TMS Details and Applications

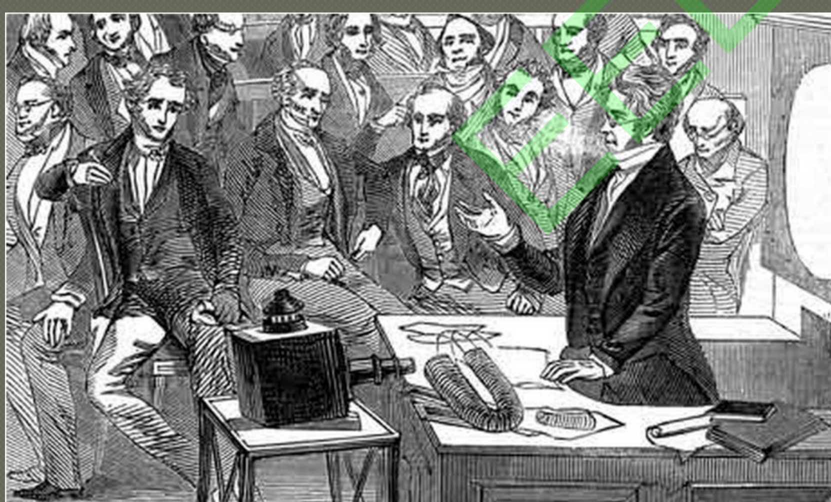
Technology Integration:

- ✓ *Stimulation* - **TMS**
  (Transcranial Magnetic Stimulation)
- ✓ MEP *Response* - **EMG**
  (Electromyography)
- ✓ *Guided Navigation*
  - ***MRI with Stereotactic Camera***
- ✓ *Sophisticated 3D Modeling and Visualization*
  - **Nexstim NBS Software**

BASIC PRINCIPLES OF MAGNETIC STIMULATION

- Principle of Electromagnetic induction (Michael Faraday (**English scientist**) in 1831).

- Anthony Barker in 1985 (University of Sheffield, UK).

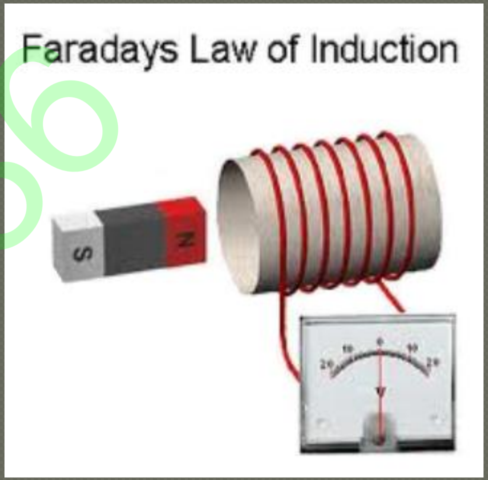


Magnetic Stimulation

- Electromagnetic induction (Faraday's law) forms the physical basis of magnetic stimulation.

- In TMS, magnetic induction is when current is produced in the brain through changing magnetic fields produced by the TMS stimulation coil.

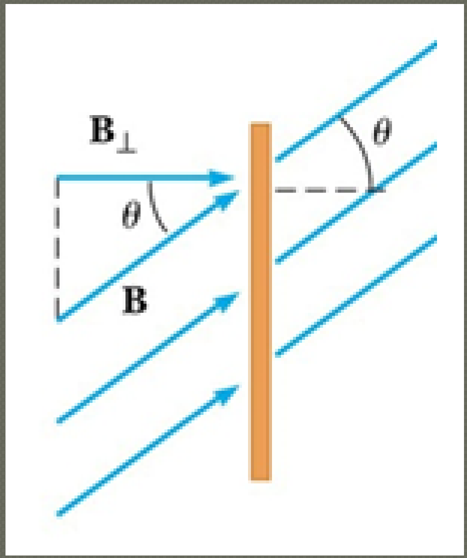
- A time varying current in a primary circuit (coil) will induce an electric field and a current flow(eddy current) in a secondary circuit(brain).



The interaction is mediated by the magnetic field B(t) generated by the changing current in the coil. The induced electric field is proportional to the rate of change of B; no neural excitation occurs with slowly changing or stationary B.

Faraday's Law

- **E=dB/dt (**how fast the flux changes with time**)**
- "**E**" is the value of **voltage** induced. The change in time is "dt". (measured in seconds). "**dB**" (change in magnetic flux).
- Flux is equal to BA, where **B** is the magnetic field strength, and **A** is the area.
- The amount of voltage created is equal to the change in magnetic flux divided by the change in time.

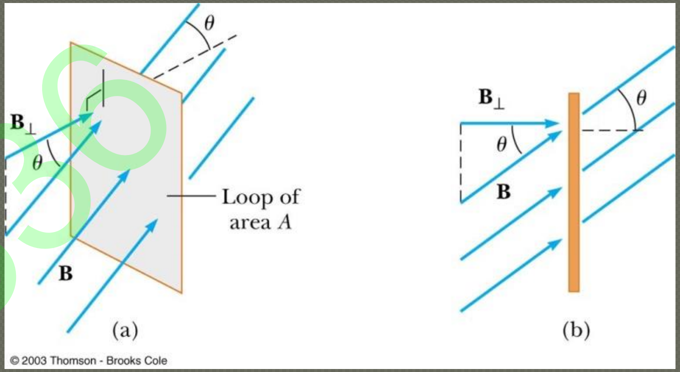


Note:
The bigger the change you have in the magnetic field, the greater amount of voltage induced in the brain.

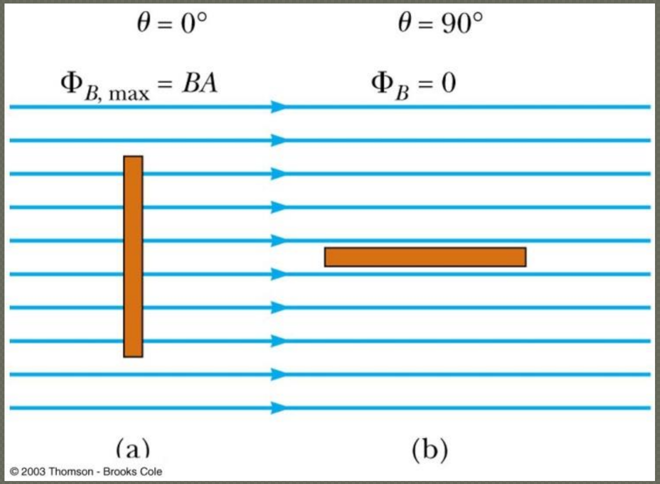
Magnetic Flux

- Induced Emf is due to a change in *magnetic flux*
- Magnetic flux is defined:

$$\Phi_B = B_\perp A = BA\cos\theta$$



- The value of the magnetic flux through a loop/surface is proportional to the total number of field lines passing through the loop/surface.



Faraday law

- The induced Emf, Ɛ in a coil is proportional to the negative of the rate of change of magnetic flux:

$$\varepsilon = -\frac{d\Phi_B}{dt}$$

- For a coil that consists of N loops, the total induced Emf would be N times as large:

$$\varepsilon = -N\frac{d\Phi_B}{dt}$$

Ways to Induce EMF

- Electricity produces two types of fields; an electric field and a magnetic field. These fields are also called electromagnetic fields or EMF (electromotive force).

- EMF generally refers to the magnetic field.

$$e = -\frac{d}{dt}\left(BA\cos q\right)$$

$$\Phi_B = B_{\perp}A = BA\cos\theta$$

Amount of Flux can vary with:

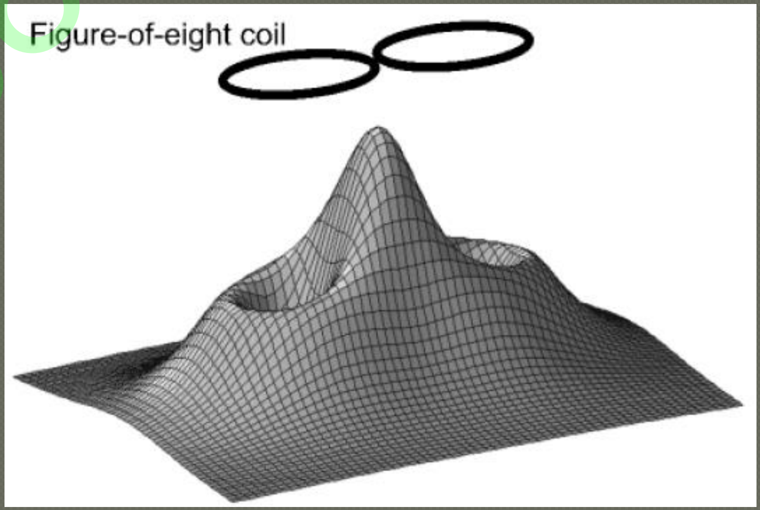
- Change of B
- Change of A enclosed by the loop
- Change of angle between B and surface (if the loop moves)

Solution to the equation gives an estimate of the induced ***E*** that ignores the effects of conductivity variations between and within the brain, skull and scalp.

Magnetic fields encountered in magnetic stimulation travel freely in air and can easily penetrate through tissue. Therefore, magnetic stimulation can readily reach brain cells even through the highly resistive skull.

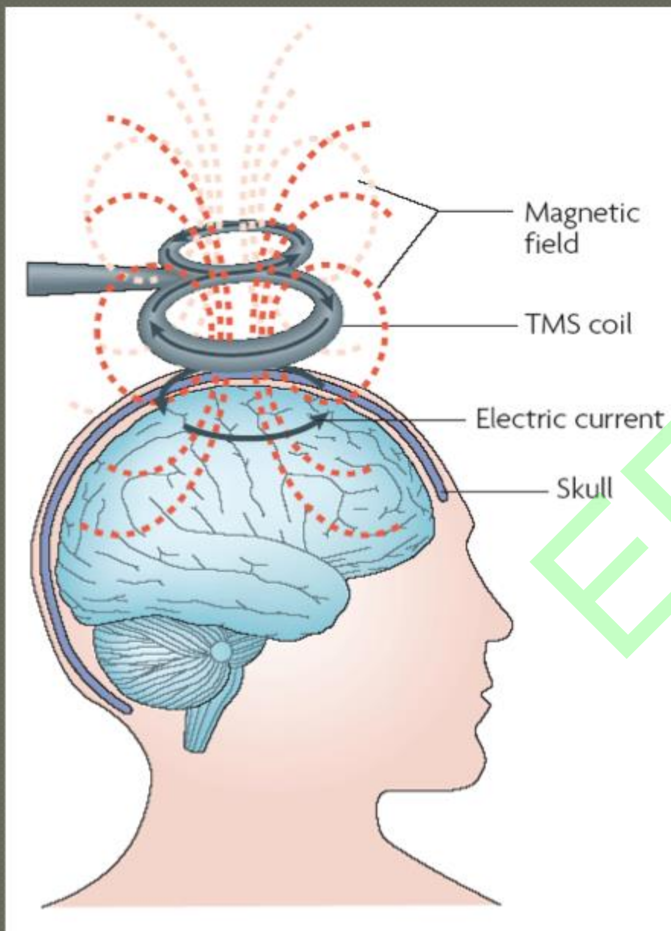
E-field computation

- Electric field induced in the tissue depends on:
- (1) coil shape
- (2) coil location and orientation
- (3) electrical conductivity structure of the head.



The strength of **E** below the coil.

Figure-of-eight coil

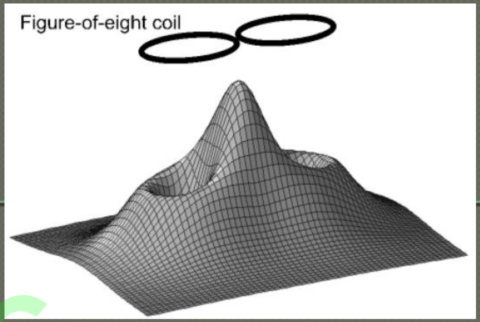


In research and clinical applications, the figure-of-eight coil is the most used coil type.

Due to heating and internal repulsive forces, the shapes and sizes of coil designs are quite limited, and the efficiency of TMS decreases as the coil size decreases.

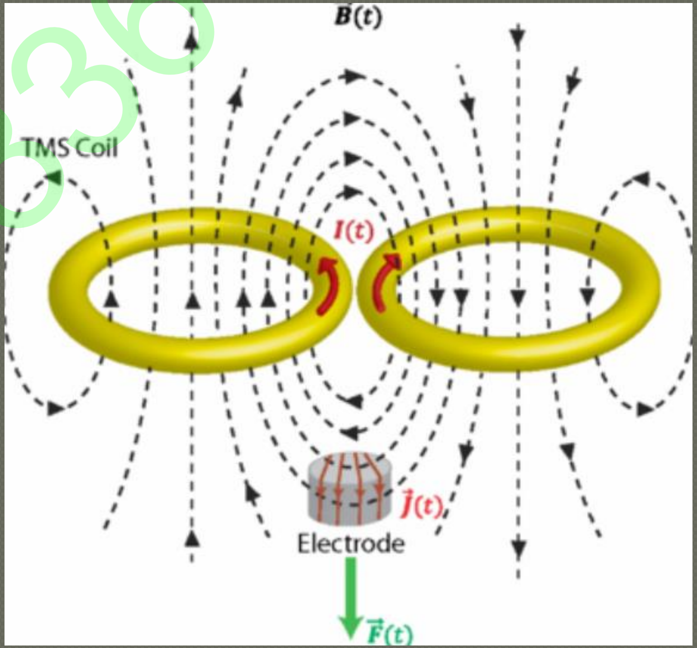
Magnetic stimulation is essentially painless because the induced current does not pass through the skin, where most of the pain fiber nerves endings are located. The currents induced by magnetic stimulation are relatively diffuse.

Figure-of-Eight Coil



- The region activated by the figure-of-eight coil is under its center. The total induced field is the sum of the fields from the two wings of the coil. The resulting field is much more focused than the field produced by a single coil of the same size.

- Figure-of-eight coil has an excellent stimulation focality than single circular coils, but the depth of the stimulation penetration is smaller than the circular coils.

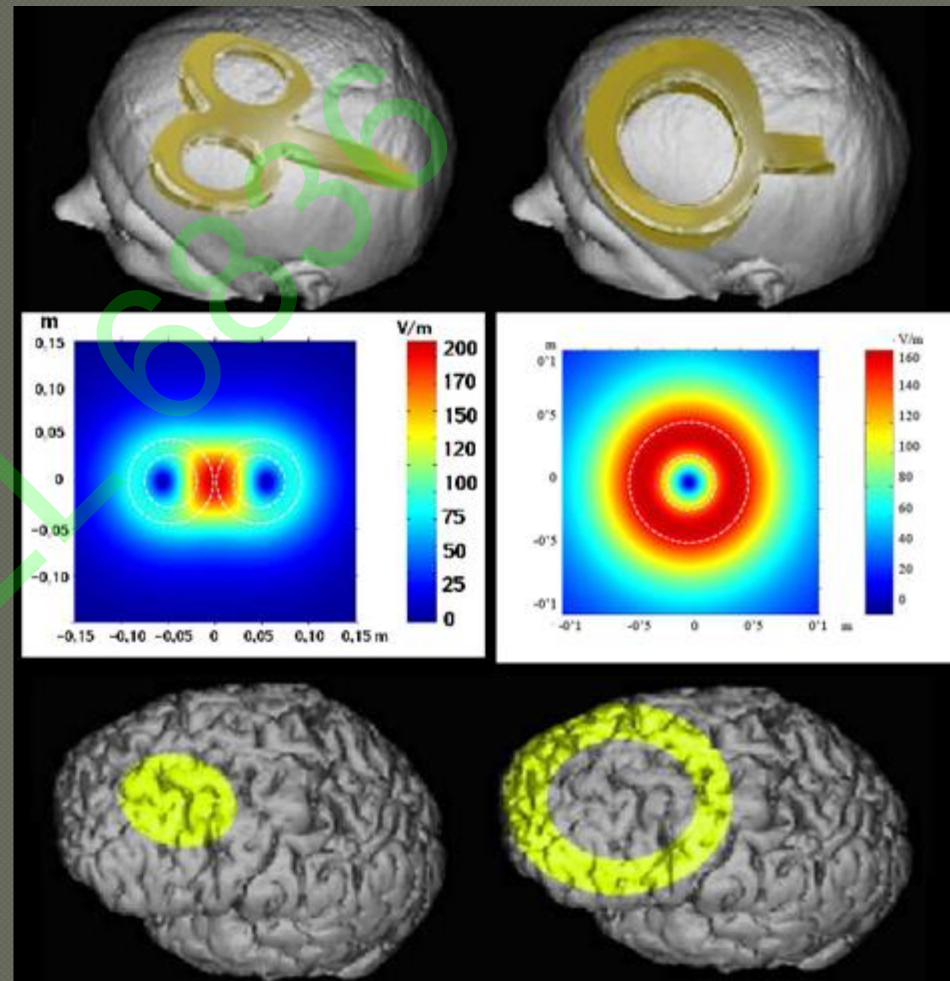


The currents in the coils flow in opposite directions. At the junction point of the circular coils, the currents have the same direction and they summate.

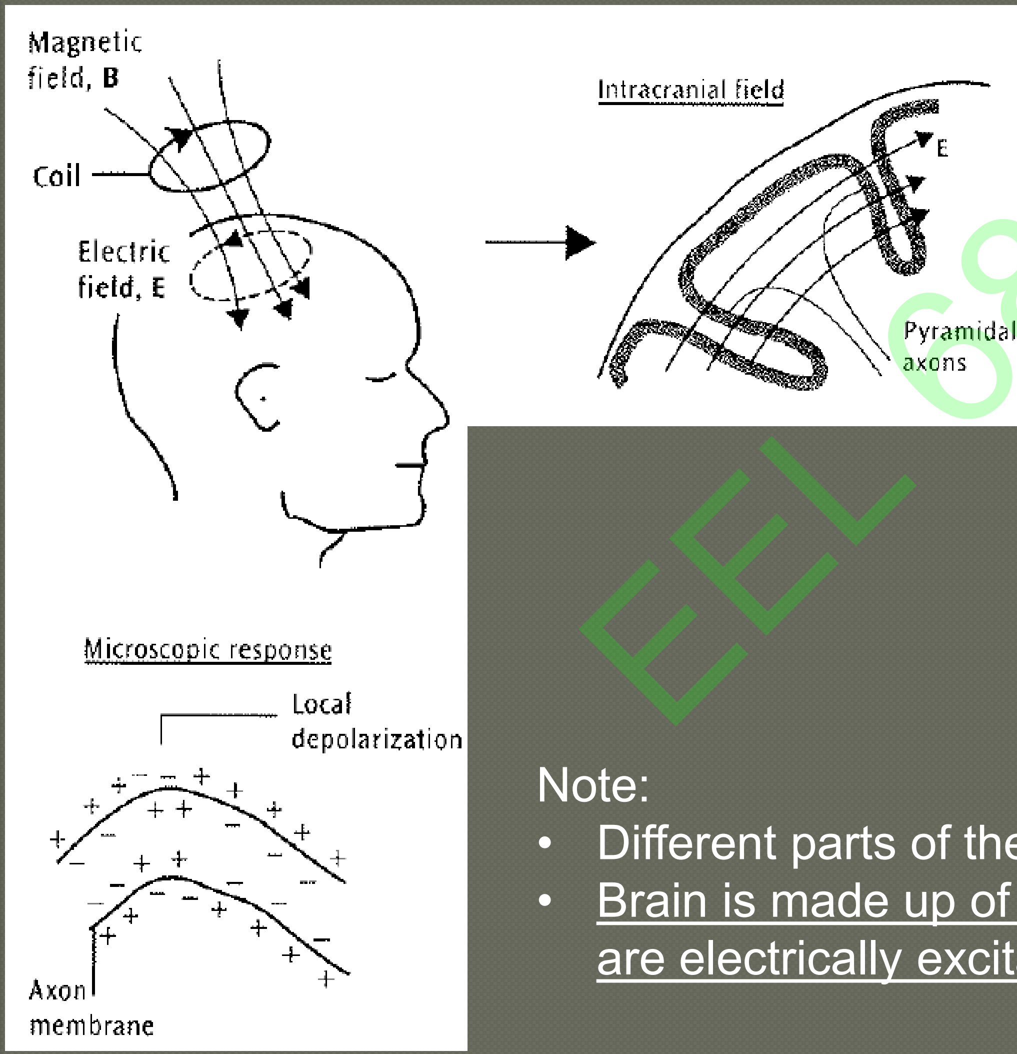
Practical considerations
Coil shape

- The <u>geometry of the coil determines the focality</u> of the magnetic field and of the induced current - hence also of the targeted brain area.

- *Induced current decays with square of distance.*



Principles of TMS



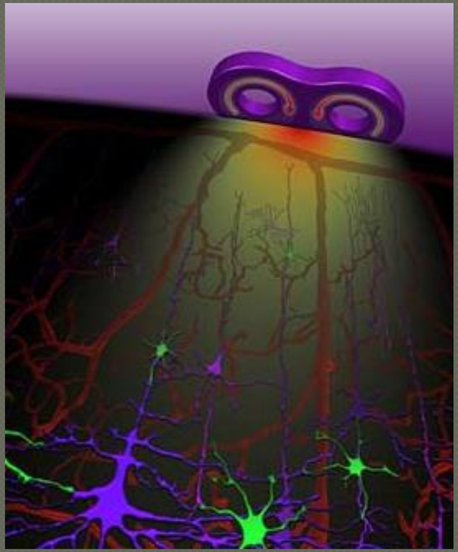
- The current in the coil generates a changing magnetic field **B** that induces an electric field E in the brain.
- **E** affects the transmembrane potential, which may lead to local membrane depolarization and subsequent neural activation.

Note:

- Different parts of the brain have different functionalities.
- Brain is made up of neurons and neuron clusters that are electrically excitable.

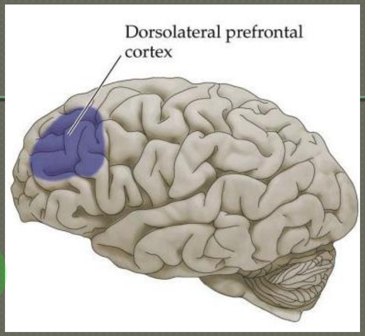
TMS

- When a TMS coil is placed on the scalp ready for a TMS pulse, a large capacitor of up to several kilovolts in the stimulator is discharged within approximately 100μs, generating a changing current in the coil.
- This produces a changing magnetic field around the coil, which induces an electric field in the neural tissues beneath.
- TMS causes nerve cells to fire, which then leads to the release of neurotransmitters. You can think of TMS as "focal drugs". It changes neurotransmitters in specific regions. This is unlike a pill, which you take by mouth and goes to your stomach, some of which goes to your whole body, some of which then goes to the brain, and a little bit gets to where it is needed.



How does TMS work?

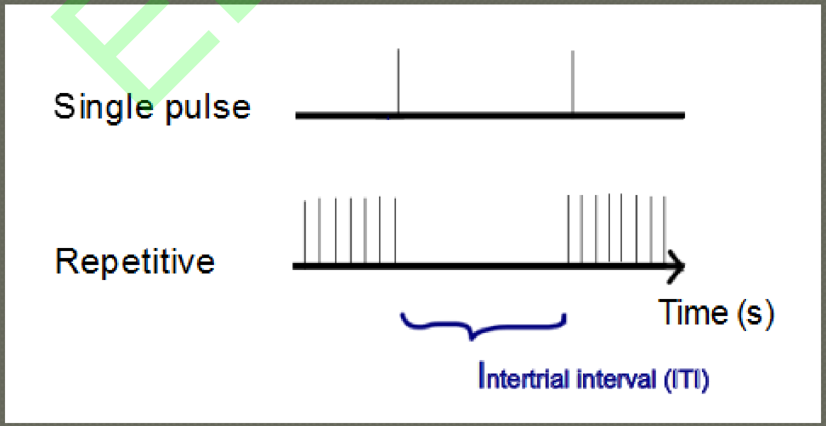
- It uses an electromagnet to noninvasively stimulate the brain of a patient. A rapidly changing magnetic field created by a magnetic coil causes weak electric currents in the brain through electromagnetic induction.
- By stimulating different areas of the cortex, it is possible to elicit a therapeutic response.
- For example, studies have shown that applying stimulation to the left prefrontal cortex increases activity below the stimulation site and produces a statistically significant reduction in depressive symptoms.
- TMS can currently target sites in the brain to within a few millimeters.



Note: Cerebral cortex: 2.5 mm

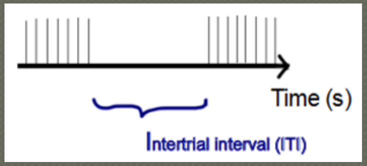
What does TMS stand for?

- TMS is short for Transcranial Magnetic Stimulation.
- rTMS, which is a newer form of TMS, stands for repetitive transcranial magnetic stimulation. rTMS improves on TMS by allowing for multiple magnetic pulses per second.
- The word "transcranial" simply refers to the fact that the magnetic field passes noninvasively through the head and no surgery is required.



TMS PARAMETERS

- **INTENSITY**:
  - ↑↓Current flowing in the coil → magnetic induced field → induced electric current
- **FOCUS**: COIL GEOMETRY
- **FREQUENCY**: ↑↓
- **LOCATION**: different brain regions → different behavioral effects
- **ORIENTATION**: aligned with axons
- **PATTERN**: length & separation of train pulses

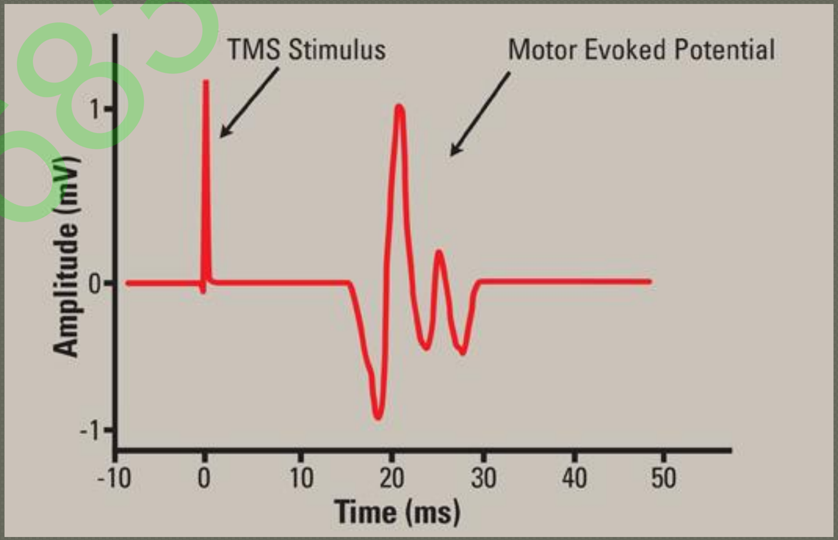


Brain's electrical EEG response to TMS

- By recording EEG evoked by TMS, one can deduce by inverse analysis the location, orientation and amplitude of the neural electrical activity in the cortical area stimulated by TMS.

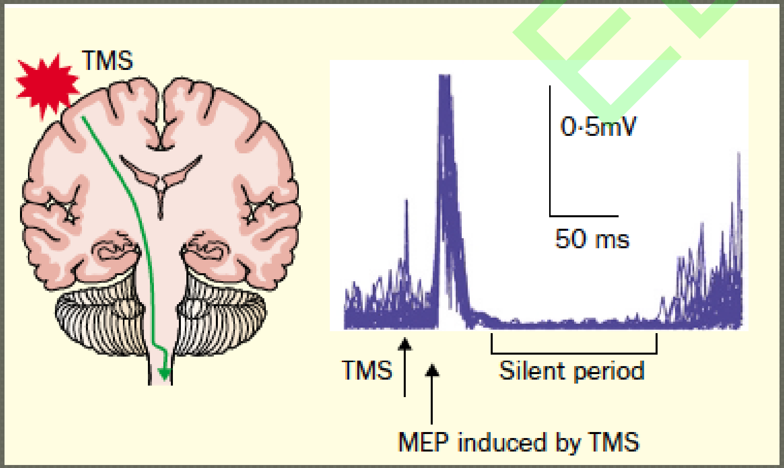
- Use to probe the reactivity and the spreading of activity.

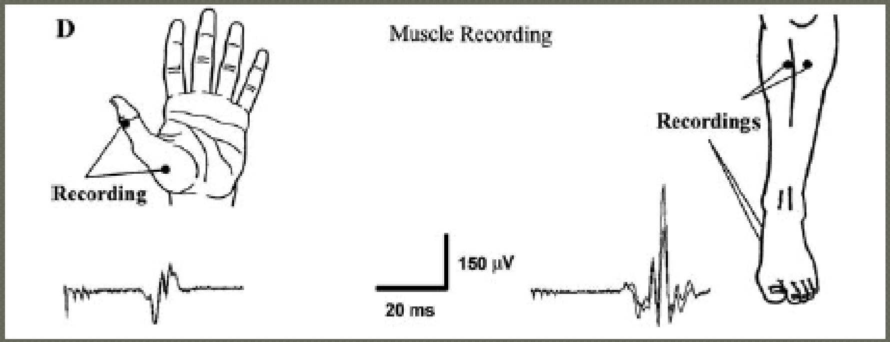
- Help understand the activating mechanisms of TMS.



MOTOR EVOKED POTENTIALS (MEP's)

- Amplitude and latency
- Functional integrity of the corticospinal tract (CST)
- Excitability of motor cortex
- Inter-individual and intra-individual variability
  - Broad range of normal values
  - Qualitative results not quantitative

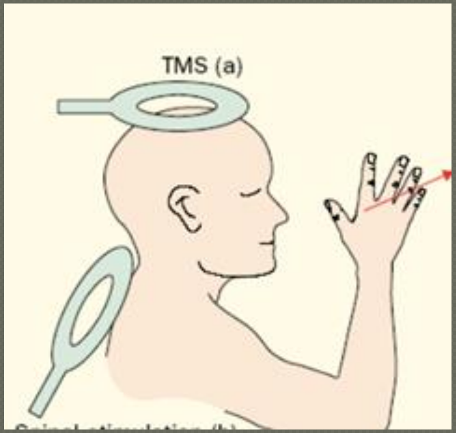




MEP latency in hand: 23 ms
Lower extremity: 30 ms

MOTOR THRESHOLD (RMT)

- Lowest intensity needed to evoke MEP of more than 50 uV peak-to-peak amplitude in at least 50% of successive trials in the resting target muscle.



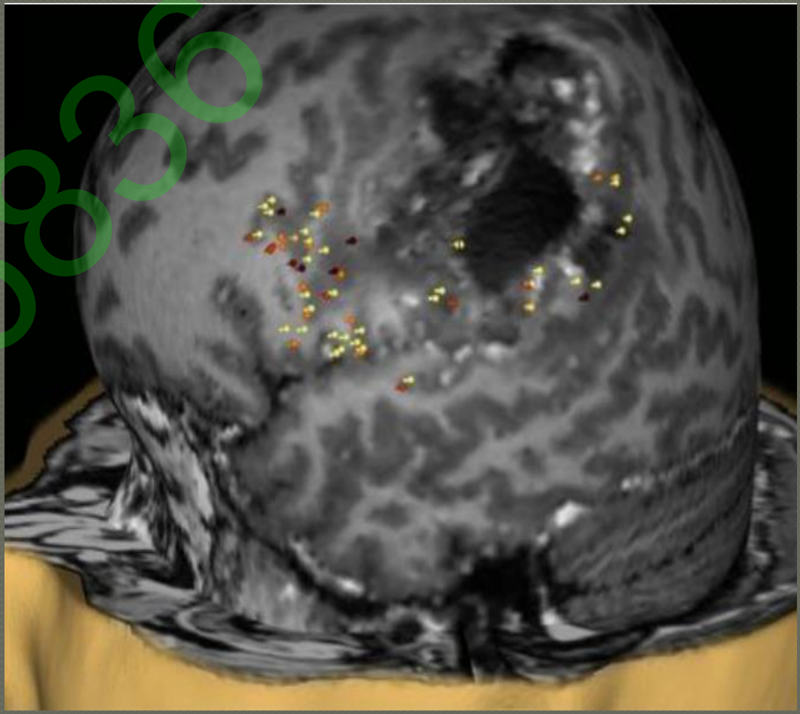
- Reflects:
  - Membrane excitability
    - corticospinal neurons
    - Interneurons
    - Motor neurons in spinal cord
  - Efficacy of a chain of synapses from presynaptic cortical neurons to muscles

- Phosphene threshold (Occipital lobe)

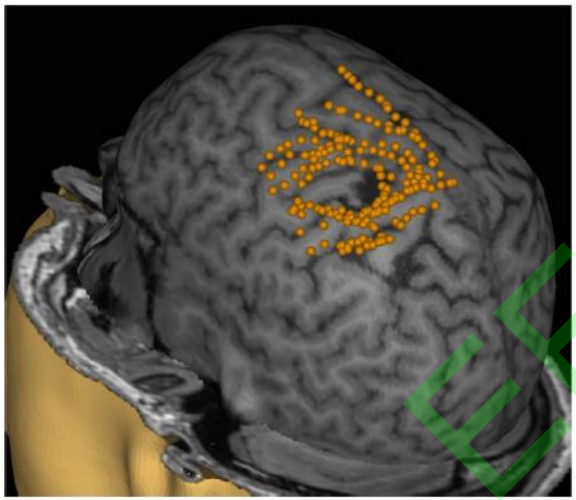
Benefits of TMS

- Reliable assessment of the functional significance of the cortical structures adjacent to the lesion.

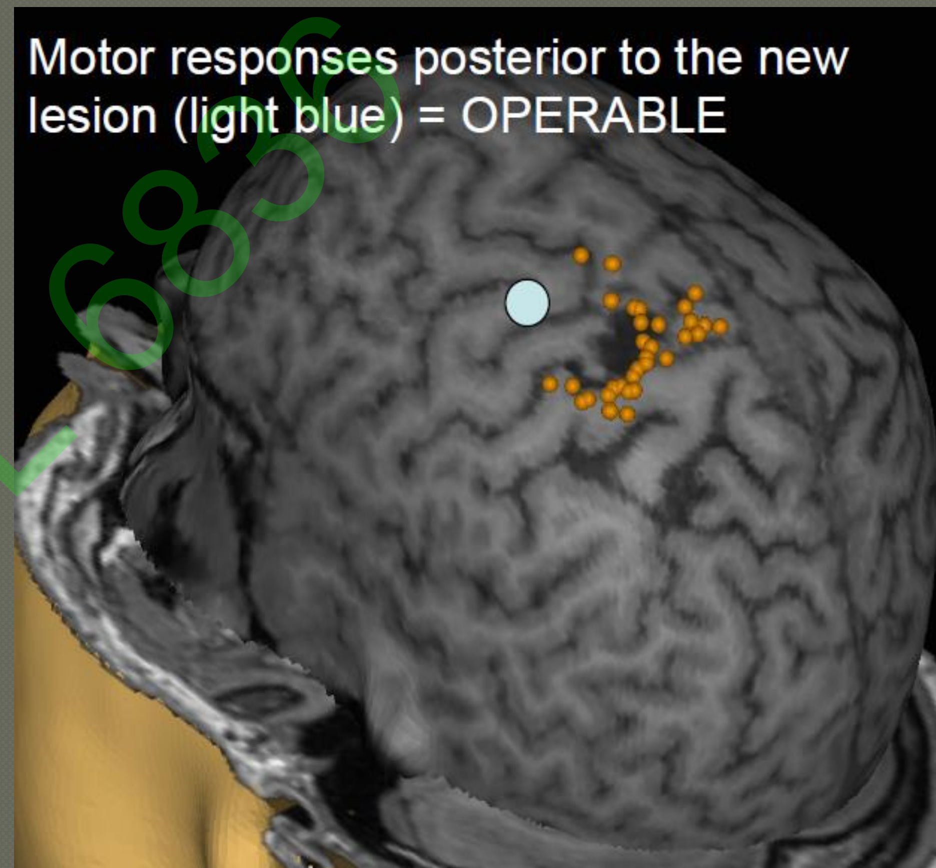
- Direct cortical and sub-cortical stimulation are well-established electrophysiological techniques for the examination of cortical functions during surgery, but until recently we have lacked a reliable method for assessing cortical function without first performing craniotomy.



Epilepsy Applications

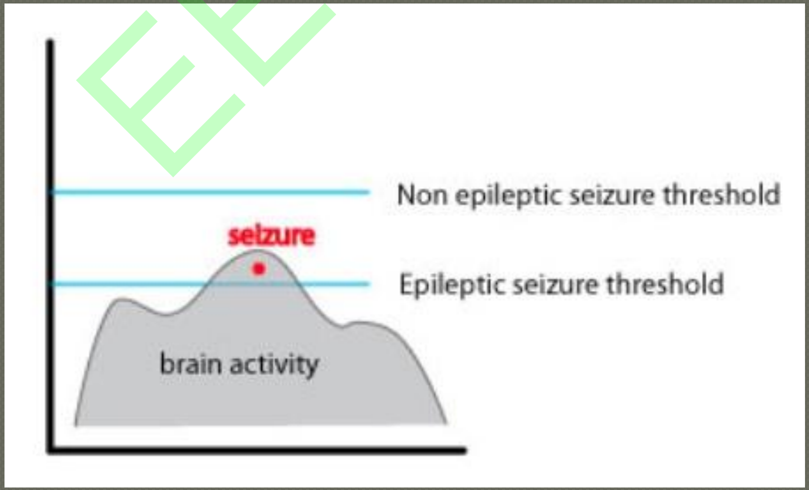


Motor mapping around the
previously resected lesion
(orange, above)



Epilepsy Applications

- Physiological and safety studies of rTMS show inhibition of the motor cortex after low-frequency stimulation (1Hz), which suggests that such stimulation may be useful for suppressing the development or spread of epileptogenic activity.
- 15 min of 1 Hz stimulation daily for 1 week produced a marked and long-lasting increase in the seizure threshold.



Epilepsy Applications

- Investigation of underlying cortical excitability and determination of the effects of antiepileptic drugs (AEDs)
- preoperative localization of epileptic foci
- functional mapping.
- seizure treatment modality.

FACTS:

- TMS results suggest that patients with generalized epilepsy syndromes have increased cortical excitability.
- TMS has been used in an attempt to elucidate the mechanisms of action of several AEDs.
- Motor threshold is increased by drugs that stabilize active sodium channels.