

# Using Transcranial magnetic stimulation to improve our understanding of Transverse Myelitis

Kathy Zackowski, PhD, OTR  
Kennedy Krieger Institute  
Johns Hopkins University School of Medicine



- TMS (transcranial magnetic stimulation)
  - Definition
  - Applications
    - > Diagnostic tool
    - > Therapeutic intervention
- Studying brain and spinal cord function in Transverse Myelitis

- In the last 3 decades our view of the CNS has changed.
- Formerly believed to be a rigid structure, not plausible of changing, now believed to be plastic and dynamic, constantly changing.
- The change in dogma resulted from technological advancement in all levels
- Human studies => PET, fMRI, TMS, MEG

# TMS

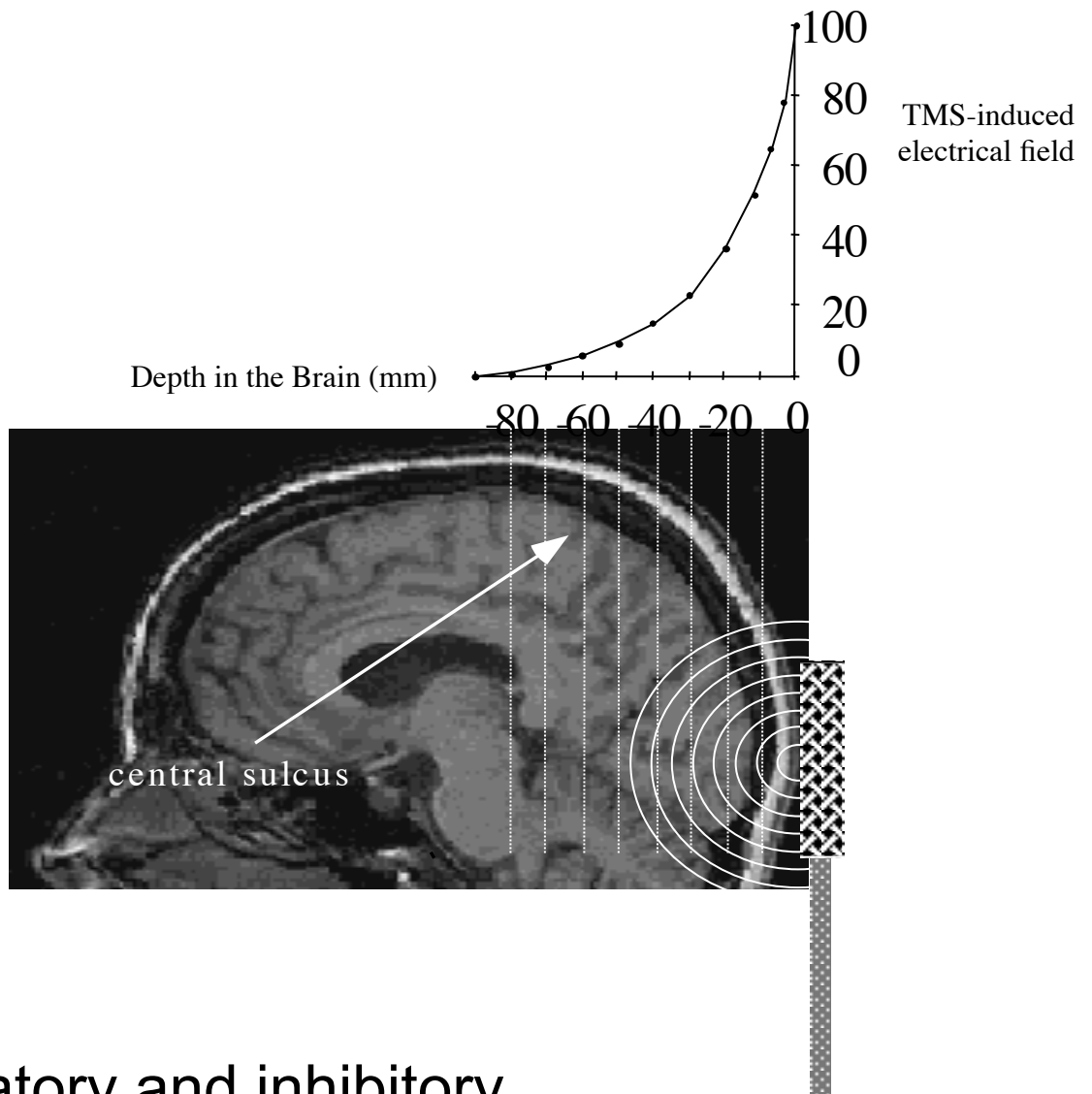
Transcranial magnetic stimulation is a tool used to study:

- connectivity of neuronal pathways
- cortical plasticity and its mechanisms
- behavioral consequences of noninvasive transient inactivation of specific cortical sites.

❖ Electrophysiological results could indicate the underlying systems or pathways effected and, provide useful insight into the mechanism of action.



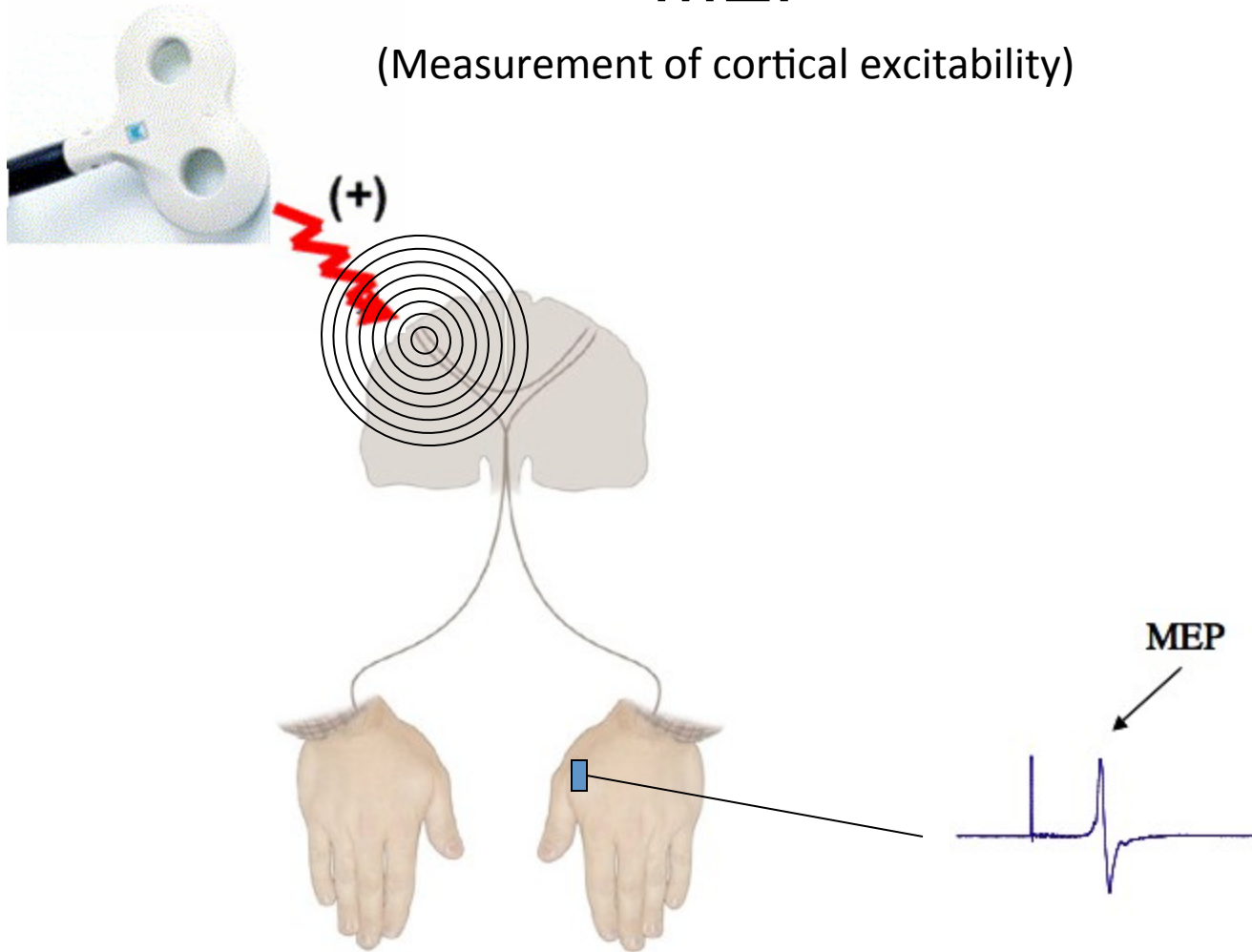
An electric pulse induces a rapidly changing magnetic field with lines of flux that runs perpendicular to the coil.



TMS activates excitatory and inhibitory presynaptic fibers to the pyramidal upper motor neuron

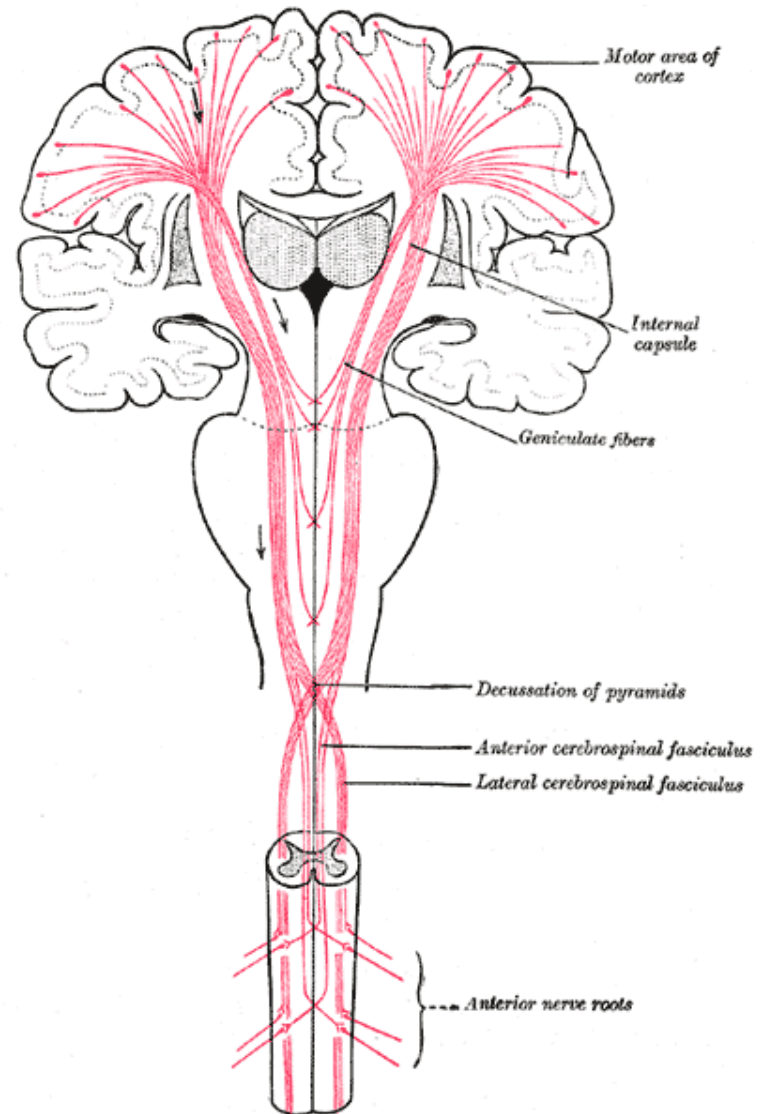
# Motor Evoked Potential MEP

(Measurement of cortical excitability)



Courtesy of Pablo Celnik

Similar to peripheral nerve studies, conduction time is measured from different stimulation sites (i.e. Motor cortex, brainstem, cervical roots)





## **1. Diagnostic tool**

- a) Central conduction time
- b) Measuring cortical excitability
  - Motor Threshold
  - Recruitment Curves
  - Intracortical Inhibition (ICI)
  - Intracortical Facilitation (ICF)
  - Interhemispheric inhibition (IHI)
- c) Probing cortical function

## **2. Therapeutic intervention**

- a) To induce plasticity
- b) To modulate behavior

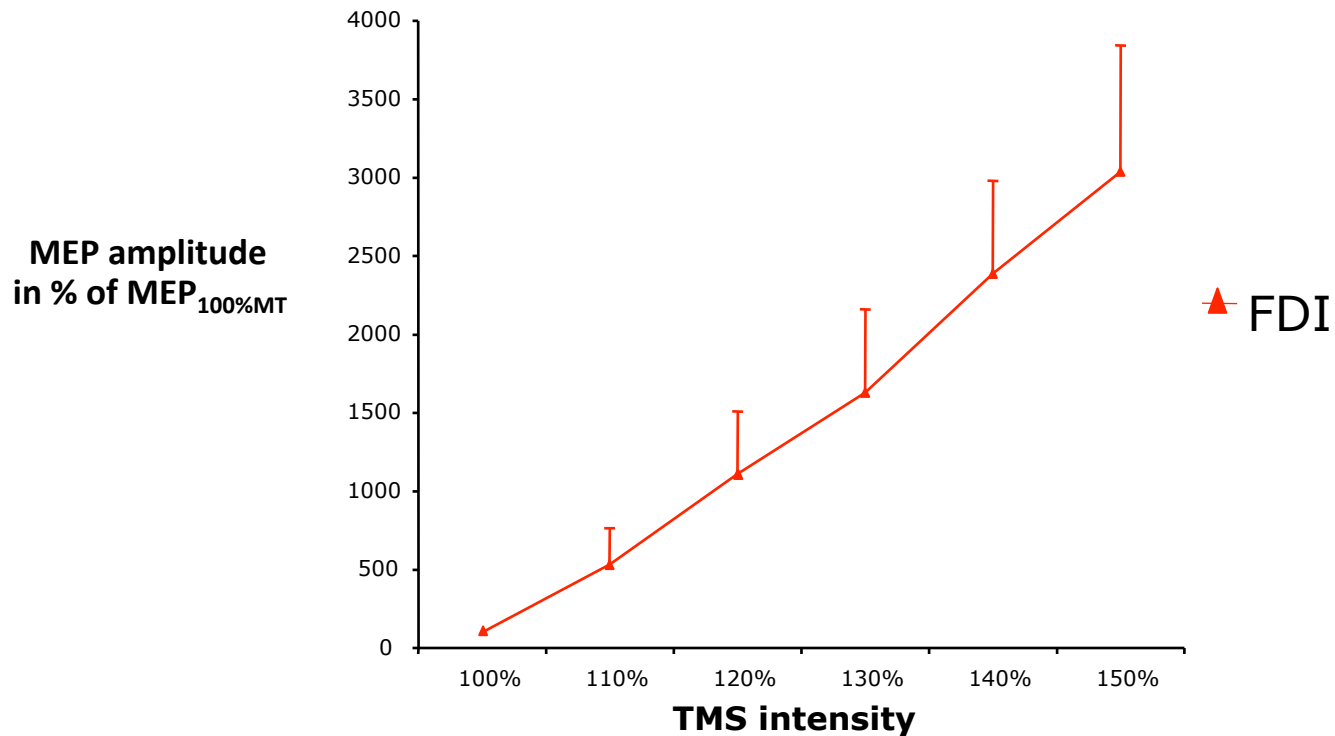
## **Motor Threshold (MT)**

- Lowest stimulus intensity that evoke MEP of 50 mV in 5 of 10 trials in a target muscle during 2% reductions in intensity from above threshold (Rossini 1994)
- Drugs that block voltage-gated sodium channels elevate motor threshold (Ziemann 1996)

# Recruitment Curve (RC)

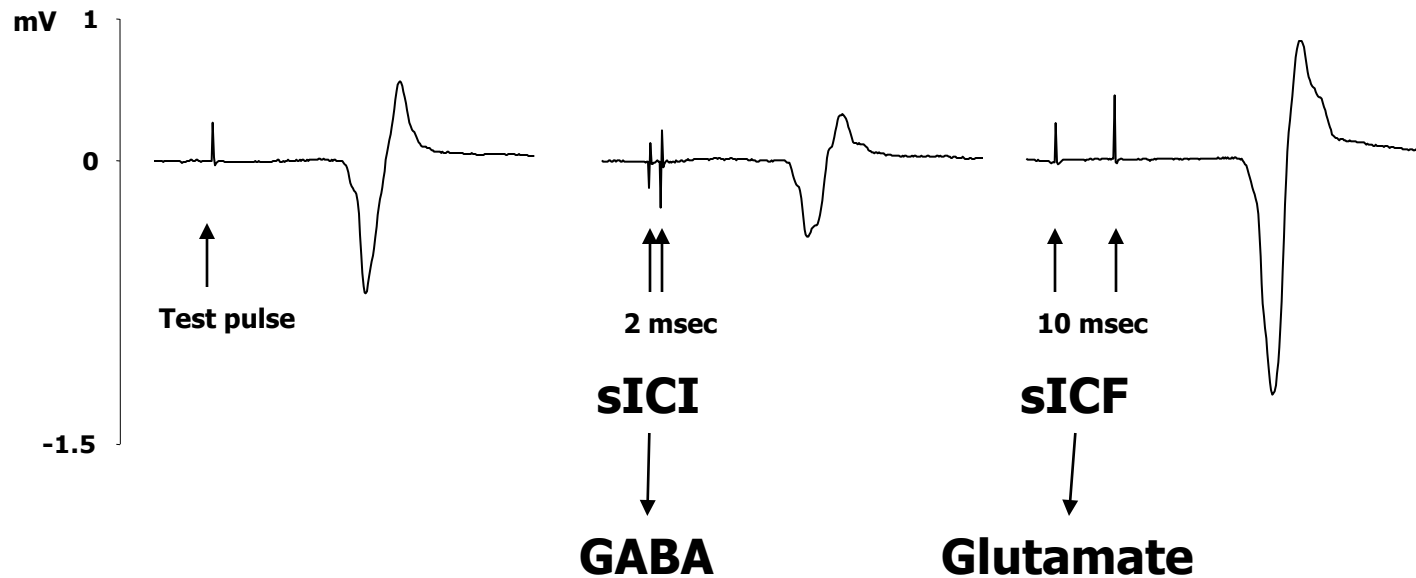
Determines the slope of the input-output curve by increasing the stimulus intensity (input) while measuring the resultant MEP amplitude (output) change (Cohen 1998).

***Provides information regarding the level of excitability of the entire network investigated.***



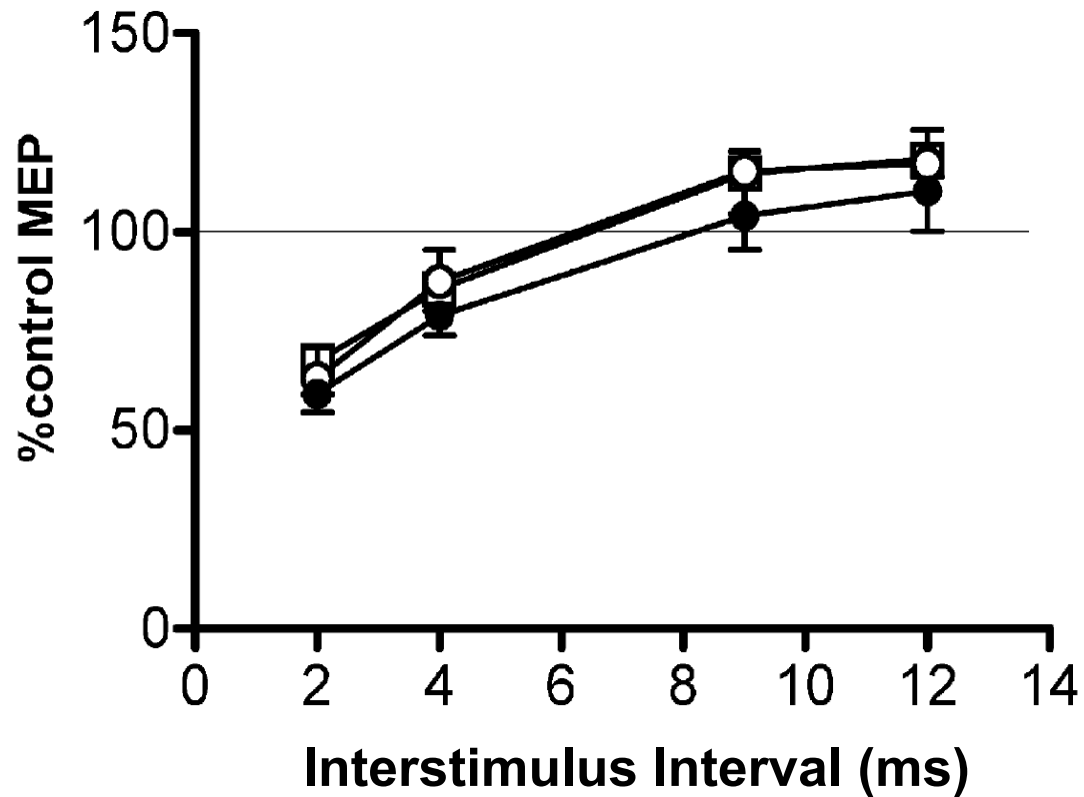
# Intracortical Excitability

- Short Intracortical Inhibition (sICI)
- Short intracortical Facilitation (sICF)



## Intracortical Excitability

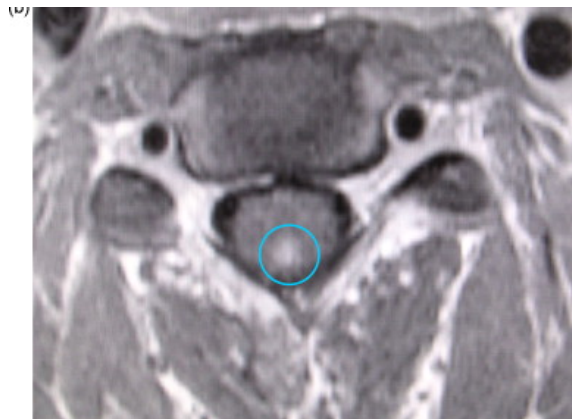
- Short Intracortical Inhibition (sICI)
- Short intracortical Facilitation (sICF)



**What studies have been done involving  
transverse myelitis?**

## Motor cortex excitability changes following a lesion in the posterior columns of the cervical spinal cord

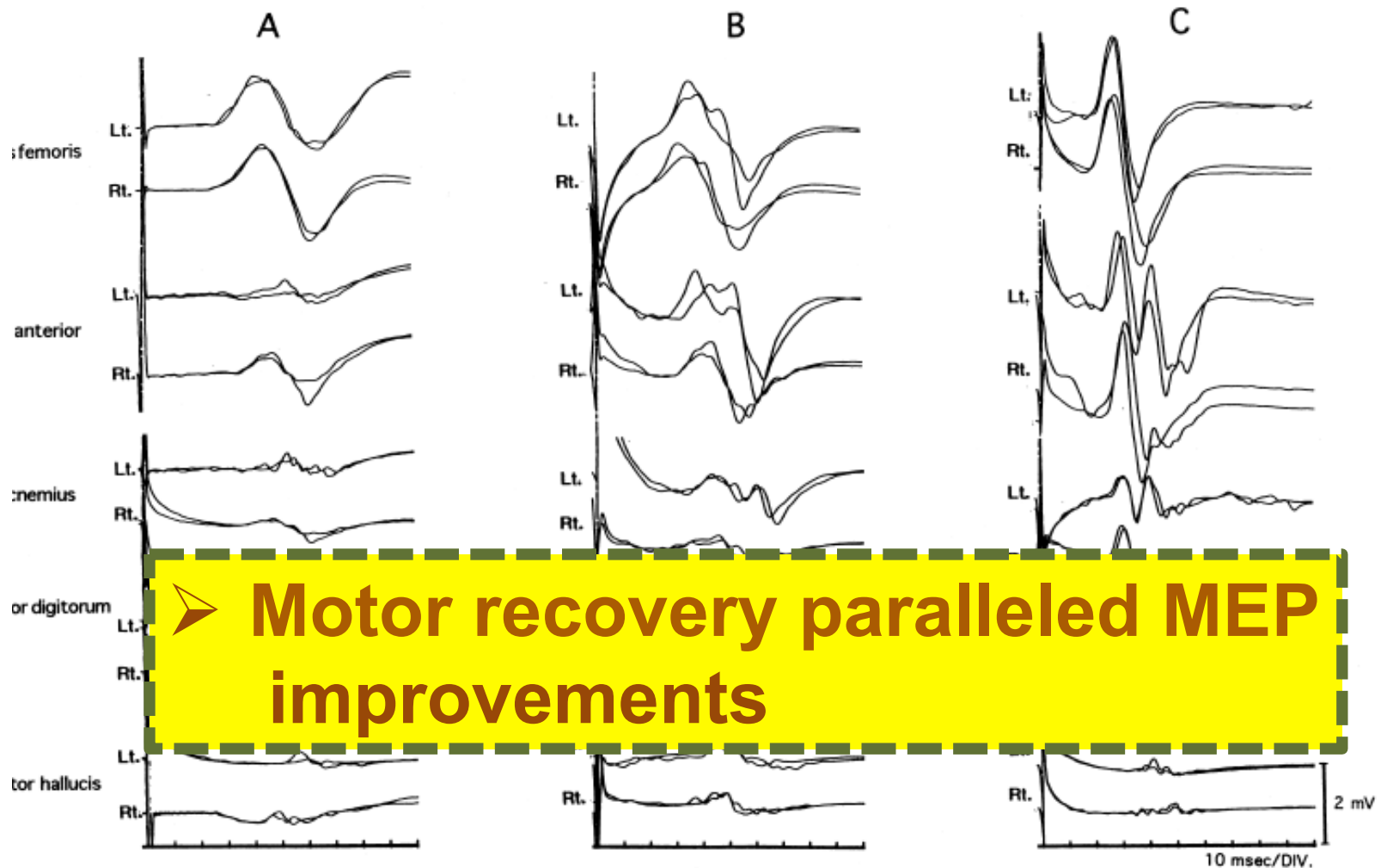
Raffaele Nardone<sup>a,\*</sup>, Stefan Golaszewski<sup>c</sup>, Jürgen Bergmann<sup>c</sup>,  
Alessandro Venturi<sup>b</sup>, Igor Prünster<sup>d</sup>, Arianna Bratti<sup>a</sup>,  
Günther Ladurner<sup>c</sup>, Frediano Tezzon<sup>a</sup>



➤ an isolated lesion in the posterior white columns of the spinal cord may lead to long-term changes in motor cortex. Can sensory training help?

# Motor-Evoked Potentials in a Child Recovering from Transverse Myelitis

Yukio Noguchi, MD, Osami Okubo, MD, Tatsuo Fuchigami, MD,  
Yukihiko Fujita, MD, and Kensuke Harada, MD





2. The Clinical Initiative—a quest for reliable and sensitive assessments of outcome after treatments for spinal cord injury (P.H. Ellaway, A. Kuppuswamy, A.V. Balasubramaniam, Maksimovic R, A. Gall, M.D. Craggs, C.J. Mathias).....
- 2.1. Sensitivity of EPT test.....
- 2.2. Reliability of EPT measures.....
- 2.3. EPT as a measure of the dorsal (posterior) column pathway.....

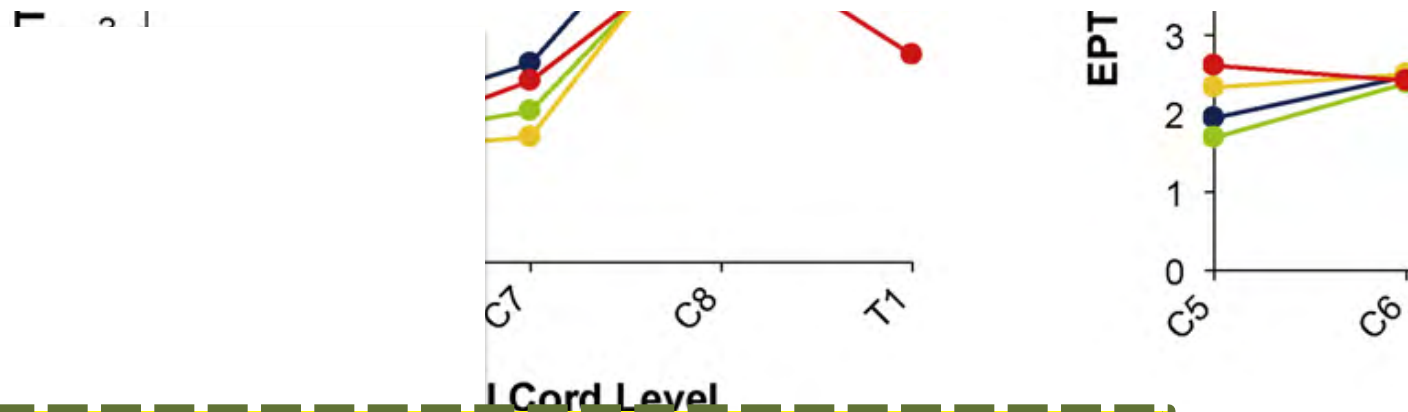
\* Corresponding author at: Department of Clinical Neuroscience, Imperial College, Charing Cross Campus, St Dunstan's Road, London W6 8RP, UK. Tel.: +44 2033117577. fax: +44 2033117577.

E-mail address: [p.ellaway@imperial.ac.uk](mailto:p.ellaway@imperial.ac.uk) (P.H. Ellaway).

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doi:10.1016/j.brainresbull.2010.08.007

Please cite this article in press as: P.H. Ellaway, et al., Development of quantitative and sensitive assessments of physiological and functional outcome during recovery from spinal cord injury: A Clinical Initiative, Brain Res. Bull. (2010), doi:10.1016/j.brainresbull.2010.08.007



➤ **Motor recovery paralleled MEP changes. Sample size small!**

Ellaway, et al., Development of quantitative and sensitive assessments of physiological and functional outcome during recovery from spinal cord injury: A Clinical Initiative, Brain Res. Bull. (2010), doi:10.1016/j.brainresbull.2010.08.007

- TMS can be used to understand brain processes (diagnostic tool) or to induce plastic changes (therapeutic tool) like excitability changes or modulation of behavior.
- Understanding the basic physiology mechanisms associated to motor behavior has permitted the development of novel strategies to enhance recovery processes in patients with CNS lesions.

**How can we use this technique to provide additional information about TM?**

✧ Evaluate the effectiveness of a known pharmacologic therapy

## New Study

Efficacy of Sustained Release Oral Dalfampridine in  
Transverse Myelitis

## Site

Johns Hopkins University, Transverse Myelitis Center

## Study Investigators

Michael Levy

Carlos Pardo

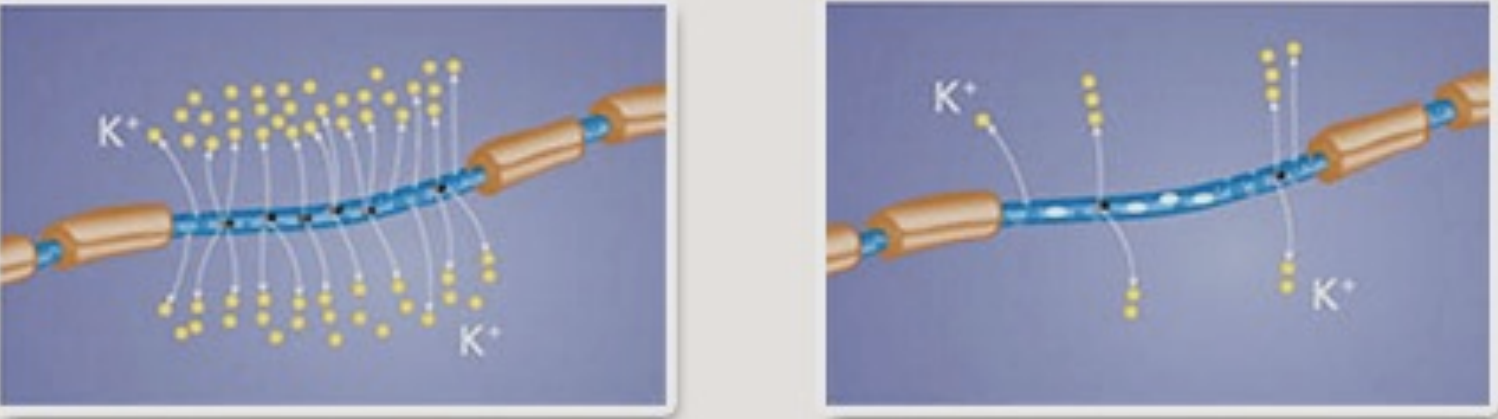
Daniel Becker

Kathleen Zackowski

## Fampridine (4-aminopyridine)

- Amplified conductivity in demyelinated peripheral nerves
- Limited therapeutic window due to stimulation of seizure activity

## What is Oral Dalfampridine (Ampyra)?



**Without AMPYRA**  
(am-PEER-ah)

Loss of potassium can disrupt the nerve's ability to conduct messages.

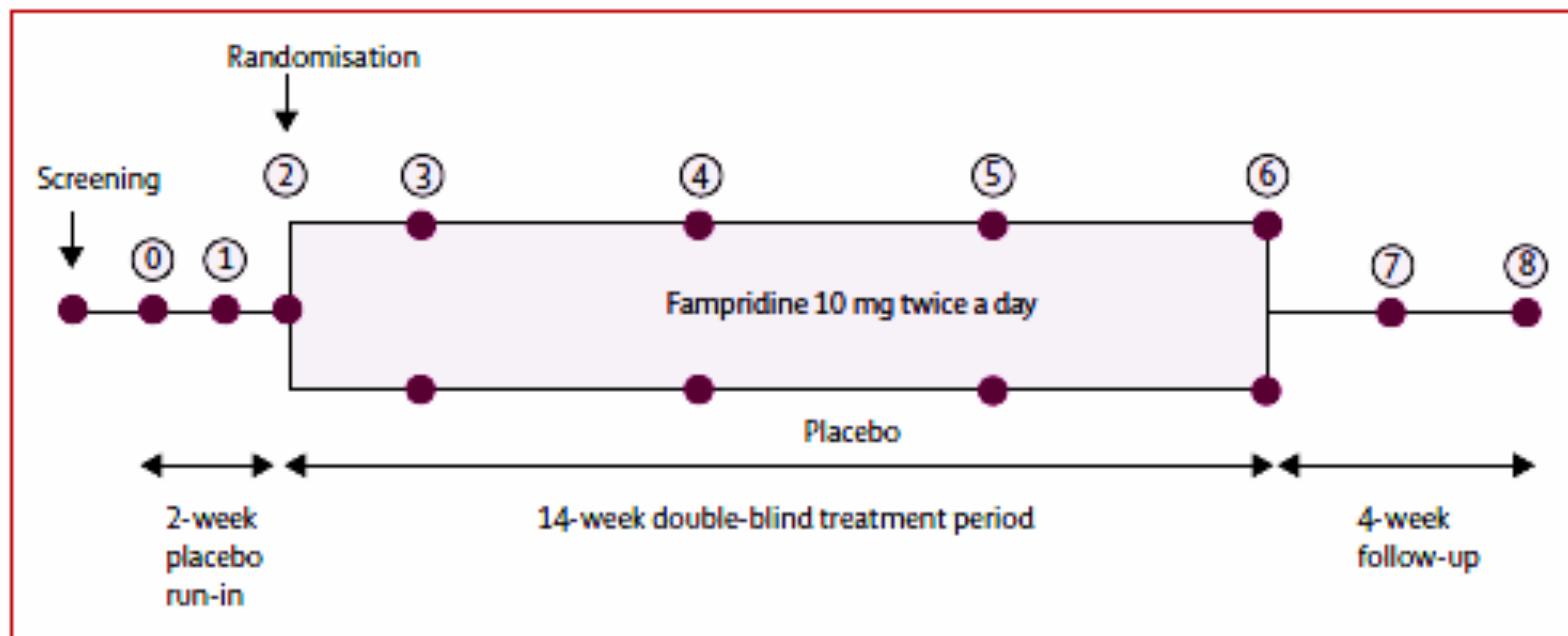
**With AMPYRA**  
(am-PEER-ah)

AMPYRA blocks potassium channels to help nerves send messages from the brain to the rest of the body.

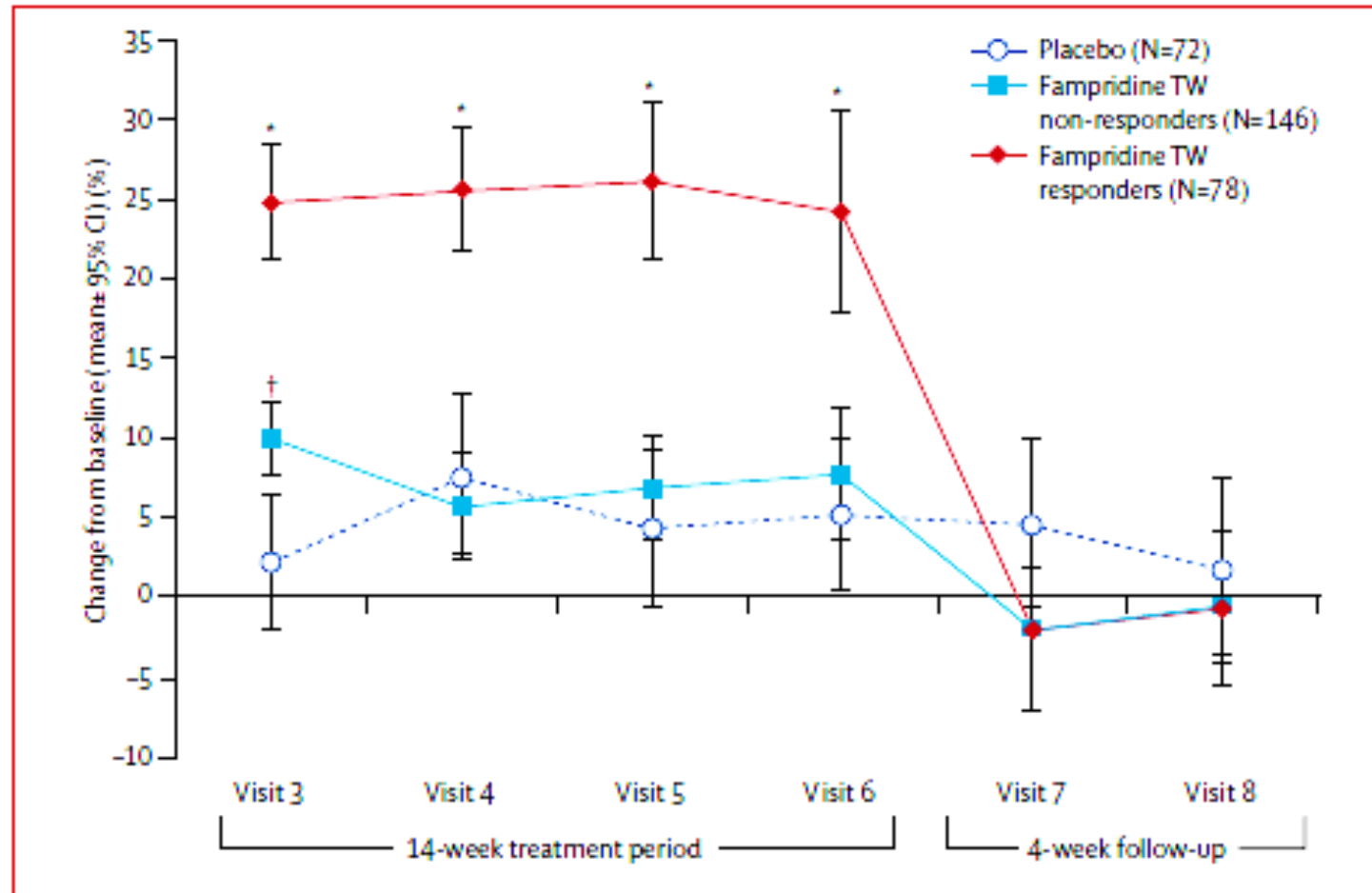
# What do we know about dalfamradine's effects?

## Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial

*Andrew D Goodman, Theodore R Brown, Lauren B Krupp, Randall T Schapiro, Steven R Schwid\*, Ron Cohen, Lawrence N Marinucci, Andrew R Blight, on behalf of the Fampridine MS-F203 Investigators†*



# Results:



**Figure 3: Percent change in walking speed at each visit after randomisation**

The fampridine-treated timed walk responders showed a sustained improvement during the treatment period that was completely reversed at 2-week and 4-week follow-up visits. The fampridine-treated timed walk non-responders showed a significant improvement compared with the placebo group only for visit 3 (2 weeks after randomisation). TW=timed walk. \*Means fampridine TW responders are greater than placebo and fampridine TW non-responders ( $p < 0.001$ ). †Means fampridine TW non-responders are greater than placebo only ( $p < 0.001$ ).

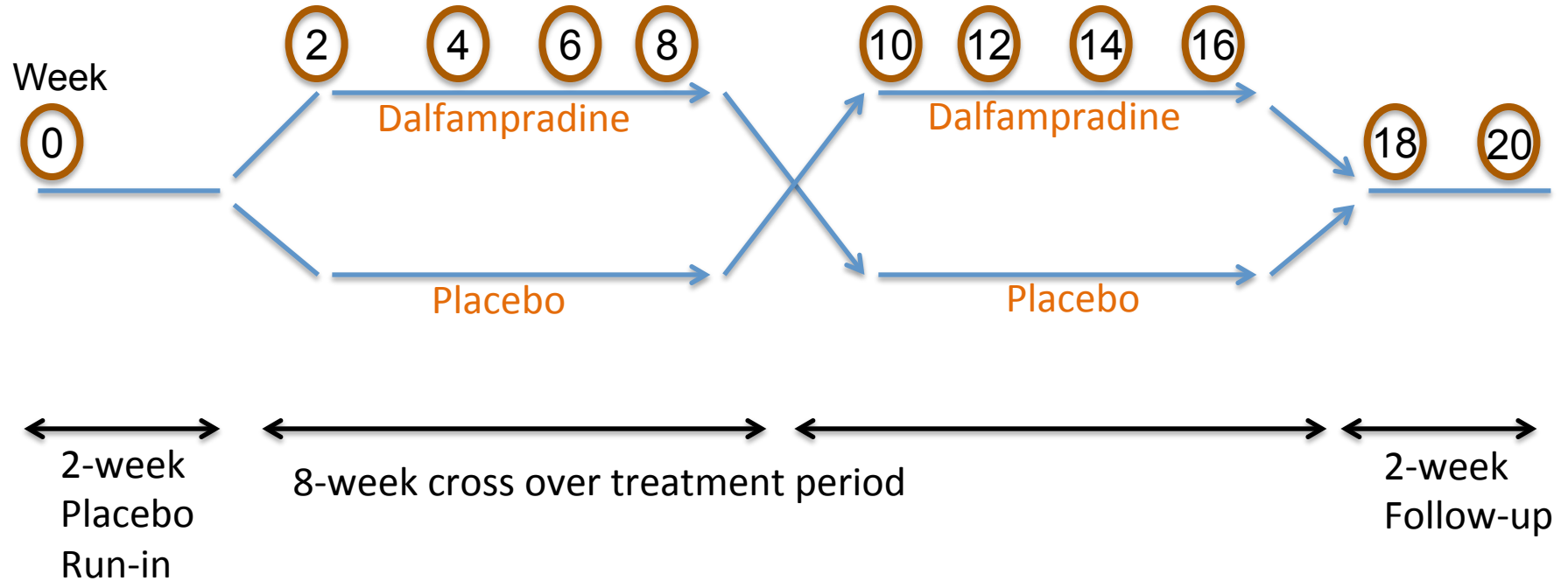
Dalfampridine, a sustained-release potassium channel blocker that has been shown to be effective in improving gait and other neurologic functions in people with MS.

Dalfampridine has the potential to improve gait and neurologic function in patients with TM because it shares a similar pathogenic process with MD.

✧ We hypothesize that Dalfampridine will improve gait and neurologic function in patients with TM, and that TMS will improve our understanding of what the characteristics are for “responders”.



# Study Protocol for TM:



Inclusion criteria for this study include:

- Diagnosis of idiopathic transverse myelitis confirmed by MRI
- Gait impairment defined by a timed 25-foot walk
- Age 18-70 yrs

We are happy to answer questions about this study.

Email Maureen Mealy at [mmealy1@jhmi.edu](mailto:mmealy1@jhmi.edu) if you are interested in participating.

Thank you for your support!

