Transcranial Magnetic Stimulation

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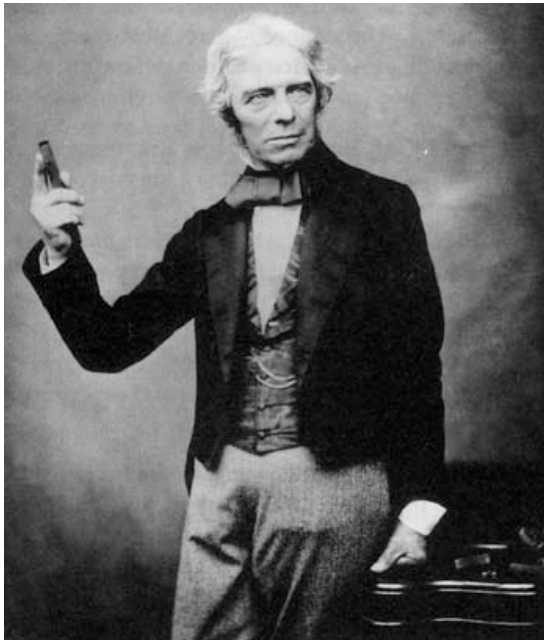
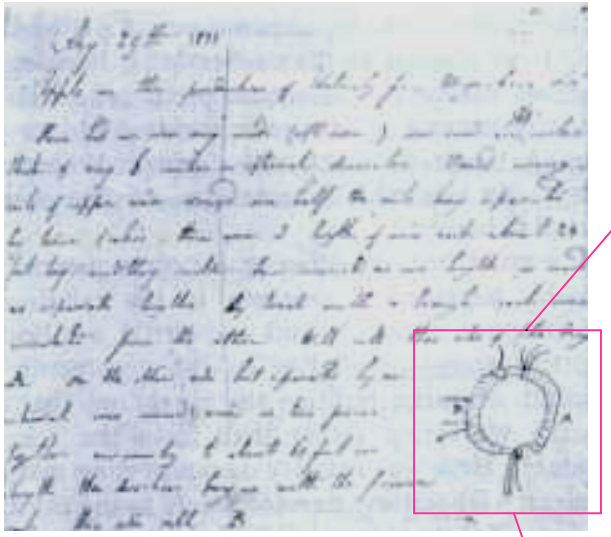
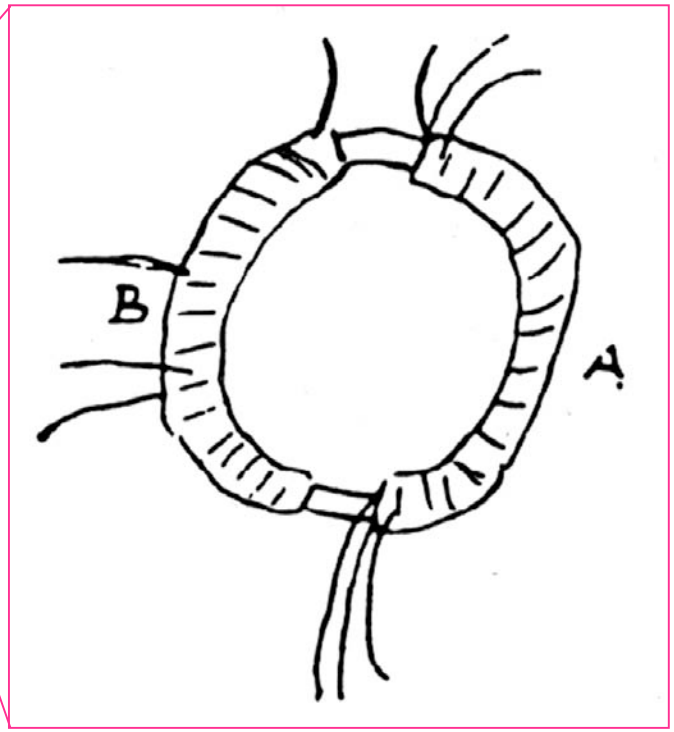
Electro-Magnetic Induction

"I think I got hold of a good thing"







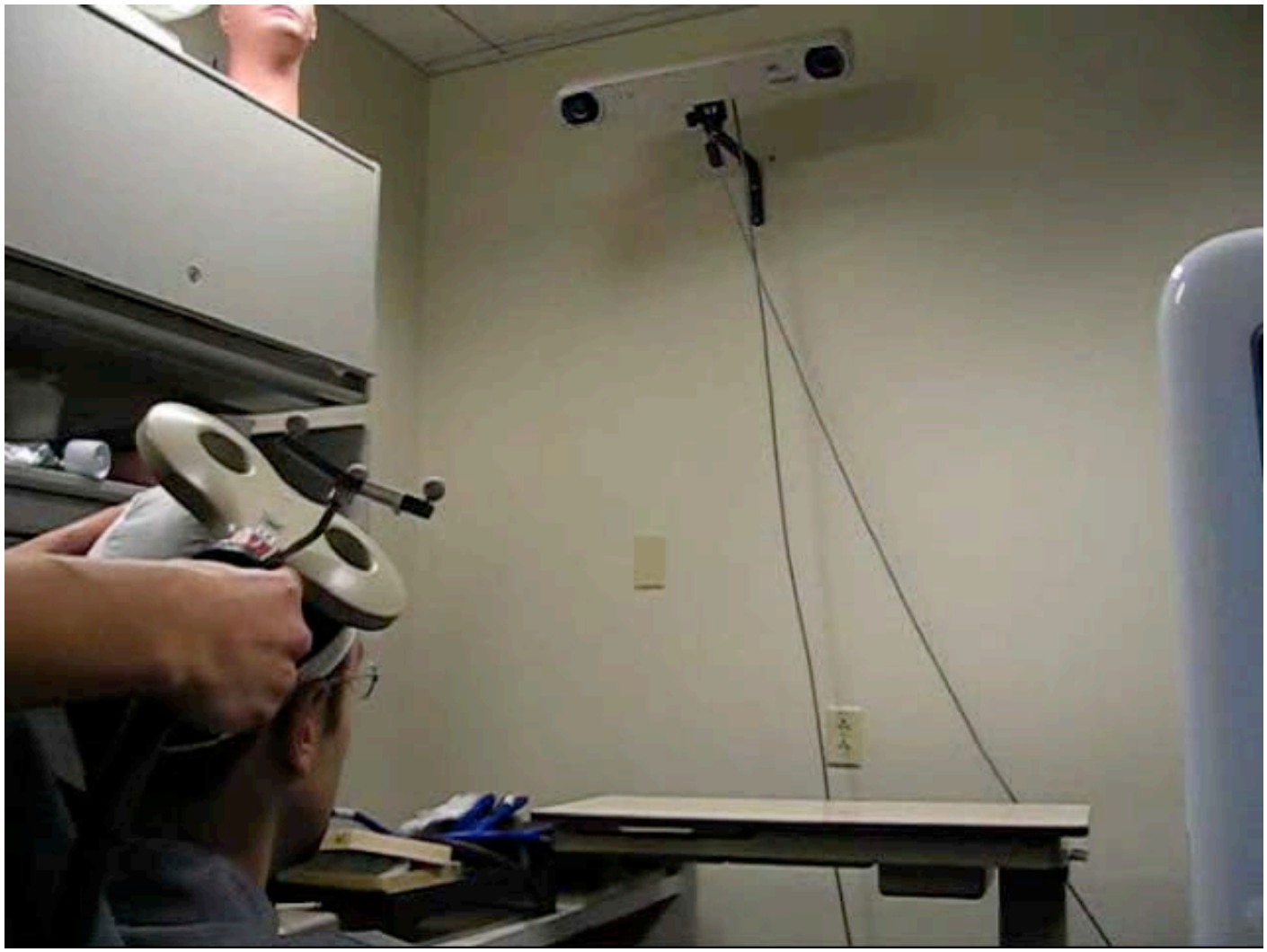
M. Faraday
29 August 1831

“Modern Era”

Anthony Barker
12 February 1985

House, MD [2006 season; Fox Television]

Noninvasive Targeting of Specific Cortical Regions: Frameless Stereotaxy

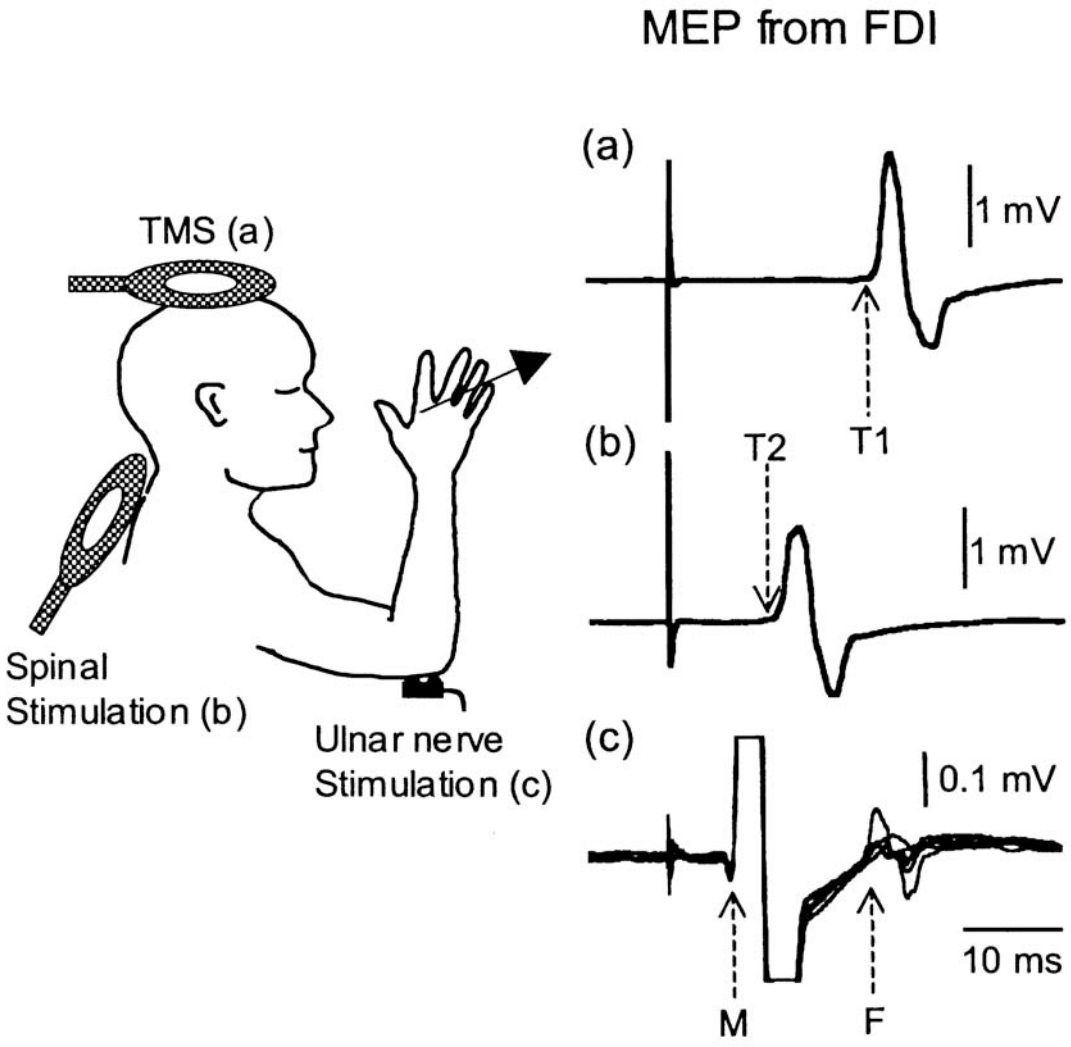


TMS Terminology

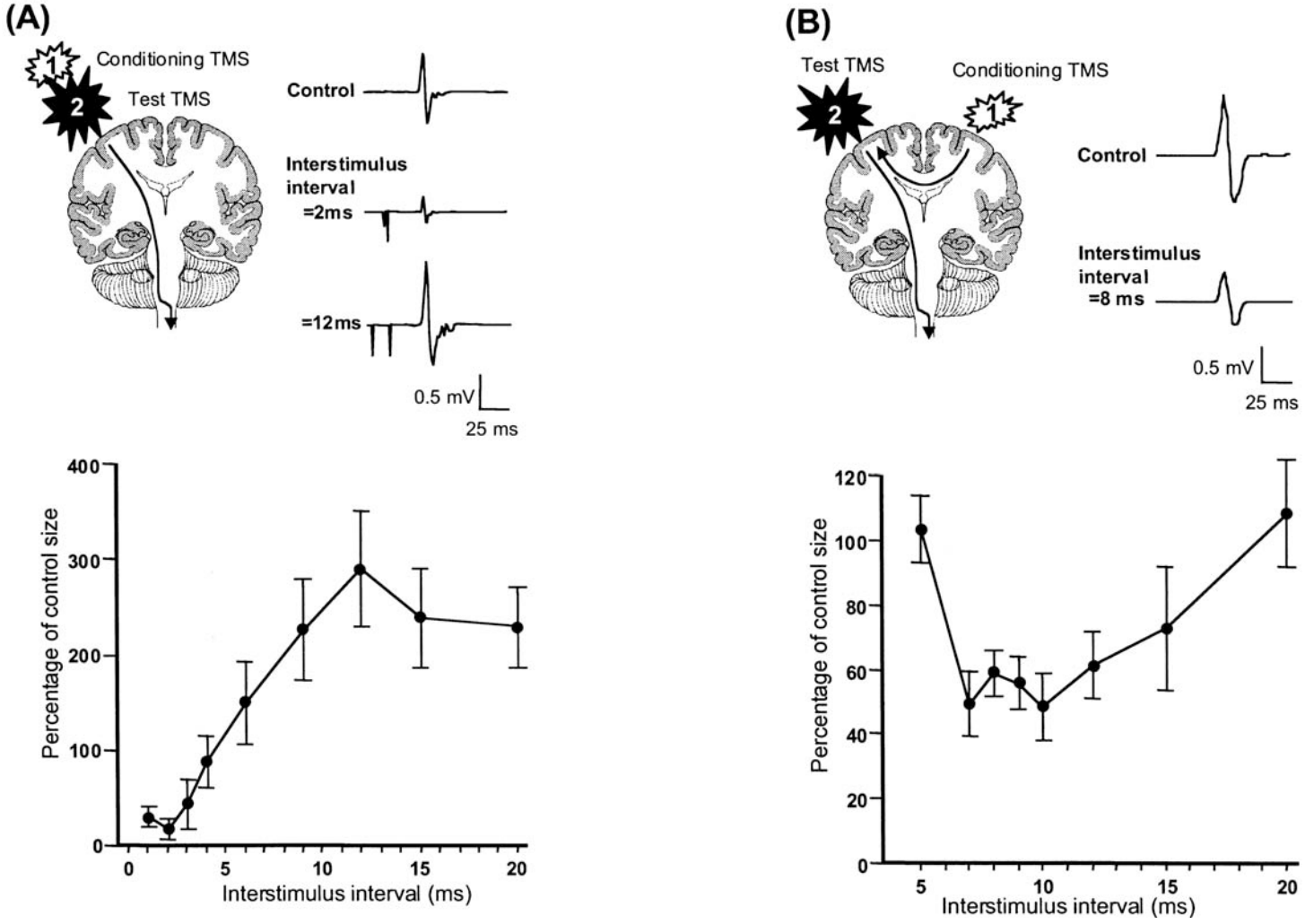
- Single pulse TMS
  - single stimulus every 5-10 sec
- Paired pulse TMS
  - subthreshold stim. then suprathreshold stim.
  - stimuli separated by 1-20 msec
- Repetitive TMS (rTMS)
  - trains of stimuli to one brain area
  - slow = low frequency
  - fast (high freq) > 1 Hz
- Asynchronous Repetitive TMS
  - Intermittent or continuous Theta Burst

A Clinical Test
Motor Central Conduction Time

A Clinical Test
Motor Central Conduction Time



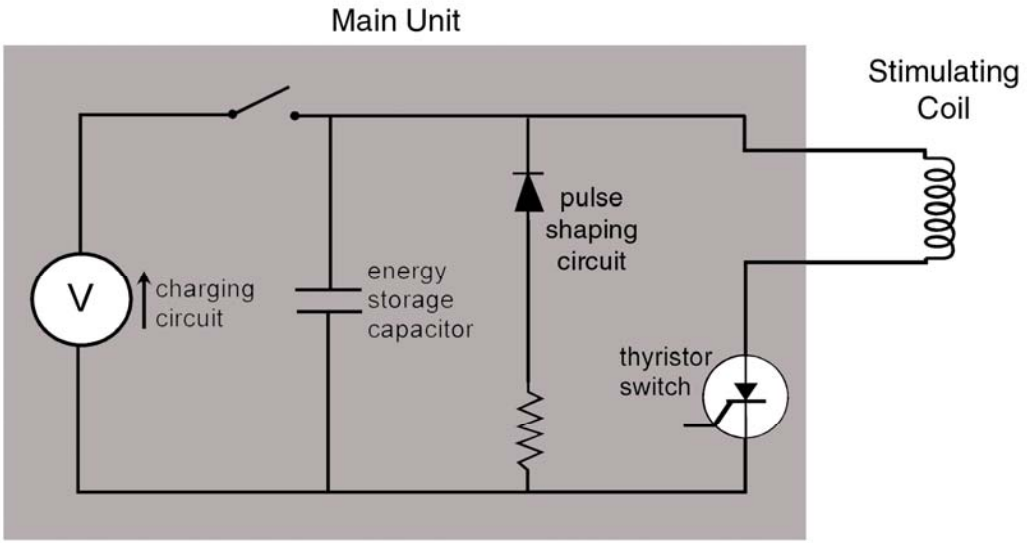
Another Clinical Test: Paired-pulse studies

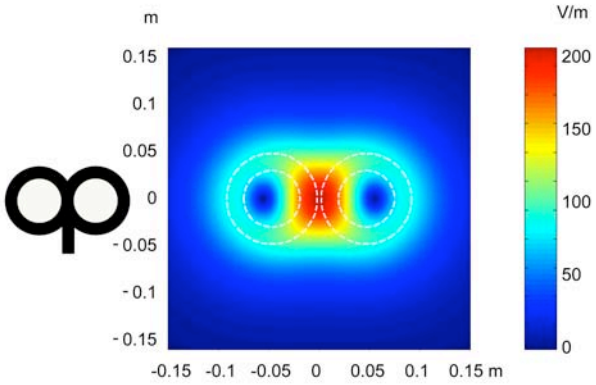


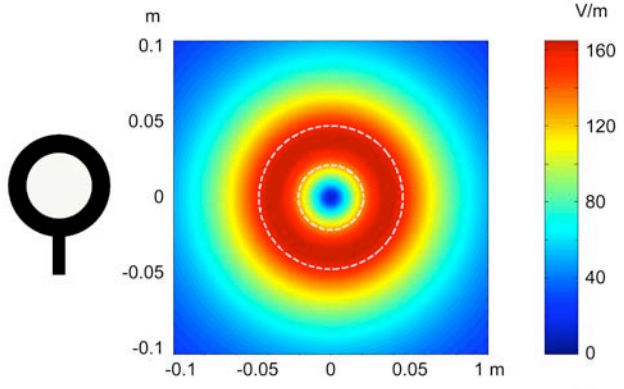
Induction of speech arrest

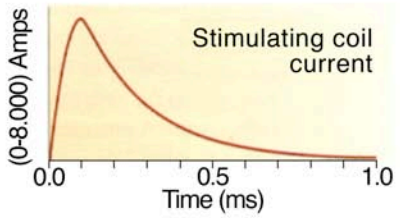
Induction of paraphasic errors

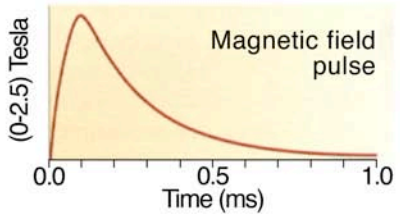
Transcranial Magnetic Stimulation (TMS)

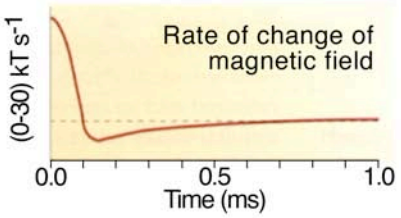


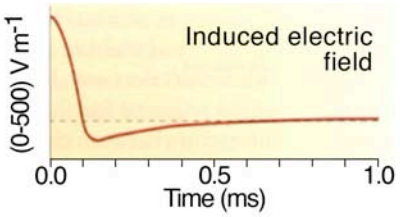


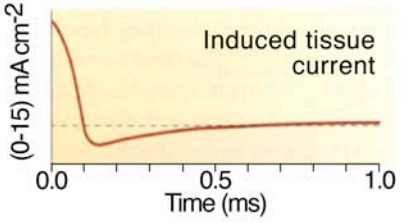






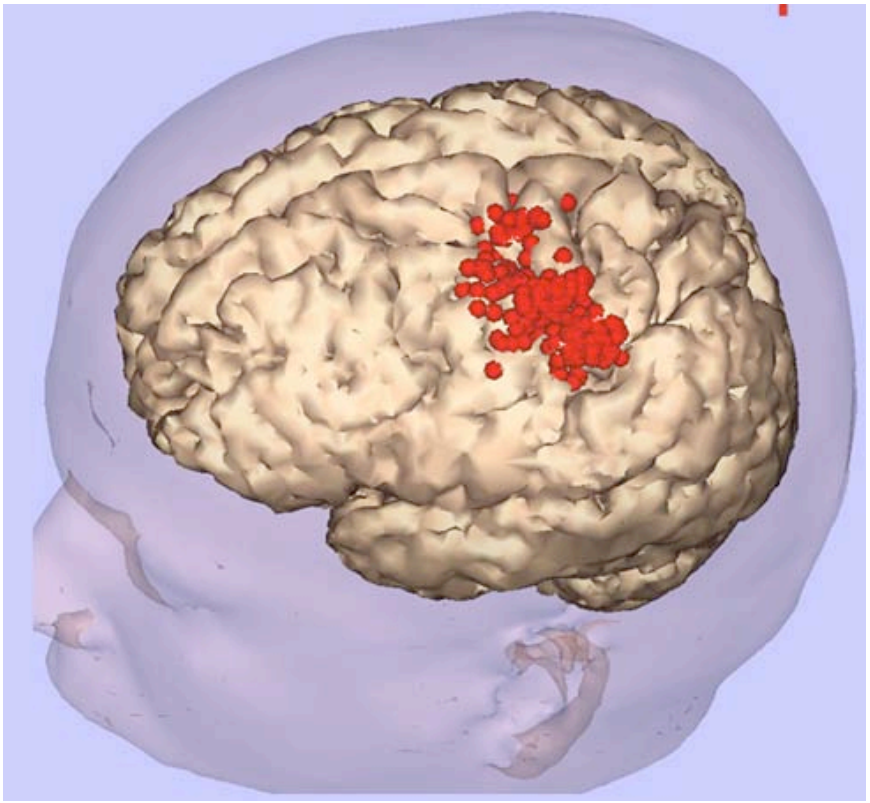




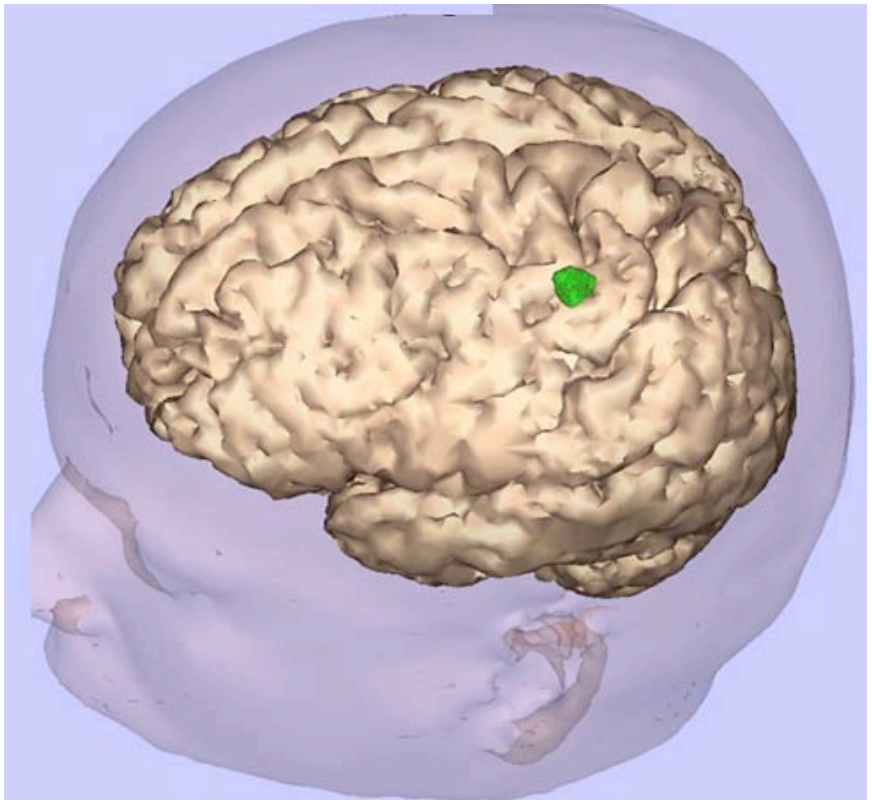


Topographic Precision

Scalp markers

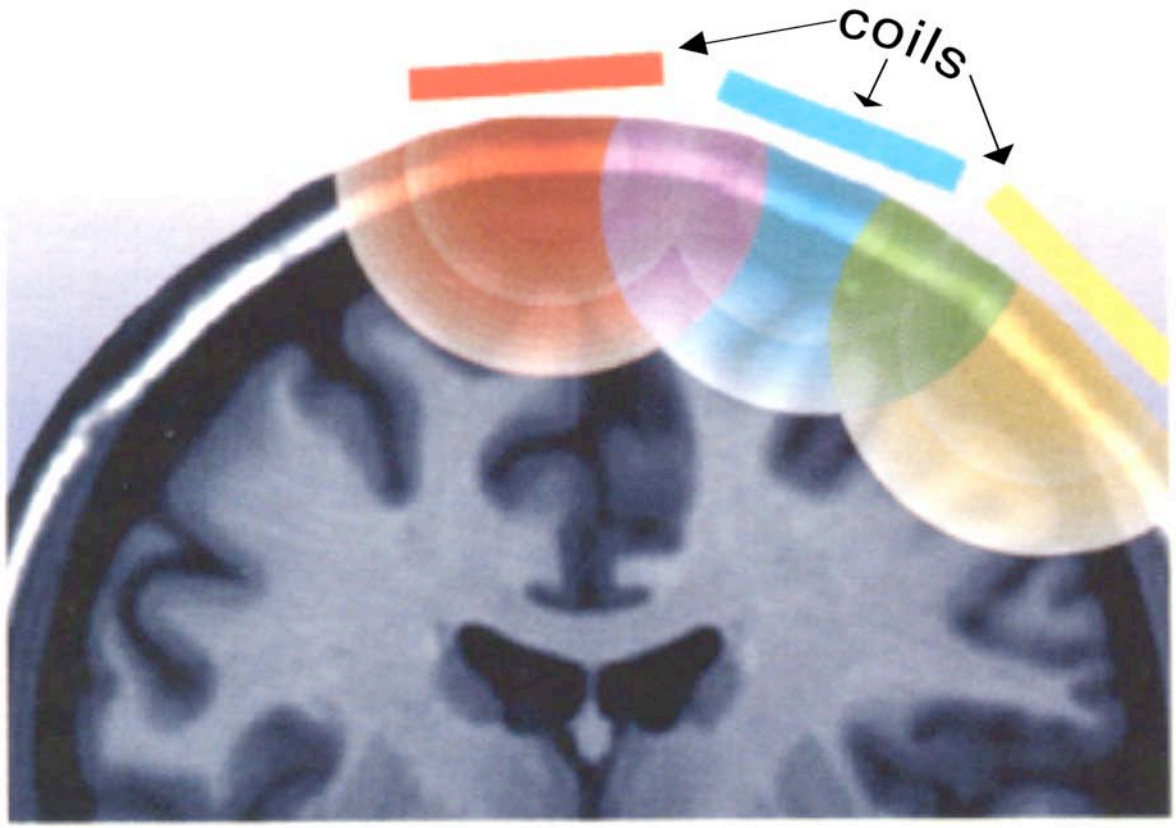


Stereotaxy

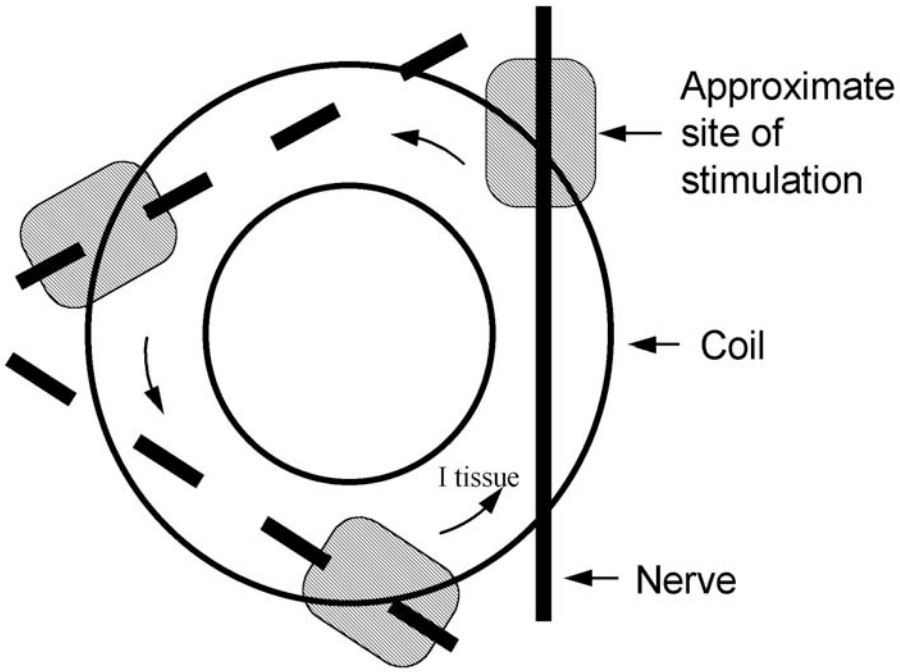


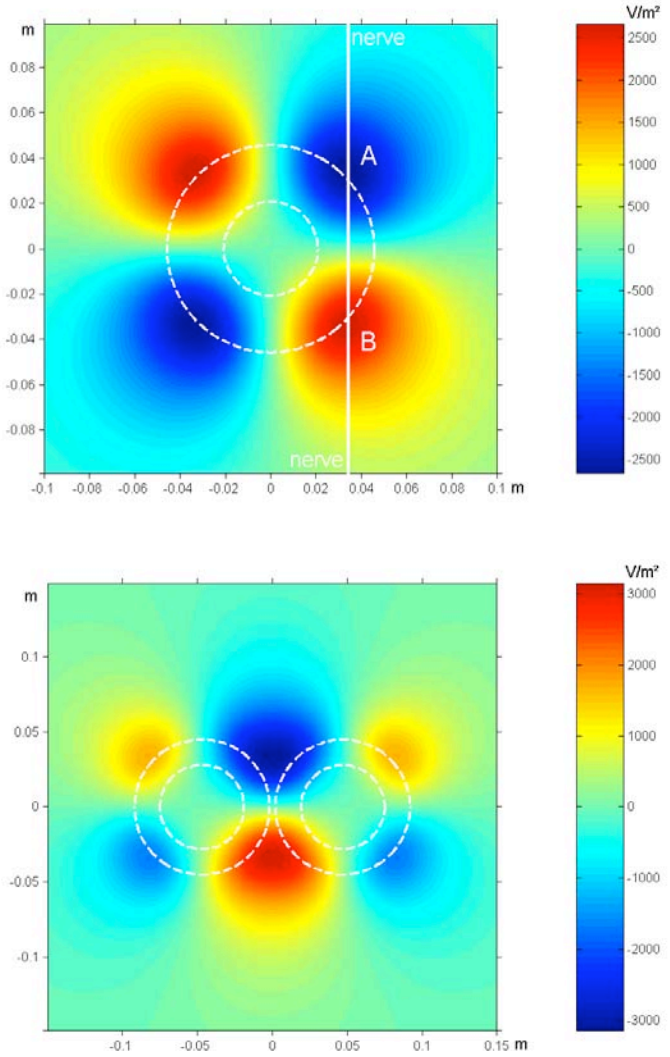
Gugino et al. *Clin Neurophysiol* 2000

Topographic resolution



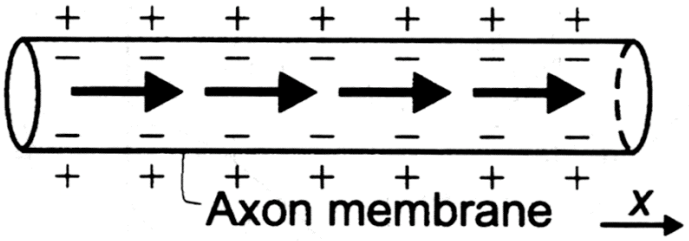
Mechanism of action

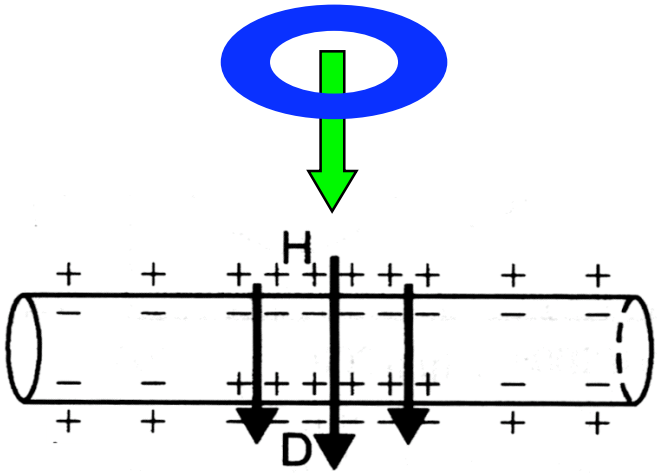


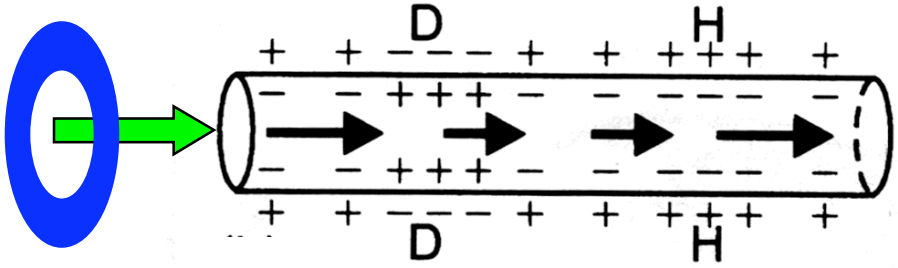


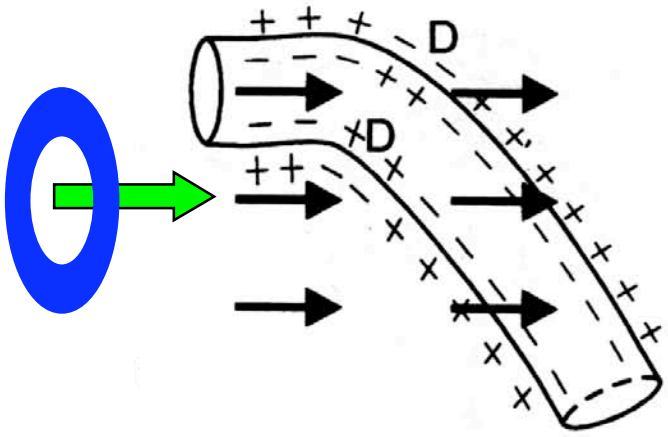
Mechanisms of action:

Interaction between induced current and axons



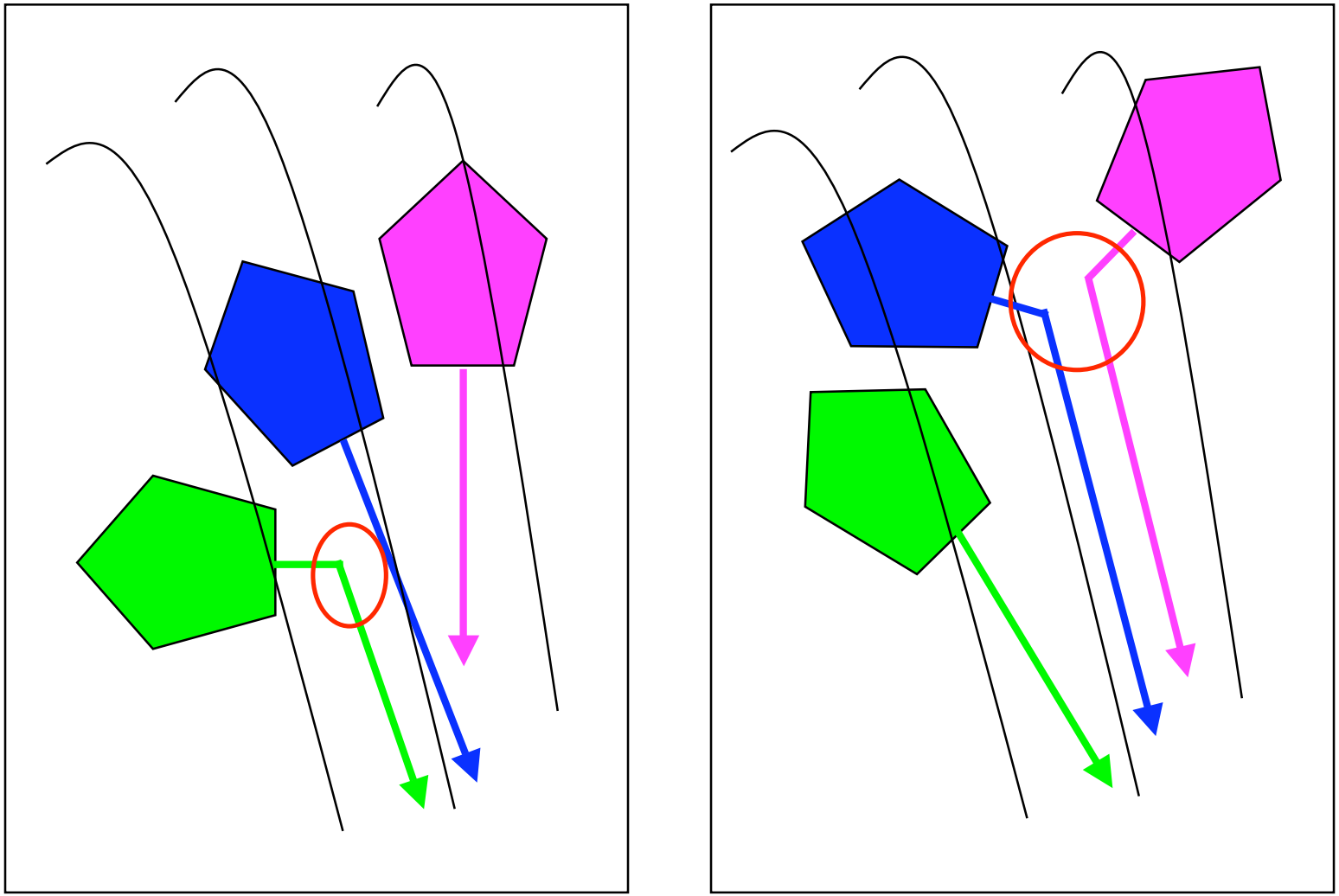






Mechanism of action:

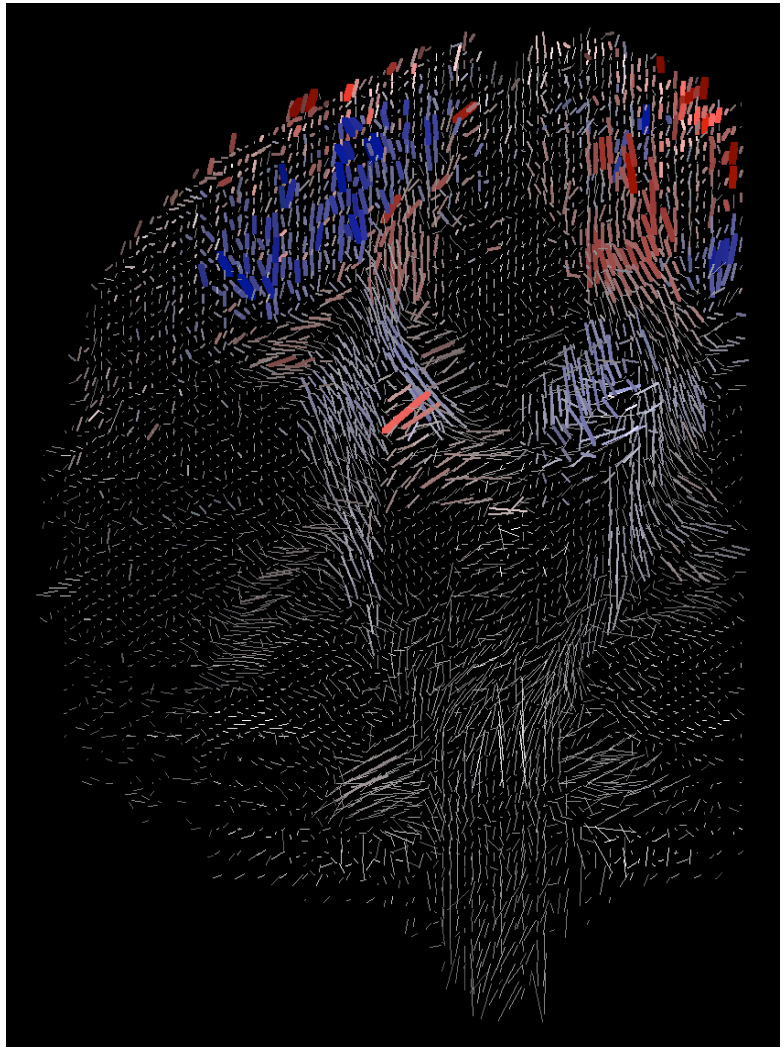
Interindividual variability



DSI-Guided TMS ?

Computed TMS interaction with cerebral white matter

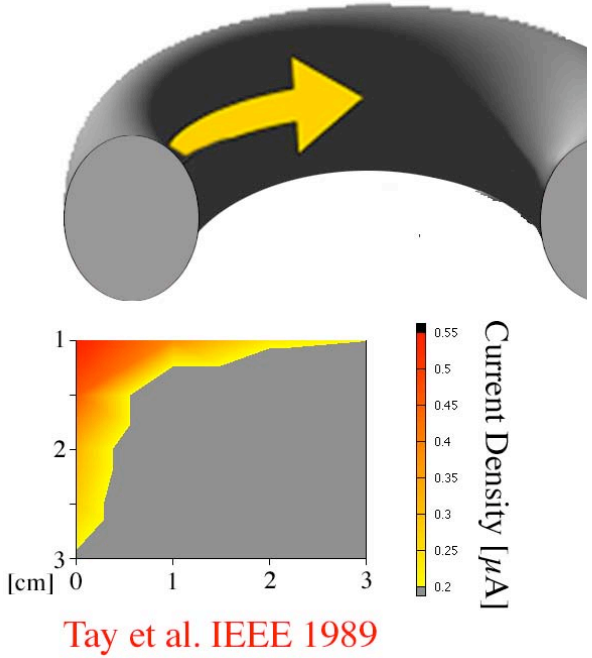
- circular 10 cm TMS coil over vertex
- DTI of cerebral white matter orientation, coronal slab
- induced axonal EMF's computed with "antenna" model: d<**E**,**s**>/ds
red +, blue -



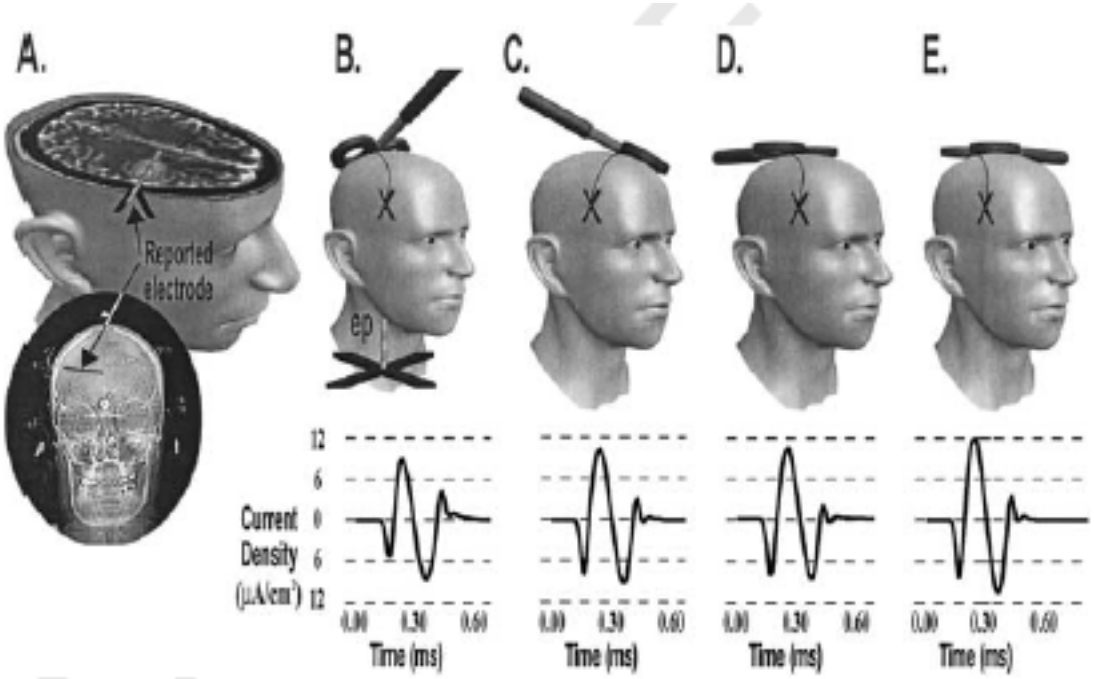
Van Wedeen et al.

Magnitude of Induced Current

Humans: measured 12μA/cm^2
1 cm from coil
7% of max. output intensity



Tay et al. IEEE 1989

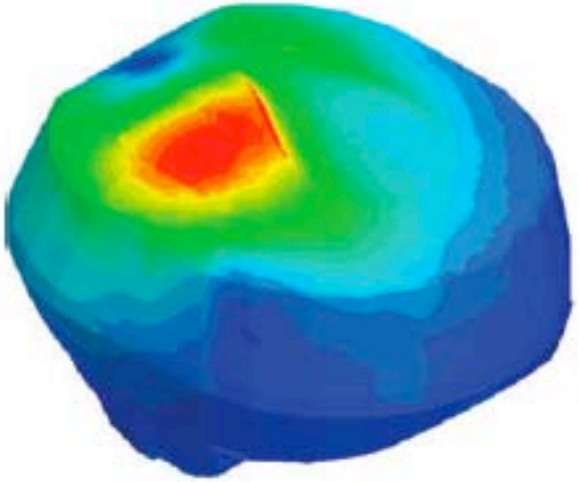


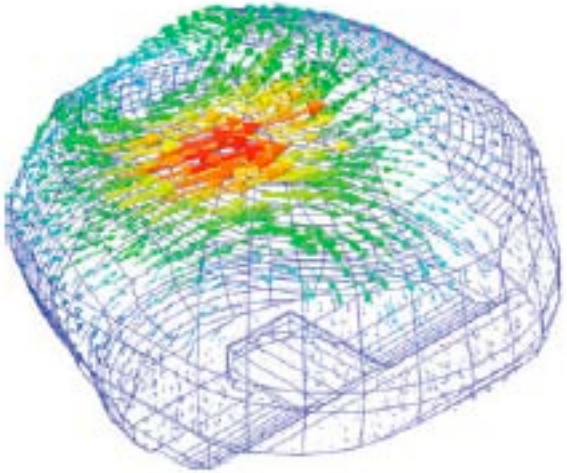
Wagner et al., *Neurosci Lett* 2003

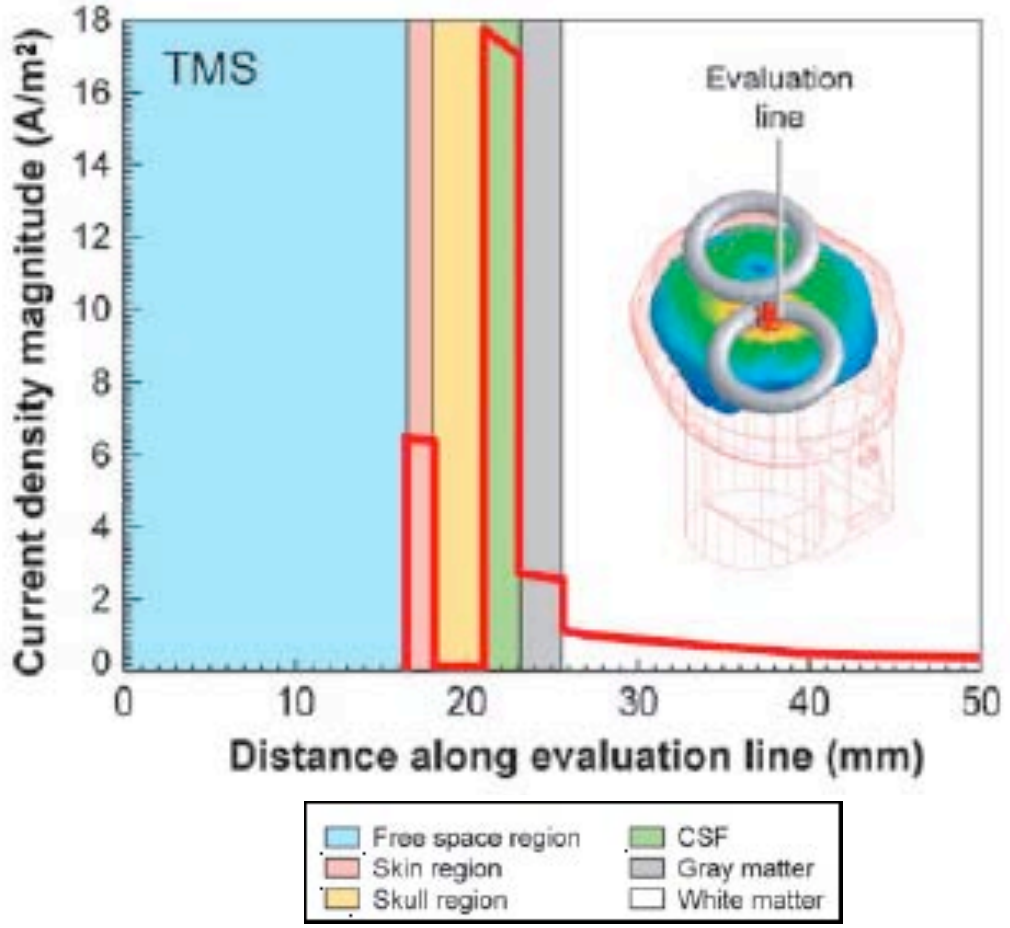
Modeling allows to understand the influence of tissue characteristics on current distribution

Magnetic field penetrates skin, scalp and skull practically without attenuation

The induced electric field exerts the effects (electrodeless-electric stimulation)



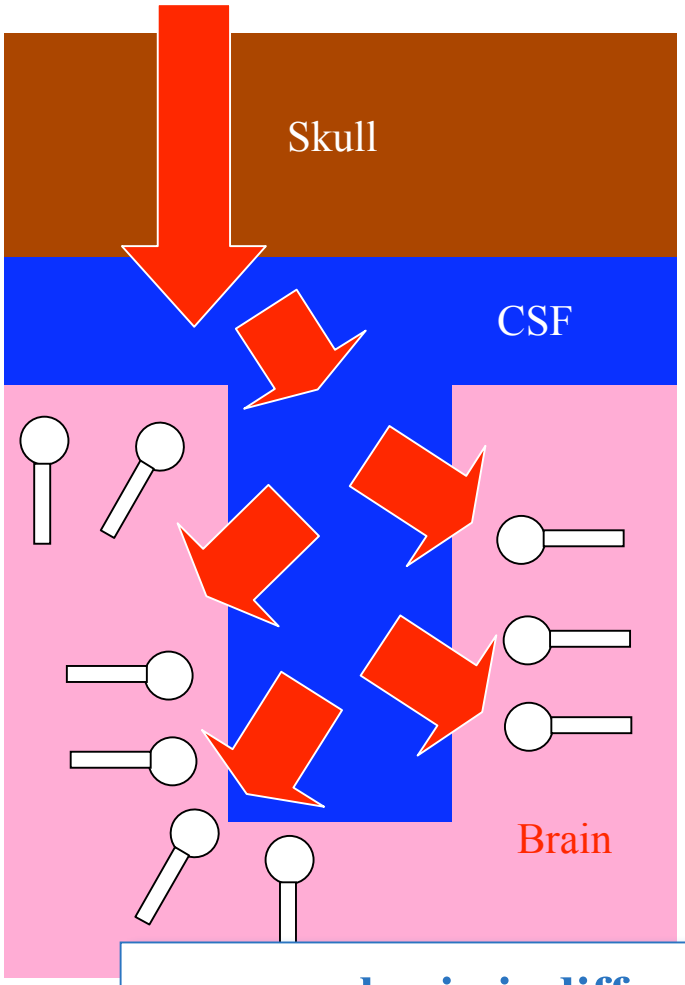




Wagner et al. *IEEE* 2005; *Neuroimage* 2006

The relationship between the current density inside and outside the brain depends on individual tissue properties.

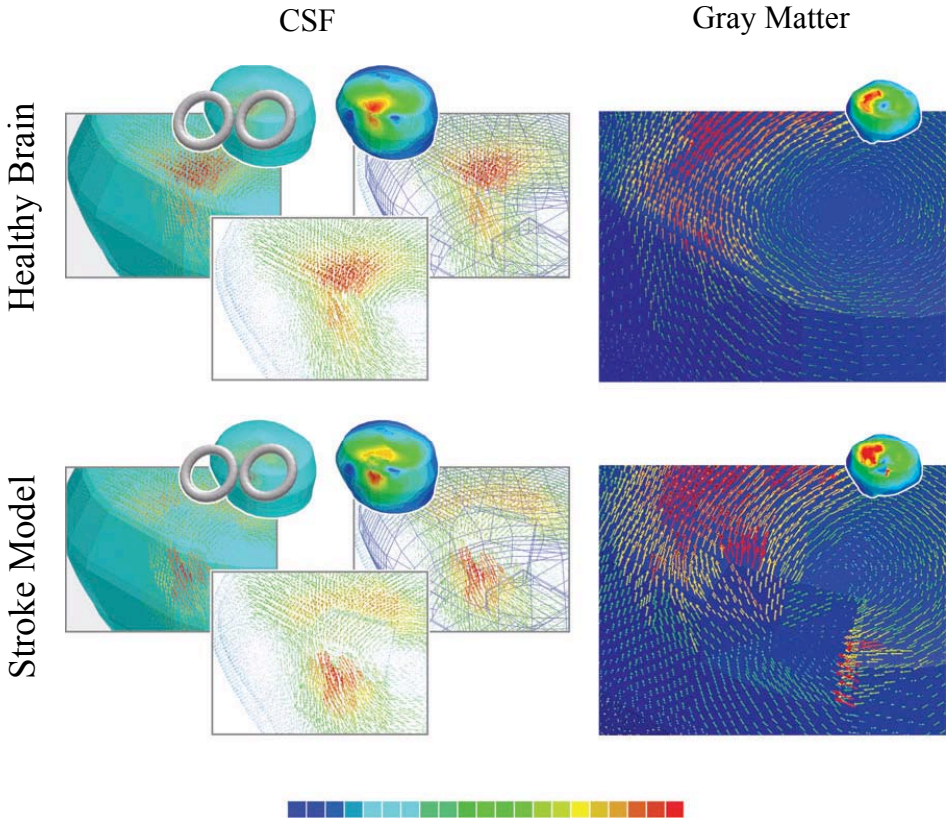
Current density varies throughout the brain due to differences in impedance and tissue geometry

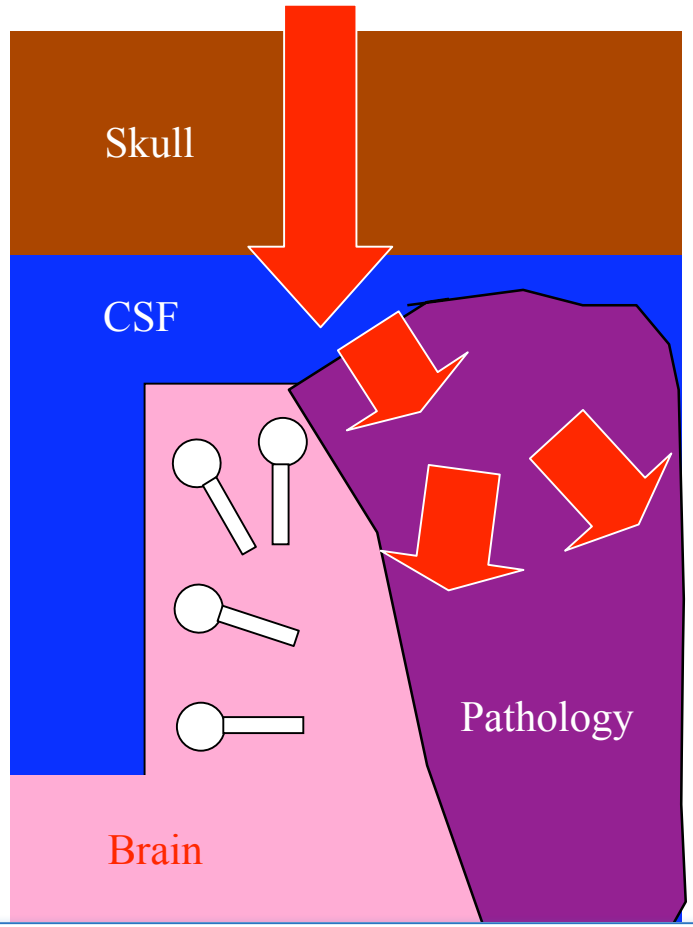


… every brain is different!

Wagner et al.

Current densities in the healthy and pathological brain are not equivalent





Relevant for safety, accuracy, and efficacy

… and every pathology is different!

Wagner et al.

Current densities in the brain are what matter

Current densities in the brain affect neural function in a complex and state dependent manner

- At least report sufficient data to be able to allow offline

  For TMS

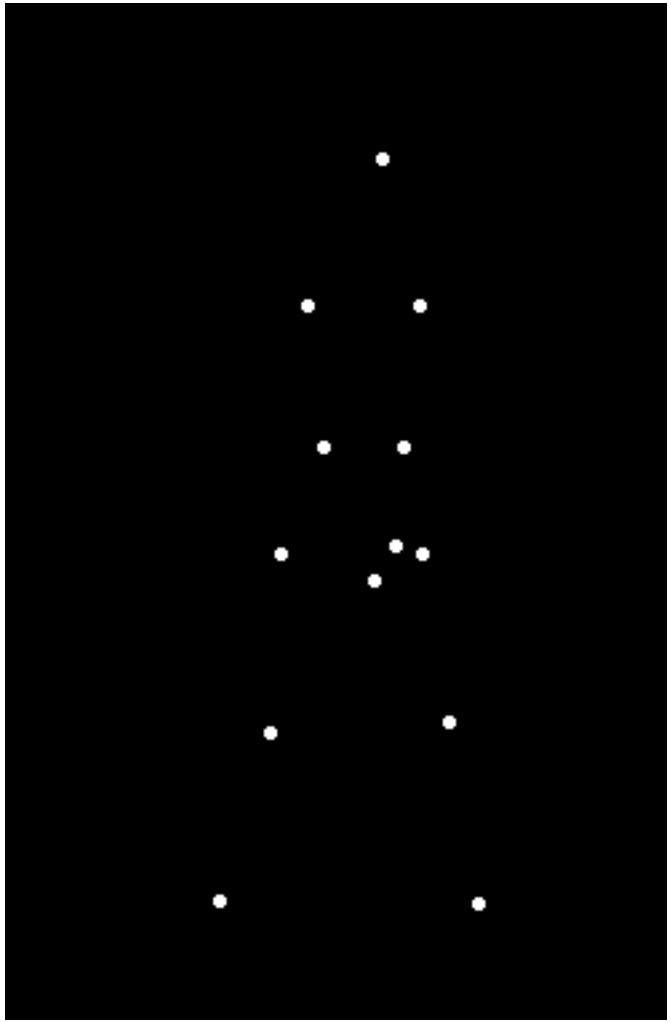
  - coil position
  - coil orientation
  - coil geometry and material
  - current over time
  - available subject data
- Computational tools can be used to determine the relative focality, orientation, penetration, and intensity of current densities across subjects/studies.

- Knowing current density distribution is a necessary, but not sufficient to determine biological, behavioral, and safety effects

EFFECTS OF TMS ARISE FROM THE INTERACTION OF THE STIMULUS WITH THE TISSUE - CONSIDER TISSUE CHARACTERISTICS

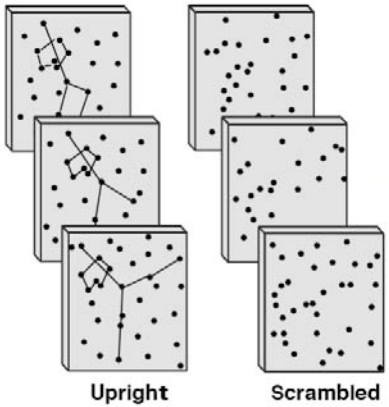
BRAIN STRUCTURES MAY SERVE AS ANTENNAS (PICK-UP COILS) OF THE MAGNETIC FIELD - ORIENTATION !

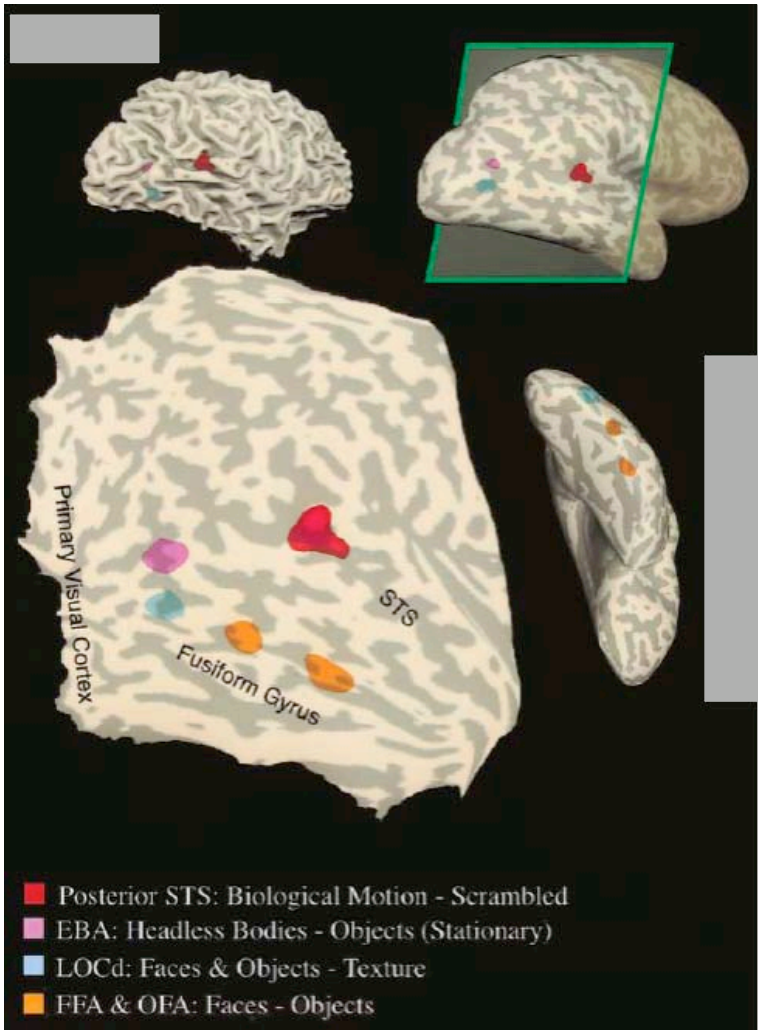
THE EFFECTS OF TMS DEPEND ON THE STATE OF BRAIN ACTIVITY



Johansson 1973

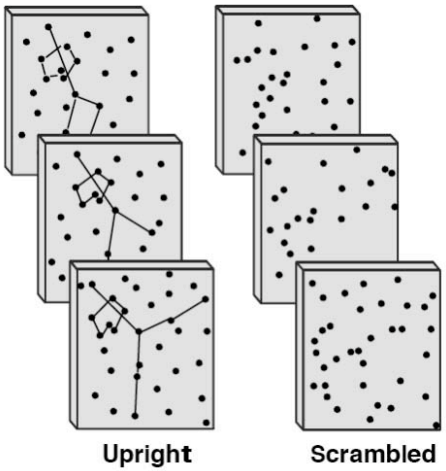
Neural correlates of biological motion perception

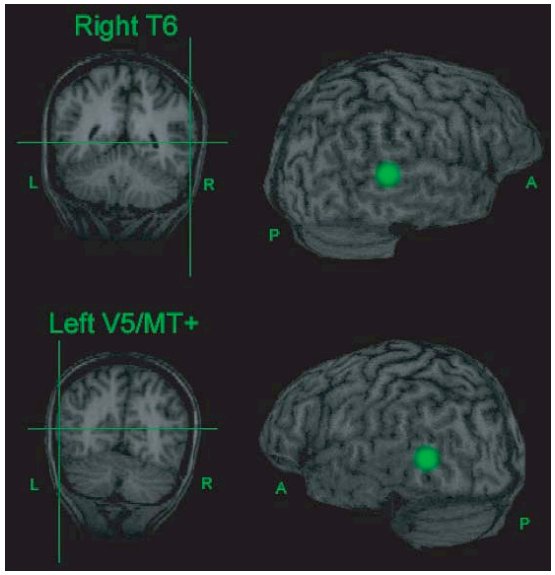


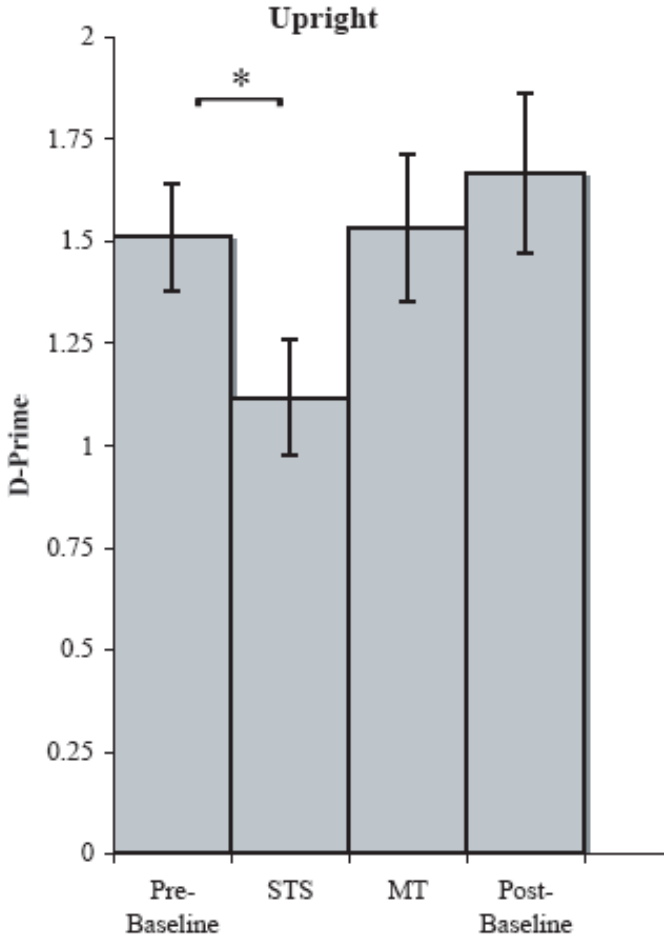


Grossman & Blake, *Neuron* 2002

Neural correlates of biological motion perception



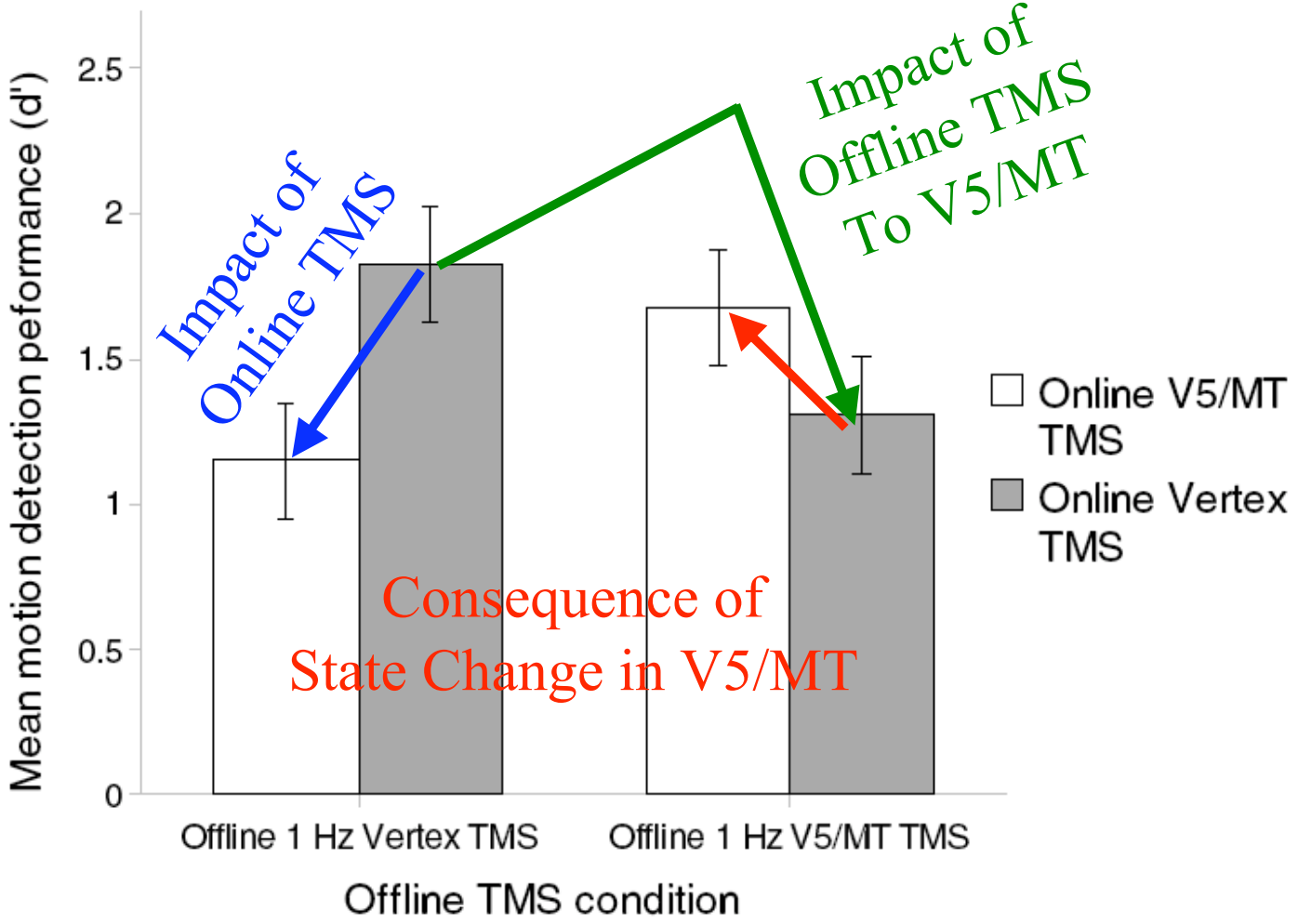




Grossman, Batelli, Pascual-Leone *Vision Res* 06

Effects of cortical stimulation depend on functional state of targeted cortex

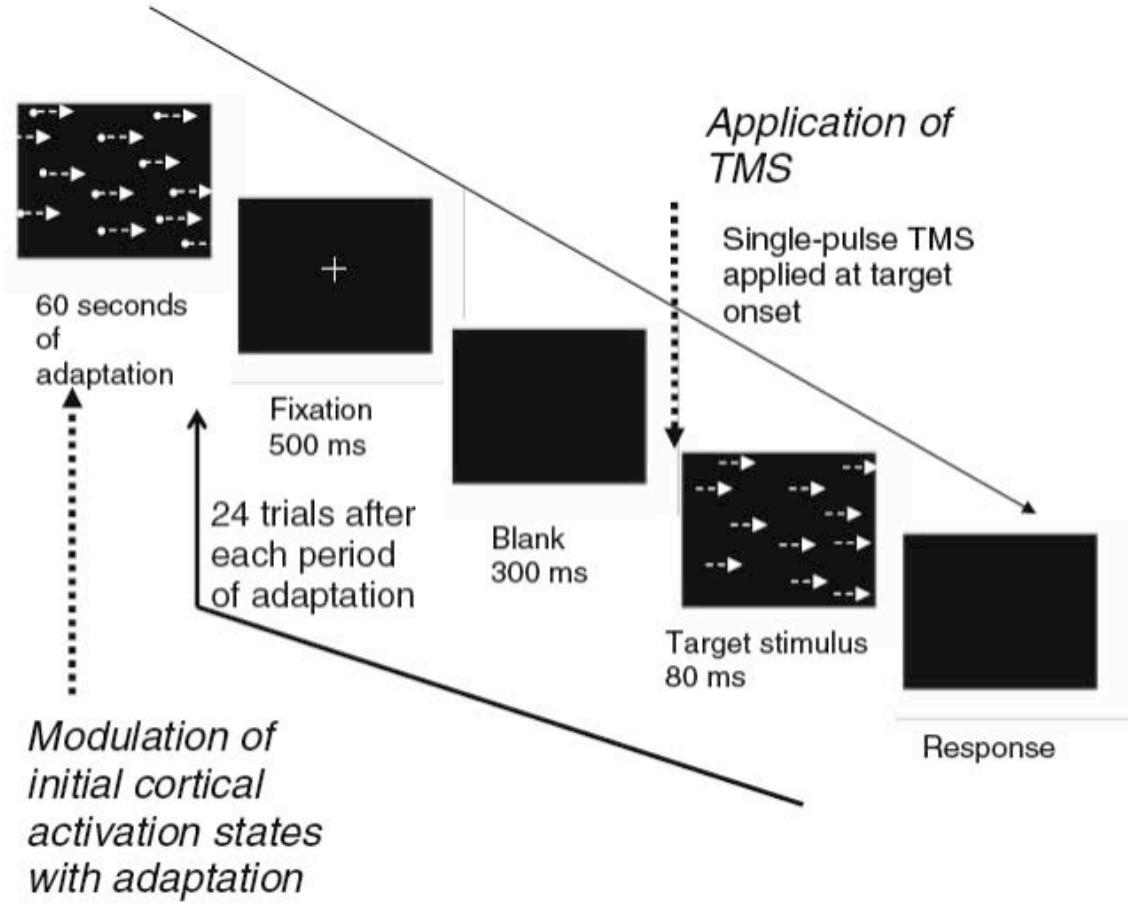
Does suppression of V5/MT by rTMS change the impact of Online TMS?



Silvanto, Batelli, Pascual-Leone *J Neurophysiol* 08

State Dependency For Specific Neural Populations

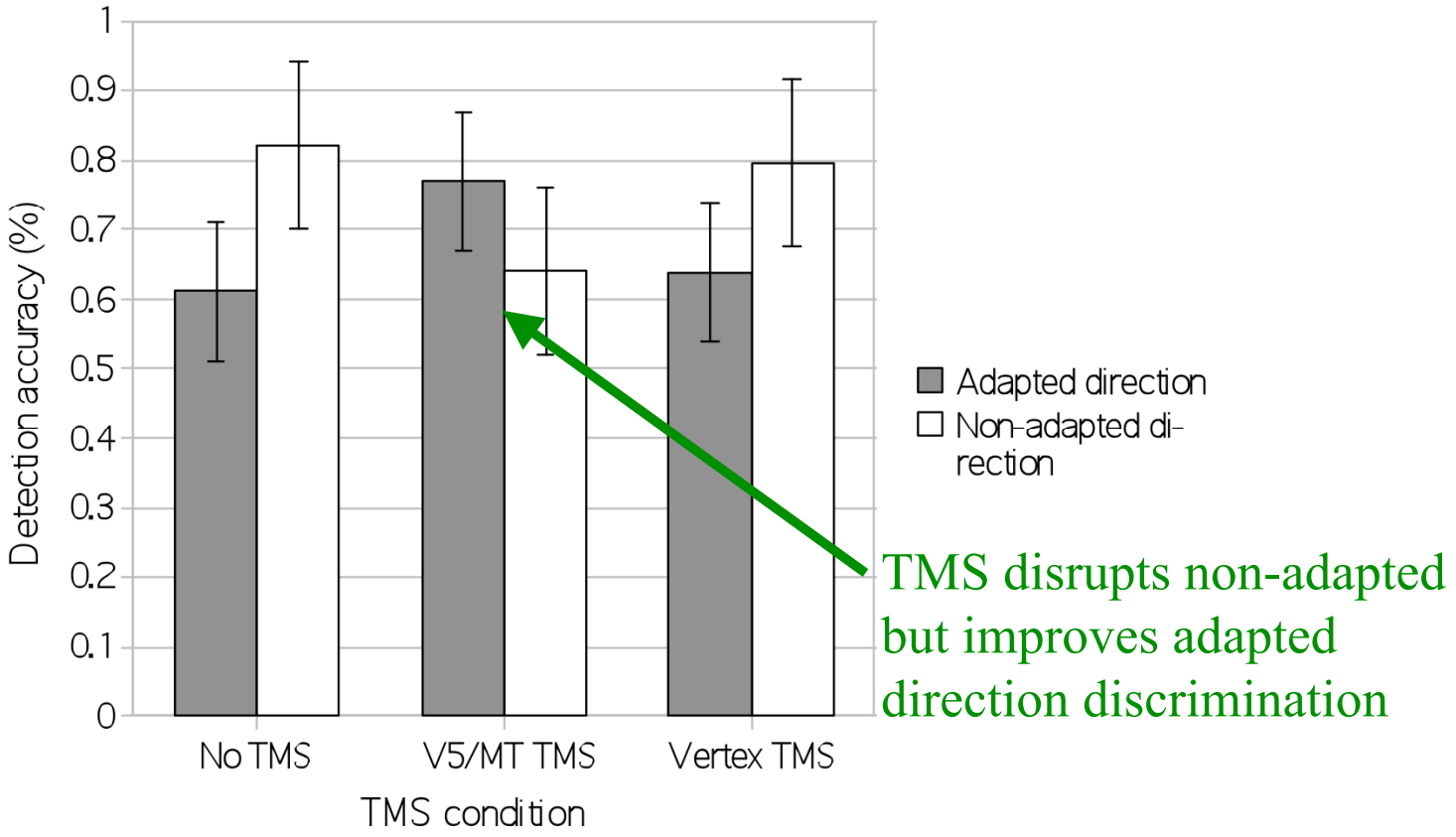
TMS-adaptation paradigm and motion direction discrimination in visual area V5/MT



Cattaneo & Silvanto *Neurosci Lett* 08

State Dependency For Specific Neural Populations

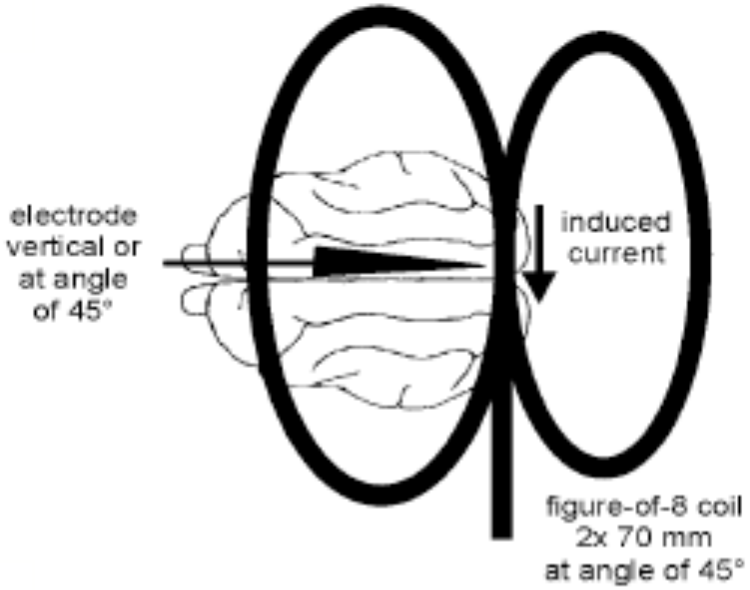
TMS-adaptation paradigm and motion direction discrimination in visual area V5/MT

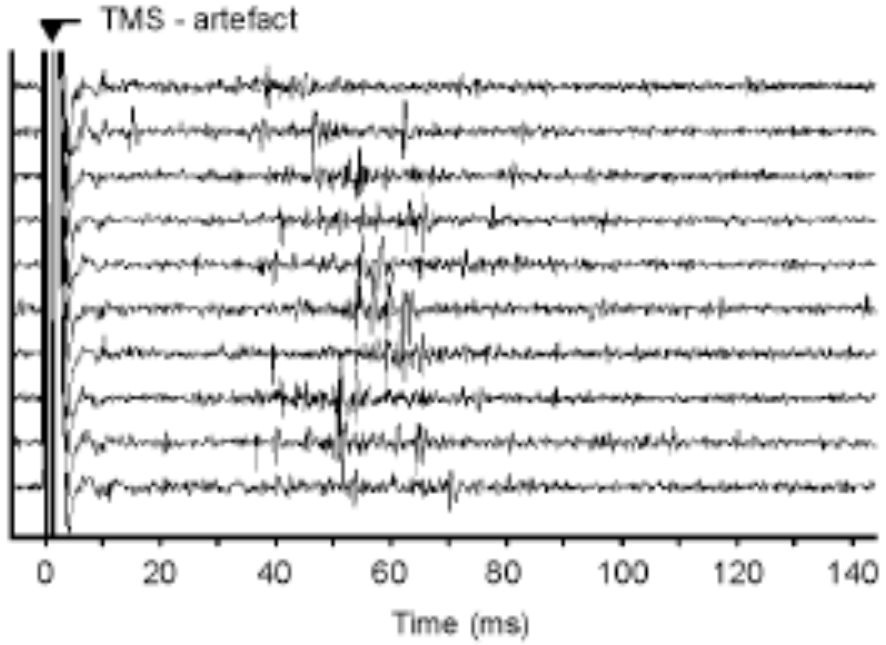


TMS disrupts non-adapted but improves adapted direction discrimination

Cattaneo & Silvanto *Neurosci Lett* 08

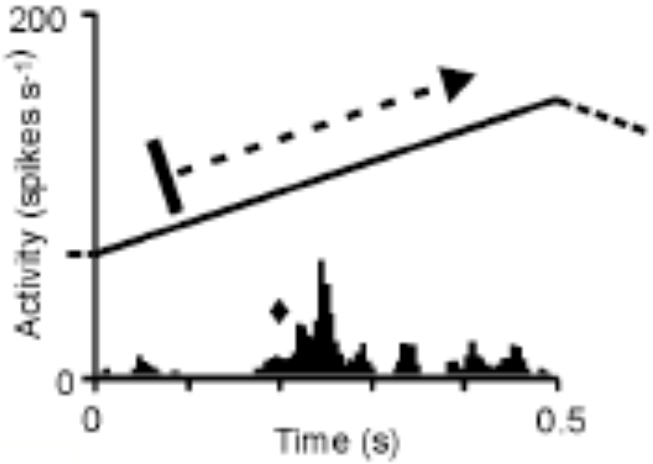
Interaction with tissue depends on TMS parameters & level of activity of targeted cortex

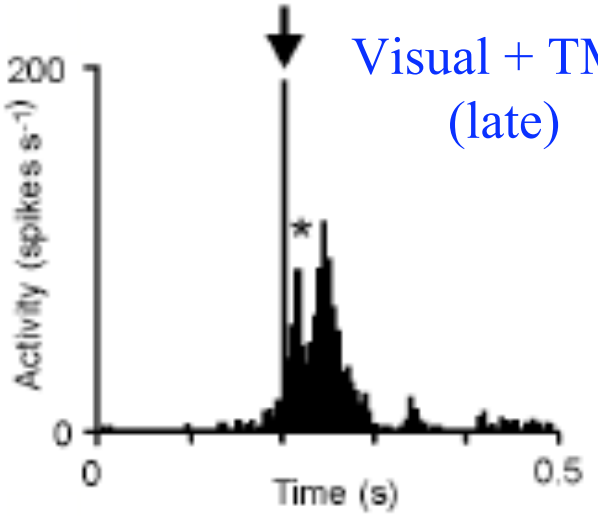


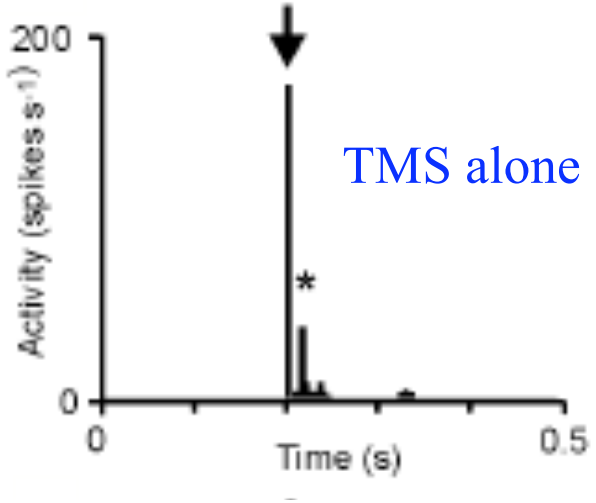


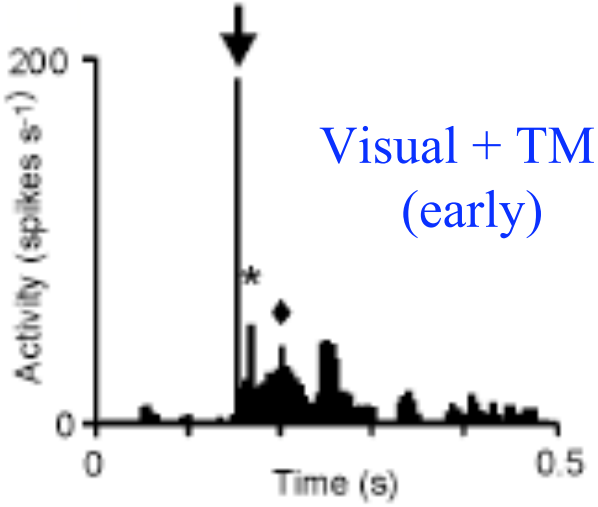
Moliadze et al. *J. Physiol.* 2003

Effect of TMS on neuronal activity modulated by visual stimuli









Moliadze et al. *J. Physiol.* 2003

Why is state-dependency useful?

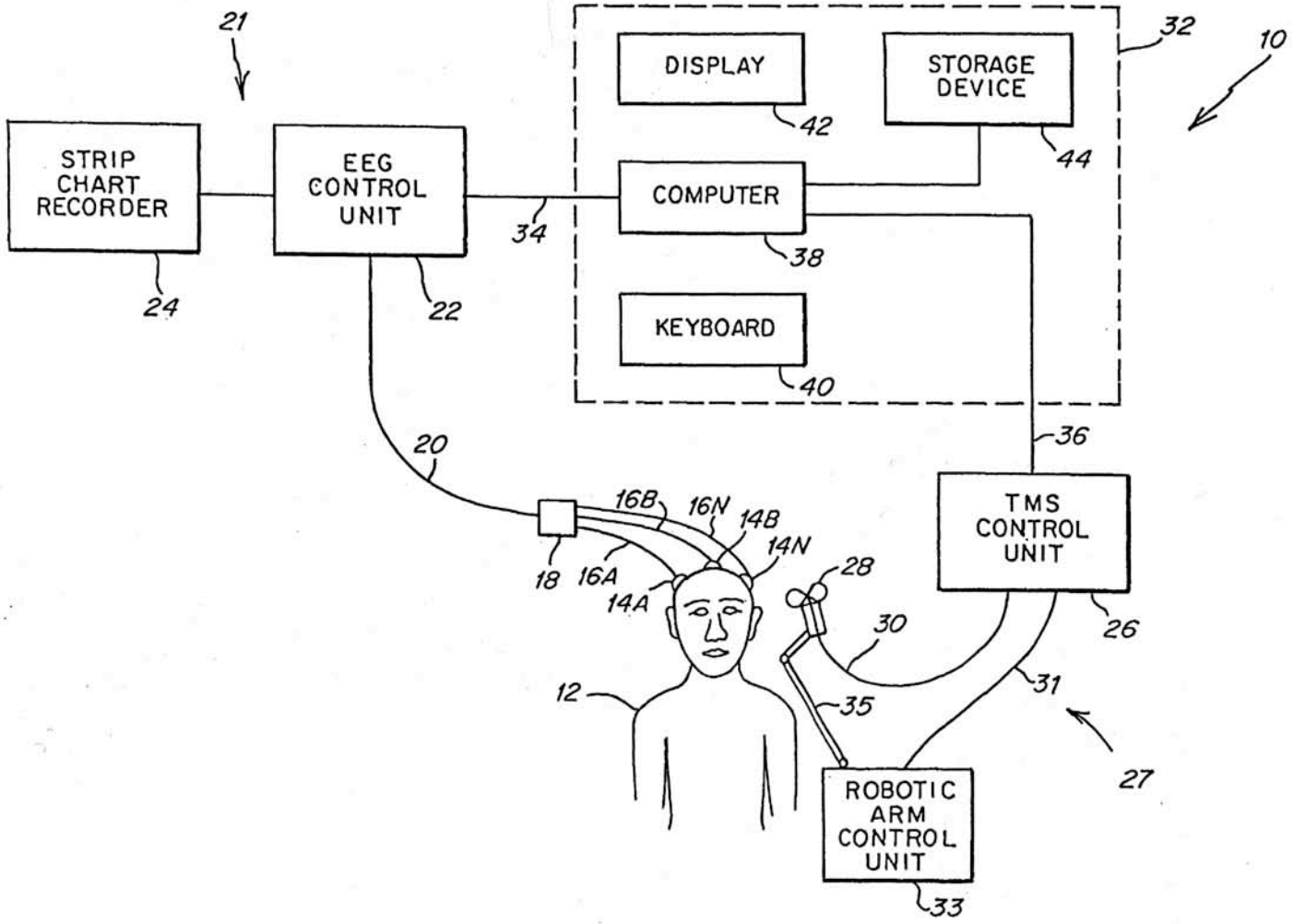
- The behavioral impact of TMS depends on the initial activation state
  - TMS behaviorally facilitates the attributes encoded by the adapted neural populations relative to attributes encoded by other neurons
- Enables differential stimulation of distinct neural populations in the targeted region
- Can enhance functional resolution of TMS
  - From causality to neural selectivity

Silvanto & Pascual-Leone *Brain Topogr* 08

THE EFFECTS OF TMS DEPEND ON THE ONGOING BRAIN ACTIVITY (BRAIN STATE) -

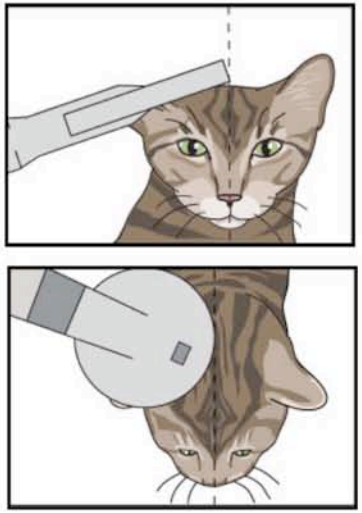
CONTROL BRAIN STATE !

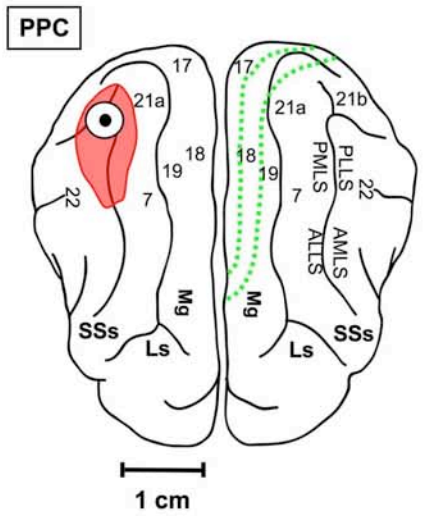
EEG Gated TMS

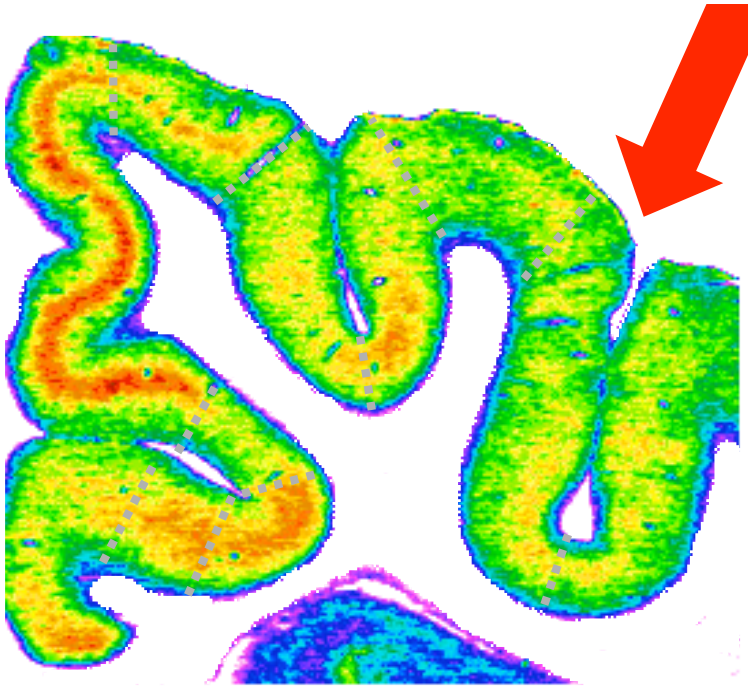


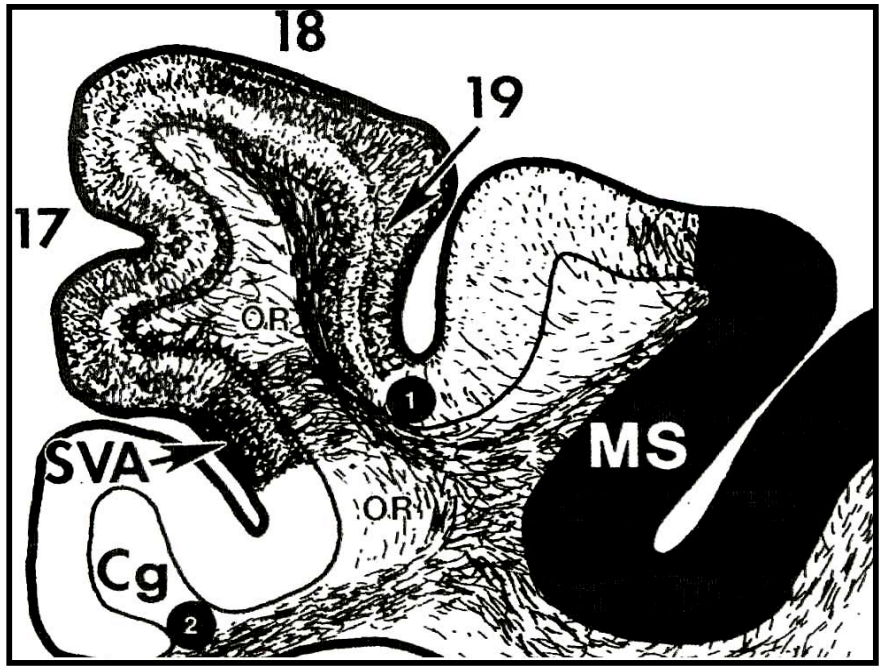
U.S. Patent No. 09/067,111
Foreign Patent License BO662/7012

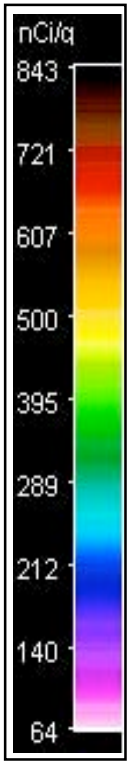
BIOLOGICAL EFFECTS EXTEND ALONG SPECIFIC NEURAL NETWORKS DEFINED BY ANATOMICAL CONNECTIVITY











SVA = Splenial visual area • Cg = Cingulate

Valero-Cabré et al *Exp Brain Res* 05

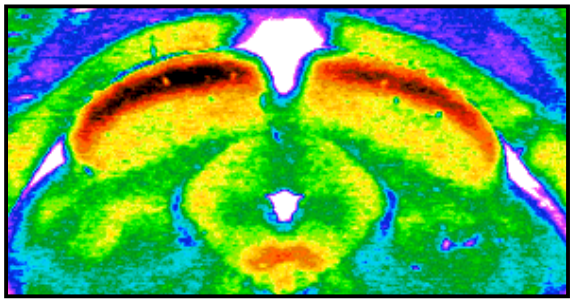
Valero-Cabré et al *Exp Brain Res* 05; 06

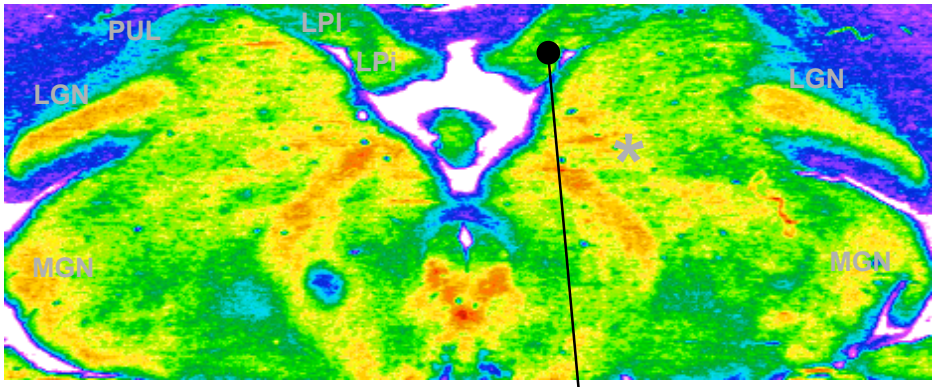
Area 17

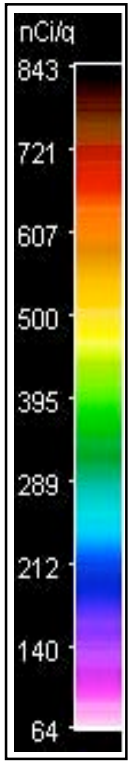
Area 19

Splenial visual area

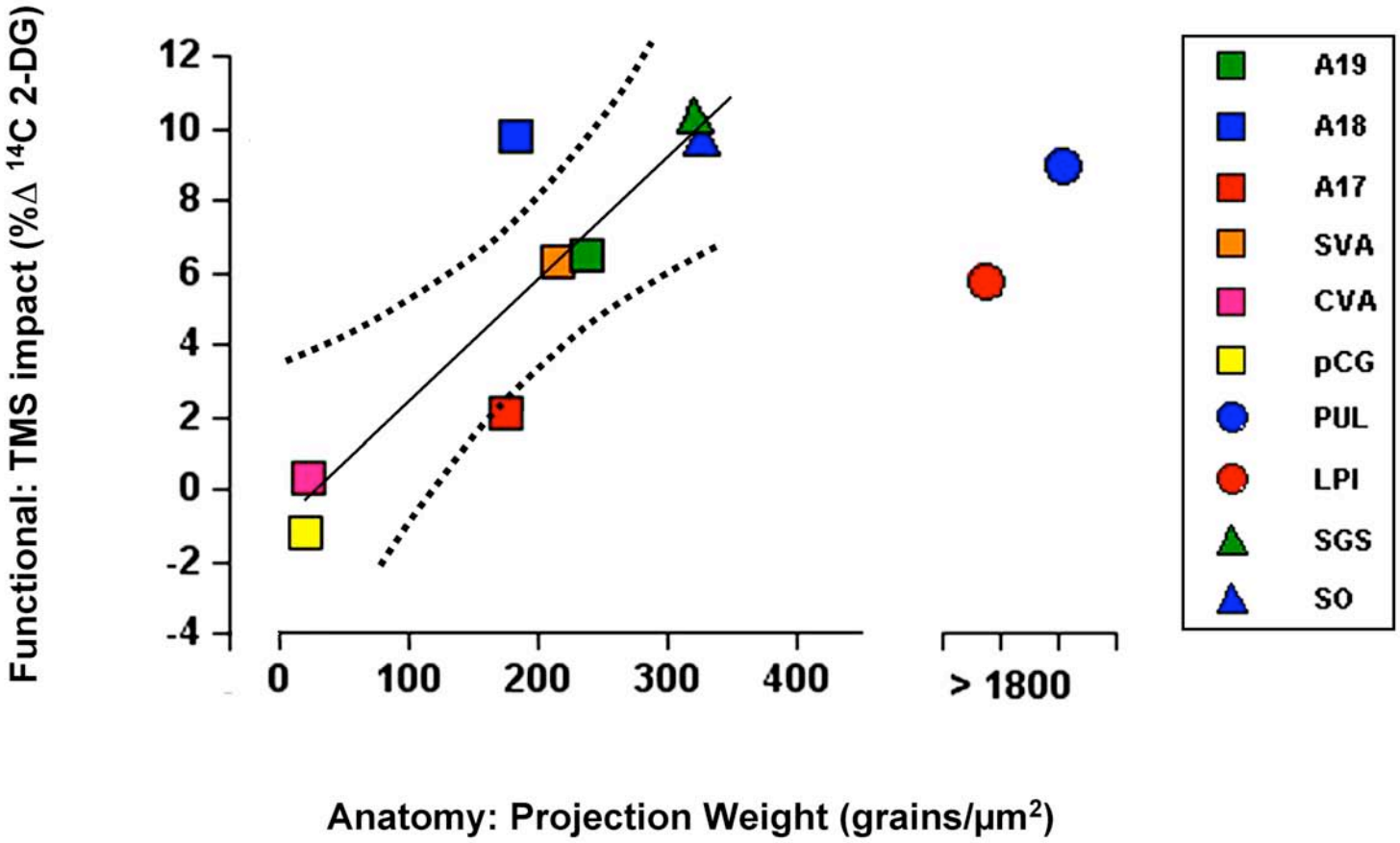
Superior Colliculus







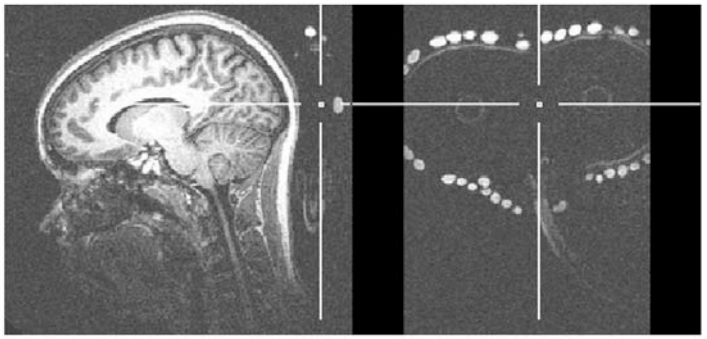
Lateral Post. Complex

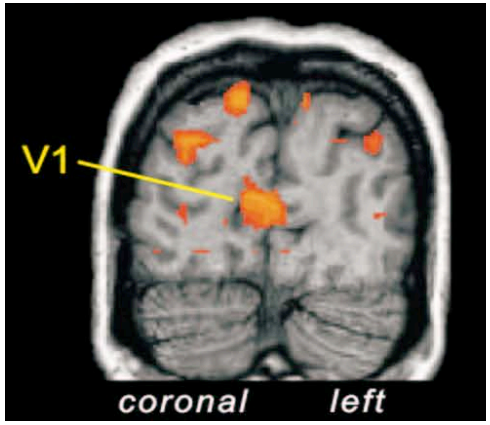


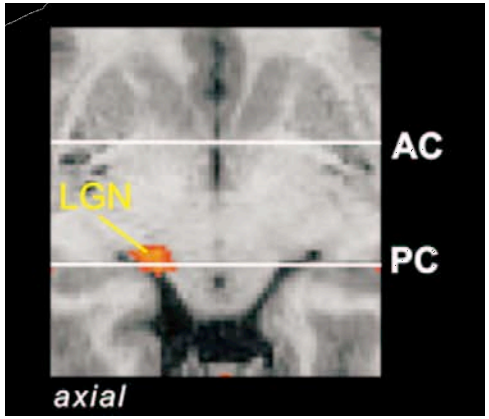
Valero-Cabré et al *Exp Brain Res* 05

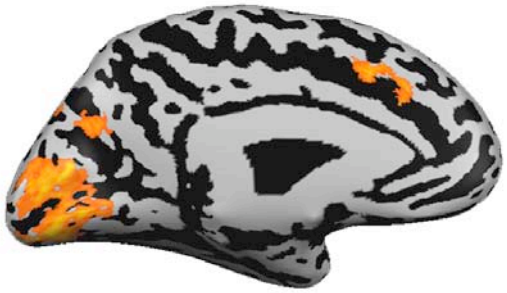
Real-Time TMS-fMRI

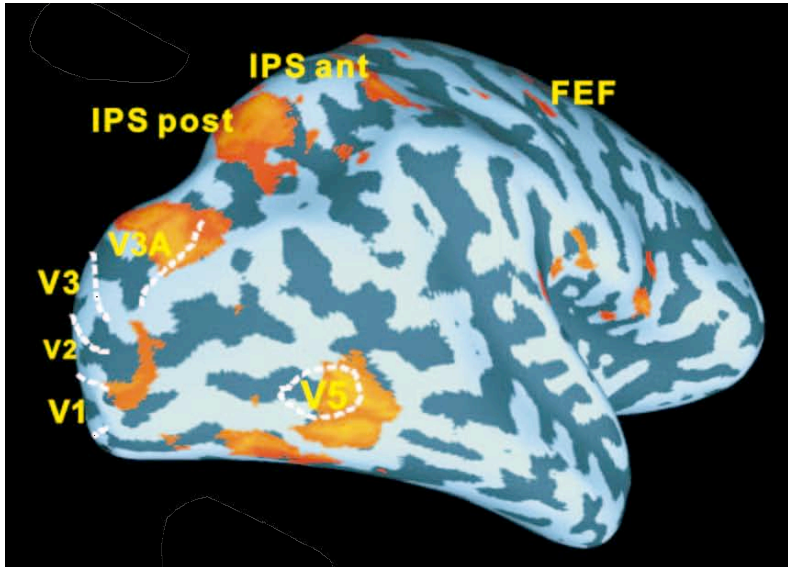
In-Vivo Studies of Connectivity
Behavioral Independence









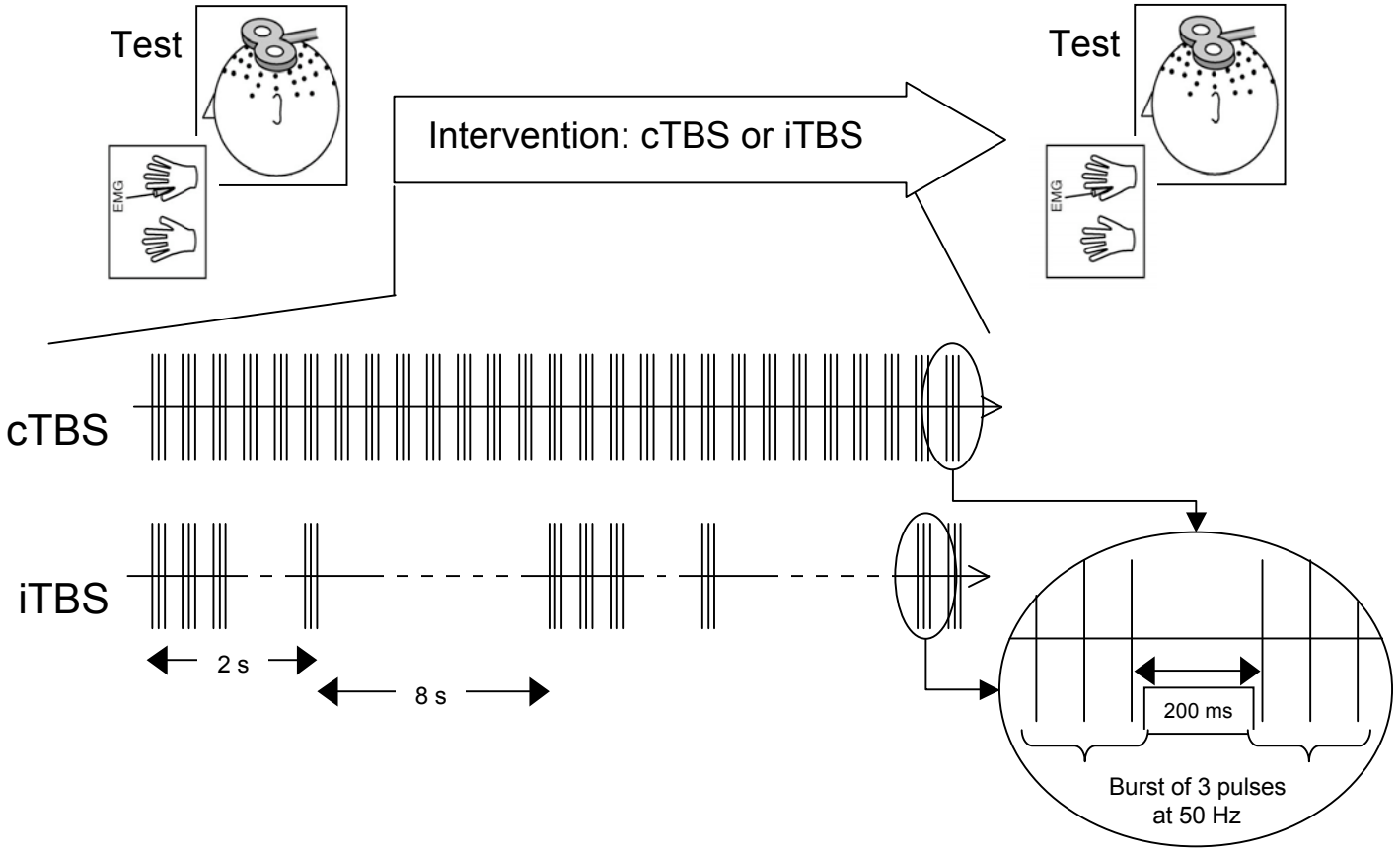


U.S. Patent No. 09/096,725
Foreign Patent License BO662/7013

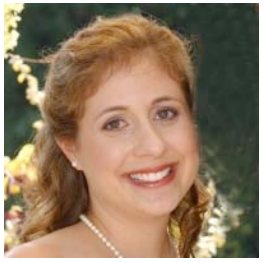
TMS TO MEASURE PLASTICITY

Measuring LTP/LTD in Humans

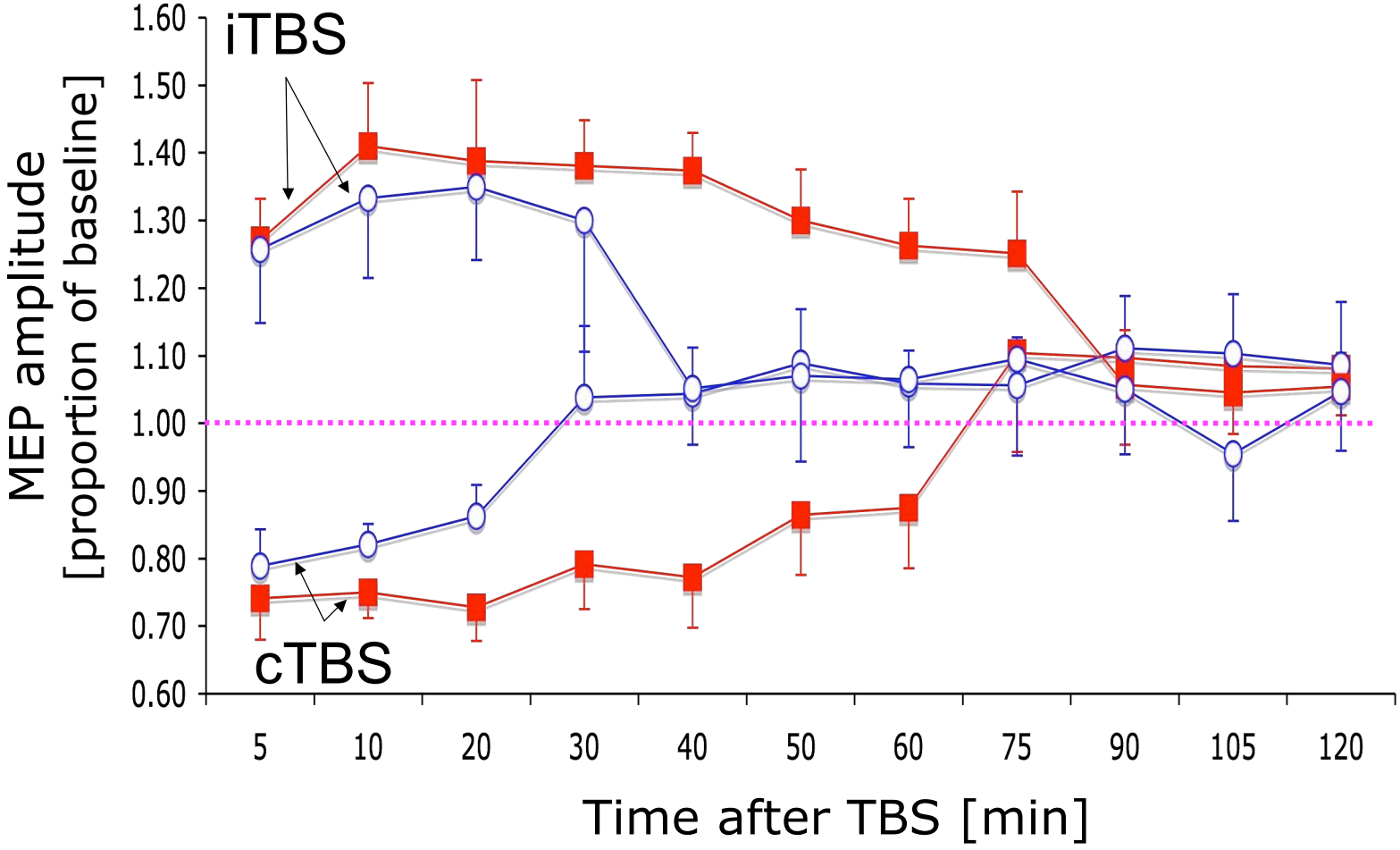
Theta Burst Stimulation (TBS)



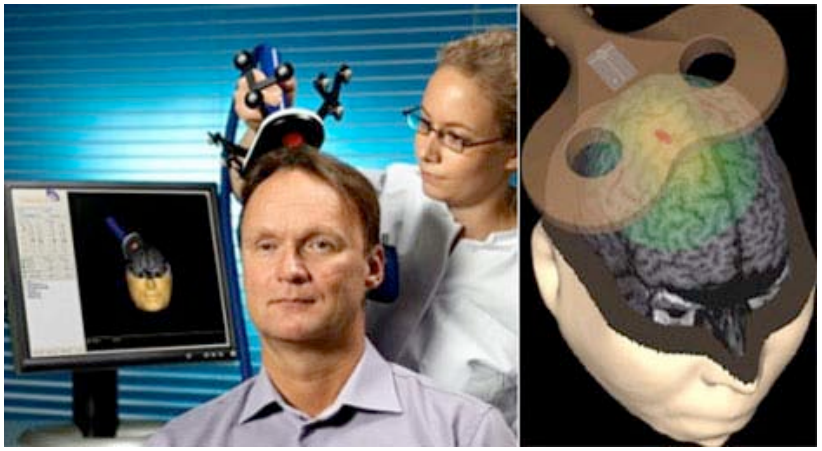
Huang et al. 2005

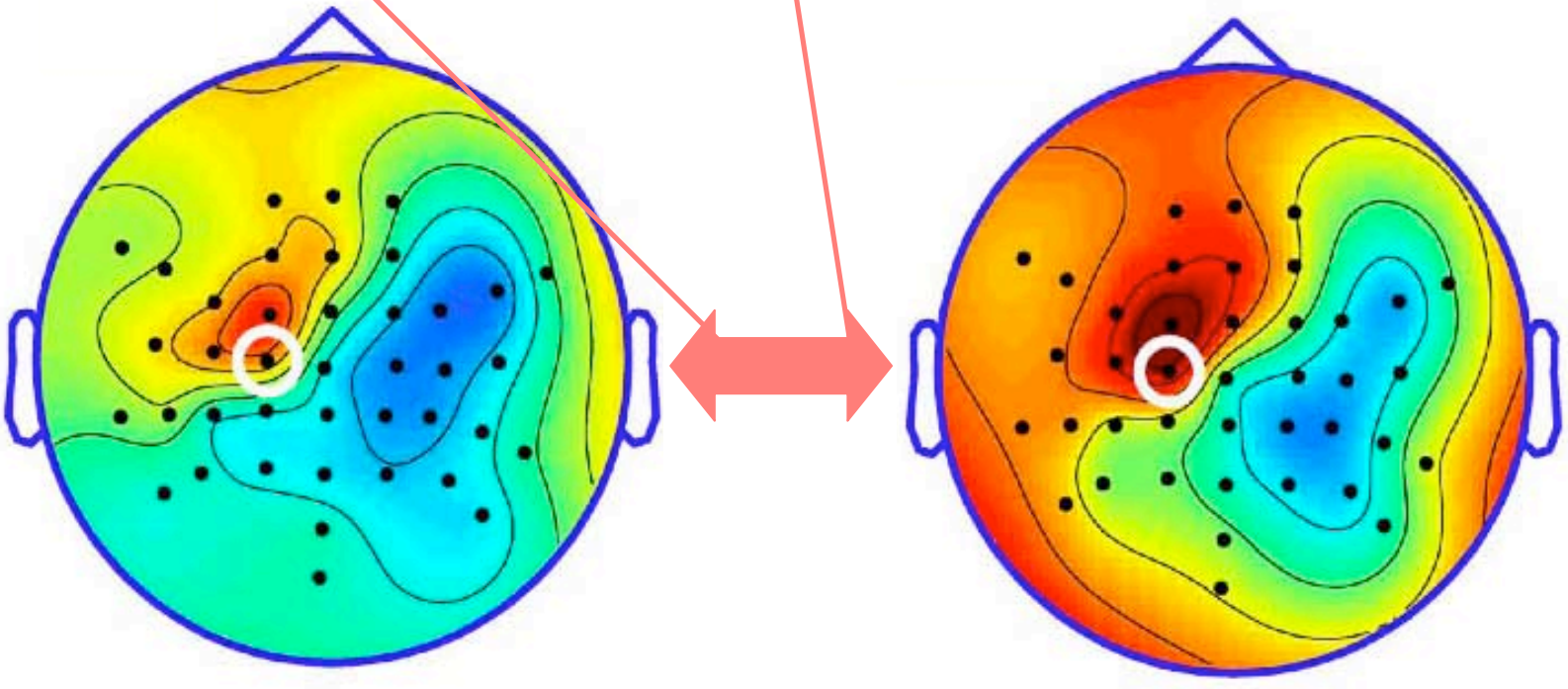


Hyperplasticity in Autism Spectrum Disorders



Intermittent TBS (iTBS)





Before

After

Esser et al. 2006

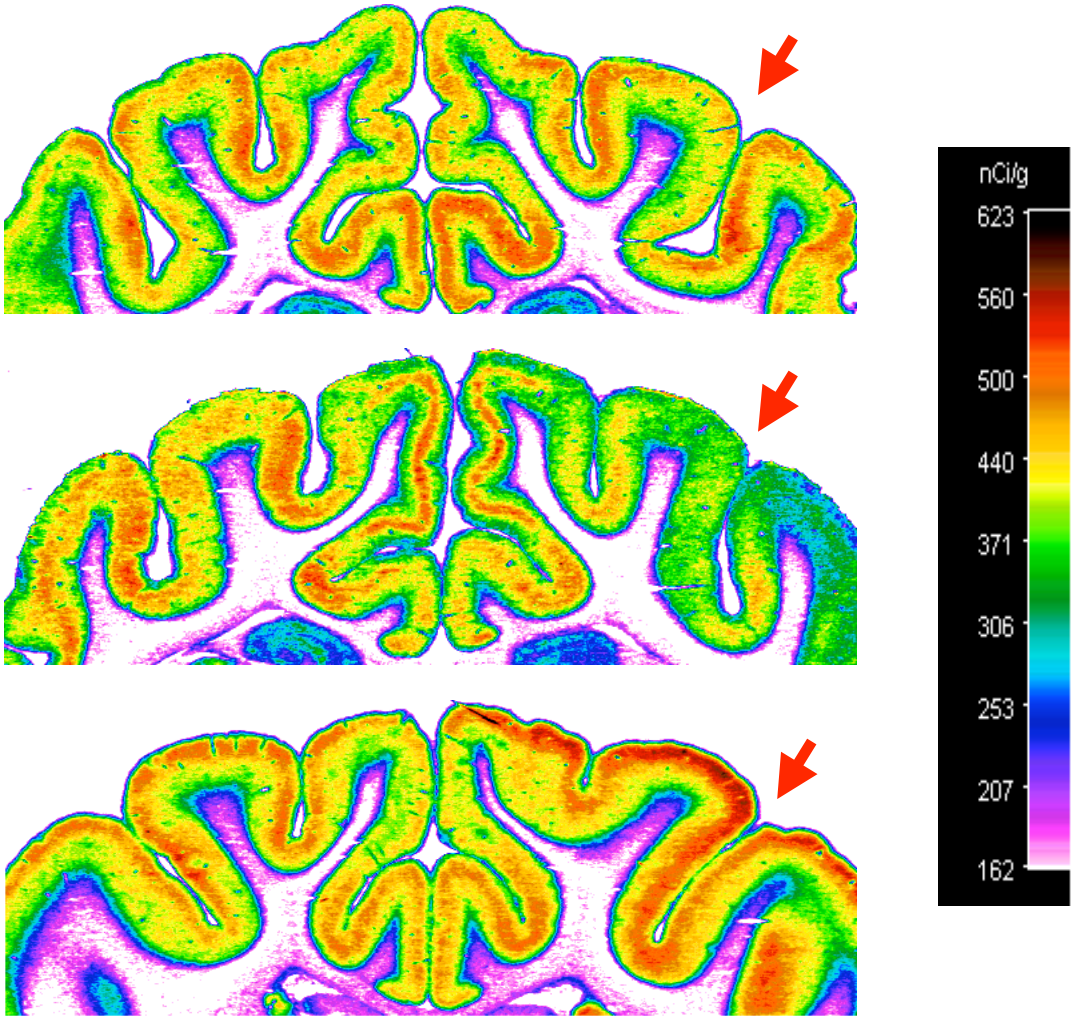
LOCAL BIOLOGICAL EFFECTS DO NOT ACCOUNT FOR THE BEHAVIORAL IMPACT

Off-line rTMS: Differential local impact depending on stimulation frequency

Sham TMS

1 Hz TMS

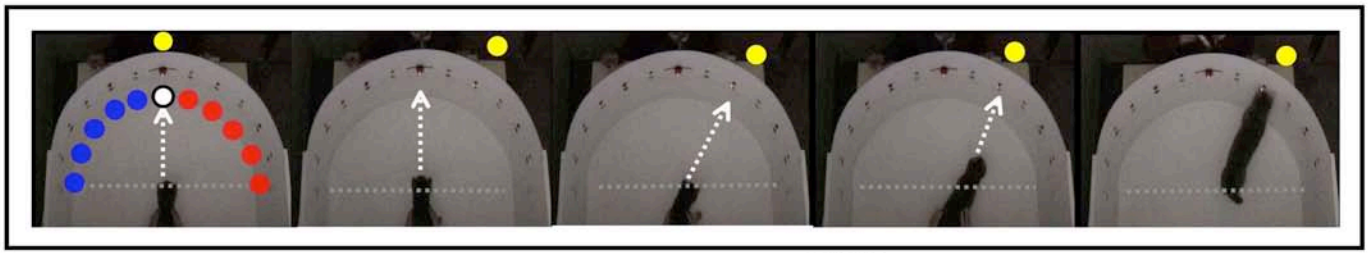
20 Hz TMS

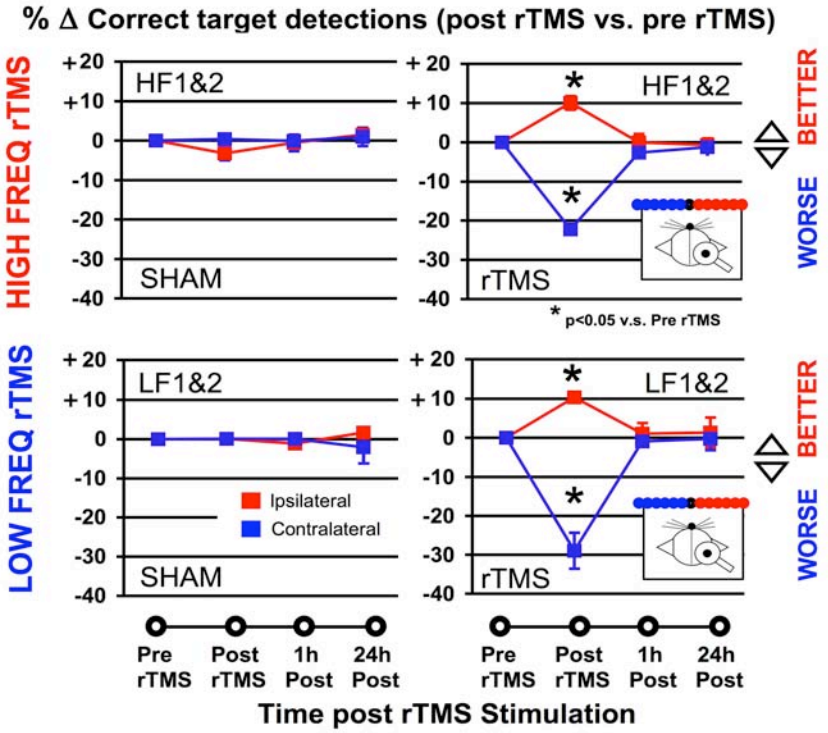


Valero-Cabré et al *Exp Brain Res* 07

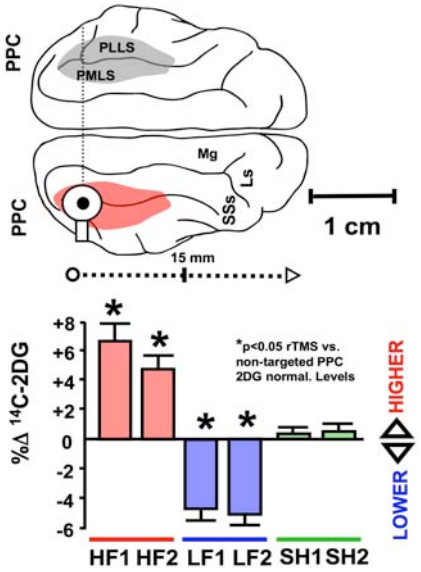
Valero-Cabré,
Rushmore, et al

Same behavioral consequences despite opposite local impact



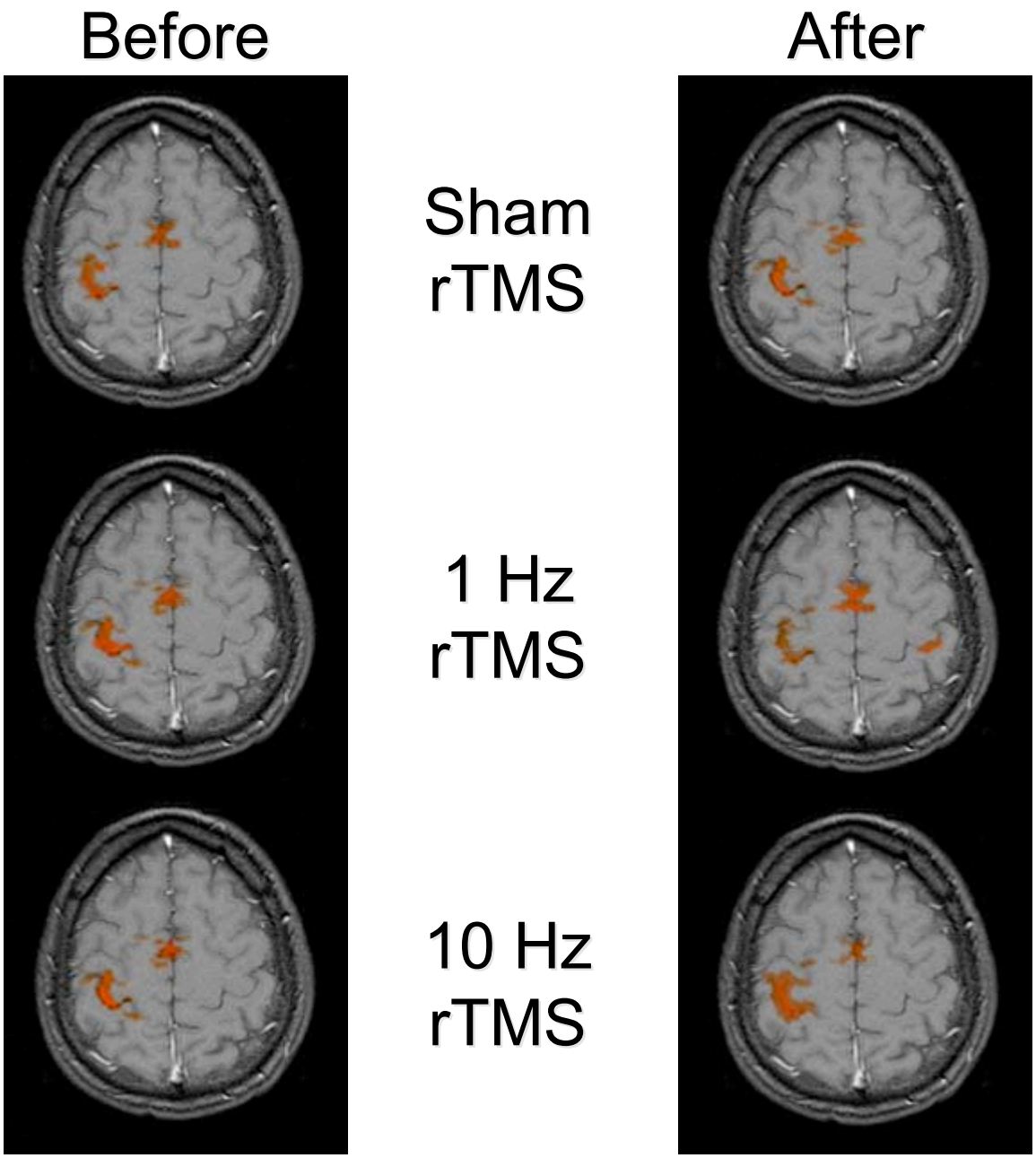


HF=High frequency rTMS 1&2
LF=Low Frequency rTMS 1&2
SH=Sham rTMS 1&2



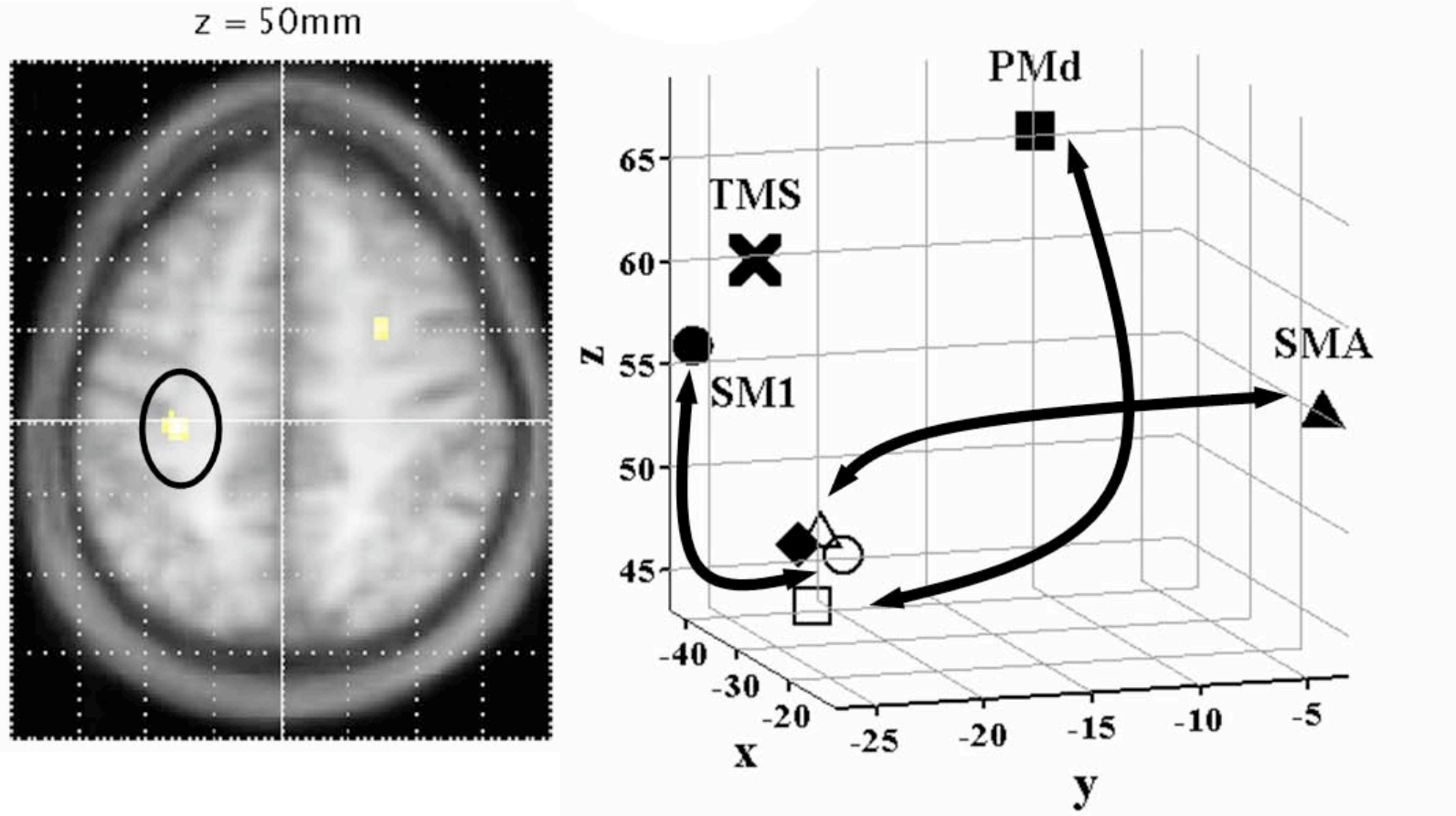
Boston University Laboratory for Cerebral Dynamics, Plasticity & Rehabilitation

BEHAVIORAL EFFECTS OF TMS REFLECT THE CAPACITY OF THE REST OF THE BRAIN TO ADAPT TO THE FOCAL DISRUPTION



rTMS to M1; subthreshold intensity; 1600 stimuli

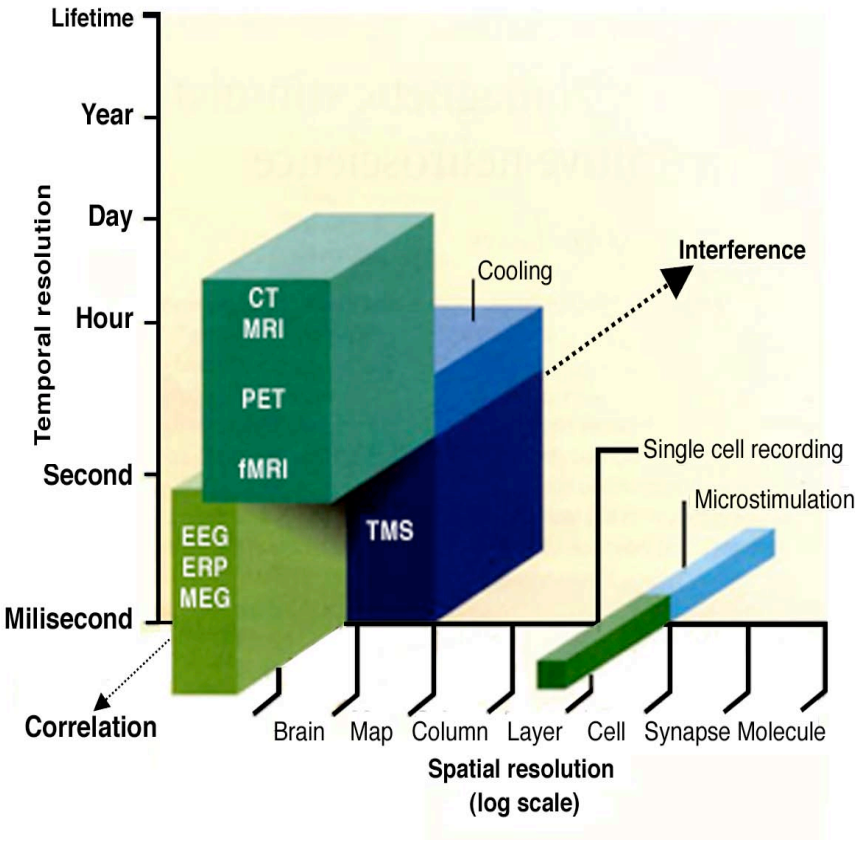
Maintained Behavior Despite Disruption By Rapid Shifts in Connectivity



Li et al. *J Neurosci*

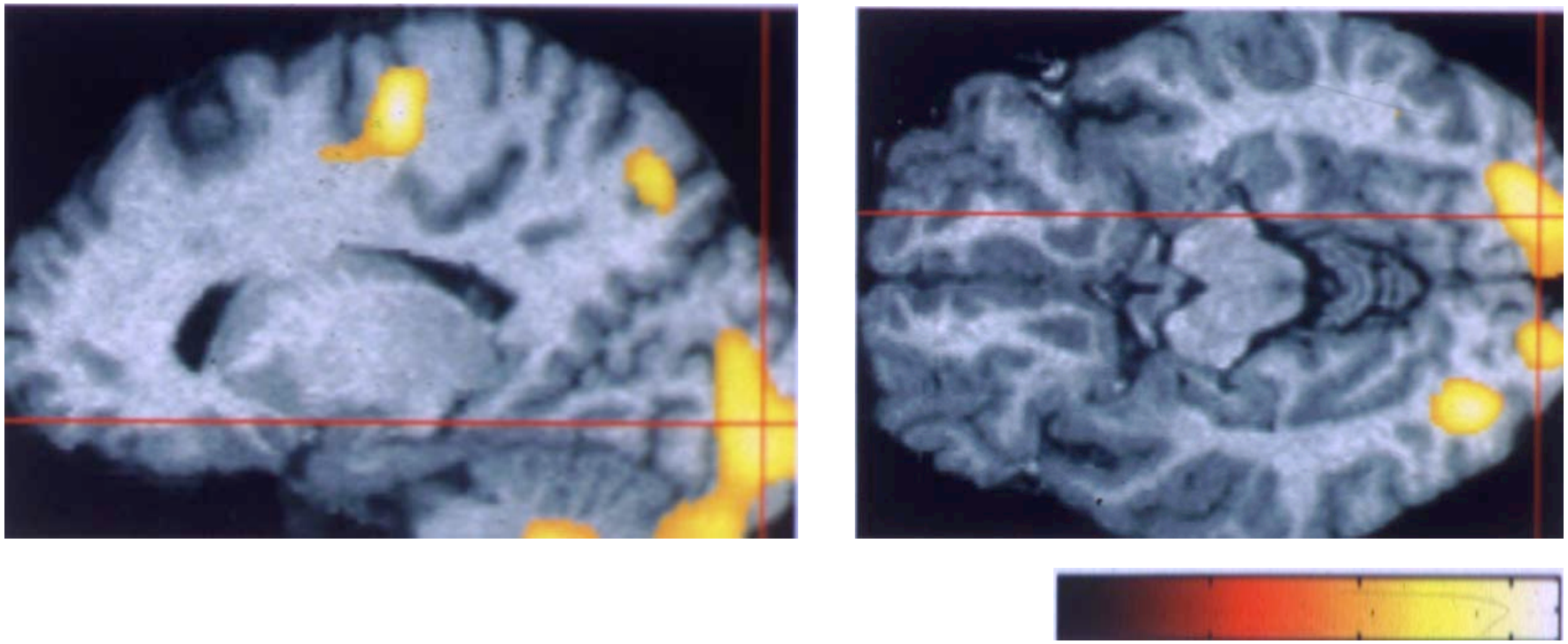
BRAIN STIMULATION PROVIDES INSIGHTS THAT CANNOT BE OBTAINED WITH OTHER TECHNIQUES

TMS: Interfering with Brain Function



- Brain Imaging 'helping' TMS
  - Localization
  - Timing
- Multimodal Integration of TMS
  - Causality
  - Chronometry
  - "Behavioral-independent" Connectivity
  - Adaptation

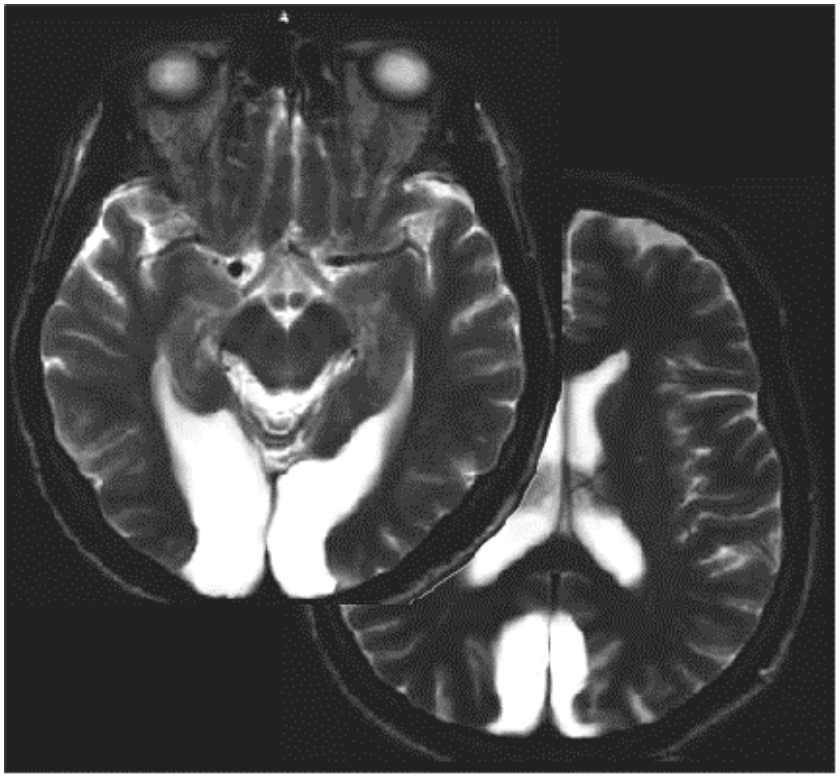
Activation of the Striate Cortex in the Congenitally Blind



Sadato et al. *Nature* 1996

Activation of the Striate Cortex is Necessary for Braille Reading in the Blind:

Serendipity of Nature

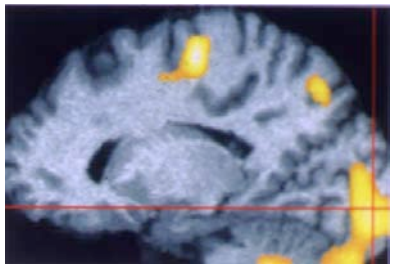


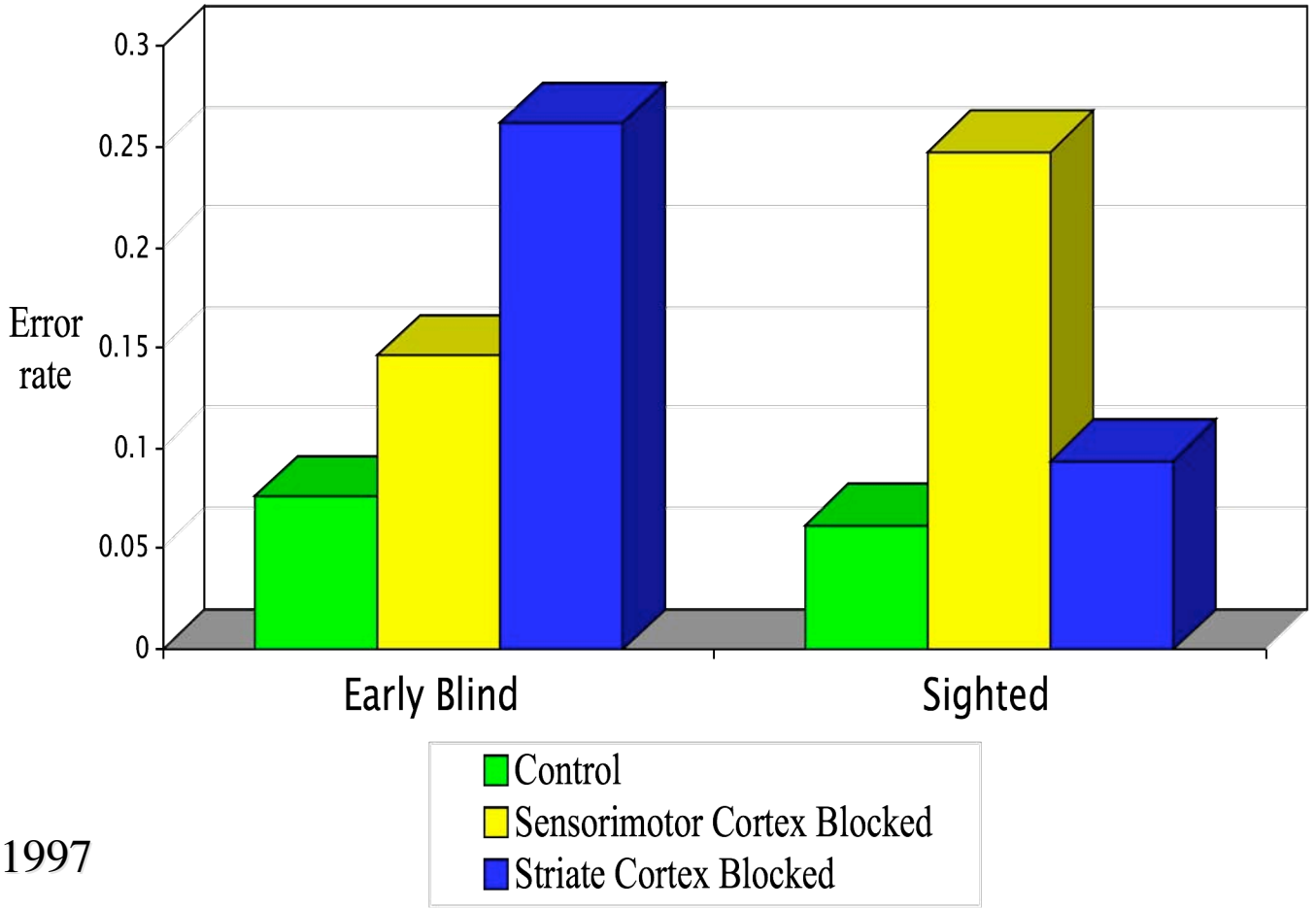
- 63 y/o woman
- Blind "since birth"
- Braille since age 7
- Braille 4-6 h/d
- Unable to read Braille after transient coma
- Normal neurological exam

Hamilton et al. *Neuroreport* 2001

Activation of the Striate Cortex is Necessary for Braille Reading in the Blind:

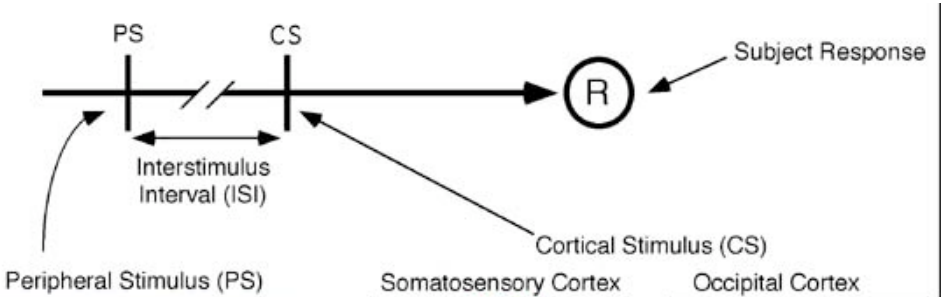
Virtual Lesion (rTMS) Experiment

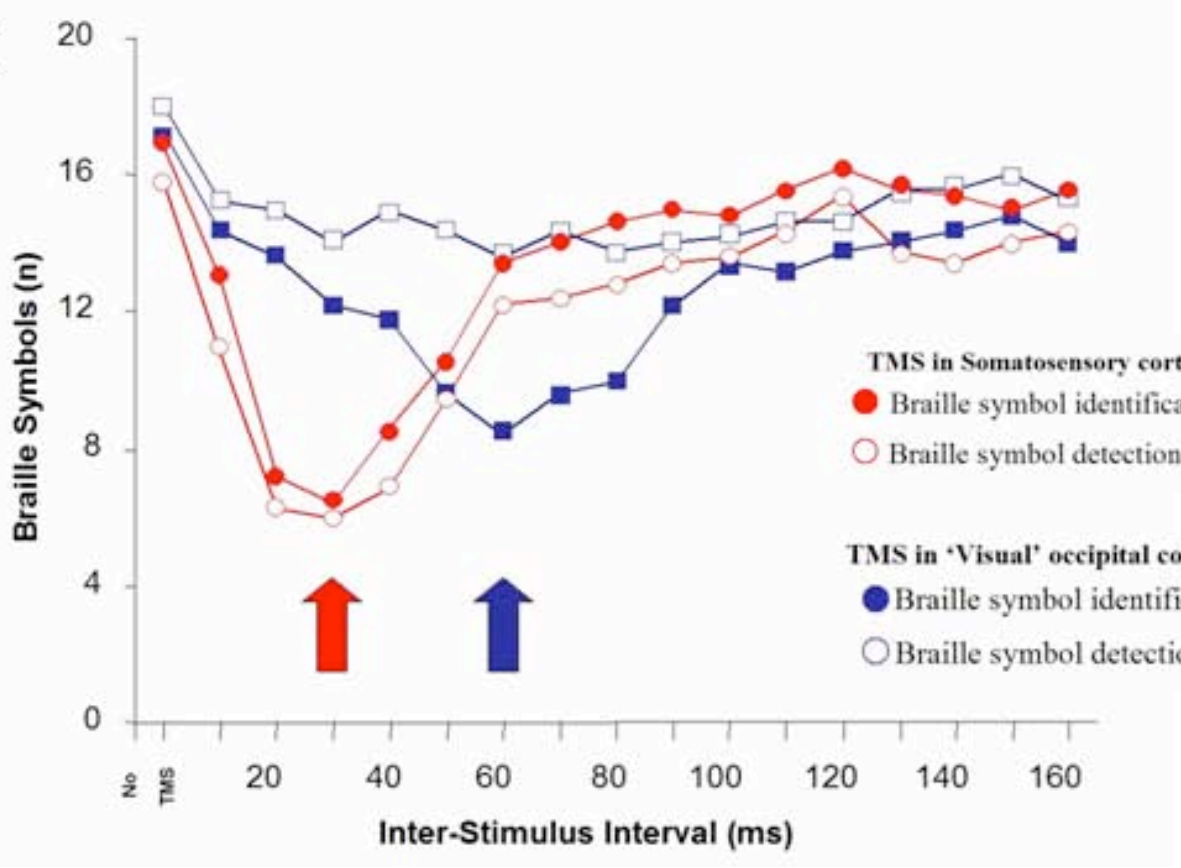




Cohen et al. *Nature* 1997

Detection and Identification of Braille Symbols in Congenitally Blind





Hamilton et al.
TICS 1998

Transcranial Magnetic Stimulation

- Electromagnetic Induction
- Effects of TMS arise from the interaction with the tissue
  - Dose according to current density
- Effects depend on the state of brain activity
  - Opportunity for selectivity of effect
- Biological effects extend along specific neural networks defined by anatomical connectivity
  - Diagnostic Utility
  - Inform study designs and interpretations
- Local biological effects do not account for behavioral impact
- TMS can provide insights that cannot be obtained with other methods