

Biomedical Technologies in Diagnostic and Therapy

Devices and methods in clinical neurophysiology

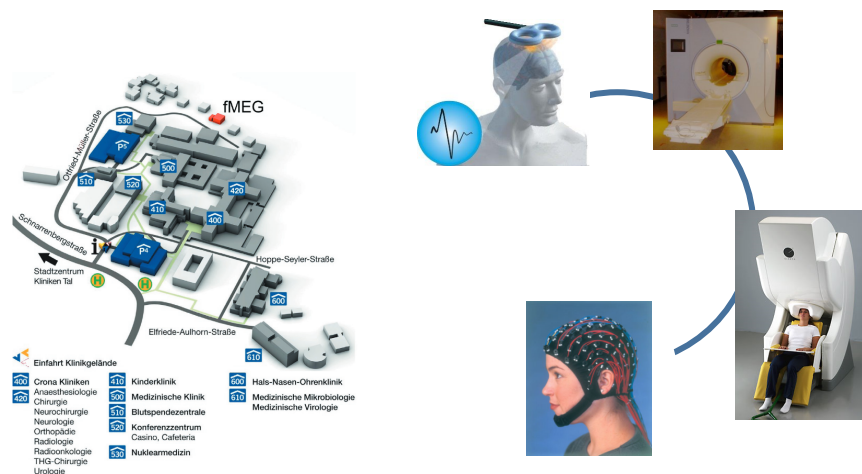
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MEG-Zentrum
Universität Tübingen

Overview

- Introduction
- Clinical Neurophysiology
- Basics
 - Neurons
 - Physical Laws
 - Brain anatomy and histology, brain function
- Functional imaging methods
 - biochemical activity
 - neurometabolic activity
 - neuroelectrical activity

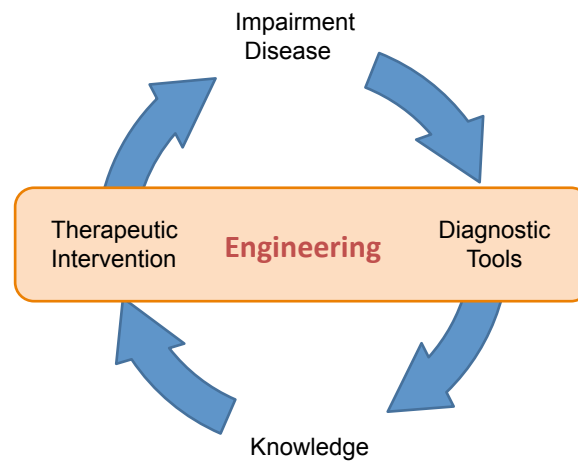
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Clinical Neurophysiology



Devices and Methods in Clinical Neurophysiology

Clinical neurophysiology is a medical specialty that studies the **central and peripheral nervous systems** through the **recording of bioelectrical activity**, whether spontaneous or stimulated.

It encompasses both **research regarding the pathophysiology** along with **clinical methods used to diagnose diseases** involving both central and peripheral nervous systems.

Wikipedia: http://en.wikipedia.org/wiki/Clinical_neurophysiology

Furthermore, it involves **therapeutic approaches** that **alter the neurophysiological activity** by **adequate stimulation** of the nervous system (electrical stimulation, magnetic stimulation, neurofeedback)

Neurobiological Basics

Neuron

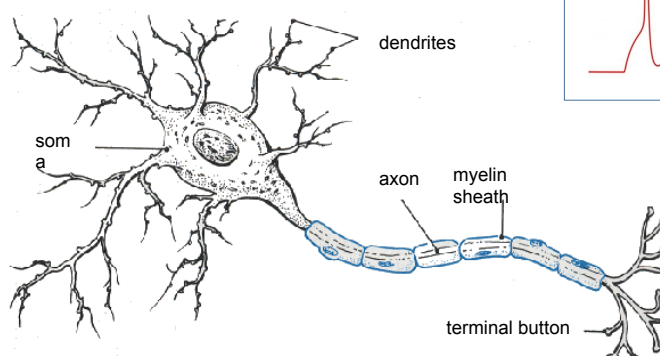
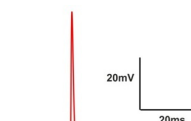
- Dendrite
- Soma
- Axon
- Synapse
- Excitatory and inhibitory postsynaptic potential
- Action potential
- Nervous system

Electrical Phenomena in Neurons

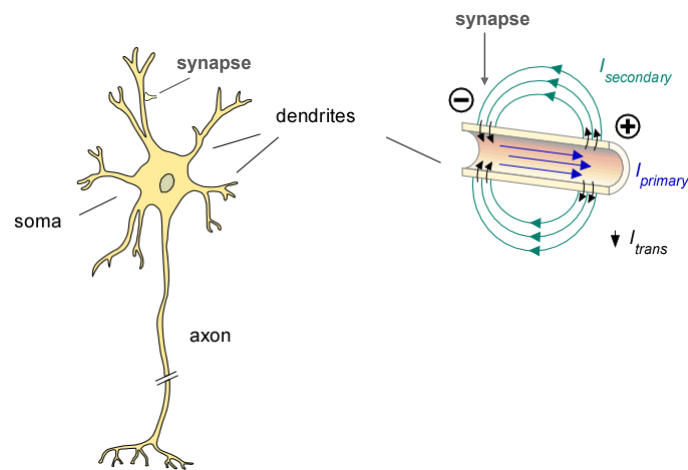
EPSP



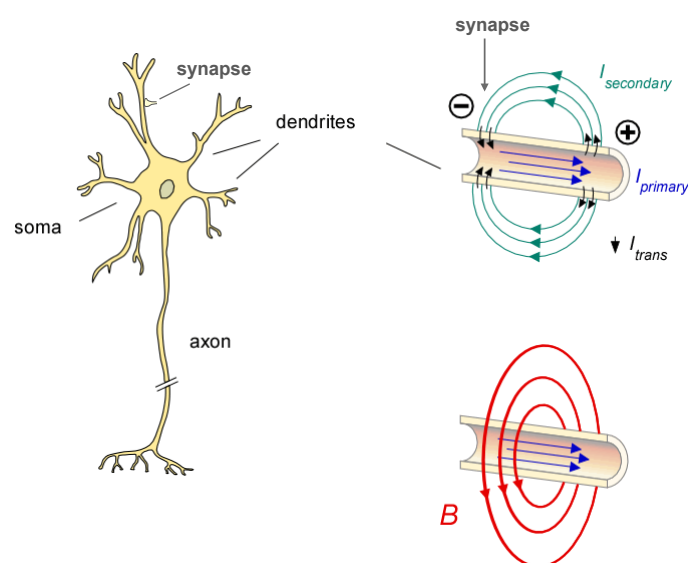
action potential



Electrical Phenomena in Neurons



Electrical Phenomena in Neurons



Clinical Neurophysiology

Methods

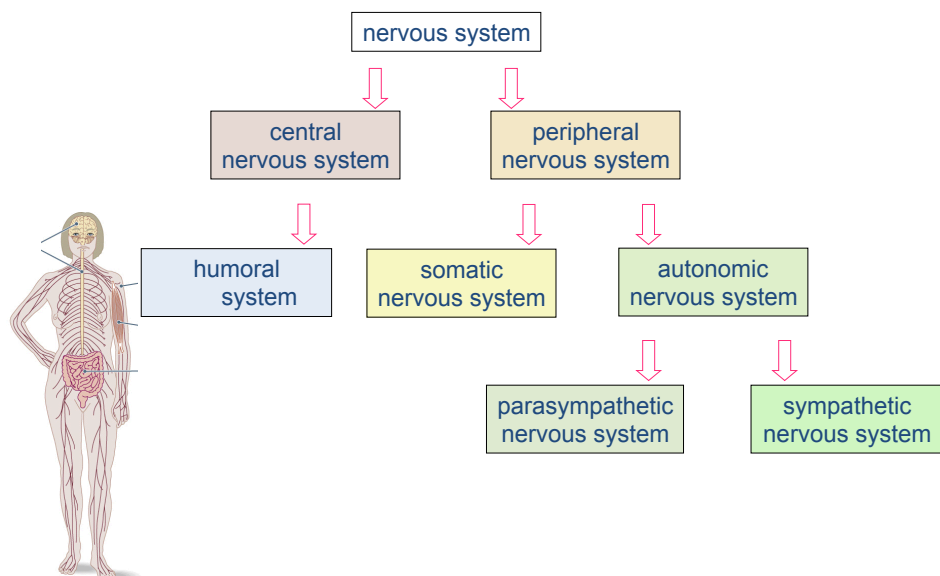
- EEG and MEG
- EMG and TMS
- tDCS and tACS
- MRI and fMRI
- NIRS

Diseases

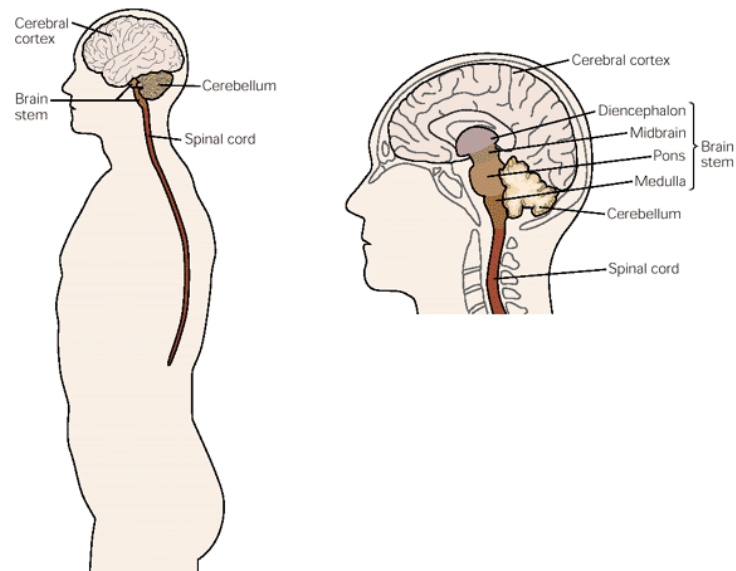
- Sensory and motor functions
- Chronic pain
- Neuropathy (Diabetes)
- Stroke and paralysis
- Amyotrophic lateral sklerosis
- Parkinson's disease
- Epilepsy
- Brain tumors
- Alzheimer's disease
- Cognitive disorders

Wikipedia: http://en.wikipedia.org/wiki/Clinical_neurophysiology

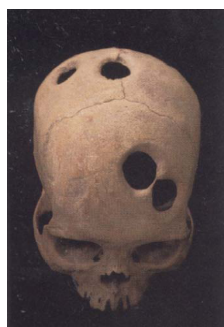
Organisation of the Nervous System



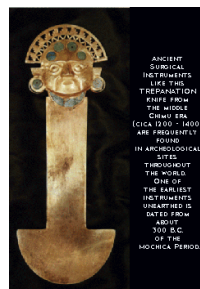
Central Nervous System



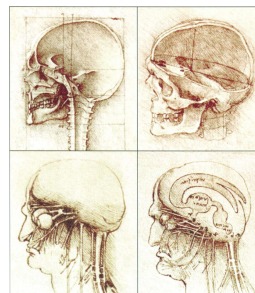
History



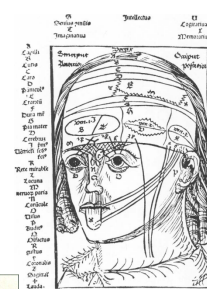
Egypt ~3000 BC



South America
~300 BC

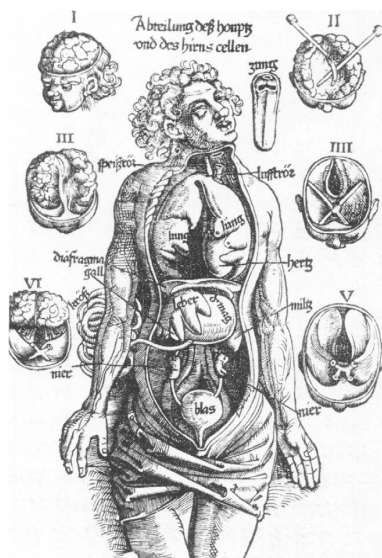


Leonardo da Vinci ~1490

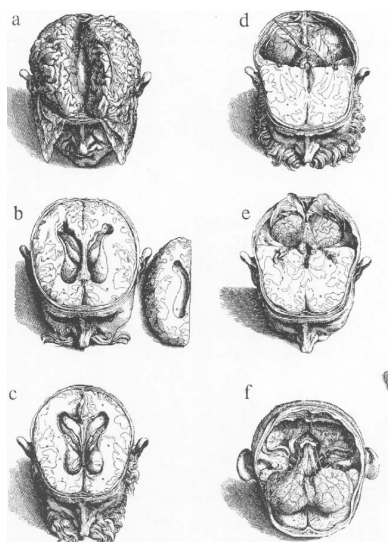


1501 by Magnus Hundt

History

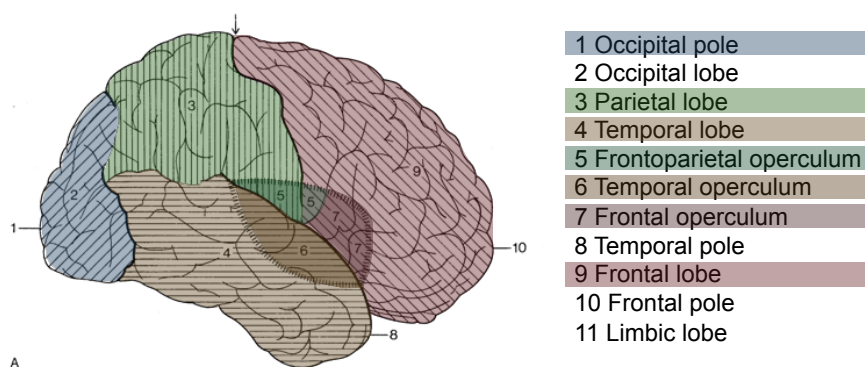


Lorenz Fries 1519



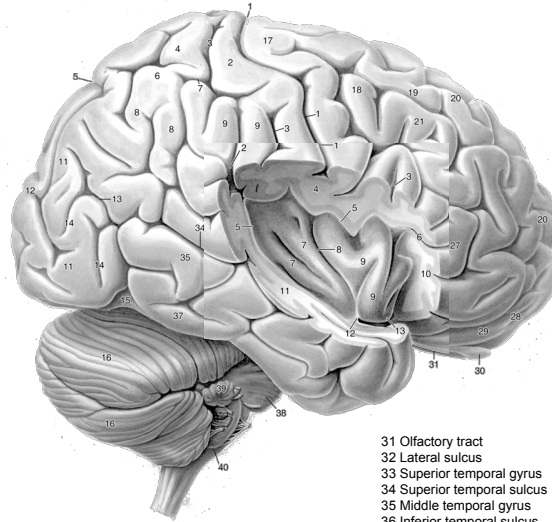
Andreas Vesalius Fabrica 1543

Organisation of the Brain



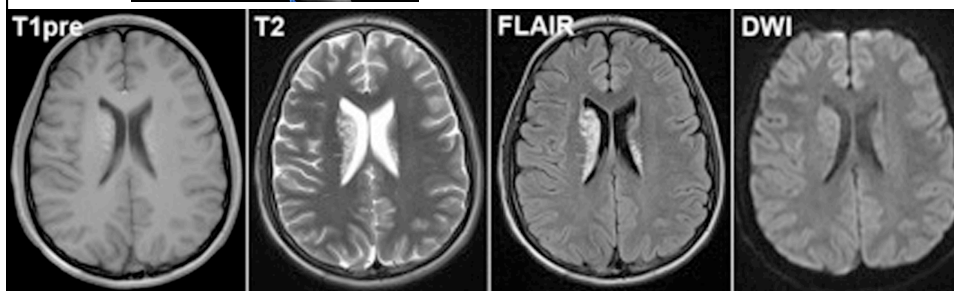
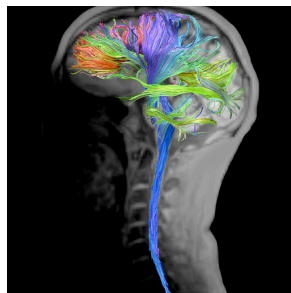
Organisation of the Brain

- 1 Central sulcus
- 2 Postcentral gyrus
- 3 Postcentral sulcus
- 4 Superior parietal lobule
- 5 Parieto-occipital sulcus
- 6 Inferior parietal lobule
- 7 Intraparietal sulcus
- 8 Angular gyrus
- 9 Supramarginal gyrus
- 10 Lateral sulcus, posterior branch
- 11 Occipital gyri
- 12 Lunate sulcus
- 13 Anterior occipital sulcus
- 14 Occipital sulci
- 15 Preoccipital notch
- 16 Cerebellar hemisphere
- 17 Precentral gyrus
- 18 Precentral sulcus
- 19 Superior frontal sulcus
- 20 Superior frontal gyrus
- 21 Middle frontal gyrus
- 22 Inferior frontal gyrus
- 23 Opercular part of inferior frontal gyrus
- 24 Triangular part of inferior frontal gyrus
- 25 Orbital part of inferior frontal gyrus
- 26 Lateral sulcus, ascending branch
- 27 Lateral sulcus, anterior branch
- 28 Orbital sulci
- 29 Orbital gyri
- 30 Olfactory bulb

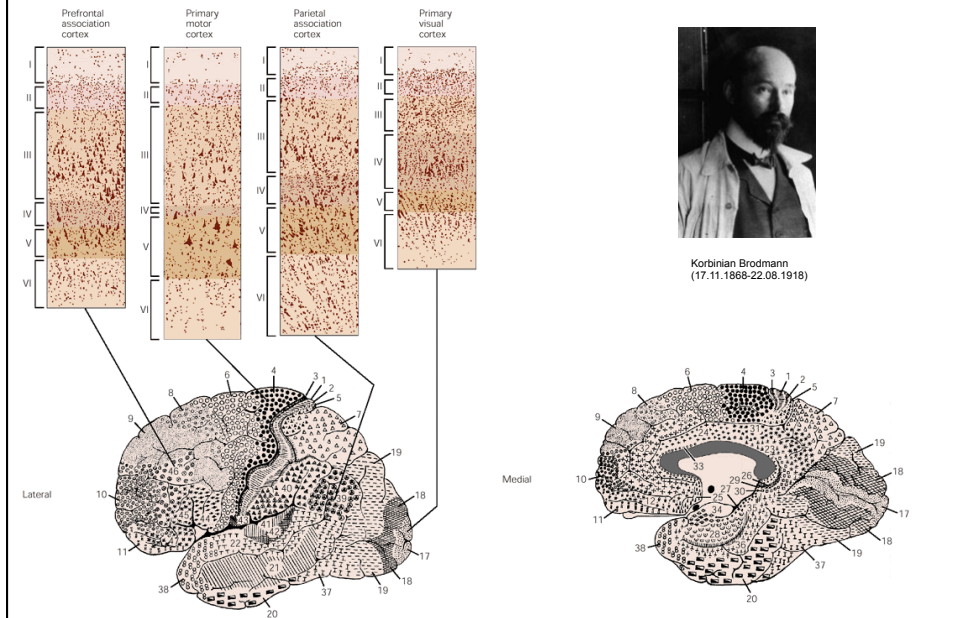


- 31 Olfactory tract
- 32 Lateral sulcus
- 33 Superior temporal gyrus
- 34 Superior temporal sulcus
- 35 Middle temporal gyrus
- 36 Inferior temporal sulcus
- 37 Inferior temporal gyrus
- 38 Pons
- 39 Flocculus
- 40 Medulla oblongata

Brain Anatomy: Structural MRI



Brain histology: Brodman areas



Phrenology: Gall and Spurzheim

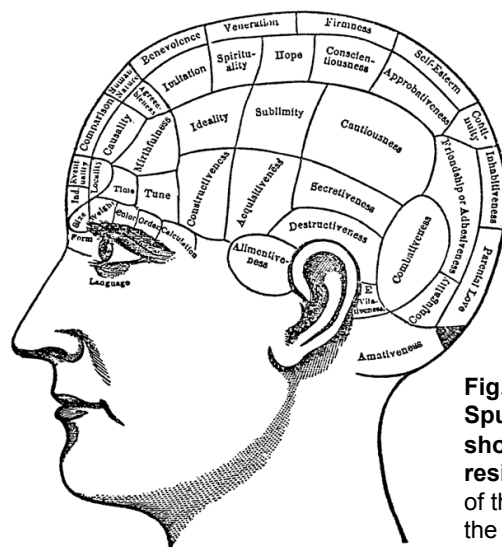
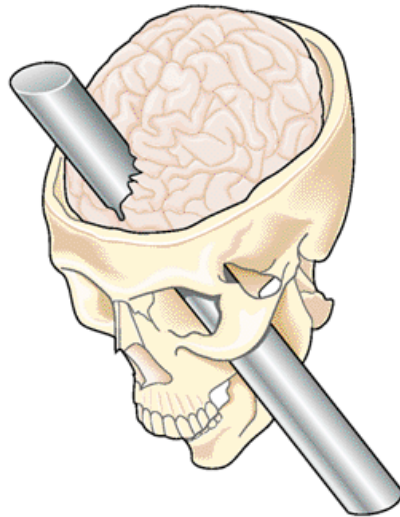


Fig. 15.16. Gall and Spurzheim's "phrenological head", showing 35 mental faculties, residing in specific organs of the cerebral cortex, projected upon the surface of the skull

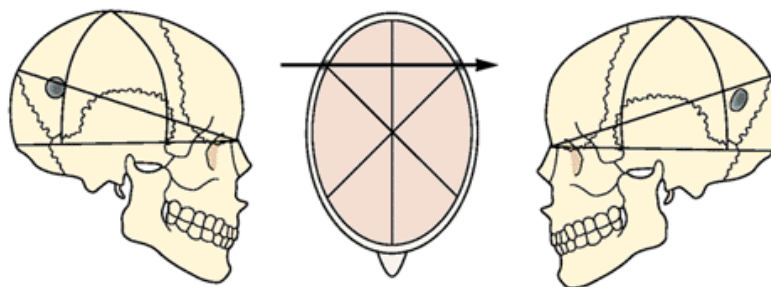
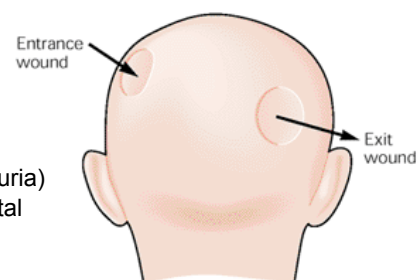
Brain functions Inferred from Injuries



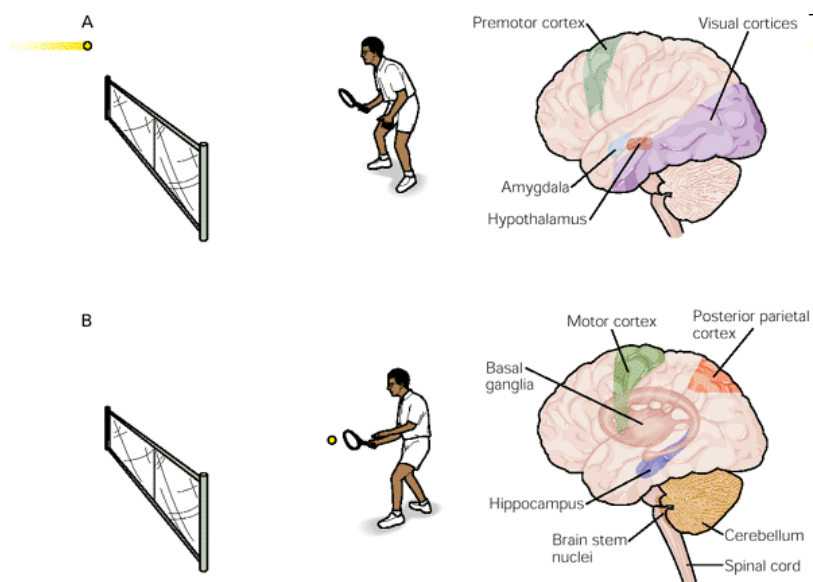
Phineas Gage
severe personality changes
after frontal lobe damage

Brain Functions Inferred from Injuries

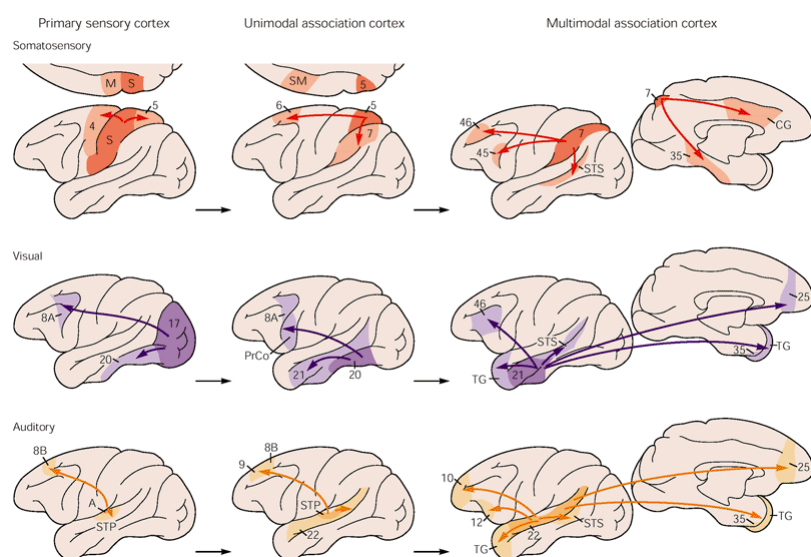
Studies in wounded soldiers
in world war I (Holmes) and II (Luria)
revealed the critical role of parietal
cortex in spatial integration



Sensory and motor functions

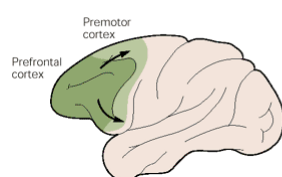


Sensory systems

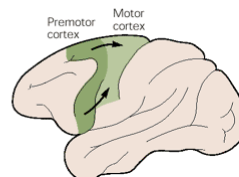


Motor system

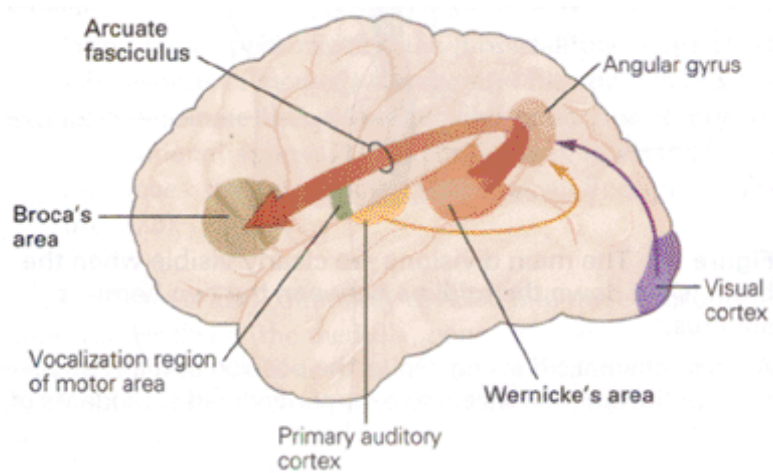
A Motor planning



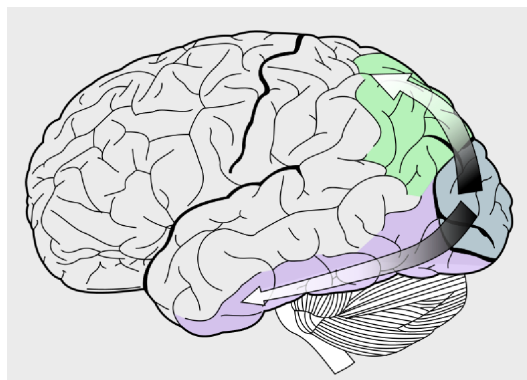
B Motor programs



Language



Visual processing



where

what

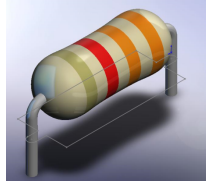
Physical Basics of Neuroimaging

Electricity and Magnetism

- Ohm's Law
- Biot-Savarts Law
- Faraday's Law
- Superconductivity
- Josephson Conjunction, SQUID

Ohm's Law

EEG

Georg Simon Ohm
(1789 - 1854)

Ohm's Law

$$\mathbf{E} = \int_V \left(\frac{\rho}{\epsilon_0} \frac{\vec{r} - \vec{r}'}{|\vec{r} - \vec{r}'|^3} \right) dV' + \frac{1}{\sigma} \mathbf{J}$$

$$\nabla \mathbf{E} = \frac{\rho}{\epsilon_0} + \frac{1}{\sigma} \mathbf{Q} = 0$$

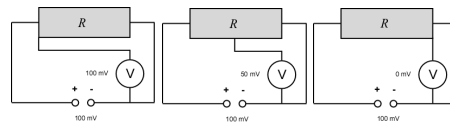
$$\mathbf{E} = \nabla U$$

$$\Delta U = 0$$

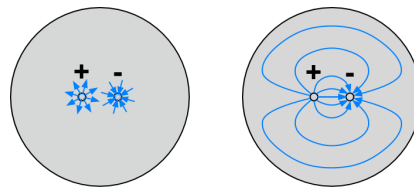
Ohm's law

$$U = RI$$

Voltage drop across a resistor

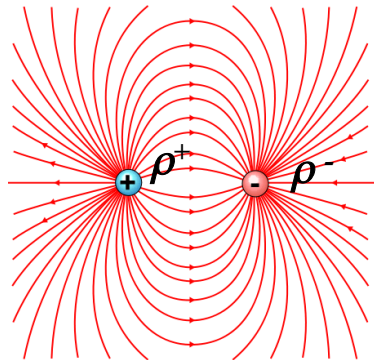


Current in a spherical conductor



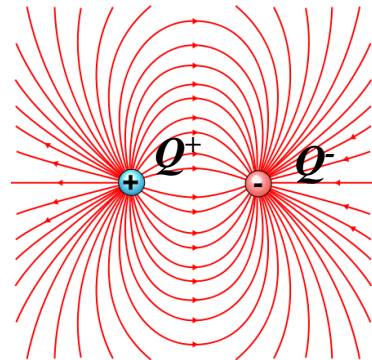
Dipole field

Electrostatics



$$\Delta U = \nabla \mathbf{E} = \frac{\rho}{\epsilon_0}$$

Electrodynamics



$$\Delta U = \nabla \mathbf{E} = \frac{1}{\sigma} \mathbf{Q}$$

Physical background of EEG and MEG

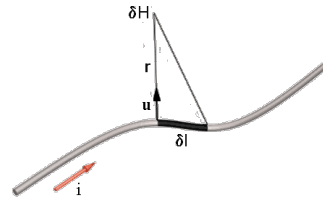
MEG

Jean-Baptiste Biot
(1774 - 1862)Biot-Savart's Law
right hand ruleFélix Savart
(1791 - 1841)

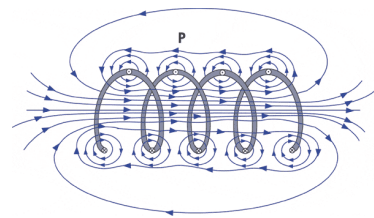
$$d\mathbf{B}(r) = \frac{\mu_0}{4\pi} I d\mathbf{l} \times \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3}$$

$$\mathbf{B}(r) = \frac{\mu_0}{4\pi} \int_V \mathbf{J}(\mathbf{r}') \times \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3} dV'$$

Biot-Savart's law: magnetic fields generated by electrical current



Magnetic field generated by a current flow coil



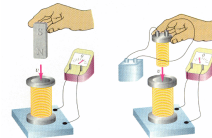
Magnetic induction: Faraday's law

Michael Faraday
(1791 - 1867)

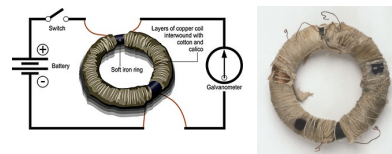
$$U = \frac{d\Phi}{dt}$$

Changing magnetic
field induces voltage

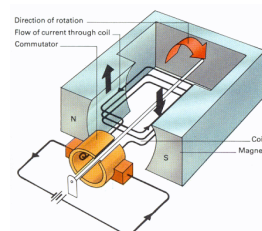
- 1) Moving magnet: increase and decrease of magnetic field



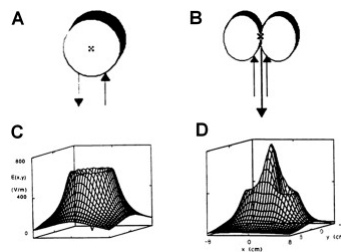
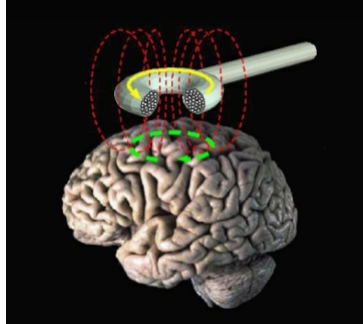
- 2) Switch magnetic field (electromagnet) on and off



- 3) Rotating coil: the coil area "sees" changing magnetic field



Transcranial magnetic stimulation

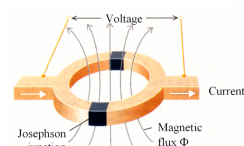
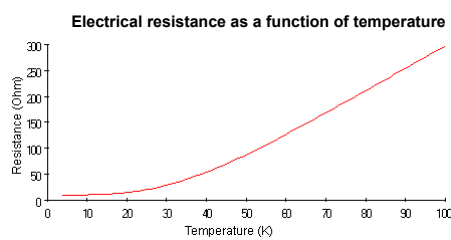
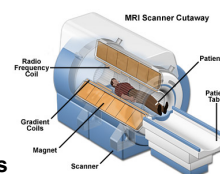


Superconductivity

Cooling down electrical conductors close to 0 K
any resistance vanishes

- strong magnets
- magnetic field sensors
- magnetic shielding

strong magnets



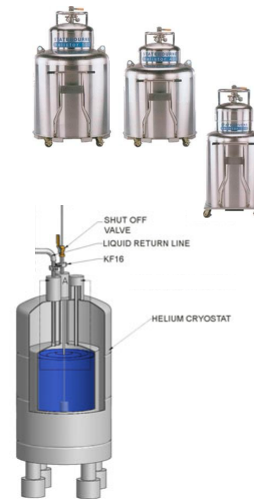
magnetic field sensors
SQUIDS

shielding



Superconductivity

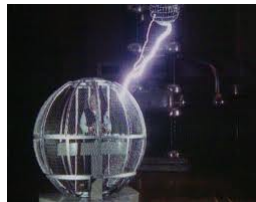
Strong magnetic fields can be generated by cooling them until they become superconducting



Superconductivity

Shielding of electrical fields:

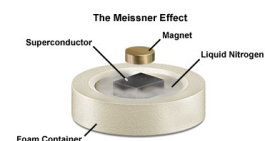
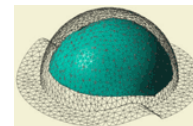
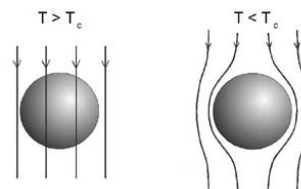
- Faraday cage



Shielding of magnetic fields:

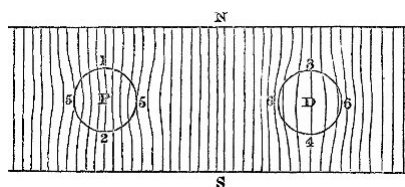
- Meissner effect
- Mu-Metal
- Eddy currents (Lenz rule)

Meissner Effect



Alternative shielding of magnetic fields

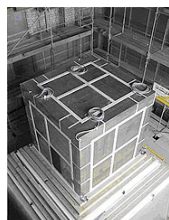
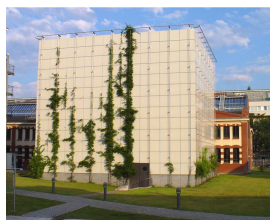
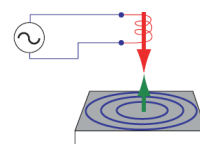
Mu Metal: Alloy of iron and nickel



paramagnetic >>
ferromagnetic
Mu-Metal
deoxyhemoglobin

diamagnetic
copper
oxyhemoglobin

Eddy currents



Brain imaging methods

Type of methods

- functional imaging methods
- biochemical activity
 - neurometabolic activity
 - neuroelectrical activity

Functional imaging methods

Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity

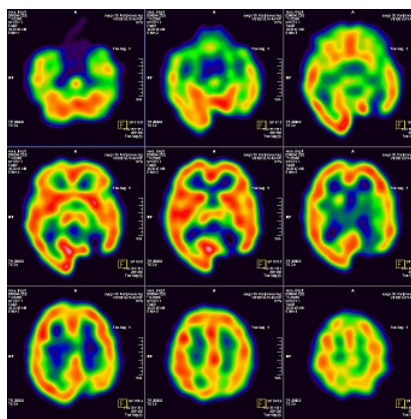
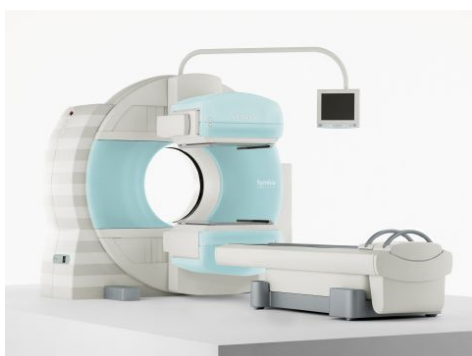


nuclear magnetic resonance tomography
(NMR, MRT, MRI)

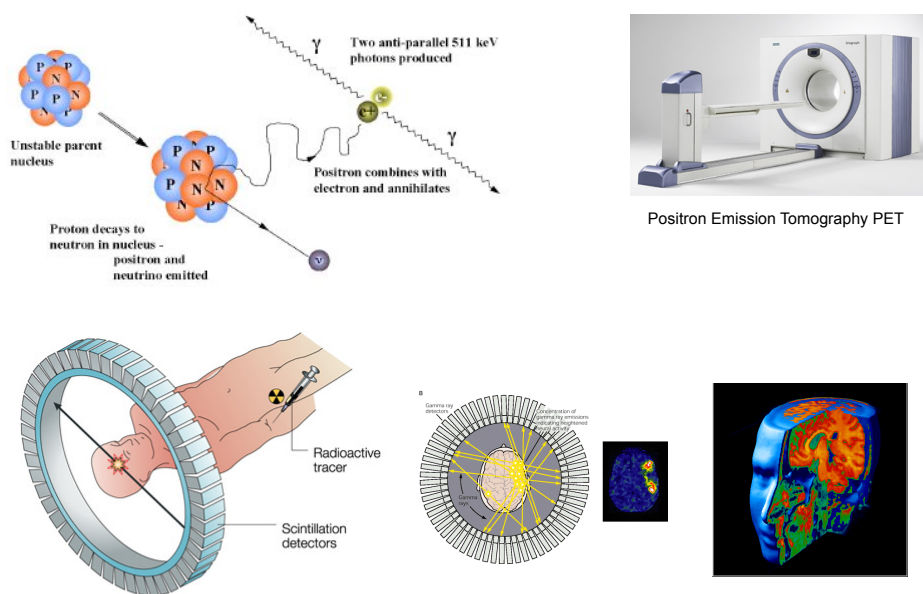


Positron Emission Tomography
(PET)

Single photon emission tomography SPECT



Positron emission tomography PET



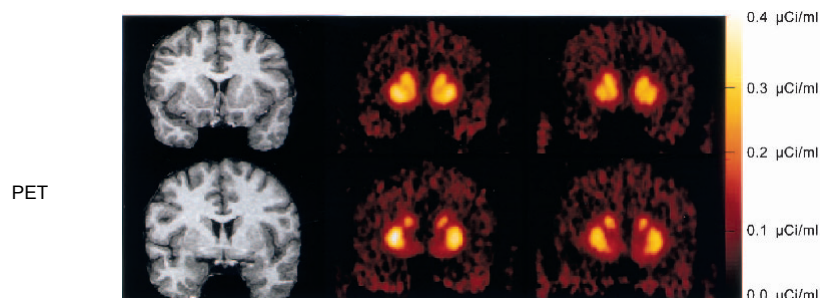
Positron emission tomography PET

Journal of Cerebral Blood Flow & Metabolism
29:285-300 © 2009 The International Society for Cerebral Blood Flow and Metabolism
Published by Lippincott Williams & Wilkins, Inc., Philadelphia

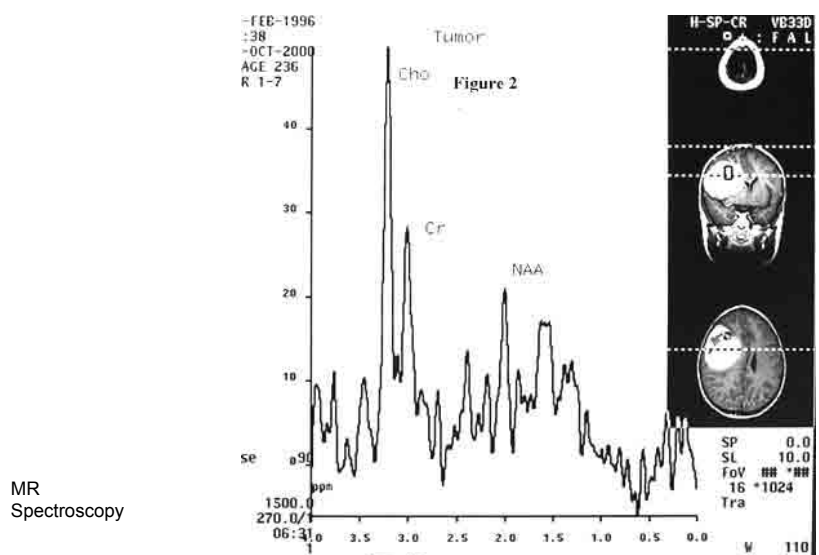
Imaging Human Mesolimbic Dopamine Transmission With Positron Emission Tomography. Part II: Amphetamine-Induced Dopamine Release in the Functional Subdivisions of the Striatum

*Diana Martinez, *Mark Slifstein, *Allegra Broft, *†Osama Mawlawi, *Dah-Ren Hwang, *†Yiyun Huang, *Thomas Cooper, *Lawrence Kegeles, *Eric Zarahn, *†Anissa Abi-Dargham, ‡§Suzanne N. Haber, and *†Marc Laruelle

Departments of *Psychiatry and †Radiology, Columbia University College of Physicians and Surgeons, New York, New York, and Departments of ‡Neurobiology and §Anatomy, University of Rochester School of Medicine, Rochester, New York, U.S.A.



Magnetic resonance spectroscopy

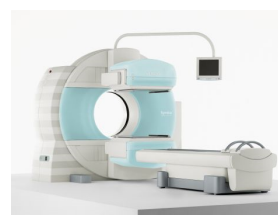


Functional imaging methods

Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity



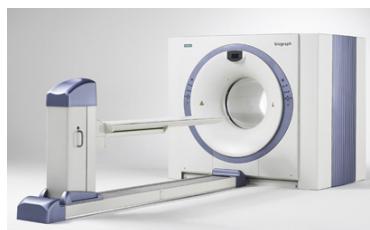
Single Photon Emission Tomography (SPECT)



near infrared spectroscopy (NIRS)

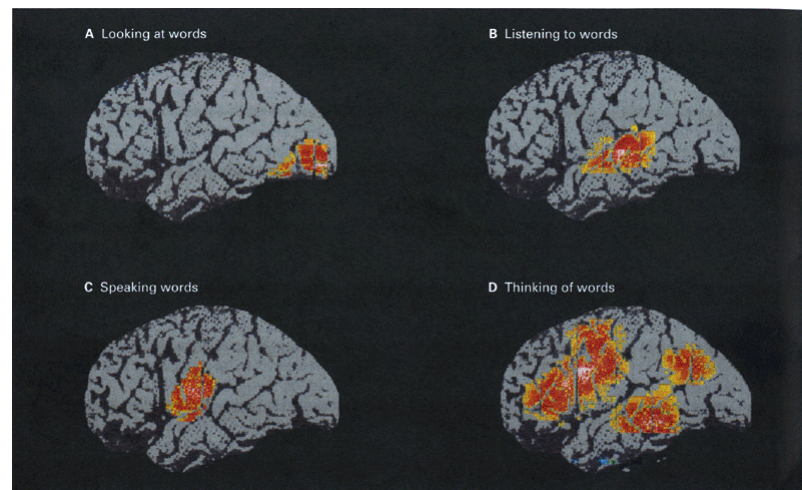


nuclear magnetic resonance tomography (NMR, MRI)



Positron Emission Tomography (PET)

Positron emission tomography PET



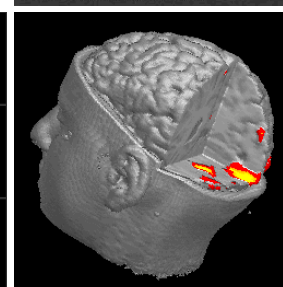
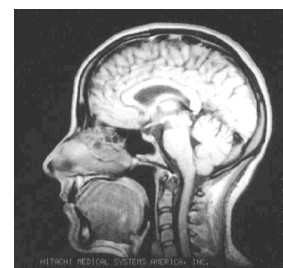
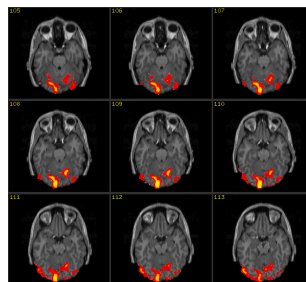
Cathy Price

Magnetic resonance imaging MRI

also
nuclear magnetic resonance NMR

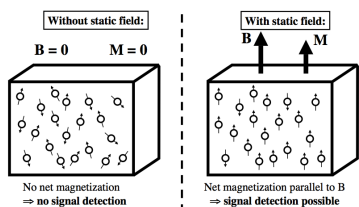


nuclear magnetic resonance
tomography
(NMR, MRT, MRI)

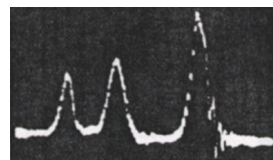


Magnetic resonance imaging MRI

How to get a macroscopic magnetization
(using a static magnetic field B)

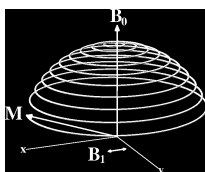
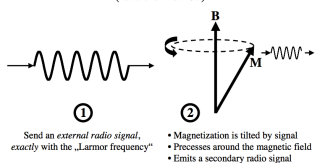


One of the first spectra of Ethanol
($\text{CH}_3\text{---CH}_2\text{---OH}$)

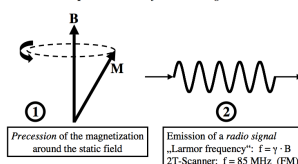


Resonance frequency of $\text{H}_1 \pm$ a few ppm

Tilt of the magnetization
(feasible method)



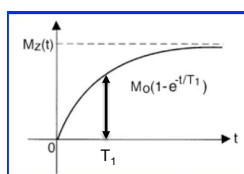
How to get a signal from the magnetization M
Step 2: Behaviour of the tilted magnetization



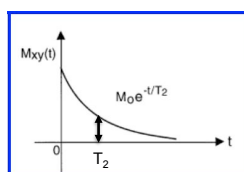
The emitted signal can be measured with a detector similar to an FM radio

Magnetic resonance imaging MRI

T1: $M_z/M_0 = (1 - 1/e) = 63 \%$



T2: $M_{xy}/M_0 = 1/e = 37 \%$



Relaxation types

T1: longitudinal relaxation
spin-lattice interaction
exchange of energy with the
near environment (molecules)

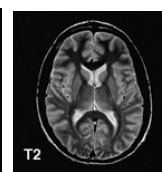
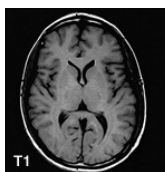
T2: transversal relaxation
spin-spin interaction

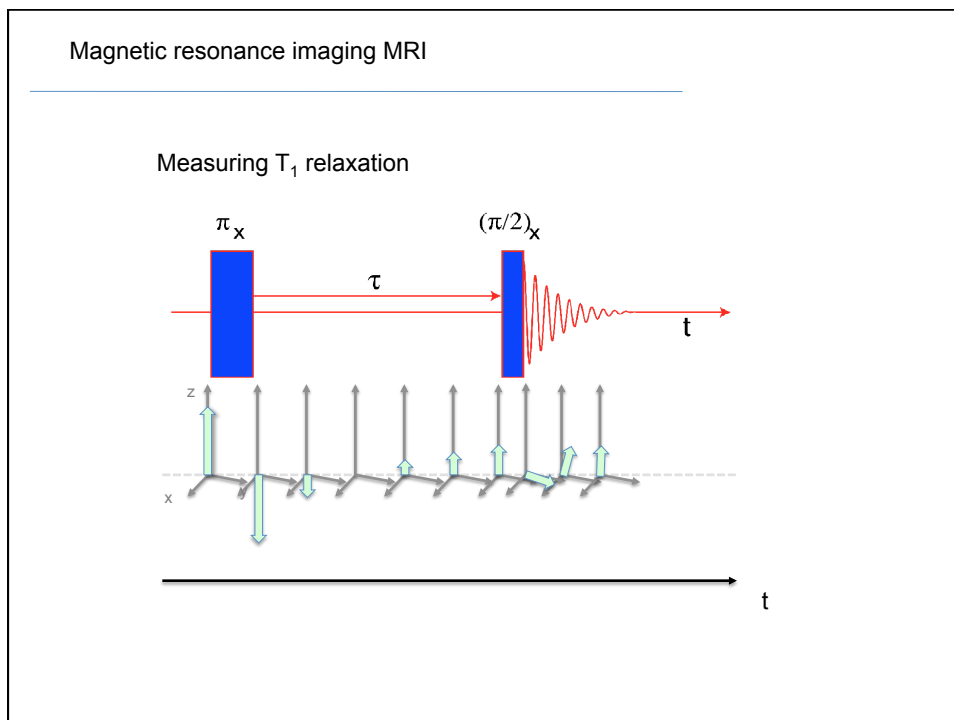
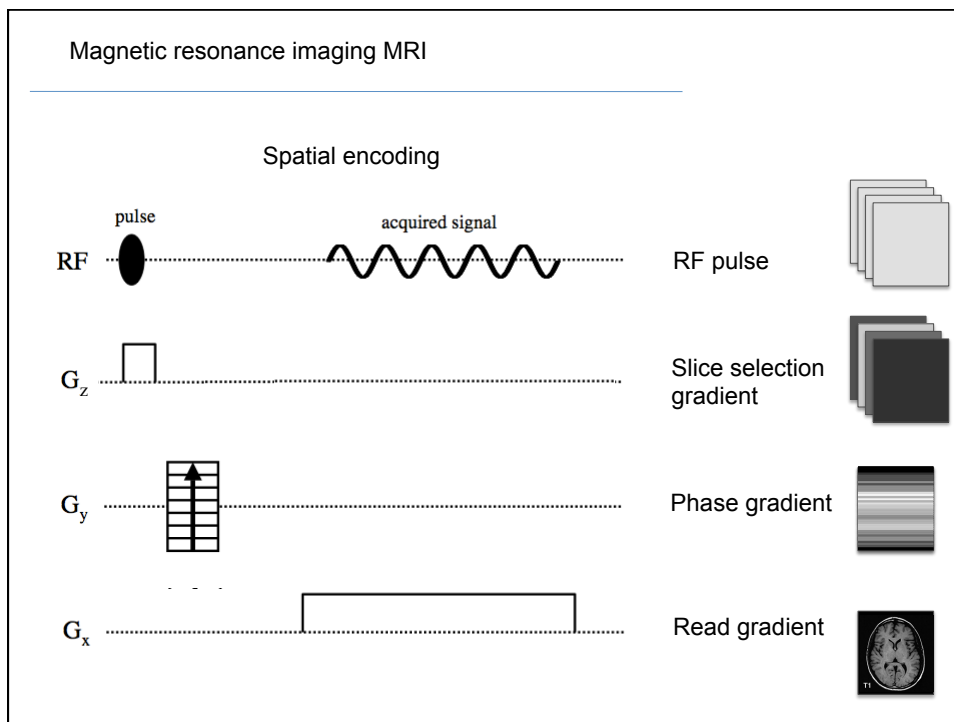
always:

$$T_2 < 2T_1$$

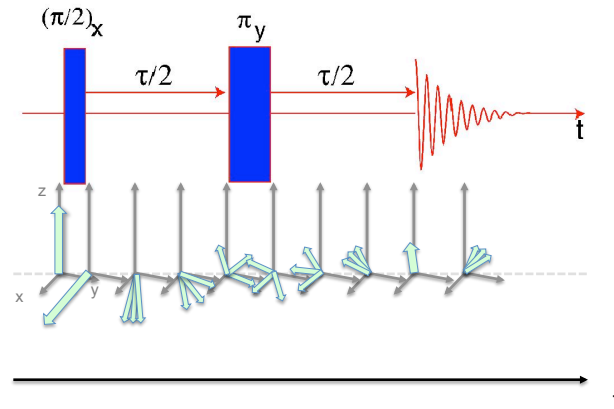
mostly:

$$T_2 < T_1$$





Magnetic resonance imaging MRI

Measuring T_1 relaxation

Magnetic resonance imaging MRI

Relaxation types

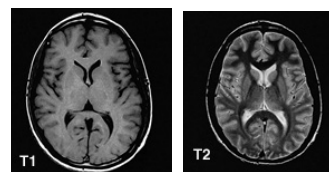
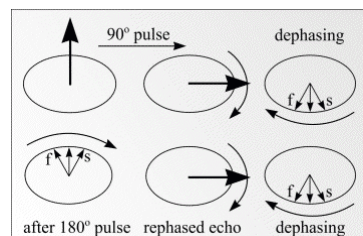
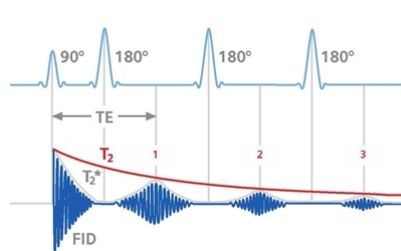
T_1 : longitudinal relaxation
spin-lattice interaction
exchange of energy with the
near environment (molecules)

T_2 : transversal relaxation
spin-spin interaction

T_2^* : inhomogeneities of local magnetic field
Fe-atoms in hemoglobin

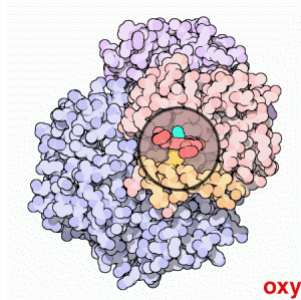
mostly:

$$T_2^* < T_2 < T_1$$

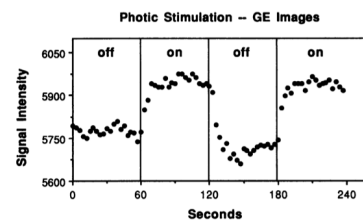
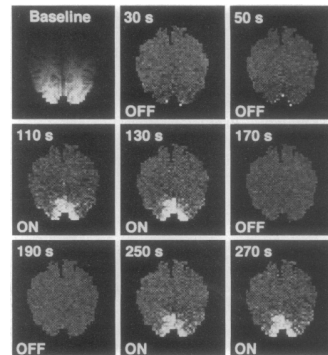


Functional Magnetic resonance imaging fMRI

Blood oxygen level dependent response: BOLD



Oxy-hemoglobin: diamagnetic
(i.e. not magnetic, no effect on T_2^*)
Deoxy-hemoglobin: paramagnetic
(i.e. magnetic, affects T_2^*)

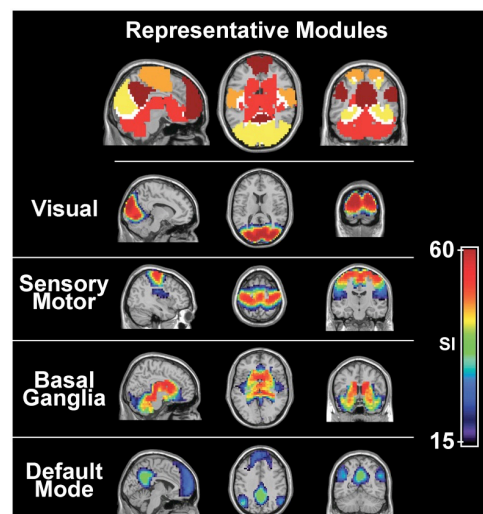


Functional Magnetic resonance imaging fMRI

Correlation between the activity of voxels:

→ functional connectivity

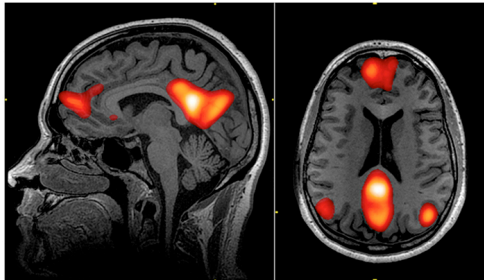
→ resting state networks



Functional Magnetic resonance imaging fMRI

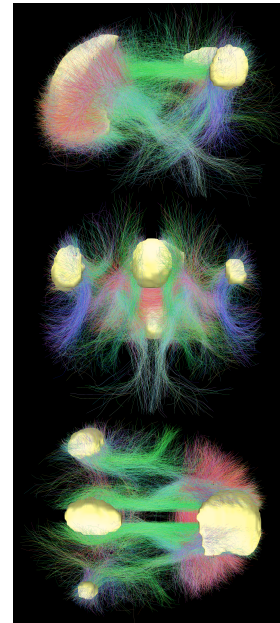
Correlation between the activity of voxels:
→ functional connectivity

→ Default mode network

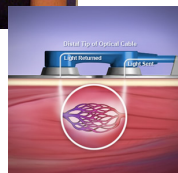


Default mode network

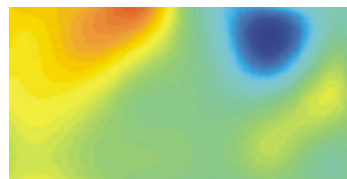
- Posterior cingulate cortex (PCC) & precuneus: Combines bottom-up attention
- Medial prefrontal cortex (mPFC): decision making
- Angular gyrus: Connects perception, attention, spatial cognition, action, and recall of episodic memories



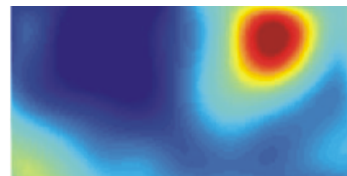
Near infrared spectroscopy NIRS



Stimulation of the left and right hemifield by an alternating black and white checkerboard. The difference between the two conditions is mapped. The red and blue spot show the maximum difference and correspond to the primary visual areas of the subject.

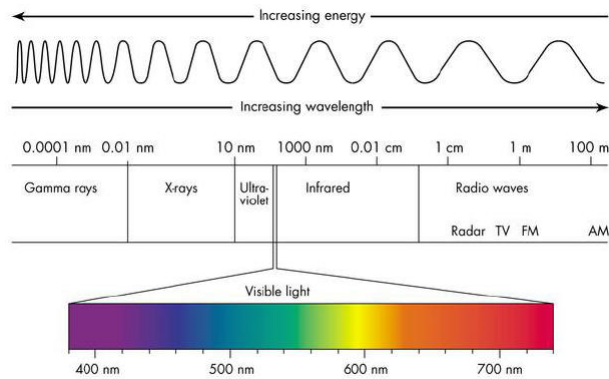


The image corresponds to the changes in the concentration of deoxygenated haemoglobin [deoxy-Hb]



The image shows the corresponding changes in oxygenated haemoglobin [oxy-Hb].

NIRS

**Bio-optical window:**

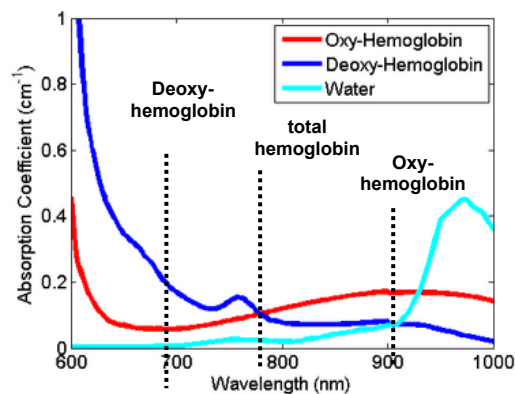
from 700 nm
to 900 nm

Relationship between wavelength λ and frequency ν :

$$c = \lambda \nu$$

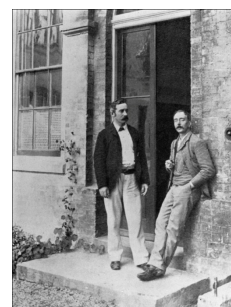
c : speed of light

NIRS: Absorption



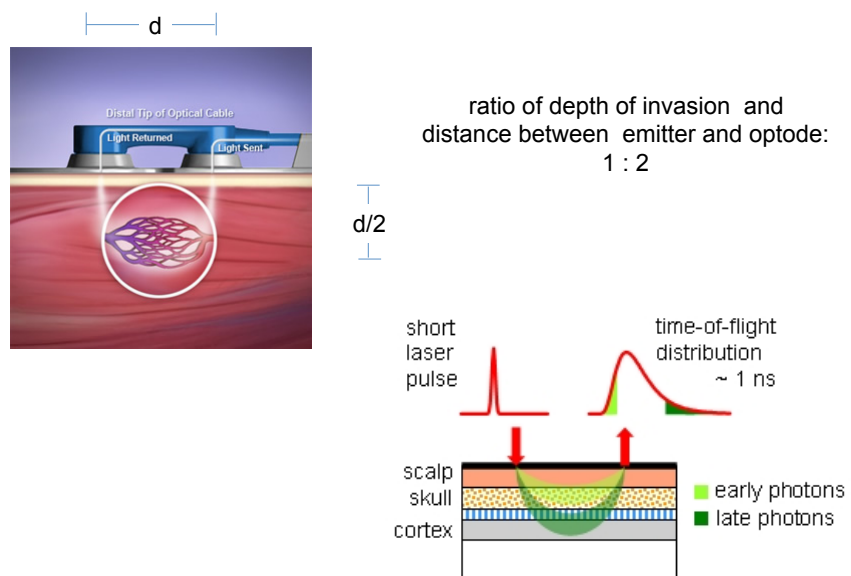
- near infrared light can invade tissue several centimeters
- skin and bone are basically transparent for near infrared light

absorption depends on concentration:
 regional cerebral blood volume (rcbv)
 regional cerebral blood flow (rcbf)
 oxygenation

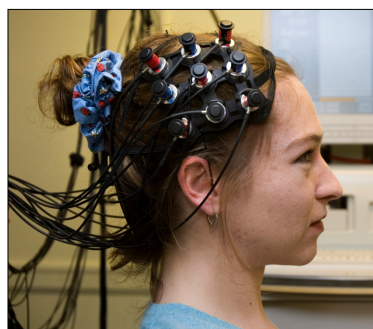


⇒ **neurovascular coupling**
 (Roy and Sherrington 1890)

NIRS

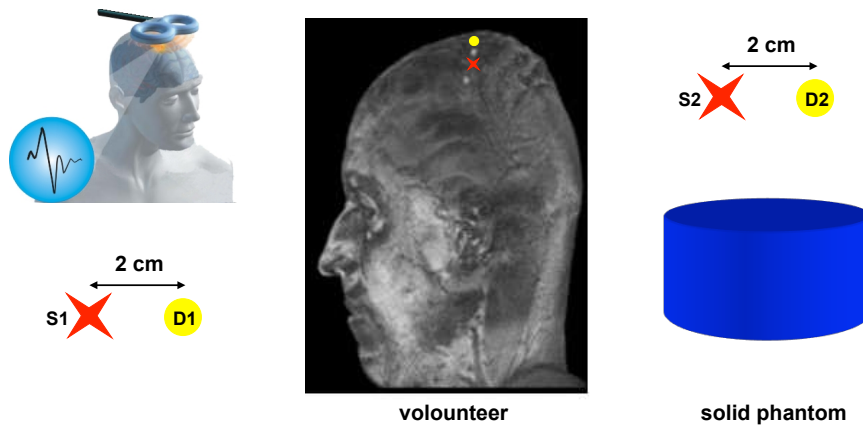


NIRS



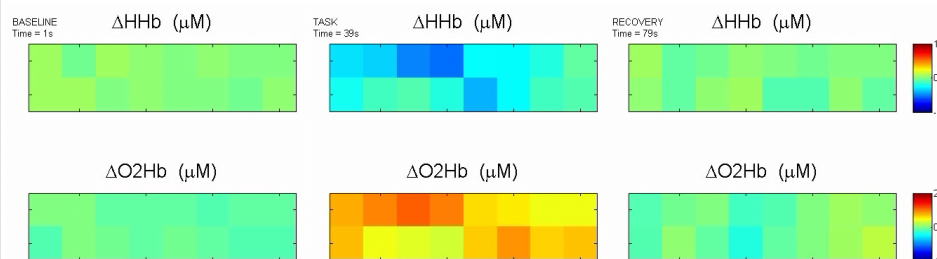
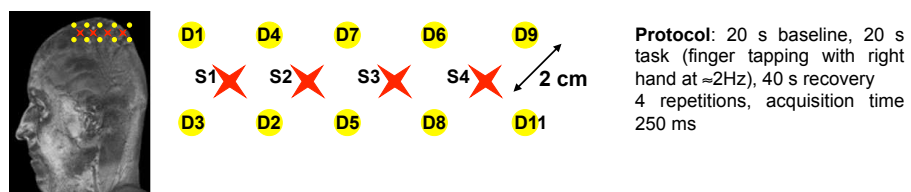
NIRS

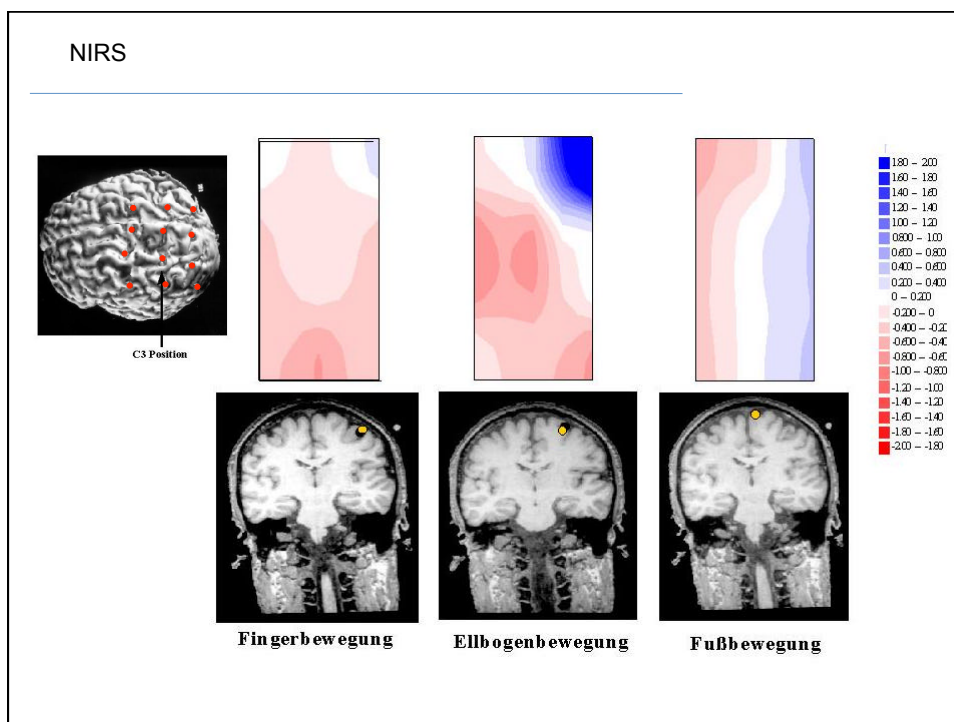
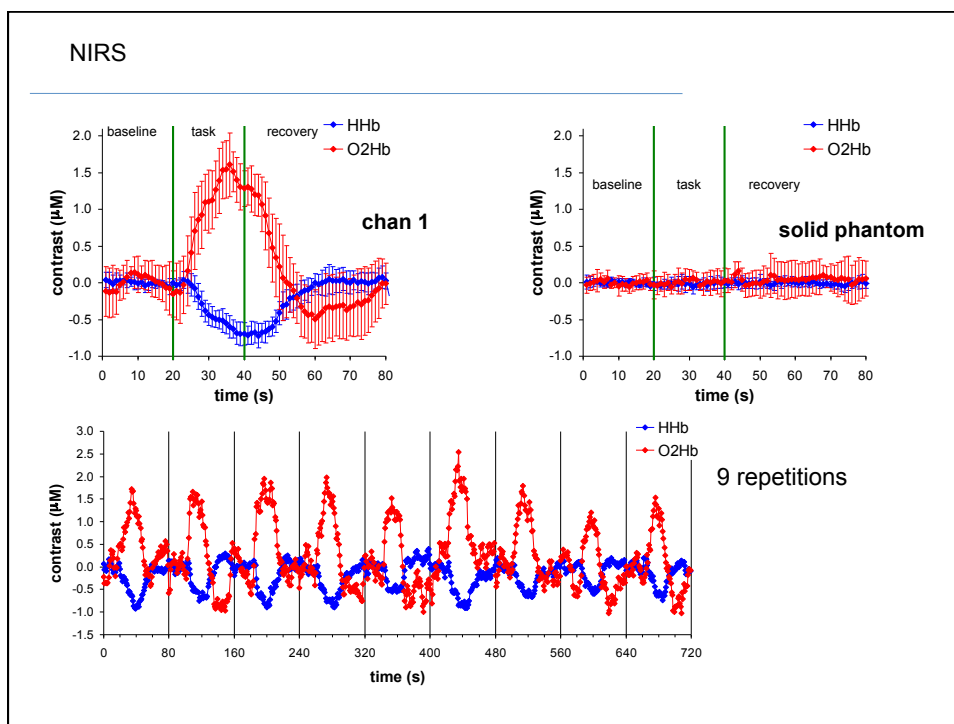
Motor area for right hand identified by Transcranial Magnetic Stimulation (TMS)



Protocol: 20 s baseline, 20 s task (finger tapping with right hand at $\approx 2\text{Hz}$), 40 s recovery
9 repetitions, acquisition time 1 s

NIRS





Functional Imaging Methods

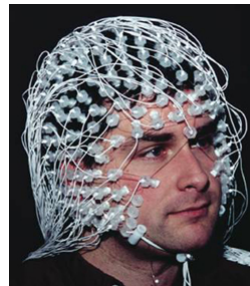
Type of methods

functional imaging methods

- biochemical activity
- neurometabolic activity
- neuroelectrical activity



Transcranial Magnetic Stimulation
TMS



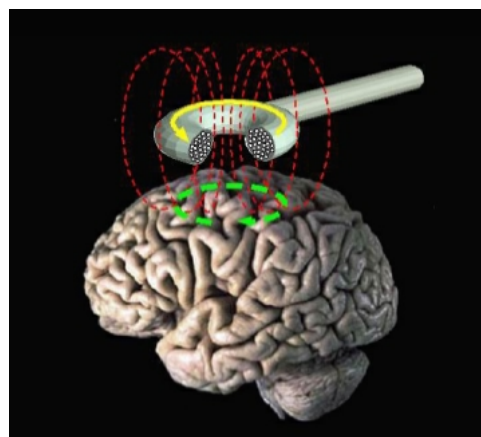
Electroencephalography
EEG



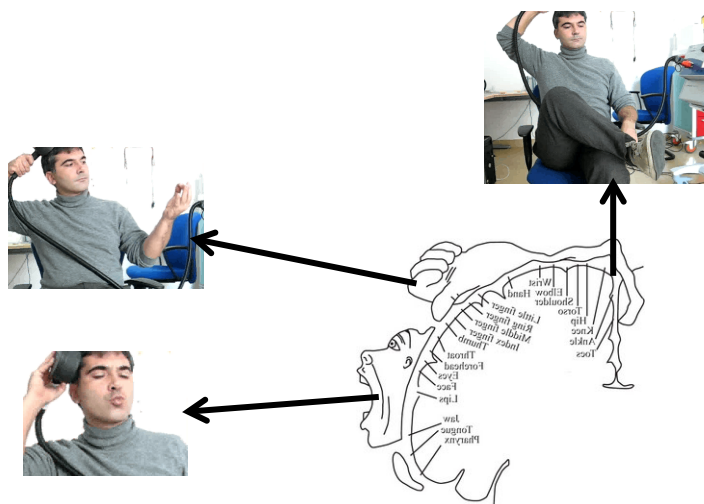
Magnetoencephalography
MEG

Physical Principle of TMS

Conductor 1 is the magnetic coil;
Conductor 2 is the extracellular fluid
of the cerebral cortex.



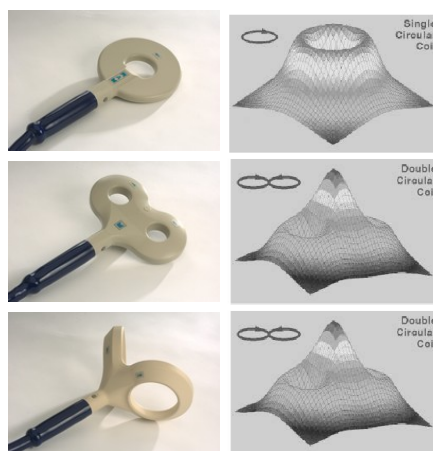
TMS: Stimulating the Motor Cortex



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TMS: Types of Coils

The shape of the coil “shapes” the magnetic field and hence the electrical field and ultimately it determines the way you stimulate the brain tissue



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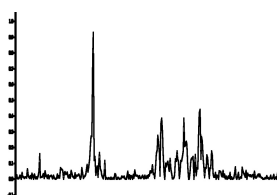
Interpretation of MEP Recordings

Tongue recordings

Raw MEP

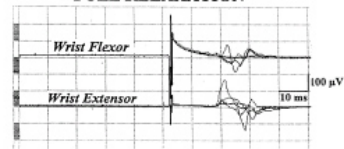


Rectified MEP

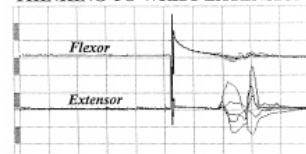


Motor imagery

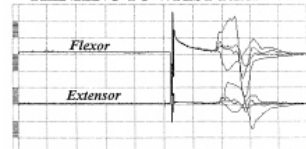
FULL RELAXATION



THINKING TO WRIST EXTENSION

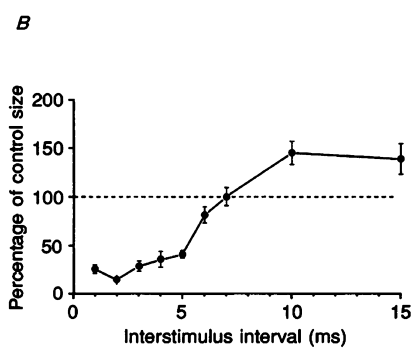
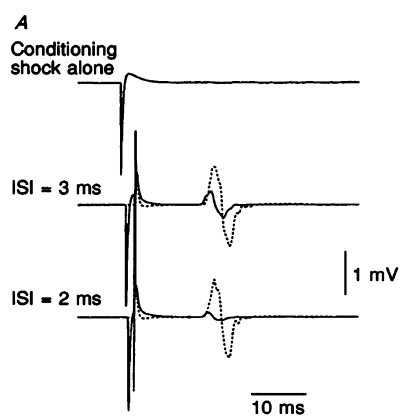


THINKING TO WRIST FLEXION



Paradigms: 1 - Conditioned TMS

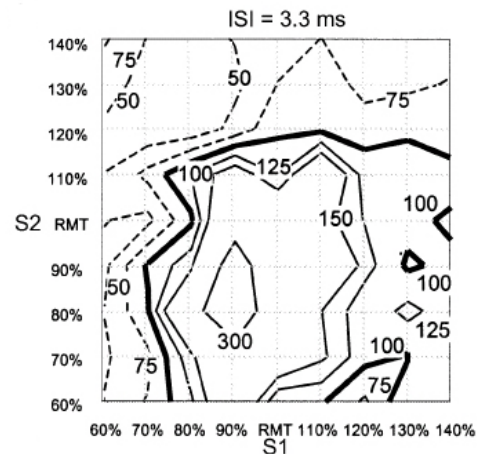
Classical paired pulse paradigm (Kujirai):



Paradigms: 1 - Conditioned TMS

It is not as simple as it looks: the interaction between conditioning and test stimulus is defined in a 3-dimensional space taking into account

- 1) the intensity of conditioning stimulus;
- 2) the intensity of the test stimulus and
- 3) the ISI



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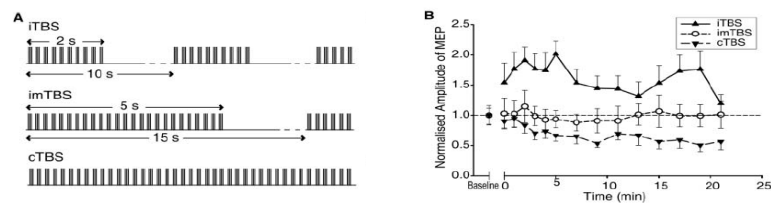
Paradigms: 2 - Shaping the Excitability of Cerebral Cortex

rTMS

A train of transcranial magnetic stimuli produces effects that outlast the train of stimuli.

We distinguish:

1. Low frequency rTMS: 0.2 Hz and 1 Hz produce inhibitory effects over the motor cortex
2. High frequency rTMS: > 5 Hz. Facilitatory effects
3. Patterned TMS: Theta-burst stimulation (TBS)
 - iTBS: intermittent TBS, cTBS: continuous TBS, imTBS: intermediate TBS

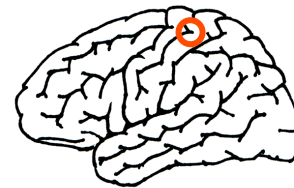
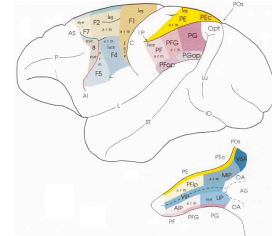


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Paradigms: 3 – Online Virtual Lesion

Virtual lesions of the anterior intraparietal area disrupt goal-dependent on-line adjustments of graspEugene Tunik¹, Scott H Frey² & Scott T Grafton¹

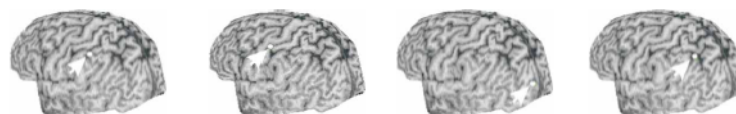
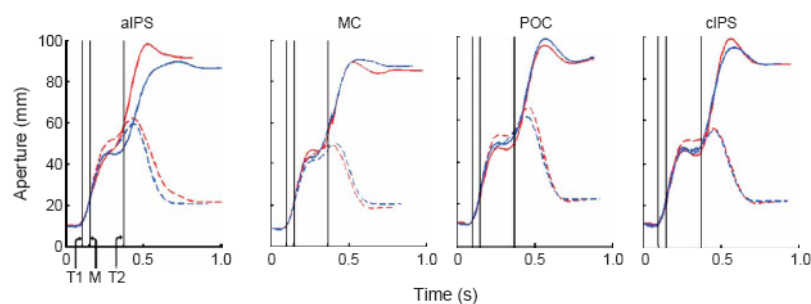
- Hypothesis: the anteriormost part of the IPS in humans in the homologue of monkey AIP and mediates visually guided grasping
- Conditioning stimulus: TMS applied over the rostral IPS at various intervals from the test stimulus.
- Test stimulus: target object perturbations during reaching, requiring online adjustments.
- Measurement: finger kinematics of grasping. Control conditions: TMS over posterior areas or over M1.



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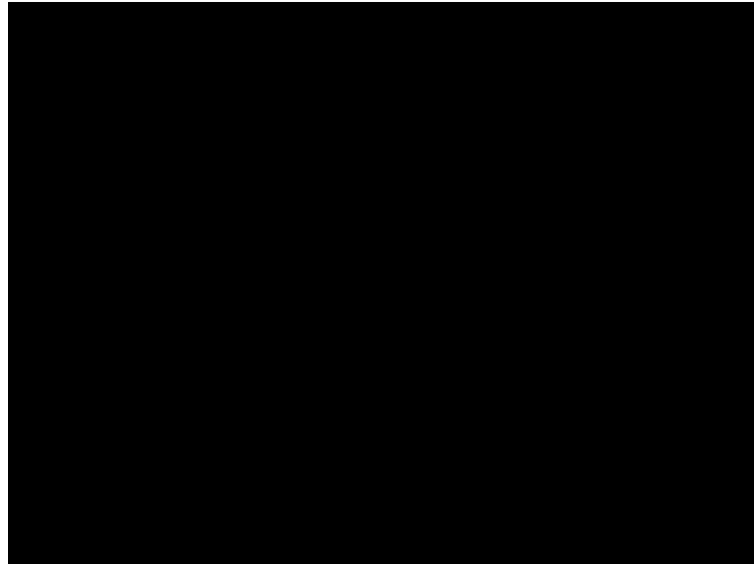
Paradigms: 3 – Online Virtual Lesion

- Results: only TMS over the rostral IPS in the time window around 65 ms from object perturbation reduces the capacity of online adjustment of grasping



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Deep Brain Stimulation in Parkinson



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Techniques – Transcranial Direct Current Stimulation: tDCS

tDCS is delivered with a pair of soaked sponges applied to the scalp



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