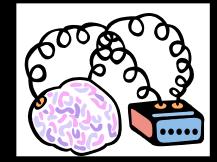


# Neuro-Modulation Techniques in Humans

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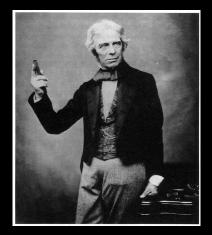
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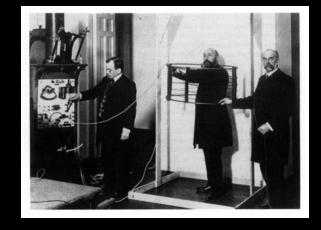


# Outline

- History
- Basic principles of Transcranial Magnetic Stimulation (TMS)
- Applications of TMS
- Therapeutic perspectives of TMS
  Transcranial Direct Current stimulation (tDCS)

## History of TMS (Early)









Michael Faraday electromagnetic induction, 1831. Arsenne d'Arsonval, 1896 *Sylvanus P. Thompson, 1910*  *Magnusson y Stevens, 1911* 

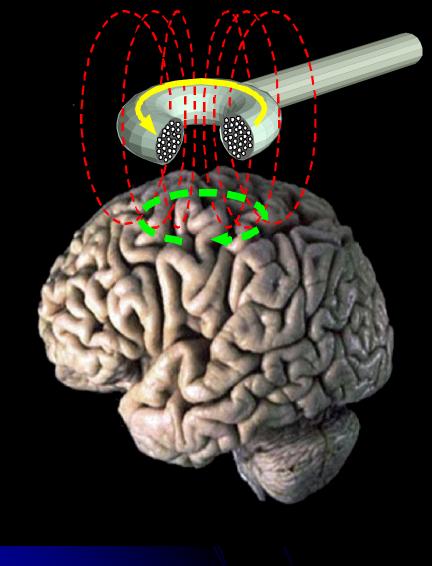
"Phosphenes and vertigo" when the subjects head was placed inside an induction coil

# History of TMS (Modern)



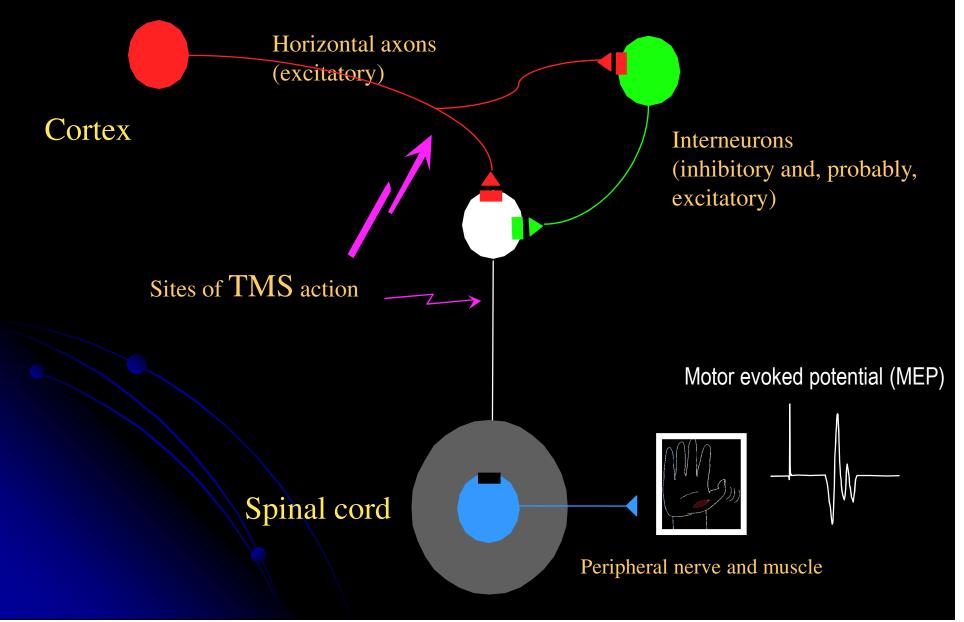
-1985 Barker et al. Noninvasive, painless, magnetic stimulation of the human motor cortex. -1988, Shoogo Ueno, figure-of-eight coil. -1988, Cadwell Laboratories Inc., repetitive stimulation with water-cooled coil.

## **TMS: Mechanism of Action**

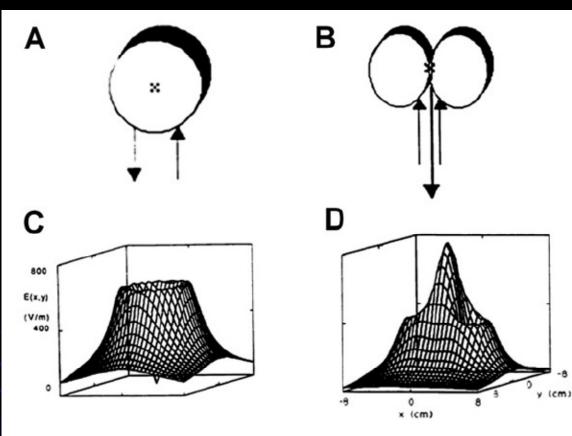


- TMS produces a magnetic field in a handheld coil placed on the scalp.
- The magnetic field induces an electrical current in underlying brain tissue, causing the brain cells to depolarize or fire.
- The amount of brain tissue stimulated depends on the stimulus intensity and coil shape.

#### Simplified schema for TMS action in the motor cortex



### Importance of Coil Shape



#### Figure 2. Magnetic Coil Shape Determines the Pattern of the Electric Field

Two magnetic coils with different shapes (A and B) and their resultant electric fields (C and D). Modified from Cohen et al. (1990), with

#### Hallett (2007)

#### Measure Motor Cortex Excitability: Motor Threshold (MT)



Single pulse TMS to optimal scalp position for induction of maximal motor-evoked potential (MEP) in relaxed contralateral hand muscle

Motor Evoked Potential (MEP) at rest

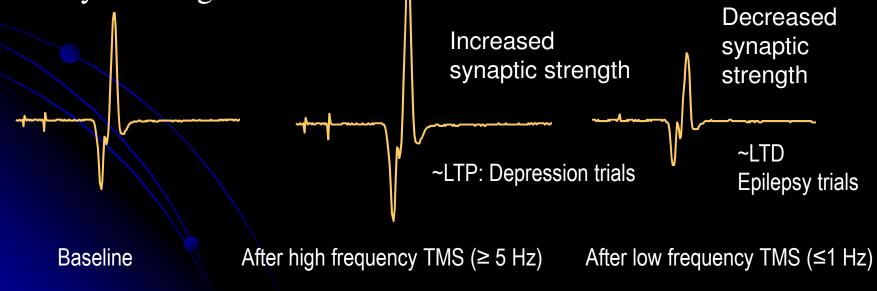
# TMS APPLICATIONS

TMS can be used to:

- Test or measure conduction of descending motor impulses
- Map functional cortico-motor representations in the brain
- Assess excitability of brain regions
- Induce a brief functional deactivation of brain regions
- Potential Treatment Tool by modulating excitability, epilepsy, PD, stroke and other brain disorders

### rTMS: Working

- Effect of repetitive (rTMS) is similar to that of electrical stimulation.
- Effects of high and low frequency stimulation show up and down regulation of cortical excitability (plasticity).
- **Potential clinical tool**, e.g. low frequency TMS proposed for the treatment of epilepsy, high frequency stimulation for depression . So far results have been disappointing as effects rarely last longer than 30 min.



rTMS has lasting effects on cortical excitability, however it has very little impact on performance.

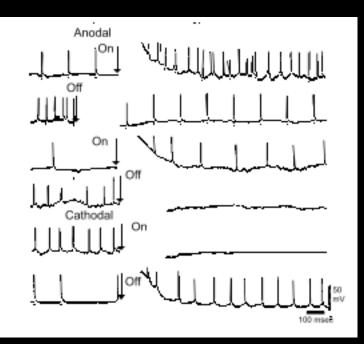
Can we improve performance?

# Improving Performance with transcranial Direct Current Stimulation (tDCS)

### tDCS: Working

A constant **direct current** (**DC**) applied to brain tissue polarizes cells and affects their excitability.

Animal studies have shown that anodal current applied to the cortical surface depolarizes pyramidal cells while cathodal current hyperpolarizes them.

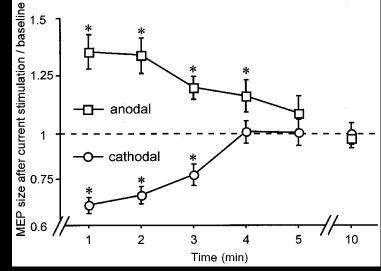


Changes in spontaneous activity of a pyramidal cell during polarization (Purpura and McMurtry, 1965).

#### Human Studies: tDCS

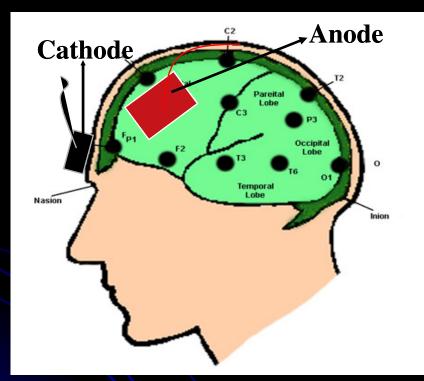
Scalp DC was first applied with electric fish and used to treat epilepsy. Later, Galvanic currents were used for treatment of behavioral disorders.

Recently, DC applied to the motor cortex changed the amplitude of TMS (transcranial magnetic stimulation)-induced motor evoked potentials (MEPs).



Changes in MEP size from baseline: 1-10 min after 5 min of DC at 1 mA (Nitsche and Paulus, 2000).

### **DC Procedures**







### tDCS Findings In Healthy Volunteers

- Performance effects appear dose and time dependent.
- DC in the range of 1-2 mA can be applied safely to scalp over human prefrontal cortex.
- Effects appear restricted to the functions of the local cortex.
- Transiently improves working memory, verbal fluency, mood, and motor performance.

### Summary of Potential Therapeutic Applications of TMS and tDCS

- Non-invasive brain stimulation produce in changes cortical excitability
- Experimental manipulation may provide a means of promoting recovery
- Studies are now addressing the effects of stimulation on various conditions (depression, stroke, epilepsy, fibromyalgia, PD, tinnitus), in the hopes that combining it with medications and / or rehabilitation sessions will be more beneficial.

### Summary of Potential Therapeutic Applications

Mechanism of action – not known.

Dosage and long term safety effects - need to be studied.

Need for parallel studies in animals.