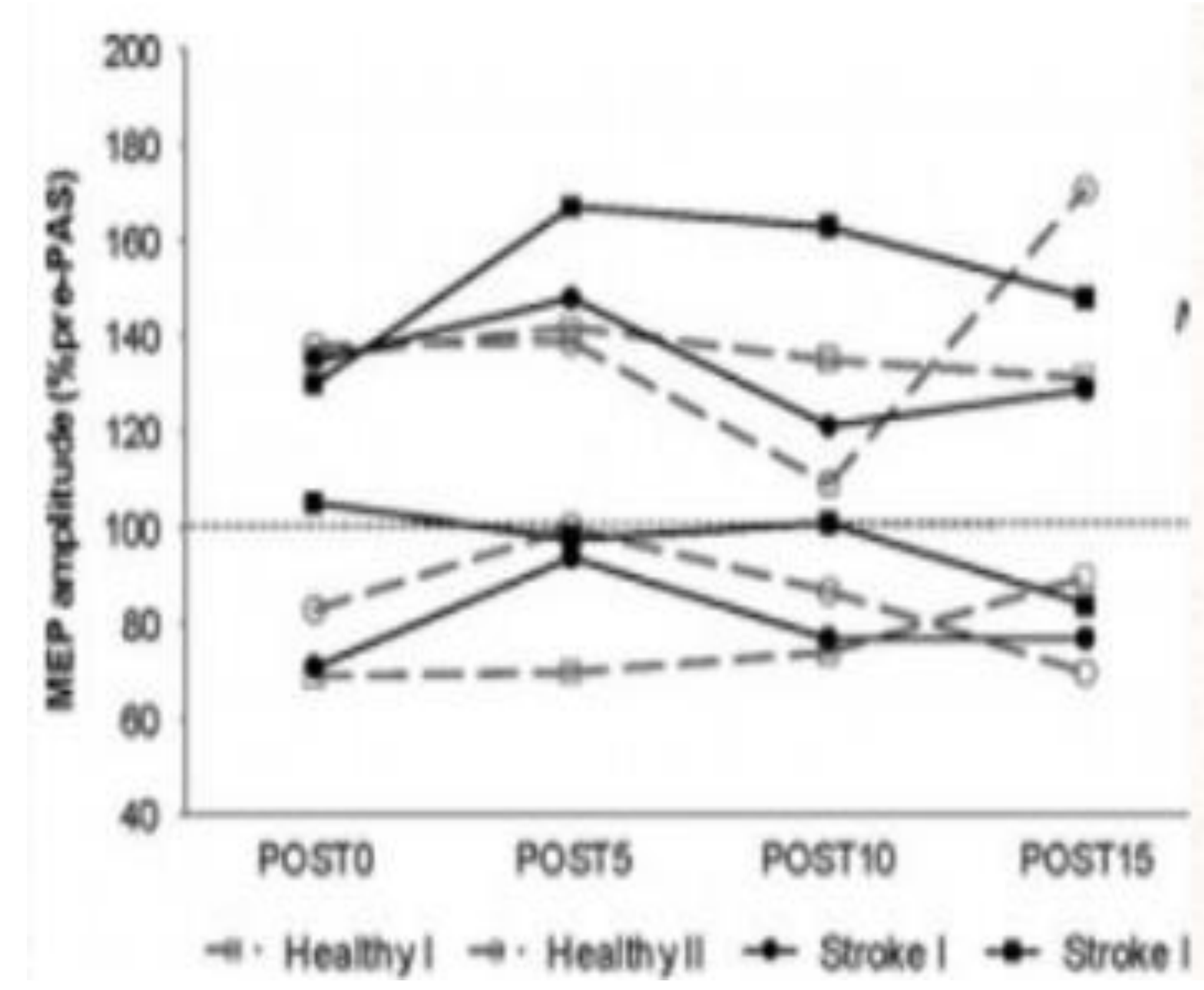
Participant Information

Subject no.	Age (years)/ Gender	Years since stroke	Impaired hemisphere	Lesion	Mobility
1	52/F	11mo	L	Basal ganglia	AFO
2	53/M	11.1	R	Internal capsule	None
3	58/F	10.8	R	Intracerebral hemorrhage	None
4	64/M	25.8	R	Striatocapsular	AFO
5	44/M	32.1	L	Striatocapsular	None
6	60/M	4.7	L	Internal capsule, frontal lobe	AFO
7	52/F	31.0	R	Carotid artery	AFO
8	60/F	5.3	R	Unknown	None
9	48/M	4.8	R	Basal ganglia, corona radiata	None
10	52/M	4.0	R	Basal ganglia	None

Jayaram and Stinear, 2008

Details of participants prior to clinical trials

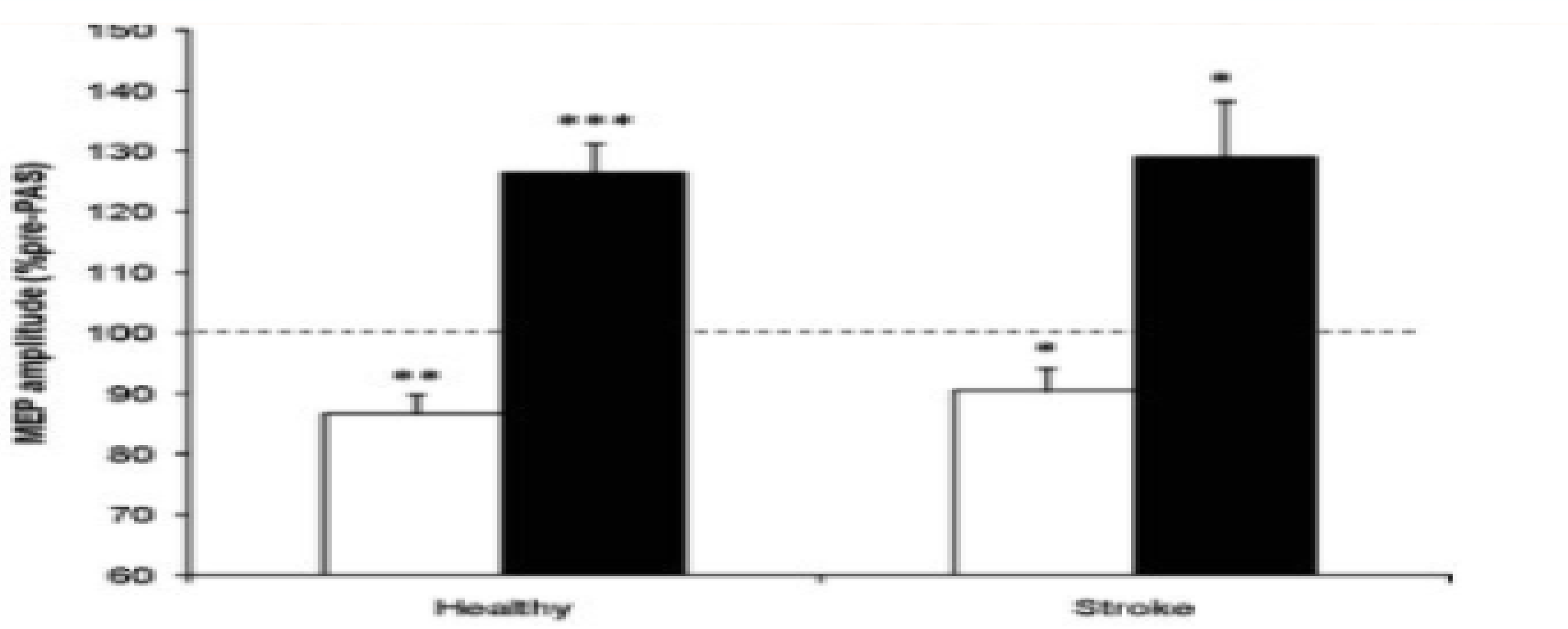
MEP Amplitudes (Time Modulation)



Jayaram and Stinear, 2008

The time course of modulation of MEP amplitude for 15 minutes following PAS.

MEP Amplitudes (Health vs. Stroke)



Jayaram and Stinear, 2008

Bilateral MEP modulation following PAS in stroke and healthy subjects.

Variance Measurements

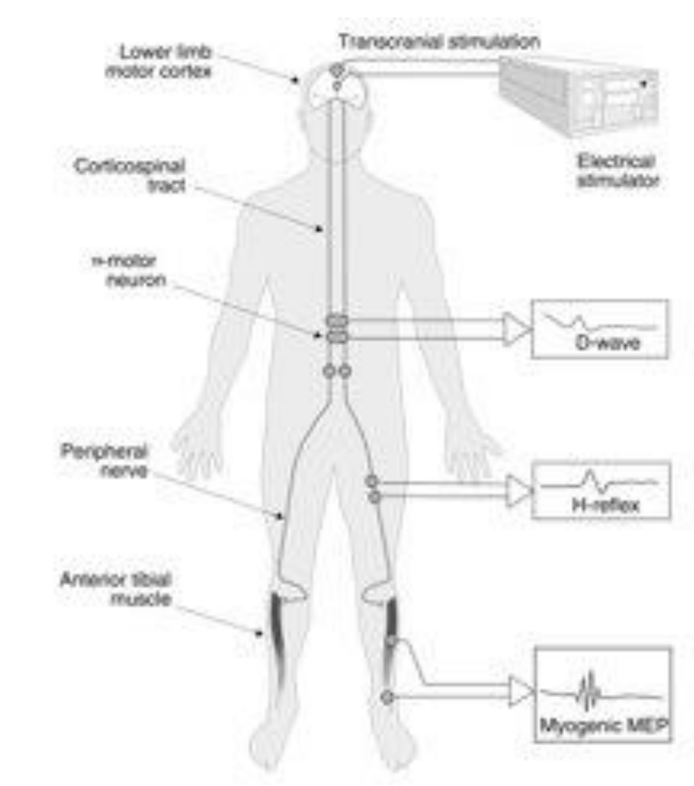
	Stroke						Healthy					
	Stimulated (Non-paretic)			Non-stimulated (paretic)			Stimulated			Non-stimulated		
	Mean (%)	SE	P	Mean (%)	SE	P	Mean (%)	SE	P	Mean (%)	SE	P
Post 0	91	5.8	0.14	134	12.0	0.02	91	5.9	0.14	118	7.9	0.05
Post 5	94	6.4	0.33	130	13.1	0.04	94	3.7	0.11	132	7.2	0.001
Post 10	89	7.1	0.16	120	8.3	0.04	85	4.3	0.01	123	8.5	0.03
Post 15	93	3.4	0.08	138	12.2	0.01	84	5.2	0.01	134	6.1	<0.001
Average	91	3.8	0.04	130	9.6	0.01	87	3.2	0.002	126	5.1	<0.001

Jayaram and Stinear, 2008

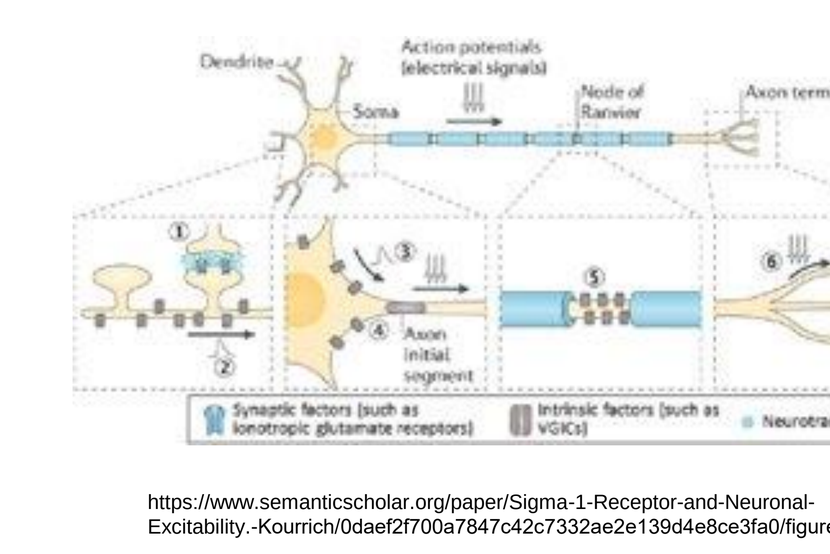
Variances from 100% for each MEP amplitude

Discussion

- Pre-PAS: non-paretic MEP amplitude decreased to 91% (8)
- Pre-PAS: paretic MEP amplitude increased to 130% (8)
- Post-PAS: non-paretic MEPs decreased to 87% (8)
- Post-PAS: paretic MEP amplitude increased to 126%. (8)
- Excitability increased in healthy and stroke patients (8,9)
- MEP amplitudes had significant differences (8,9)
- Unsure of stimulation and walking having effect on results
  - Most likely did not have effect (11)
- Healthy subjects had smaller increases in excitability (8,12)
- Indicates that PAS is an effective manner of inducing excitability (8,13)
- Unsure of efficacy of different types of PAS (8,12)
  - Inhibitory vs. facilitatory
- Can be applied in lower-limb motor cortex injuries
- Viable therapeutic target for neurological-based walking impairments (8)
- Excitability may increase with varying PAS/TMS intensities (8,11)
  - Lower excitability with higher TMS intensity
- May be applicable to upper limb injuries (8)
- Can be used to modify therapies for patients (9)
- Reduction in asymmetry in lower limb interhemispheric inhibition (3,8,9)
  - Potentially enhance motor recovery



https://neurologiclabs.com/neuromonitoring/mep/



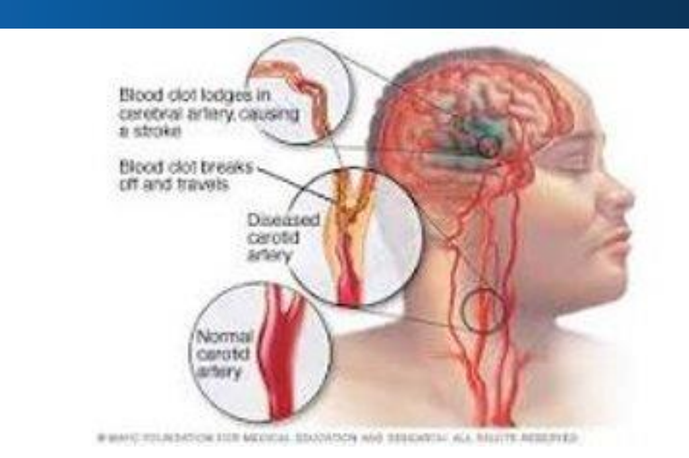
https://www.hopkinsmedicine.org/health/conditions-and-diseases/stroke/arm-care-after-a-stroke

Conclusion

- Over 795,000 strokes each year (1)
- Number of strokes are to continue to rise (1)
- Neurorehabilitation is very variable (4)
- Strokes vary patient to patient (6)
- Great need for specific and effective motor recovery methods (1-13)
- **Purpose**: Investigate PAS and implications it has on lower limb motor recovery of stroke patients
- **Methods**: PAS/TMS after walking on treadmill; electromyography; MEP amplitudes and measurements taken every 5 minutes for 15 minutes; ANOVA and student t-test analyses
- **Results**: MEP amplitudes decreased for healthy patients and increased for stroke patients before PAS, and increased MEPs for both groups post-PAS
- **Conclusions**: PAS induced excitability; increases motor recovery for lower limb patients; can be applied to therapies and upper limb patients

Future Research

➢ Investigate Inhibitory PAS vs. Facilitation PAS
➢ Task and PAS stimulation effect on results
➢ Intensity of PAS/TMS effect on excitability
➢ Investigate if a reduction in inhibitory asymmetry increases recovery



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