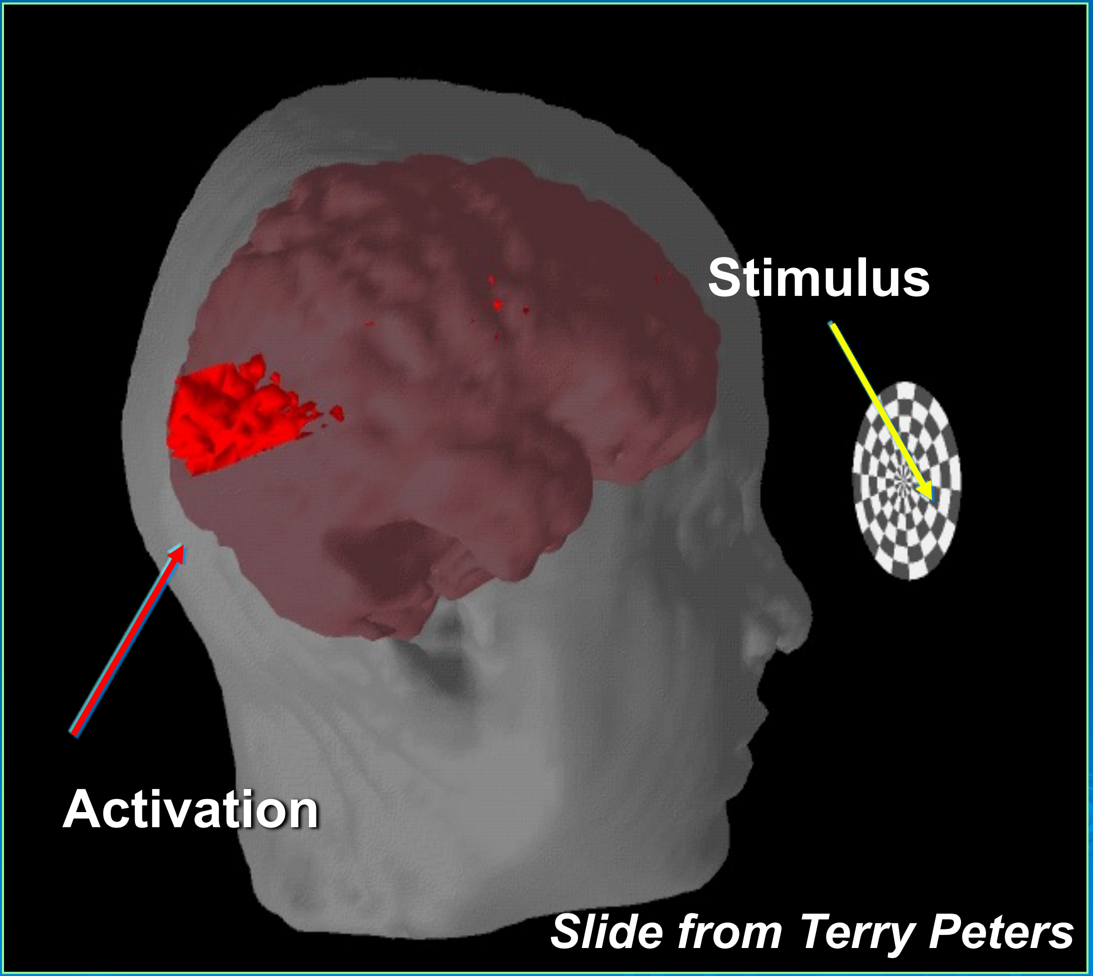
functional MRI

Subject looks at flashing disk while being scanned "Activated" sites detected and merged with 3-D MR image



http://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/introduction

Outline

- What are we going to observe ?
  - Physics and physiological basis of brain activation and of the MRI contrast
- How to collect such information ?
  - Data acquisition
- Data analysis
  - Statistical criteria
- Examples

Functional MR Imaging (fMRI)

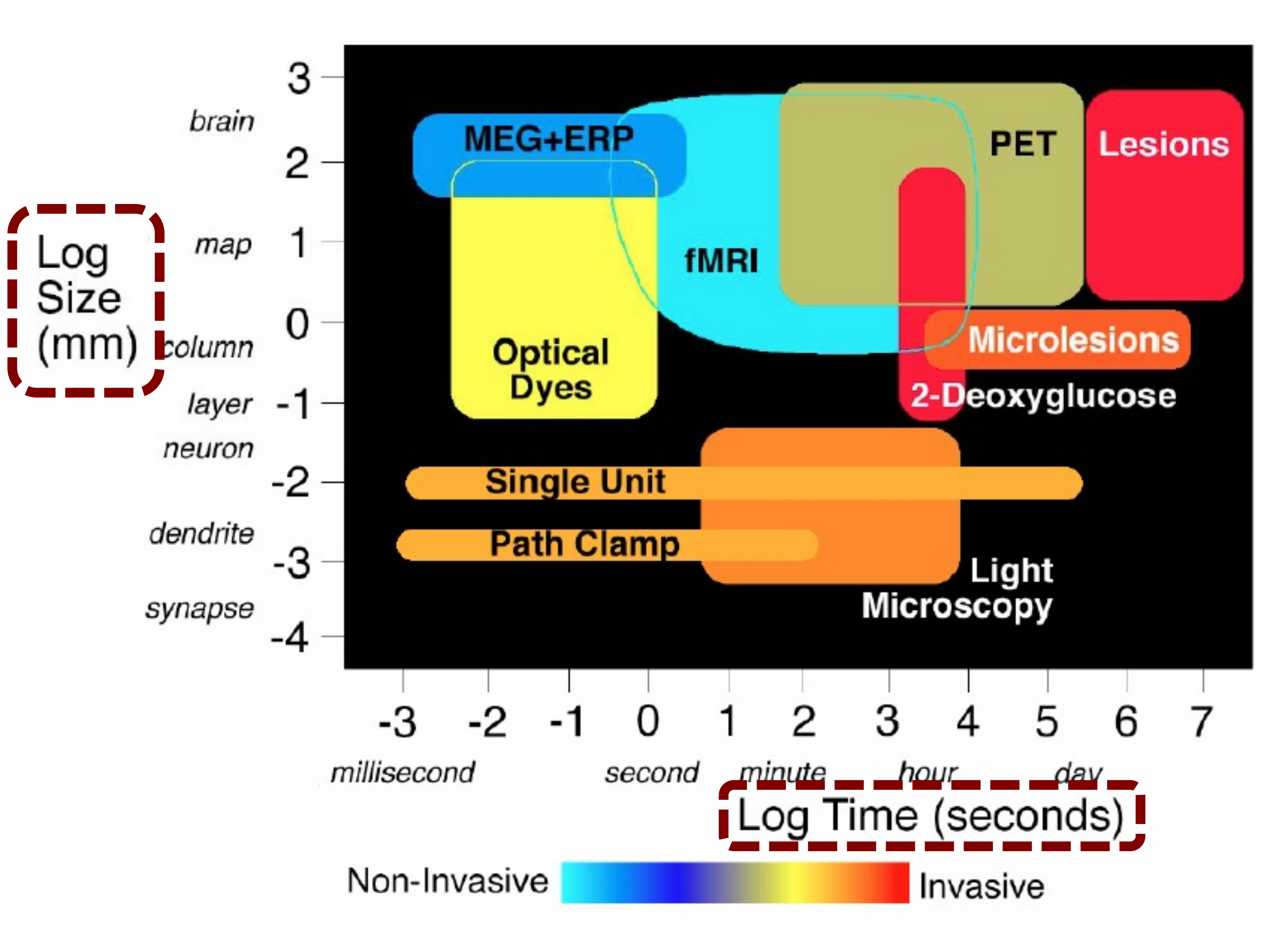
Peter Jezzard, PhD

FMRIB Centre, Oxford University,
John Radcliffe Hospital, Oxford, OX3 9DU

http://www.fmrib.ox.ac.uk/physics

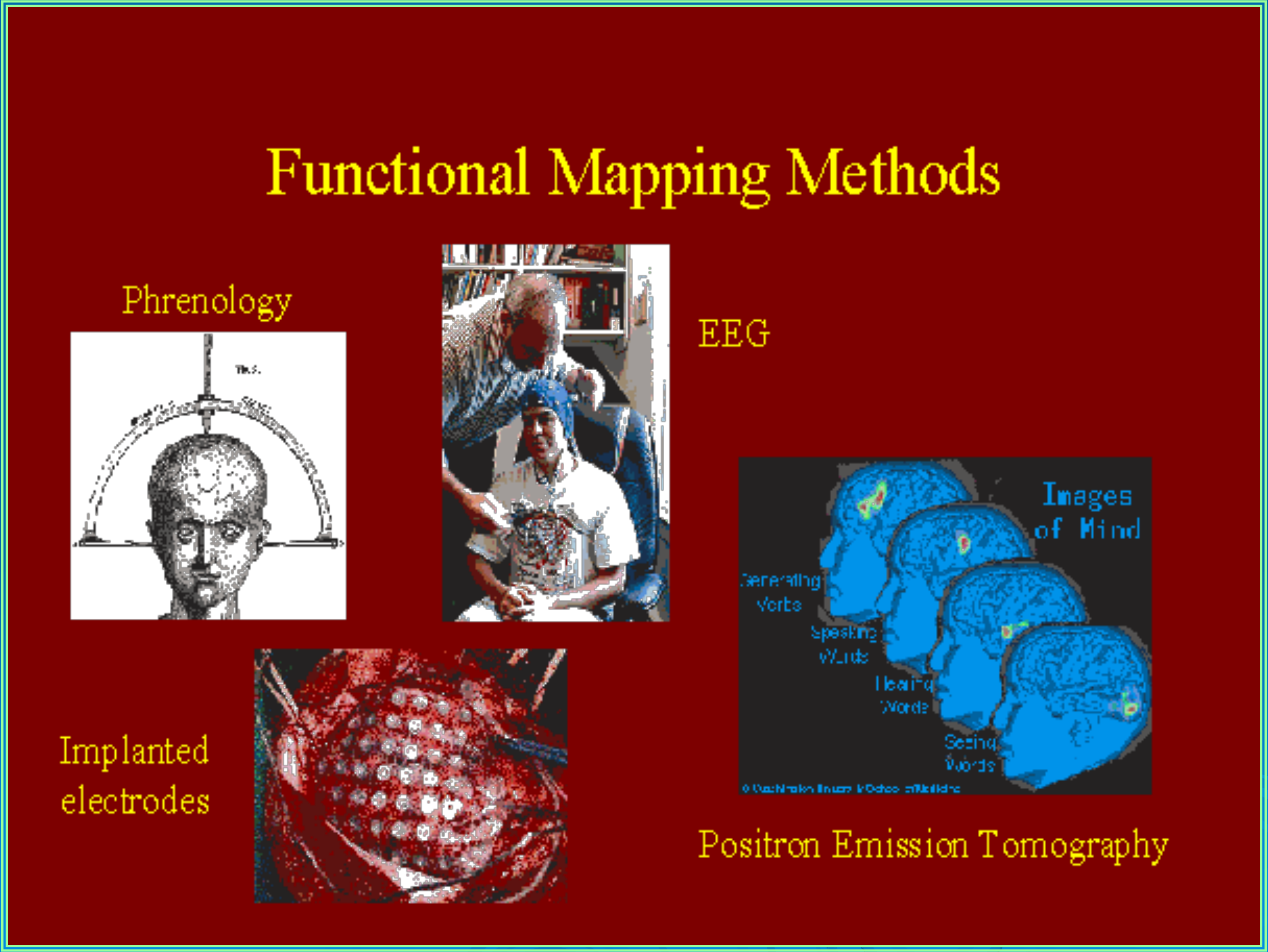
Some slides from
http://users.fmrib.ox.ac.uk/~peterj/lectures/miccai99/sld001.htm

Brain mapping techniques

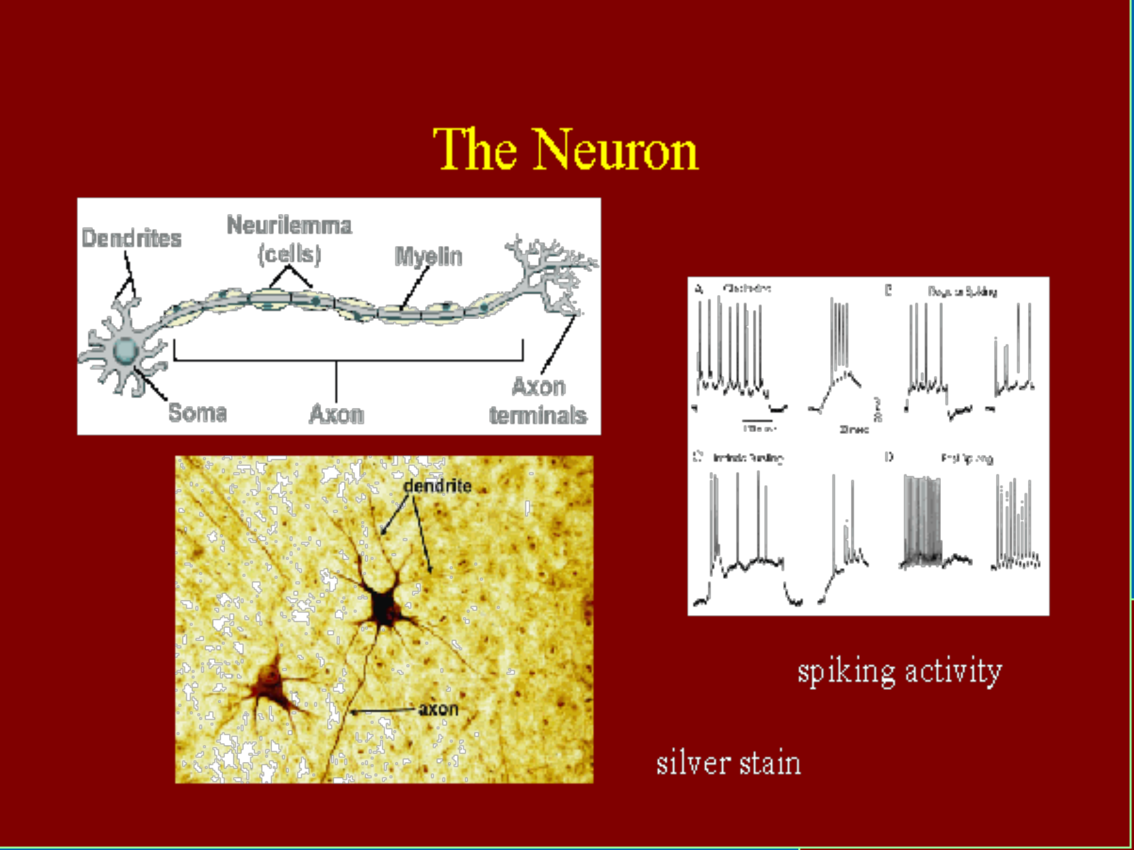


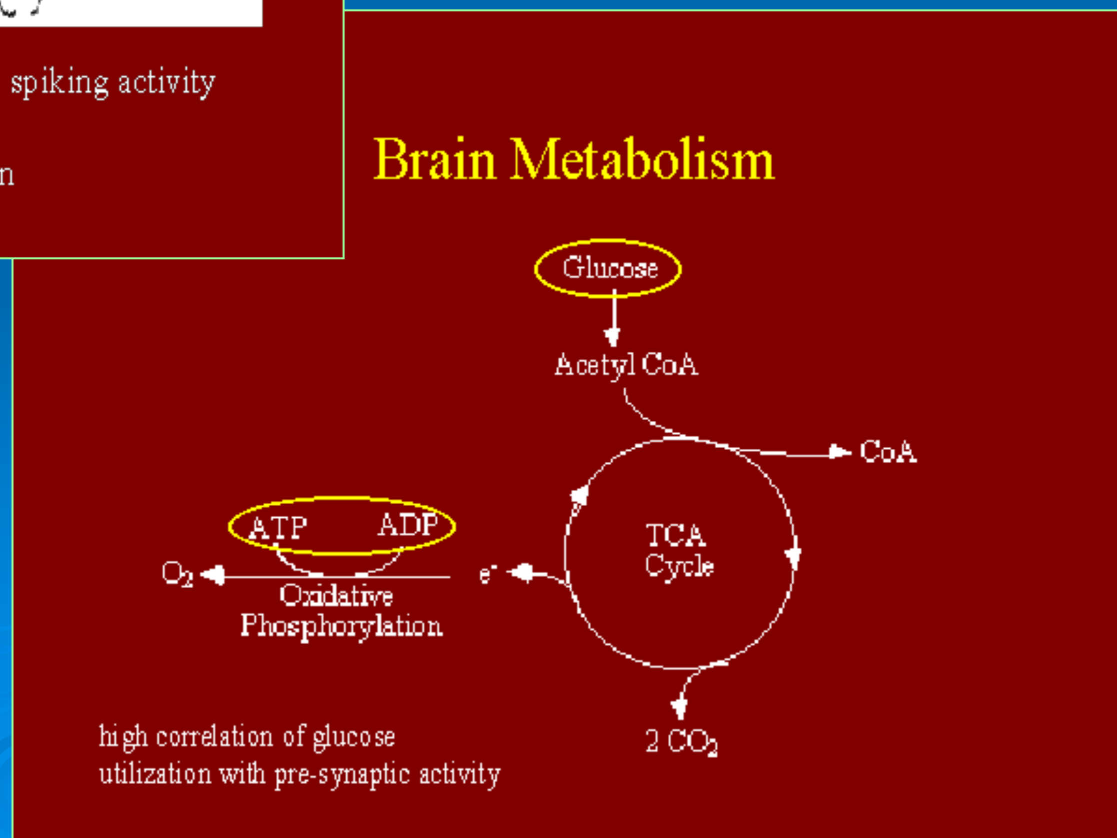
Spatial resolution (log size), time resolution (log time)

The history of brain mapping



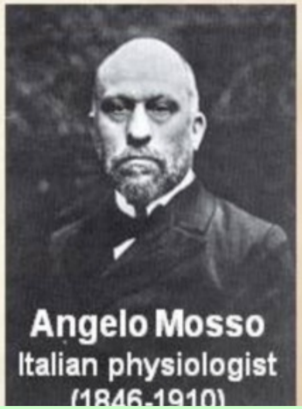
The physiology behind it





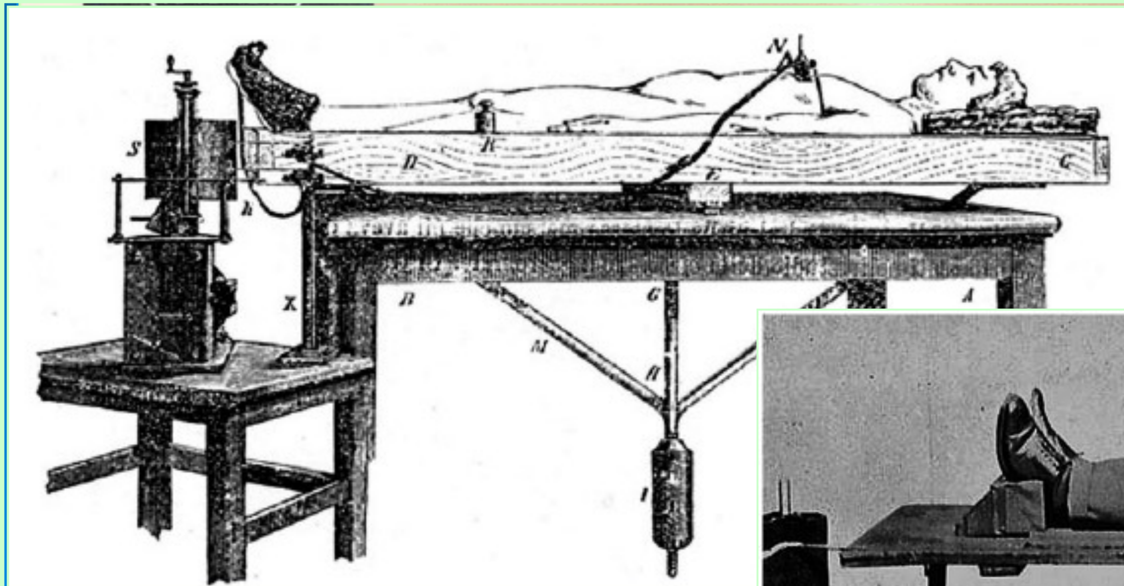
How can we meassure brain activity?

The first (and cheapest ¡) experiment

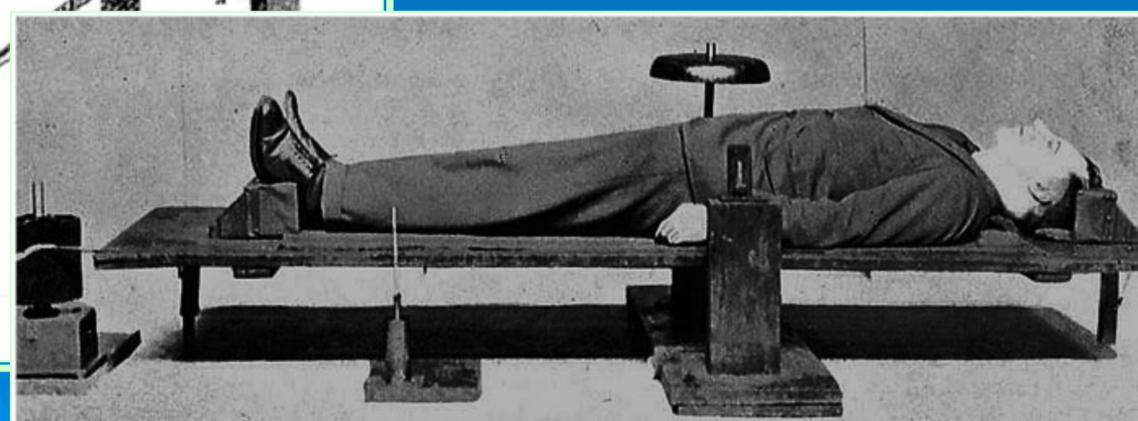


Experiment: subject resting on a balanced table. Brain activity tilts the table towards the head, due to blood redistribution in the body.

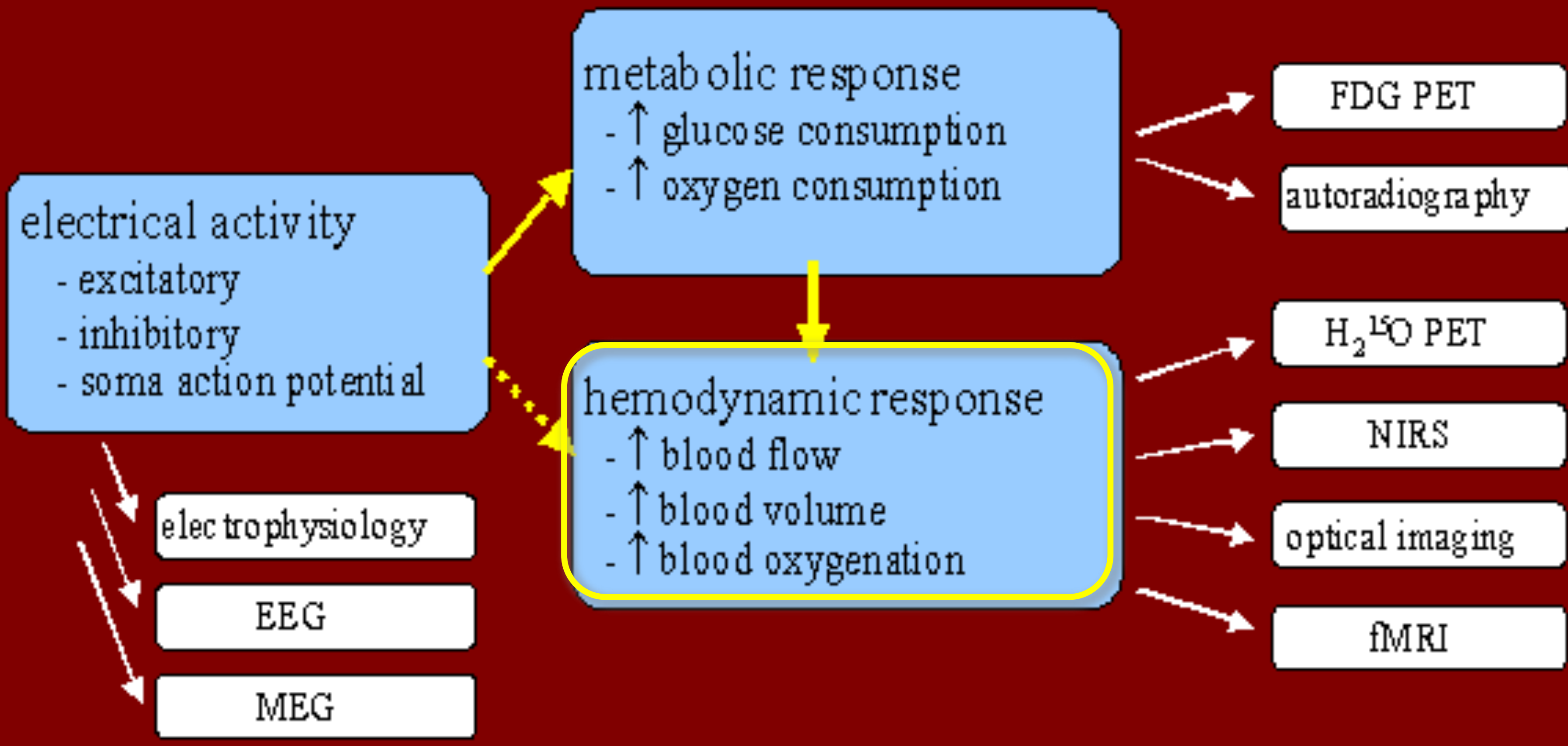
Slide from P.Ramos Cabrer, ESMRMB meeting 2008



Sandrone et al (2013) Brain



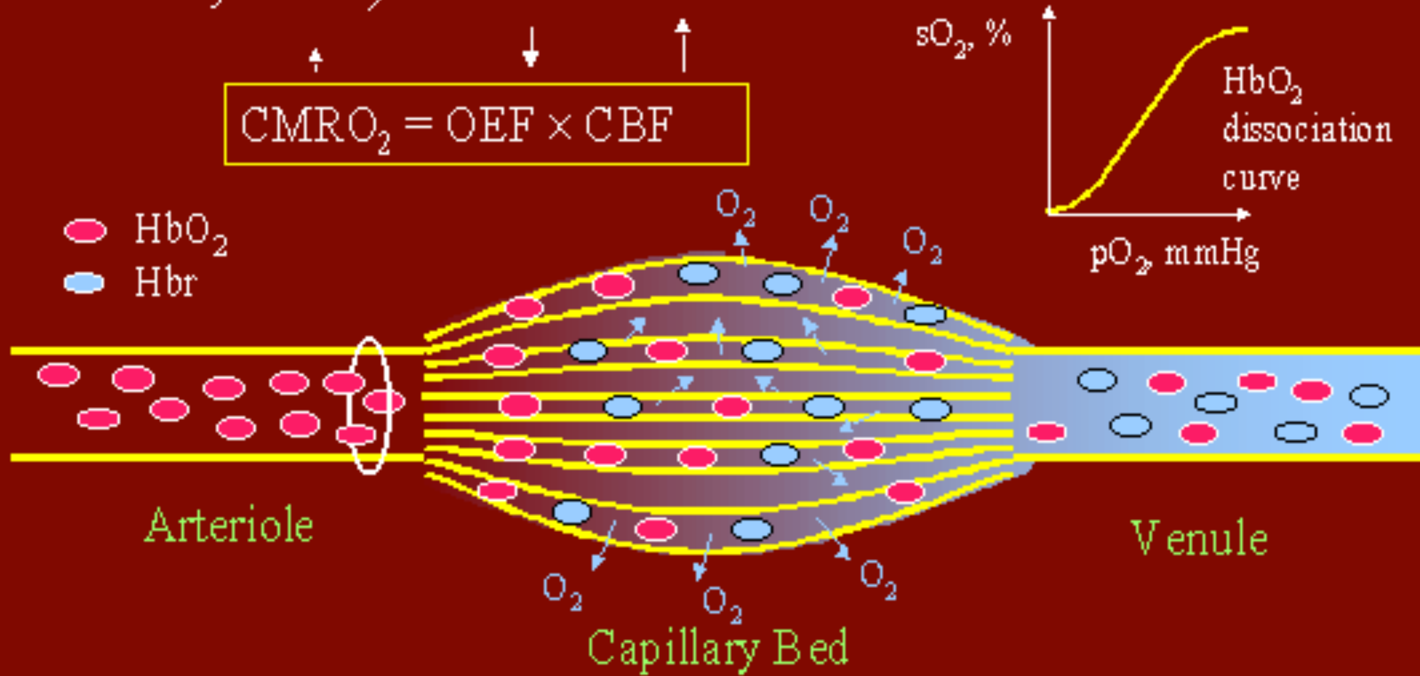
Physiological Correlates of Brain Electrical Activity



The physiology behind it

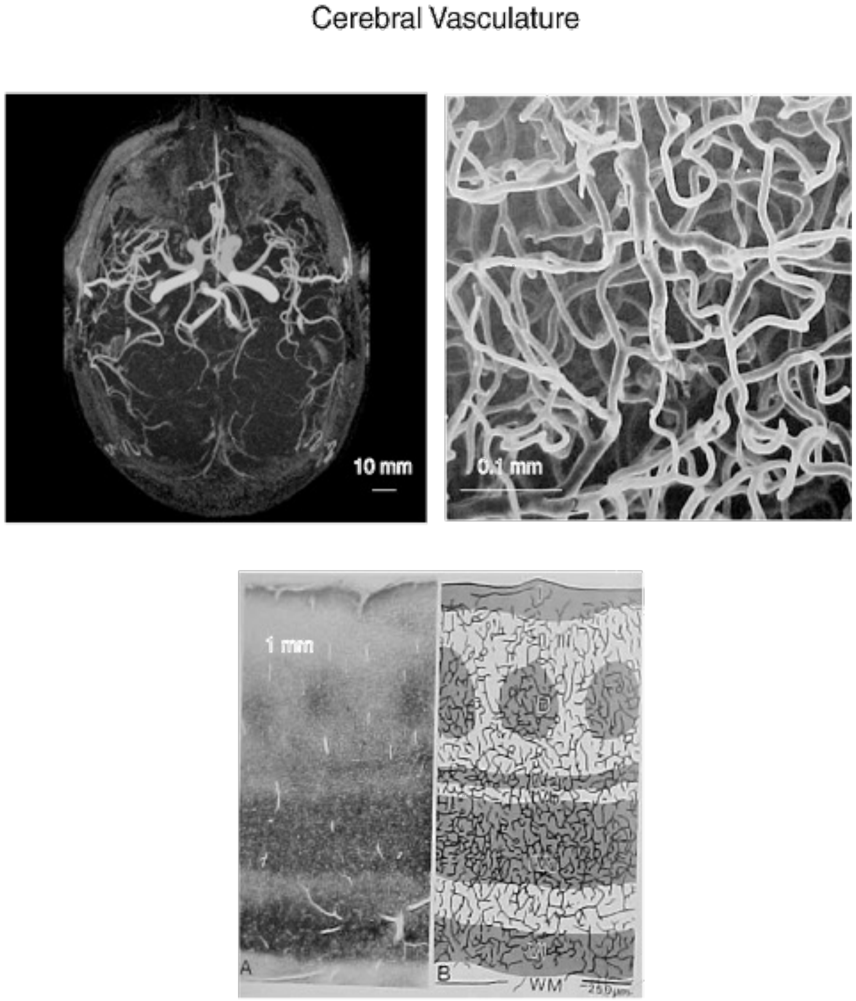
Oxygen Transport

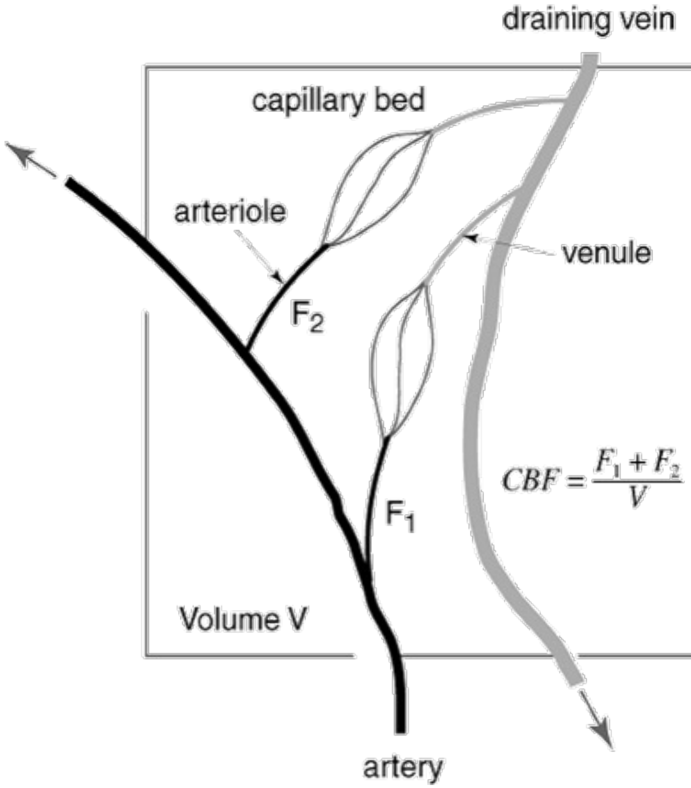
- Limited oxygen diffusion model (Buxton & Frank, 1997)



Buxton and Frank, JCBFM, 17:64, 1997

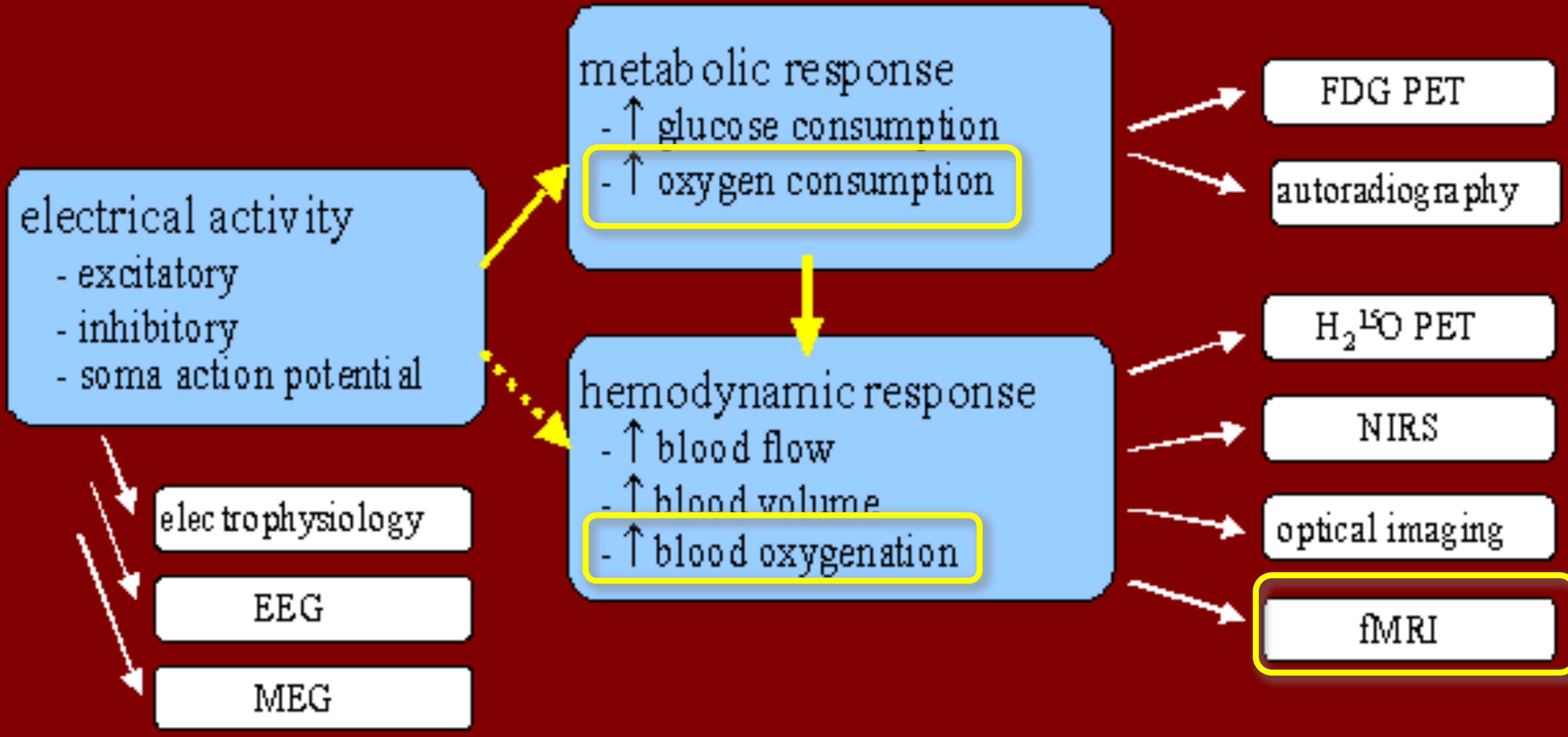
Vascular network





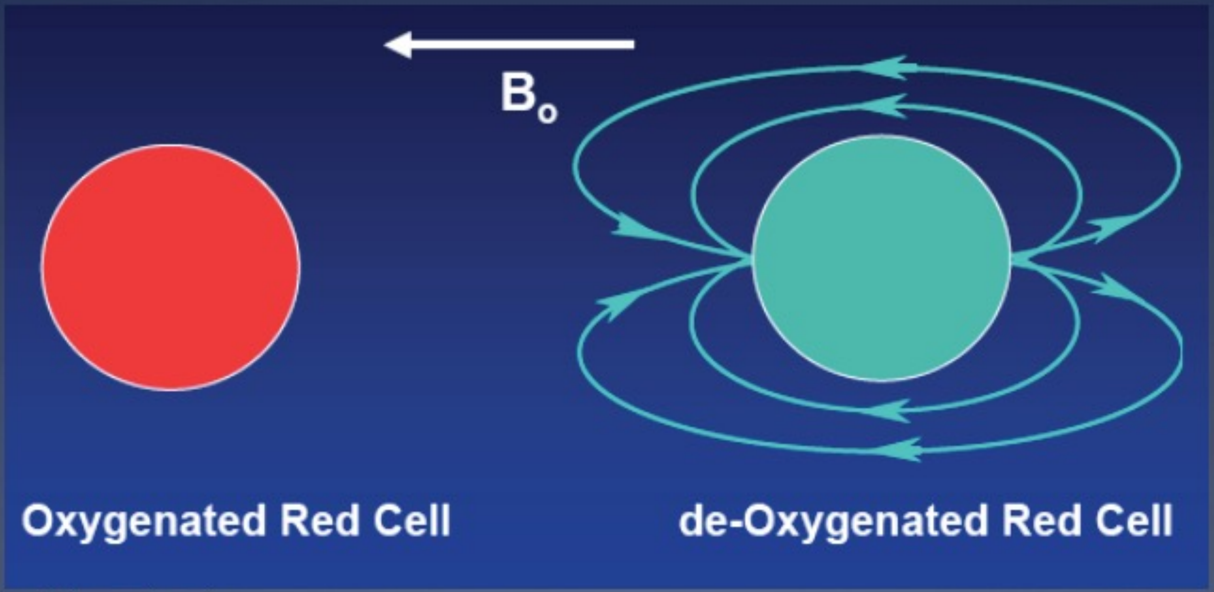
Source: Buxton book Ch 2

Physiological Correlates of Brain Electrical Activity



Magnetic properties of Red Cells

Field homogeneity & oxygenation state

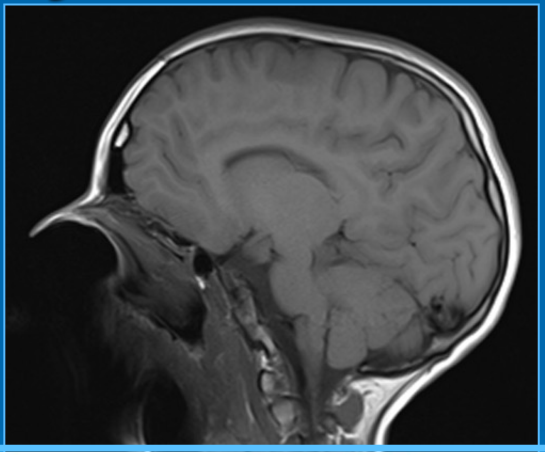


- Red blood cell
  - 6 μm diameter, 1-2 μm thick
- Susceptibility
  - An object with differing magnetic properties distorts the field

Slide by Daniel Bulte ***http://users.fmrib.ox.ac.uk/~bulte/***

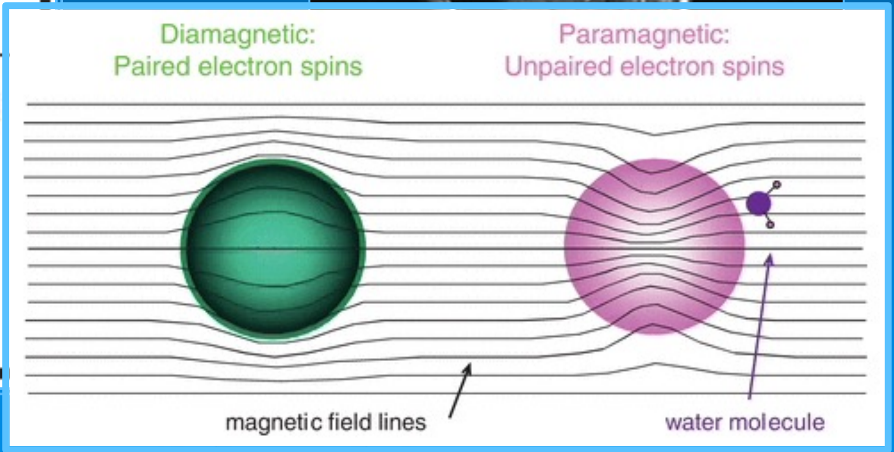
Susceptibility Artifacts

- ✓ ***Susceptibility*: generation of extra magnetic fields in materials that are immersed in an external field**
- ✓ **In T2*-weighted images, susceptibility determines signal loss**
  - **Spin dephasing**



Effects That Cause T2* and T2 Dephasing

Causes of T2* Dephasing	Causes of T2 Dephasing
Spin-spin interactions	Spin-spin interactions
Magnetic field inhomogeneities	
Magnetic susceptibility	
Chemical shift effects	



Bushberg et al, The essential physics of medical imaging 2012 Lippincott Williams & Wilkins

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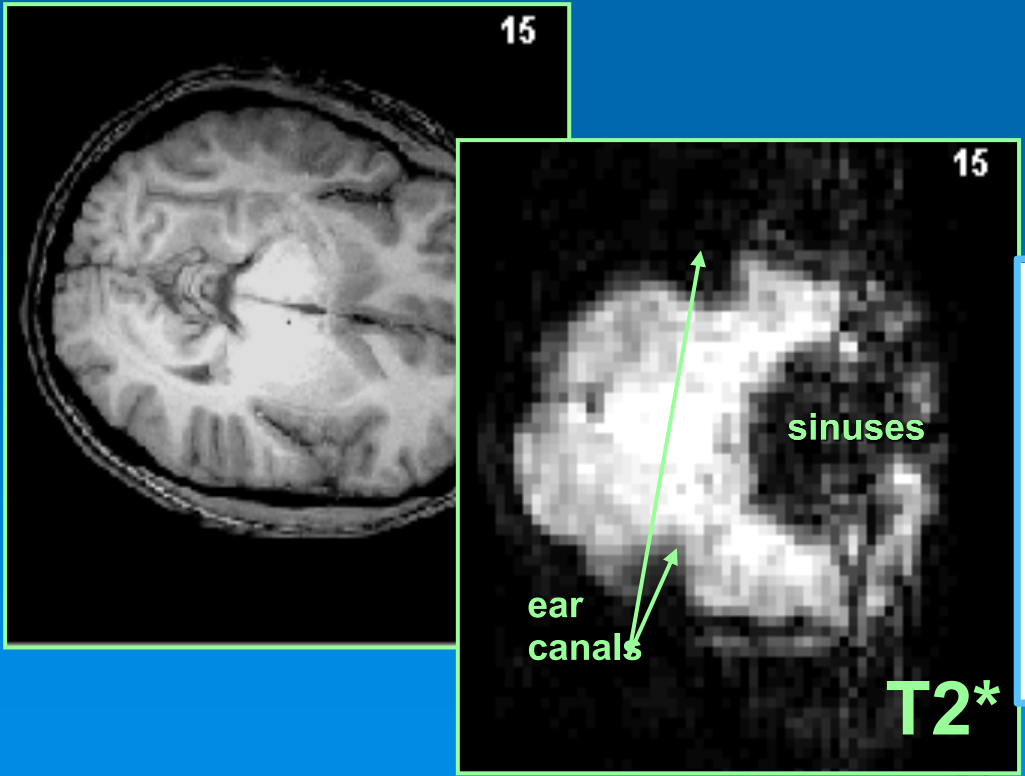
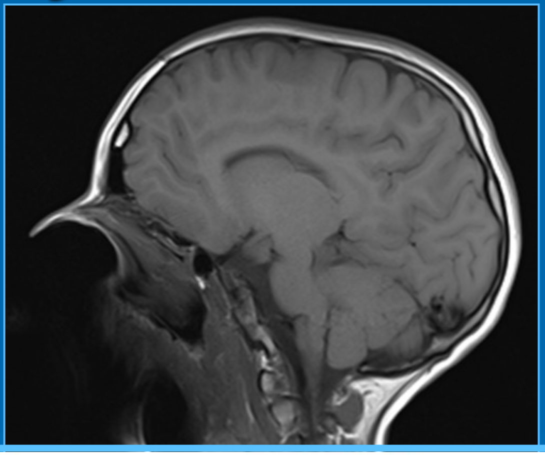
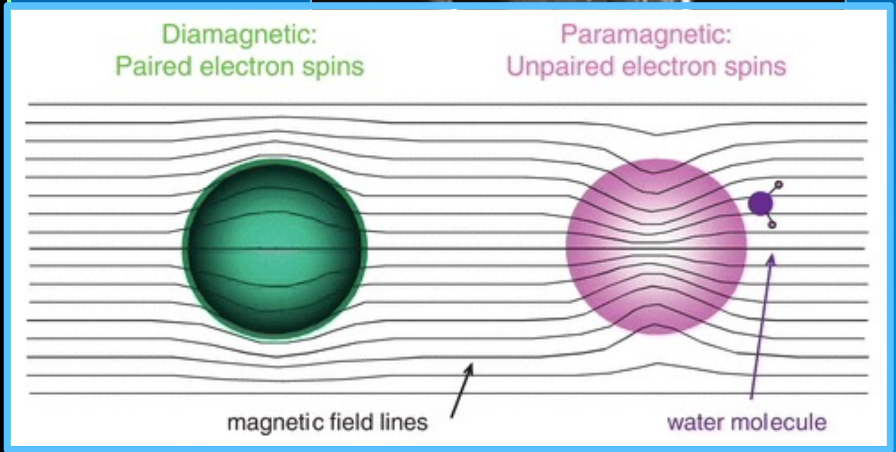
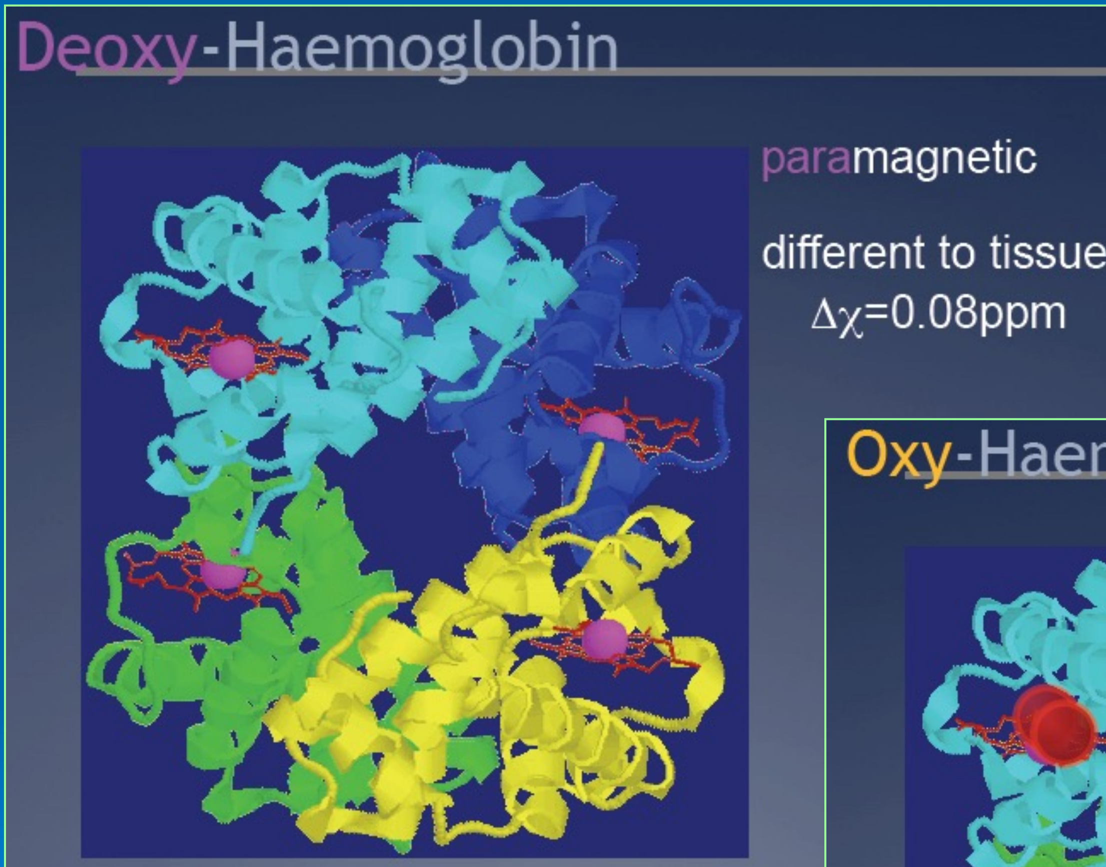


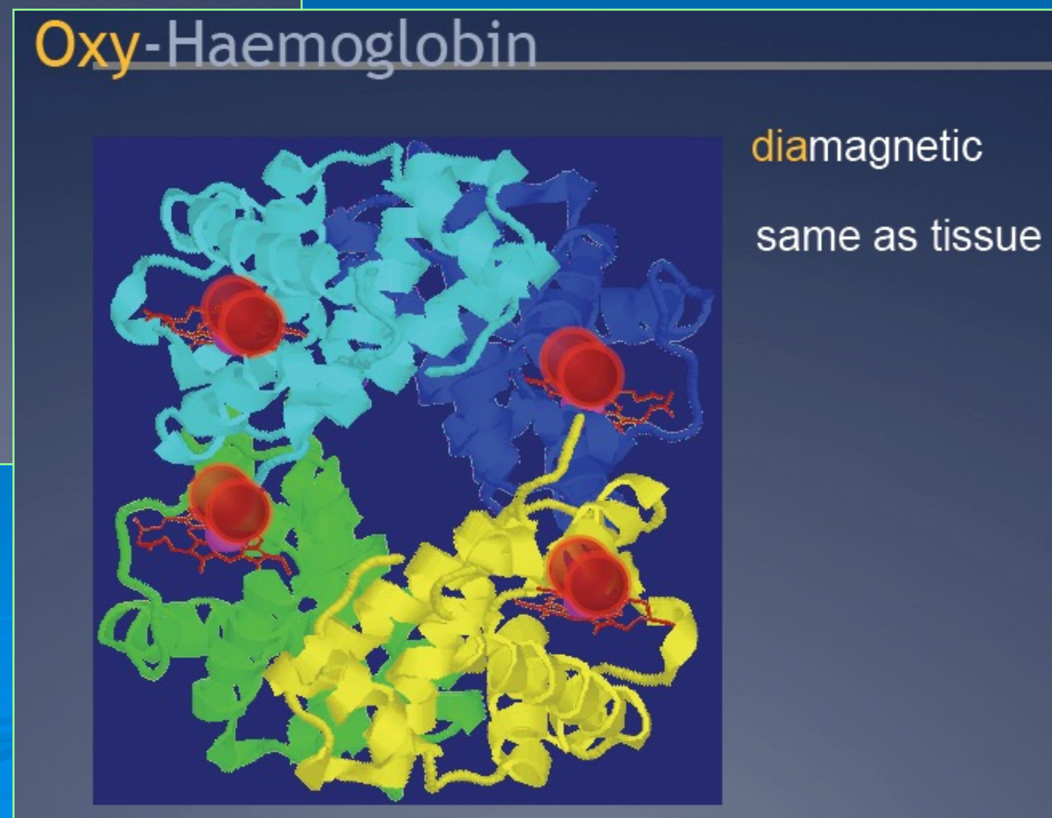




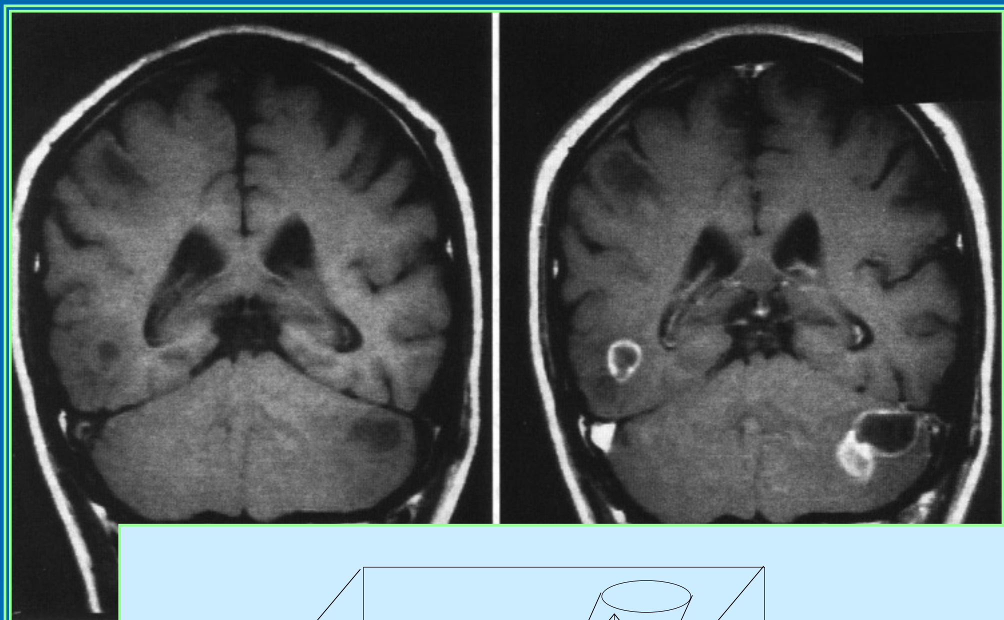
Bushberg et al, The essential physics of medical imaging 2012 Lippincott Williams & Wilkins

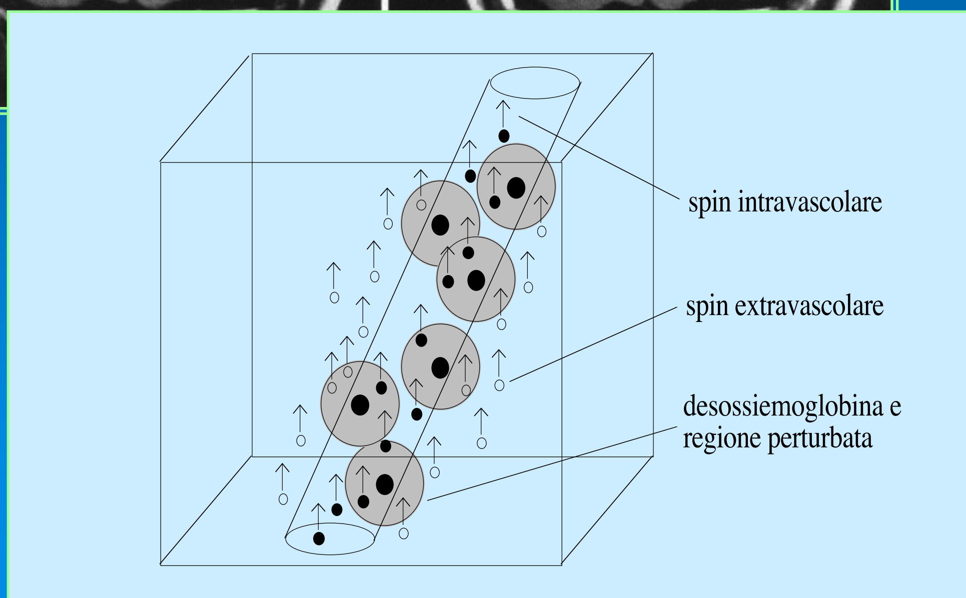
Blood magnetic properties





Paramagnetic contrast agents





In fMRI the deoxyhemoglobin is exploited as an endogenous contrast agent

- BOLD contrast
  - Blood
  - Oxygen
  - Level
  - Dependent

BOLD fMRI … on one slide!

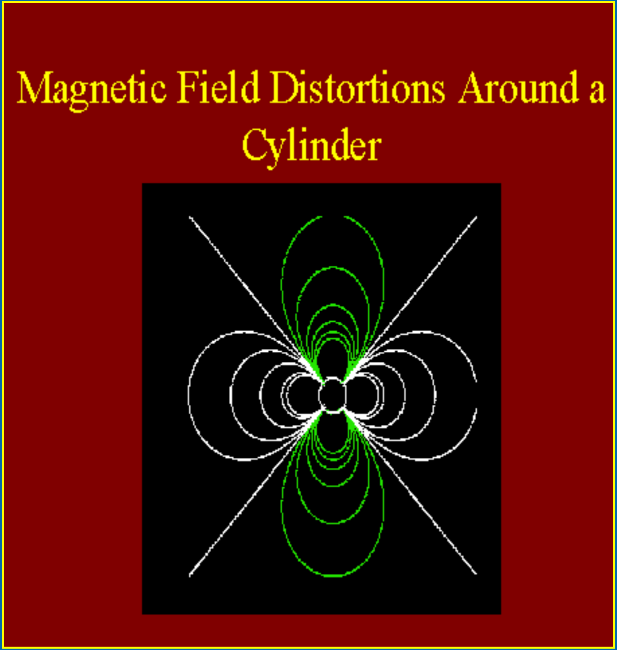
Blood **O**xigen **L**evel **D**ependent

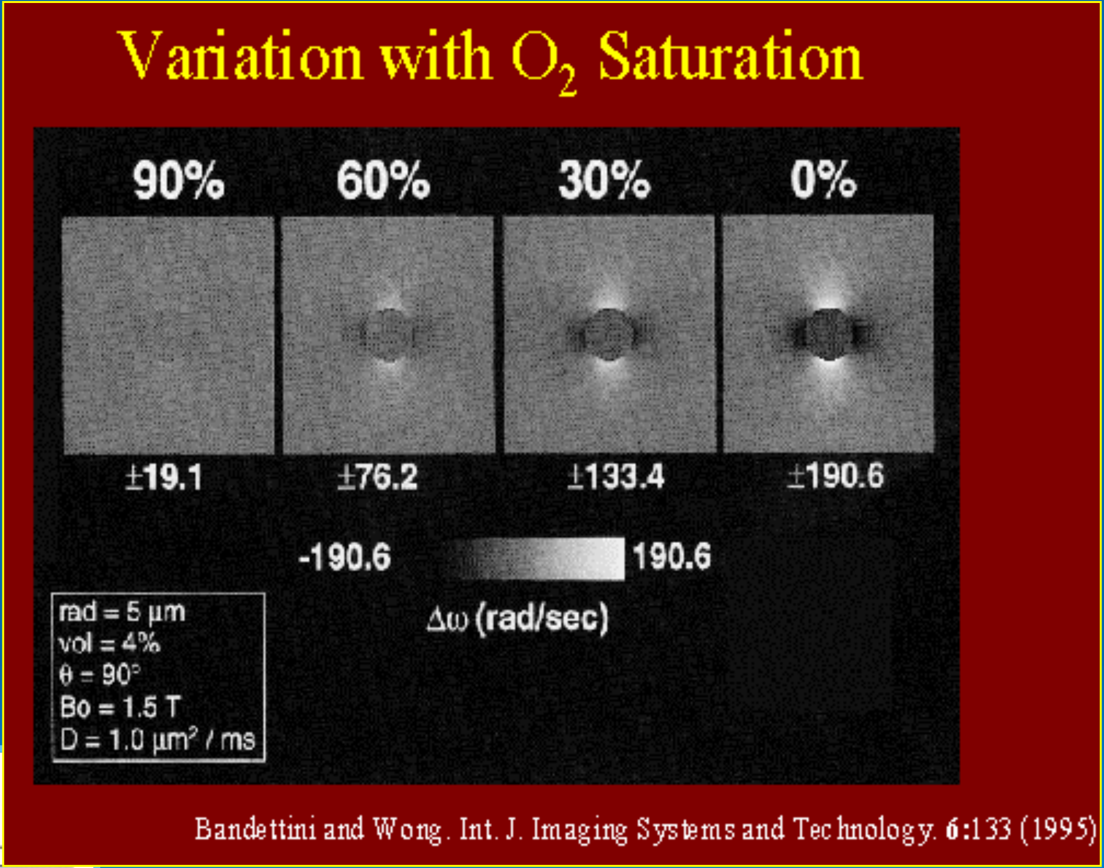
Stimulus occurs
↓
Neurons are activated
↓
Oxygen is consumed
$Hb0_2 \rightarrow Hb$
↓
Changes in $CMR0_2$, CBF, and CBV
↓
Return to baseline

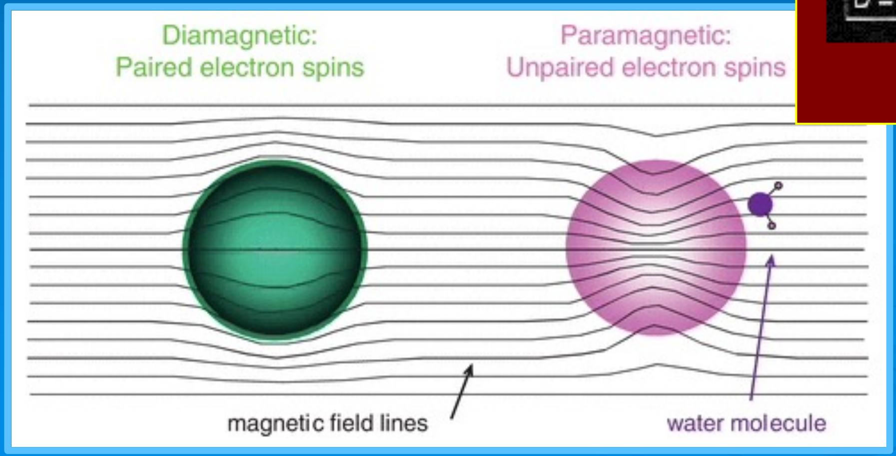
- **$Hb0_2$ is diamagnetic**
  - creates a weak opposing magnetic field
- **Hb is paramagnetic**
  - a strong additive magnetic field
- ***Increasing field strengths cause the signal to dephase more quickly, decreasing the signal***
  - T_2* effect

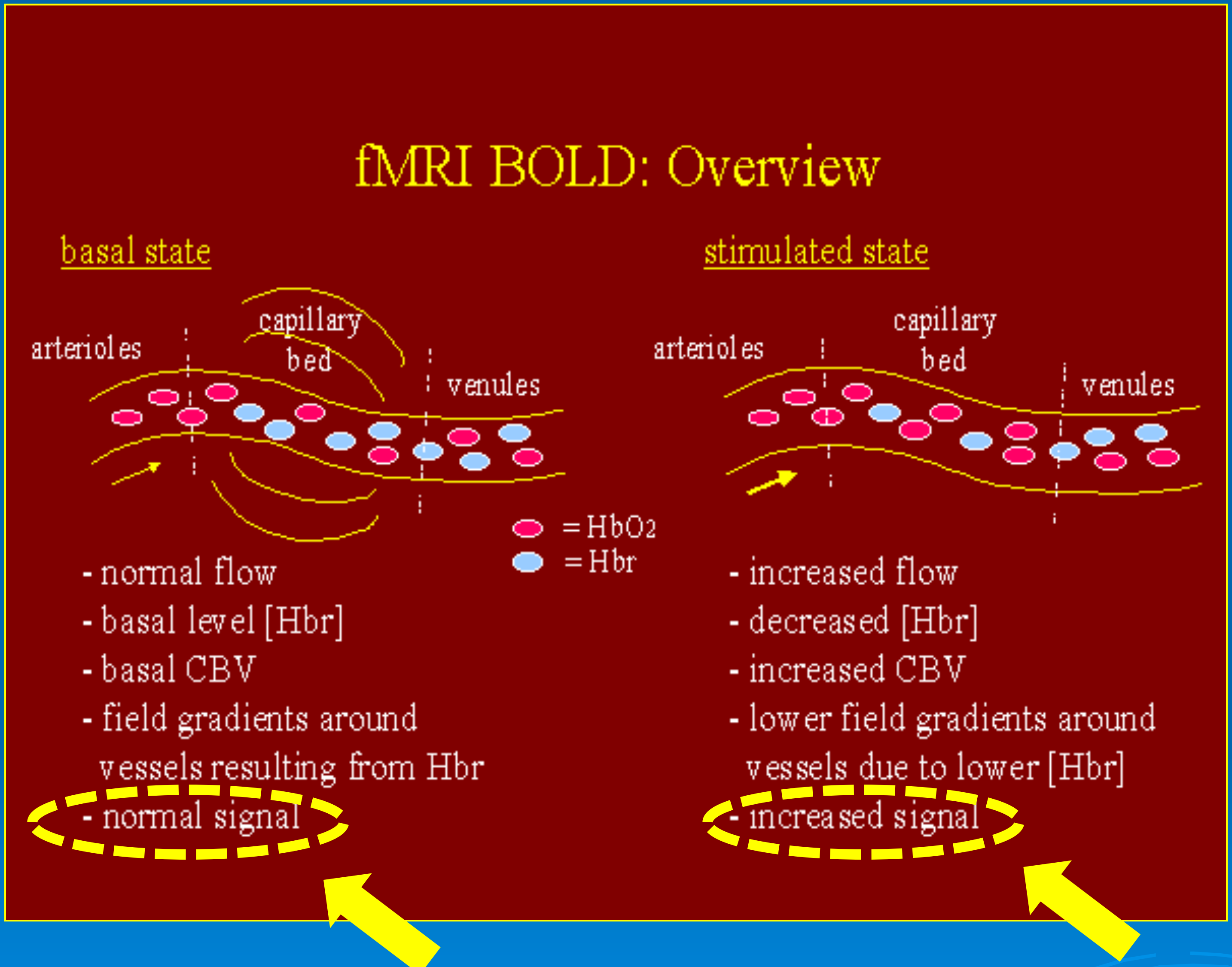
www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/brain-activation-bold-contrast

Is BOLD signal visible ?







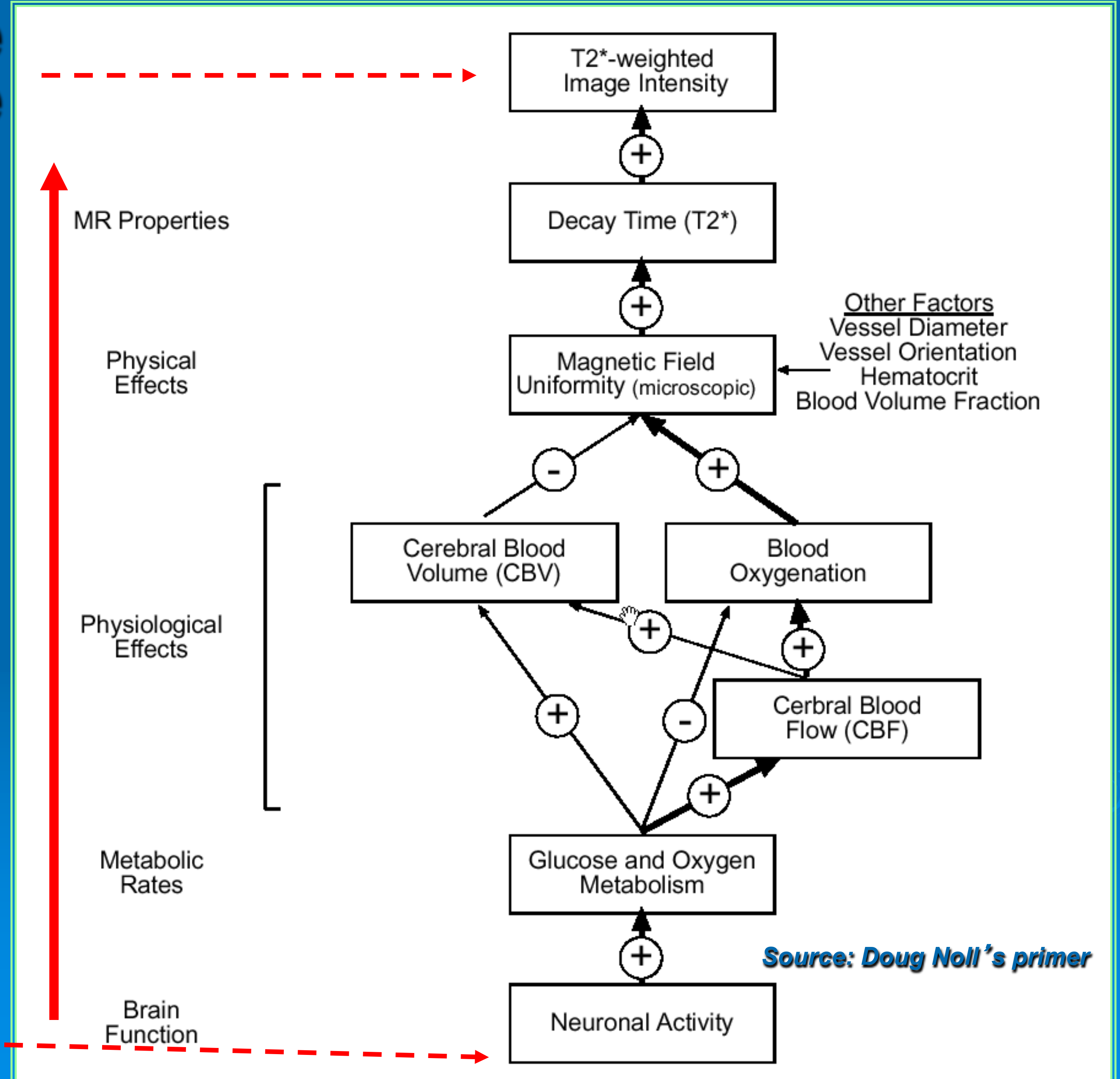


Blood Oxygen Level Dependent (BOLD) signal is a relative value:

✓It is necessary to collect both basal and stimulated images and comparing them

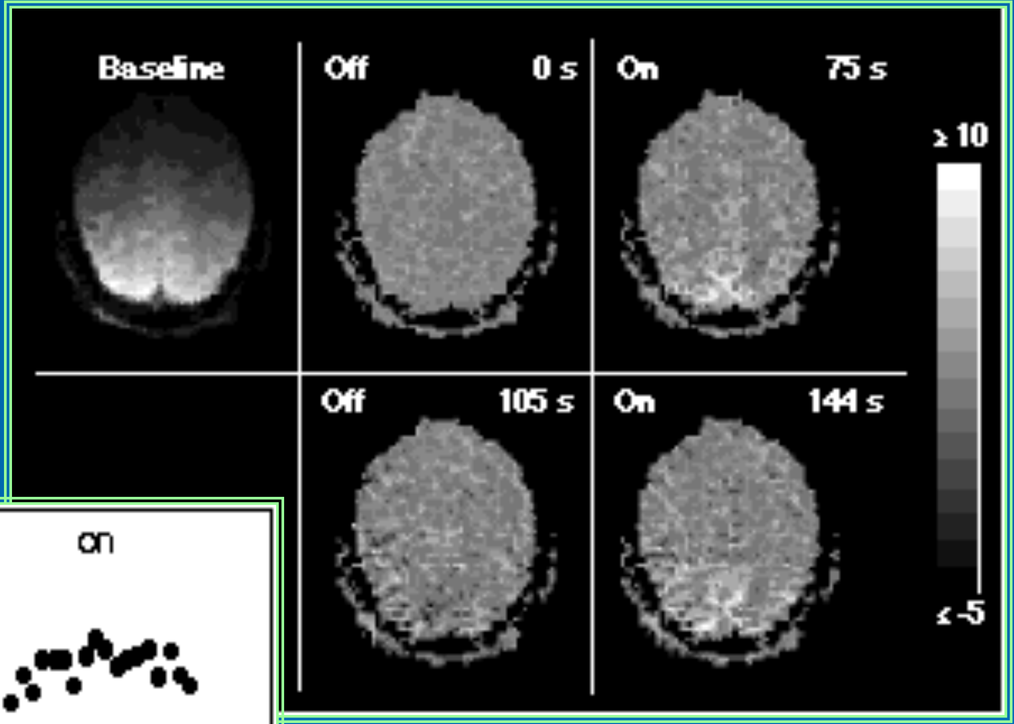
What we observe

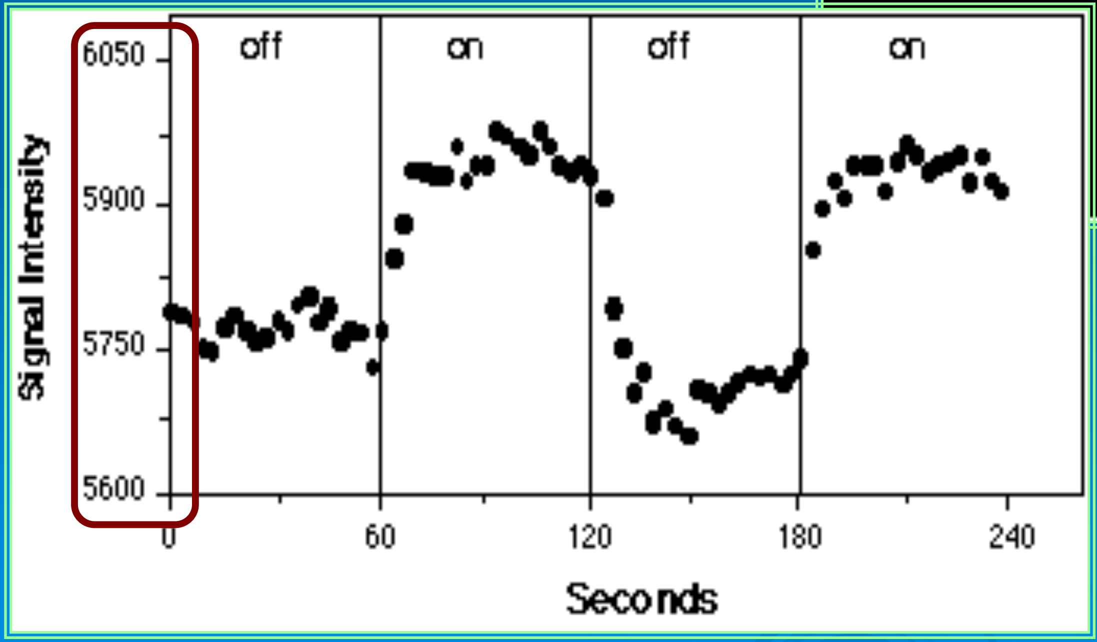
What we want to study



Source: Doug Noll's primer

First Functional Images

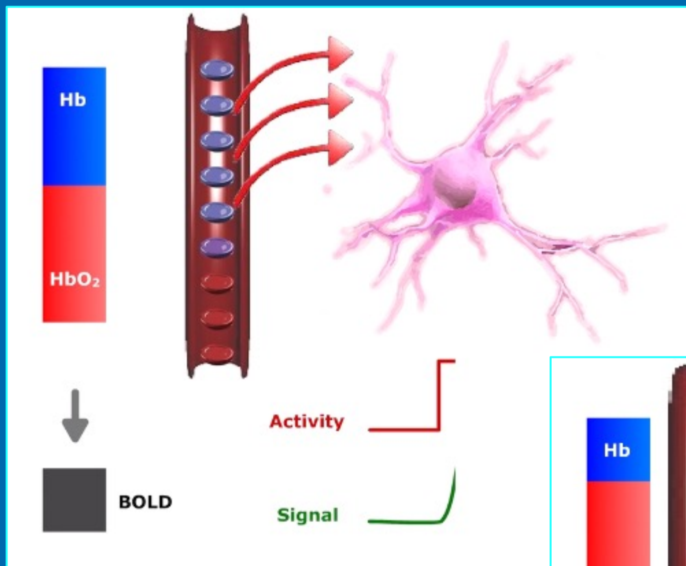


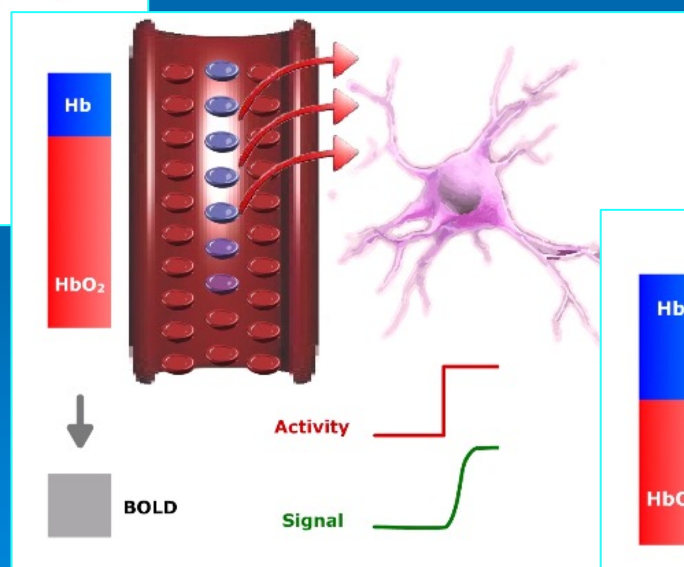


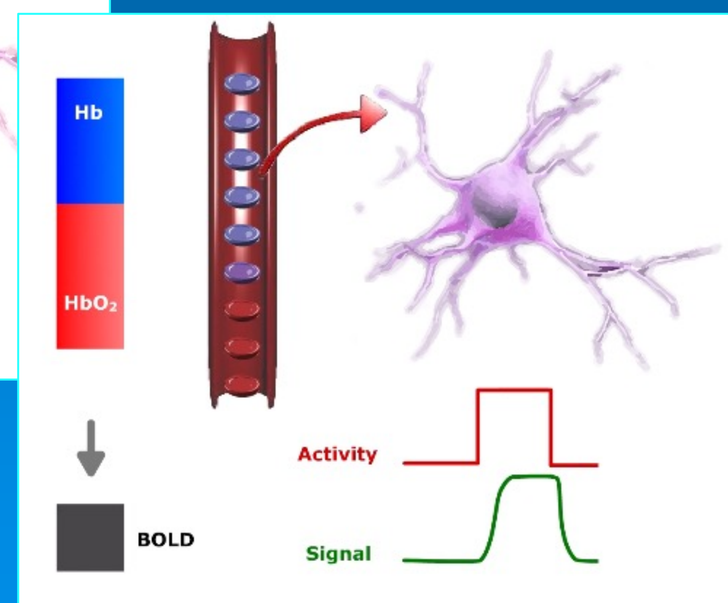
Source: Kwong et al., 1992

https://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/analysis-functional-mri-data

Hemodinamic response and MRI signal

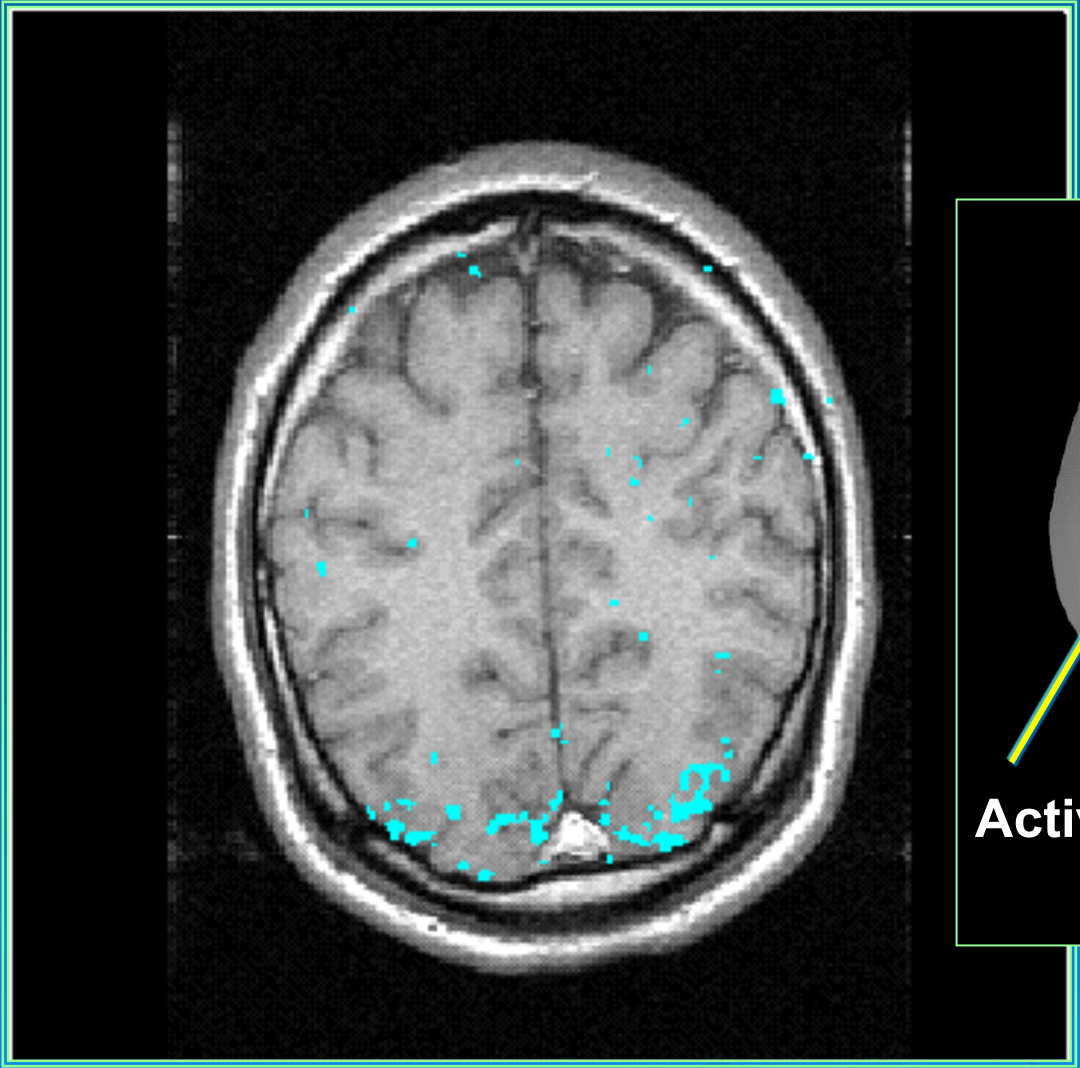


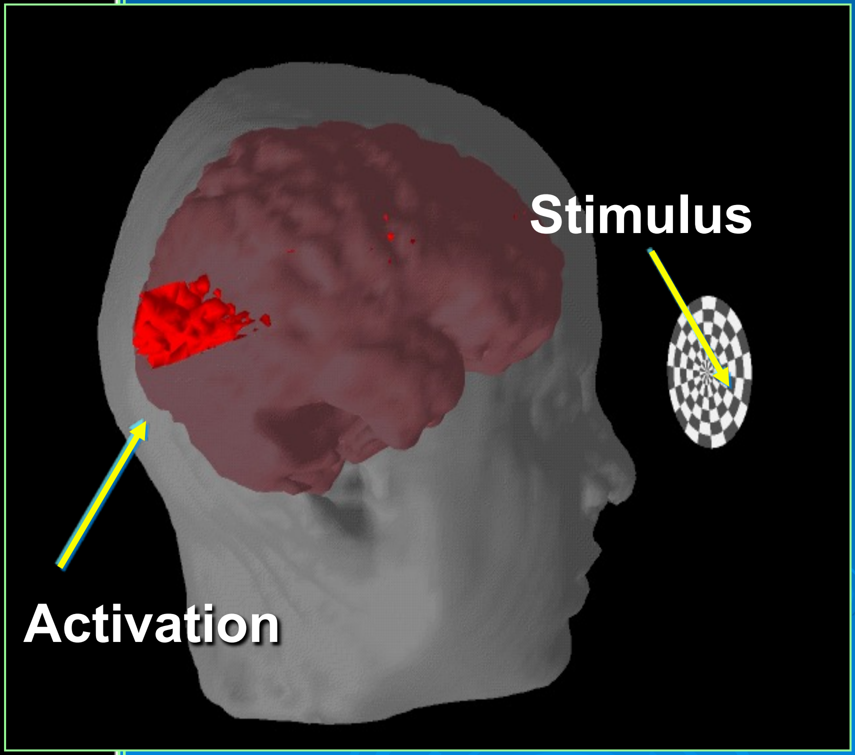




https://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/brain-activation-bold-contrast

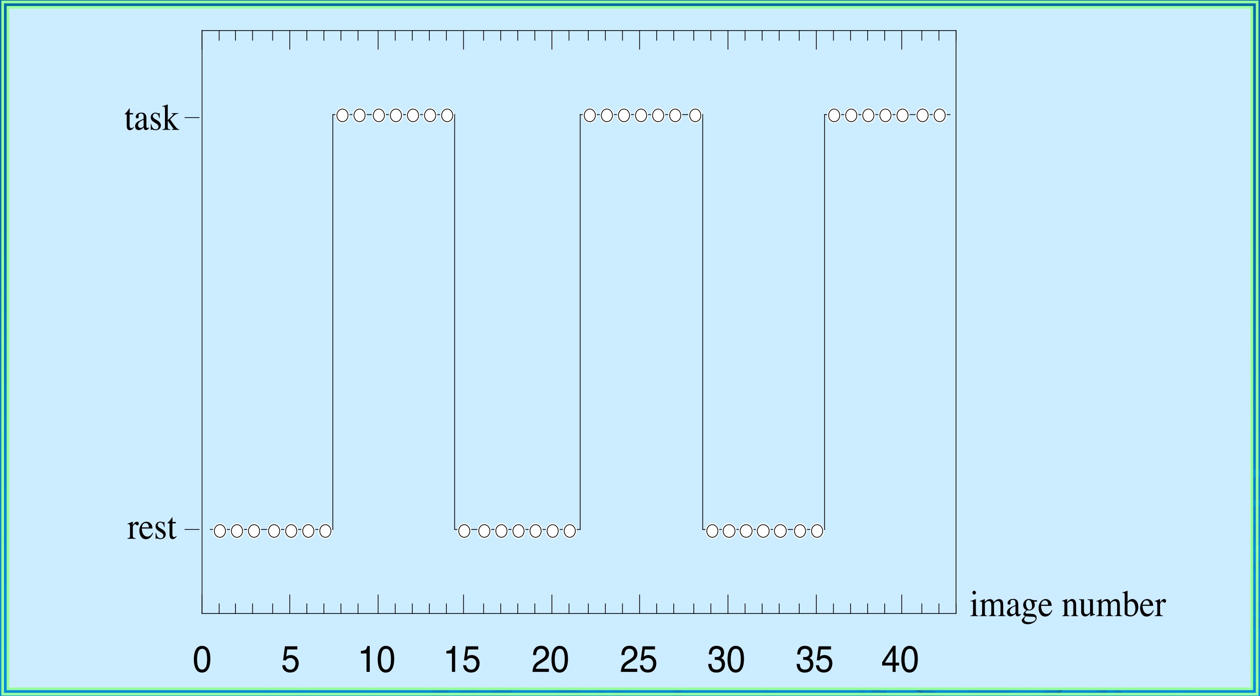
Visual stimulus





Block paradigm experimental protocol

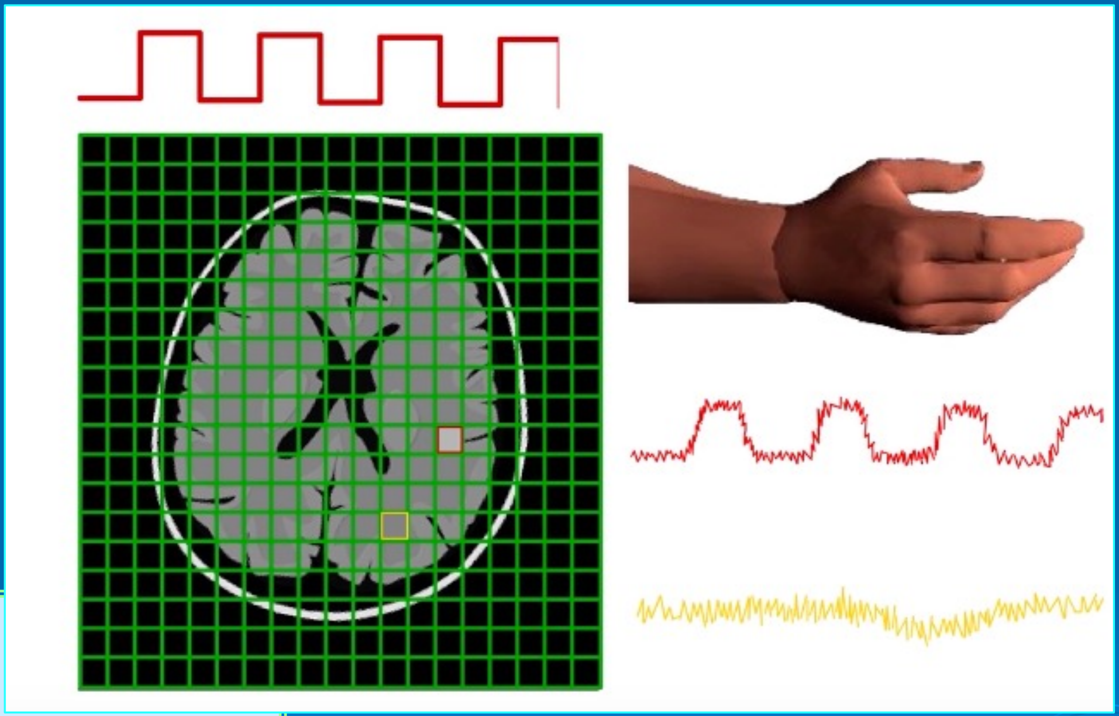
- about ~150 images
- Task and rest periods
- Total acquisition times ~5 minutes

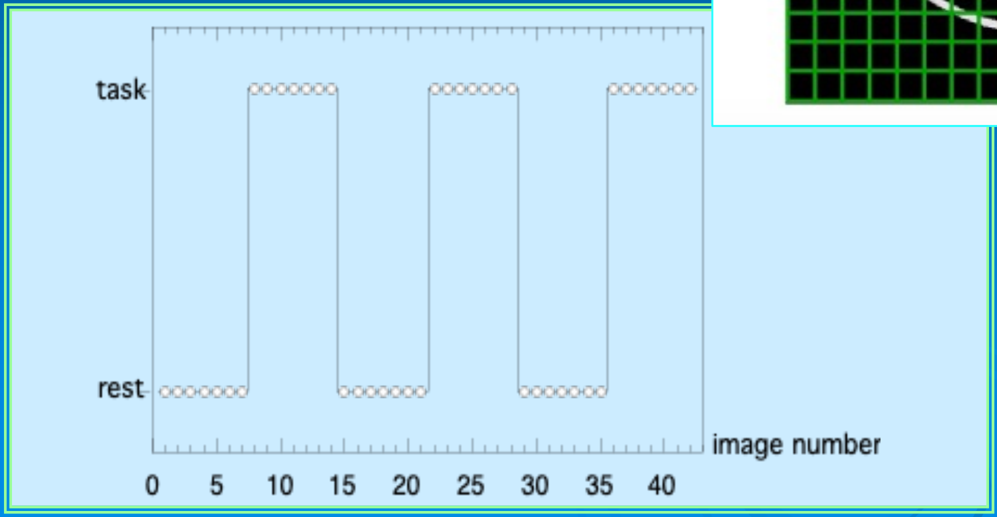


https://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/analysis-functional-mri-data

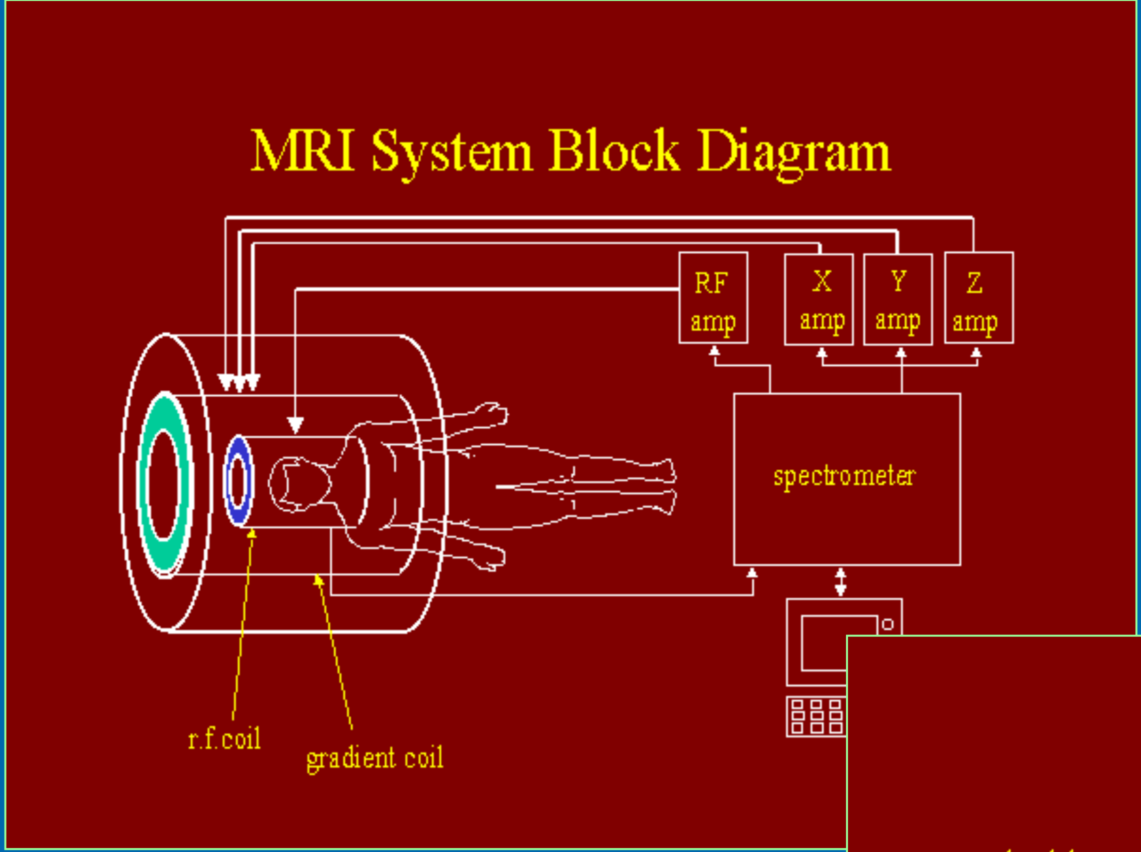
Block paradigm experimental protocol

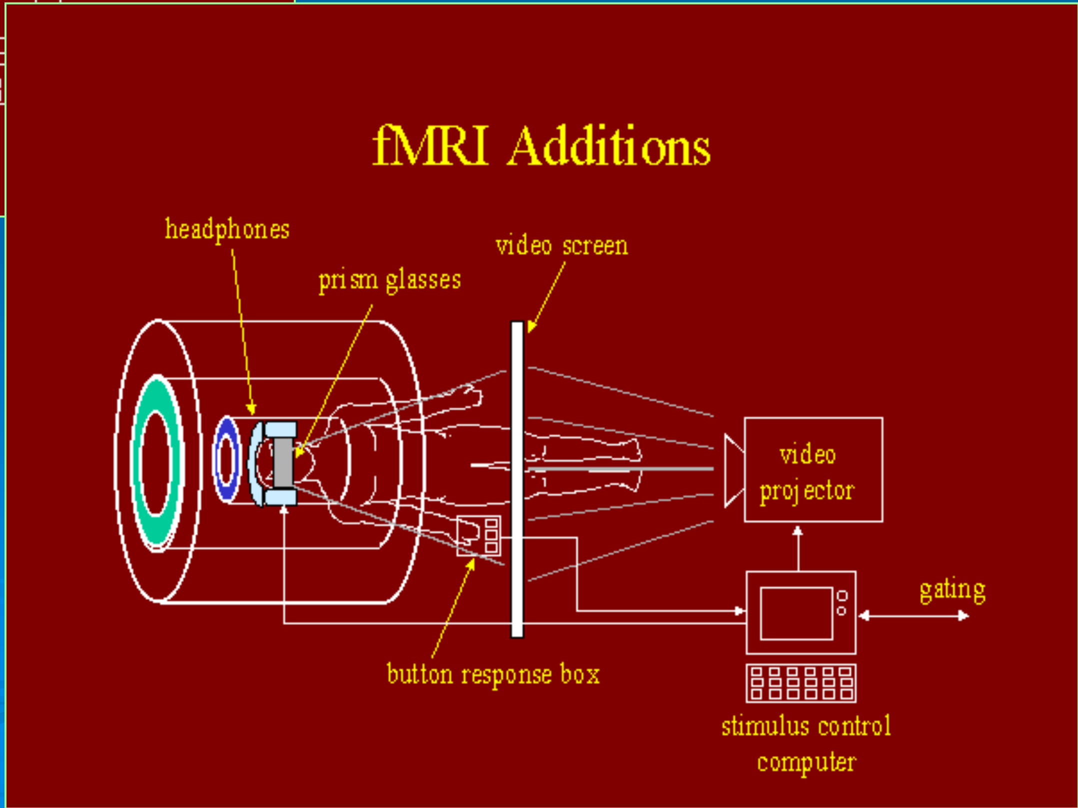
- Task and rest periods



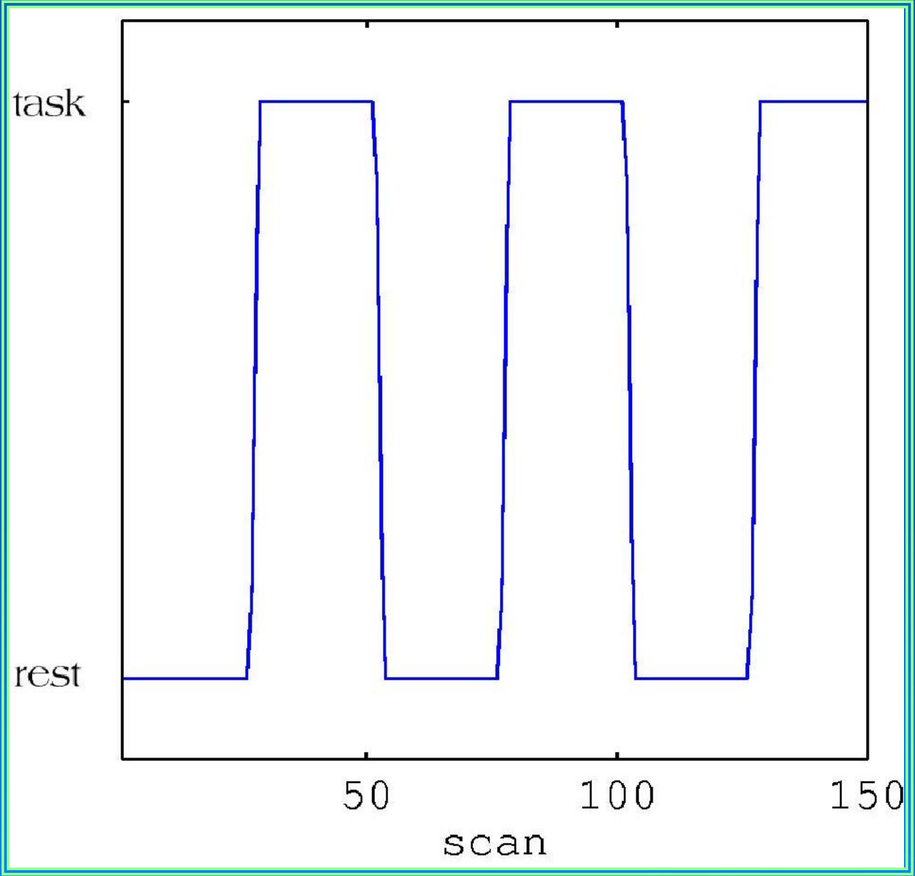


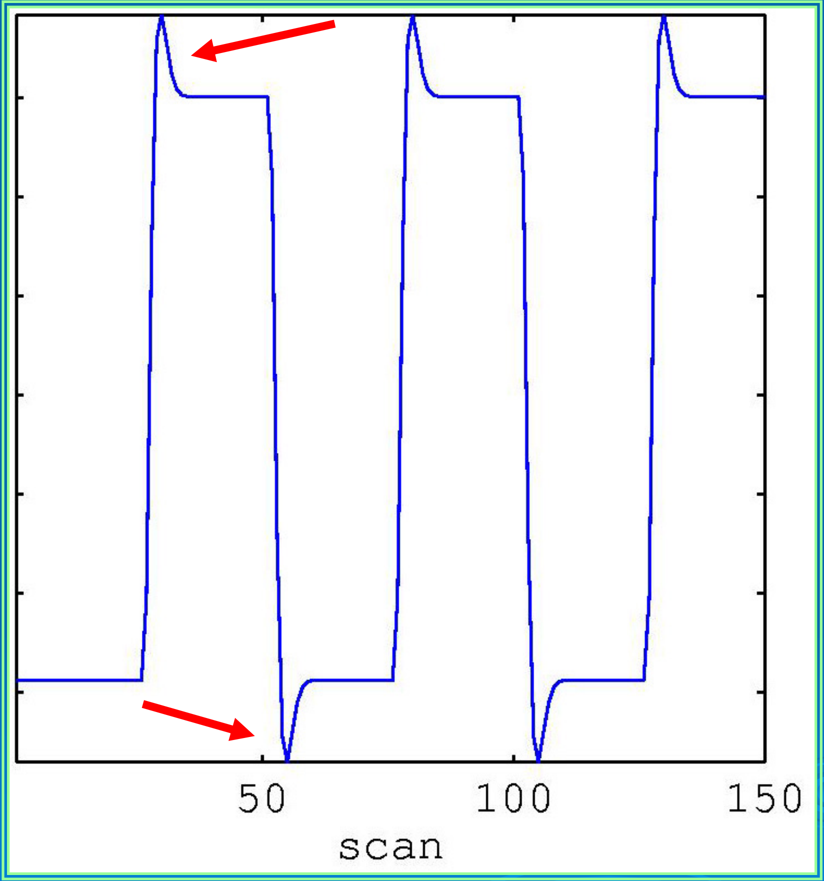
How to do


MRI System Block Diagram
RF amp
X amp
Y amp
Z amp
spectrometer
r.f. coil
gradient coil


fMRI Additions
headphones
video screen
prism glasses
video projector
gating
button response box
stimulus control computer

Block protocol and BOLD signal

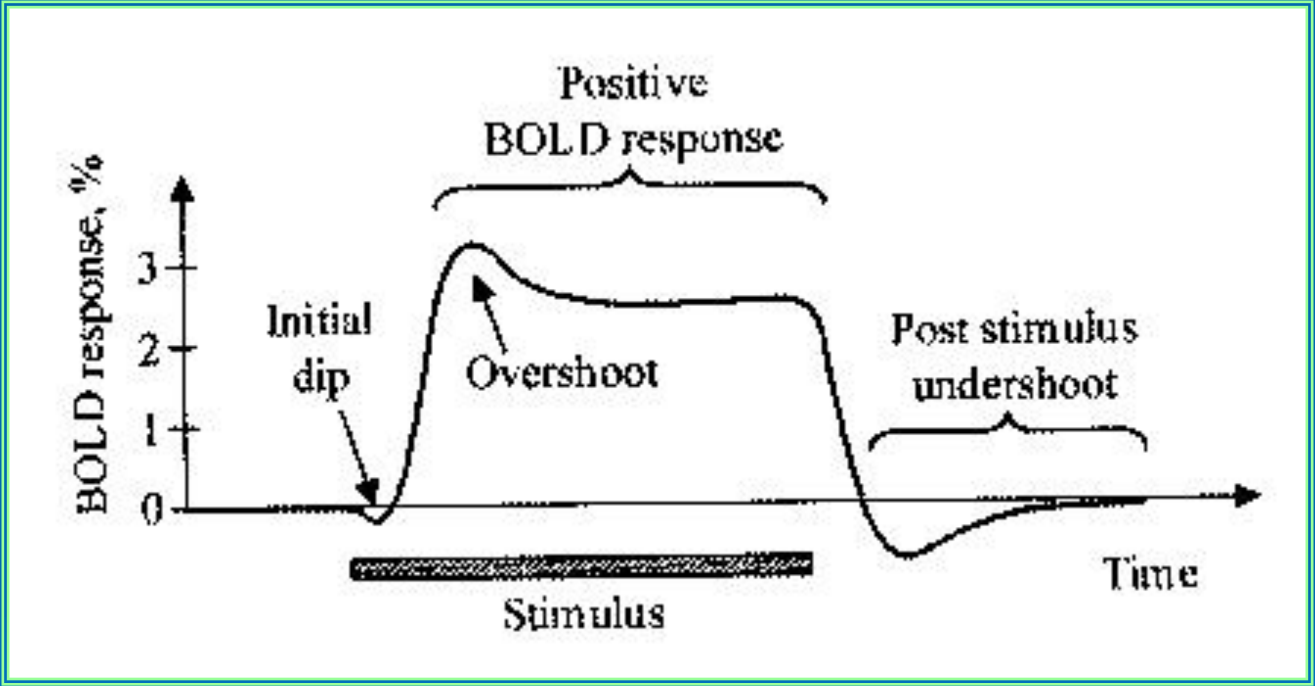




Block protocol:
Timing of the stimulus

BOLD signal:
Signal intensity of a voxel during the scans (time)

Hemodynamic Response Function



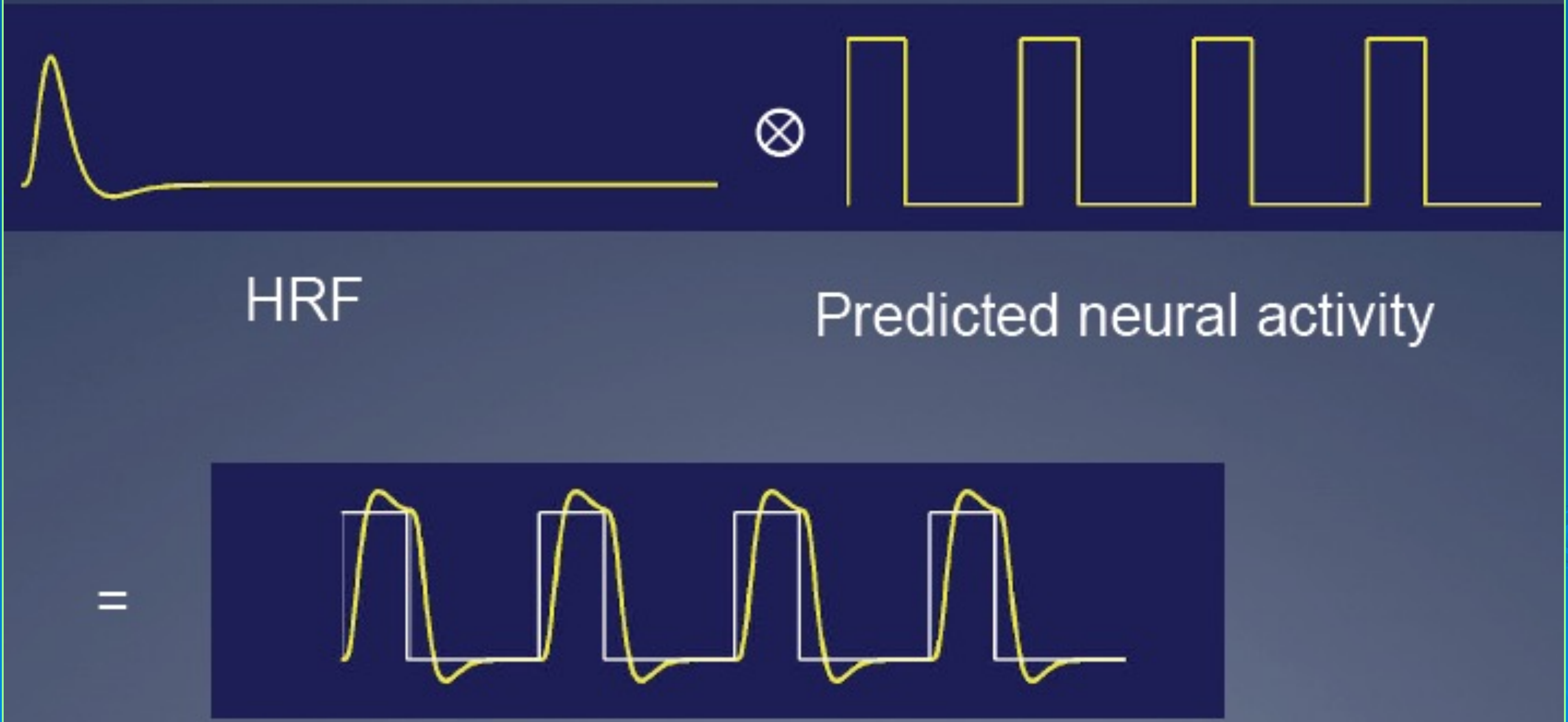
- ✓ % signal change
  - = (point – baseline)/baseline
  - usually 0.5-3%
- ✓ initial dip
  - more focal
  - somewhat elusive so far
- ✓ time to rise
  - signal begins to rise soon after stimulus begins
- ✓ time to peak
  - signal peaks 4-6 sec after stimulus begins
- ✓ post stimulus undershoot
  - signal suppressed after stimulation ends

HRF

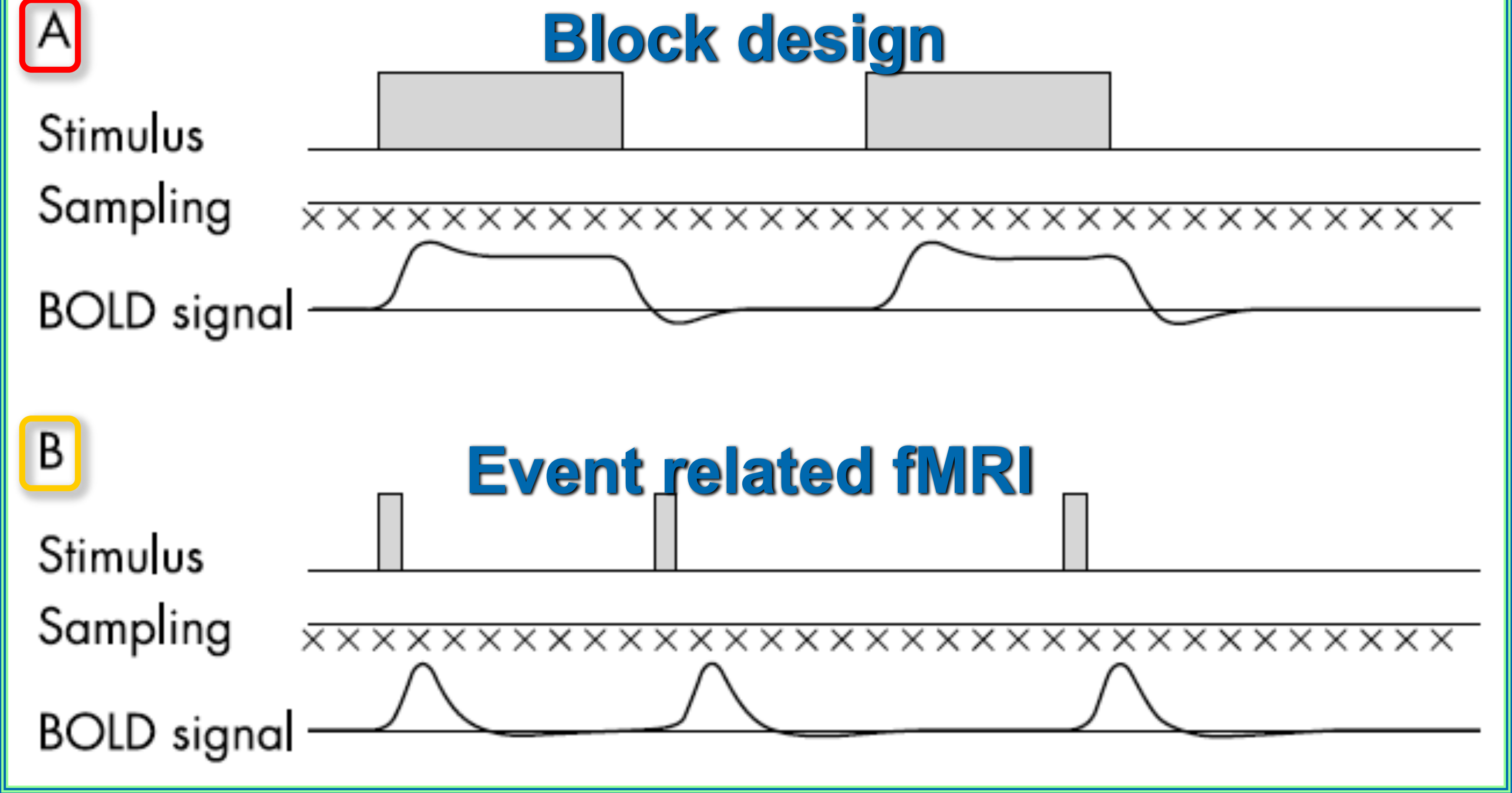
The haemodynamic response to a stimulus is blurred and delayed

Predicted Response

* The process can be modeled by **convolving** the activity curve with the HRF

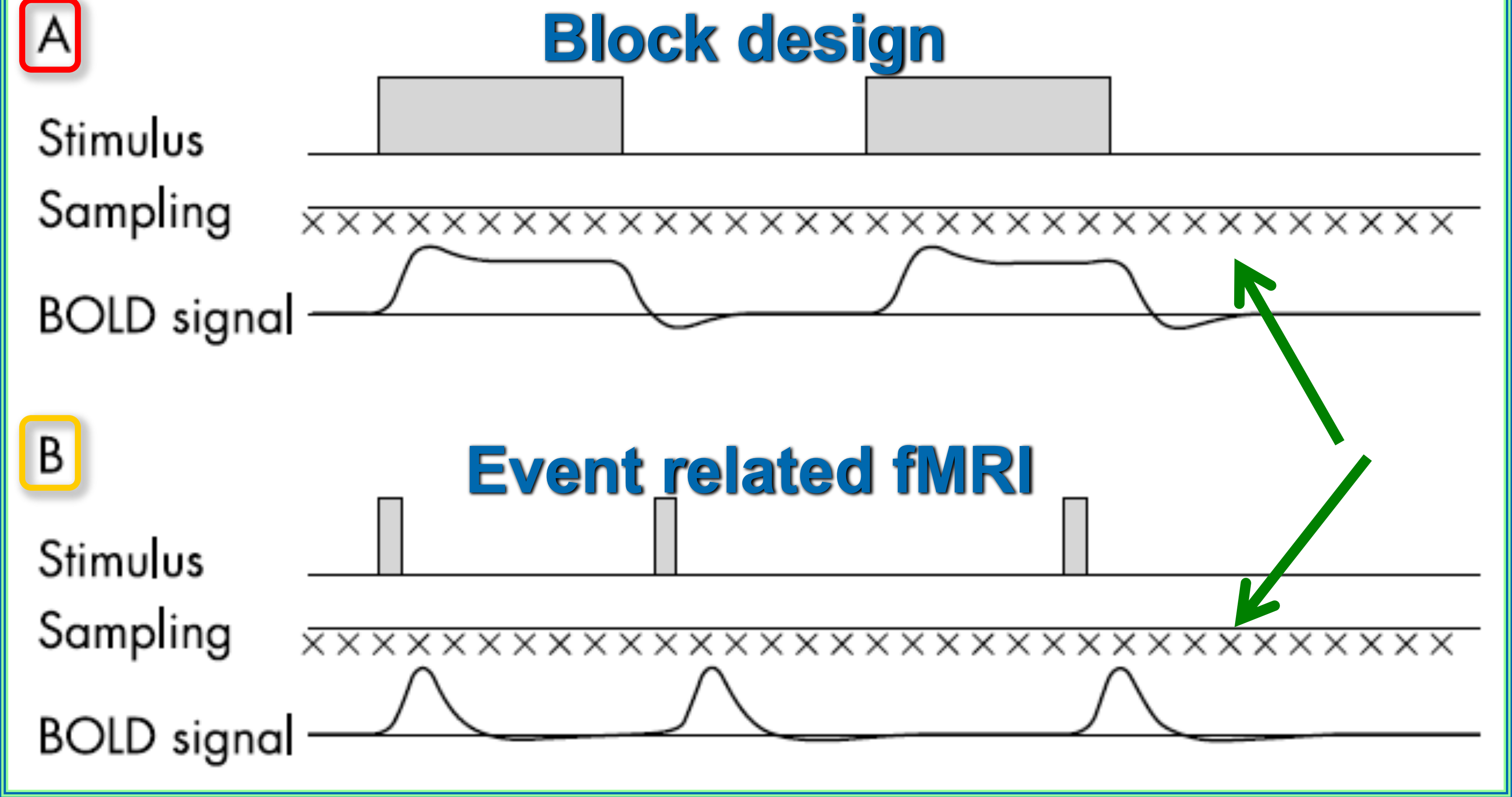


Predicted response



A. **Block design** a relatively long stimulation period is alternated with a control period
- ~ 30 second

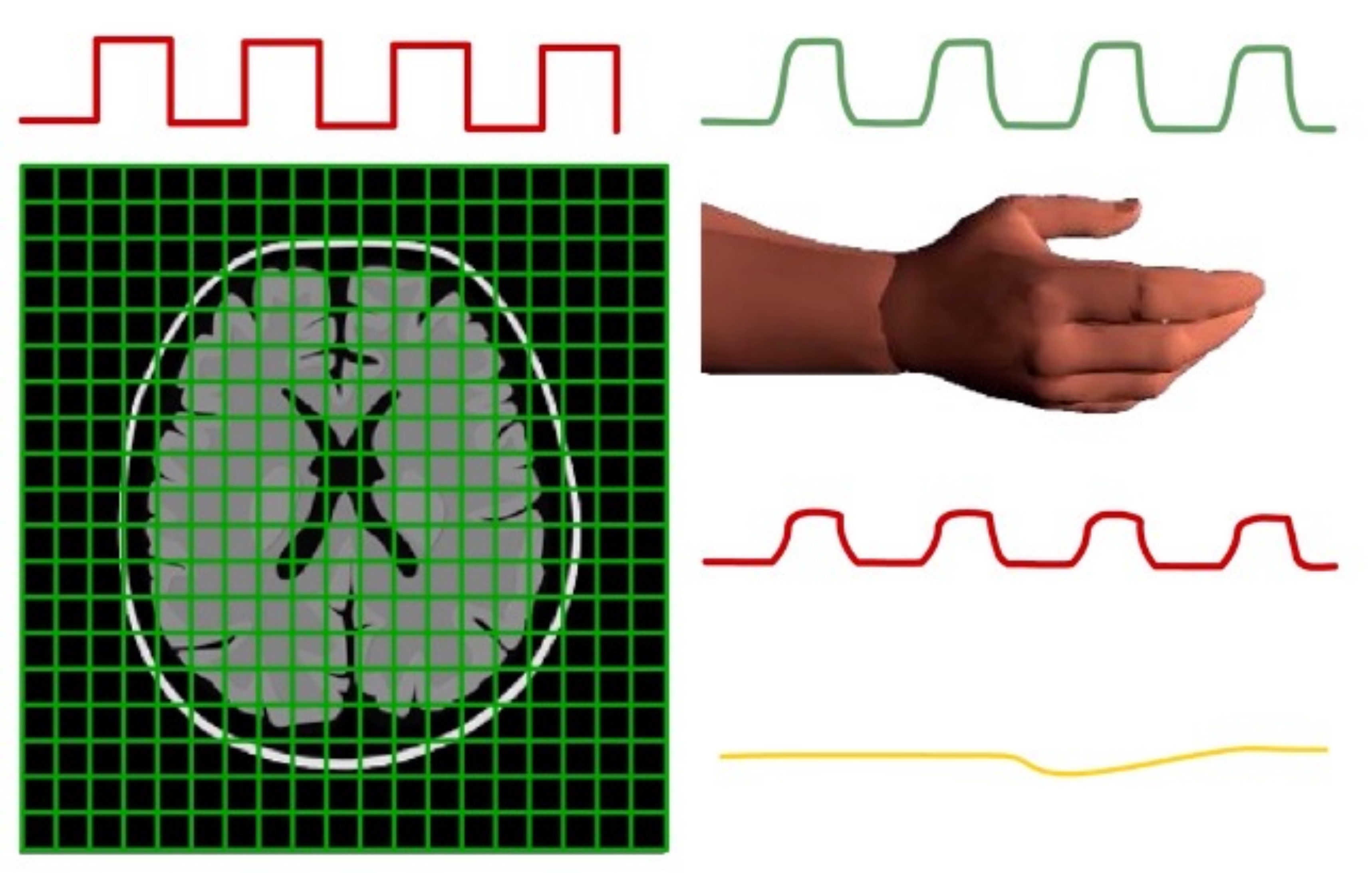
B. **Event related design** a brief stimulus period is used
- either periodic or randomized



In both cases volumes of data (indicated by the crosses) are collected continuously, typically with a repeat time of 3 to 5 seconds

- 192 repeated volumes
- ~ 20 slices per volume

fMRI modelling



https://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/analysis-functional-mri-data

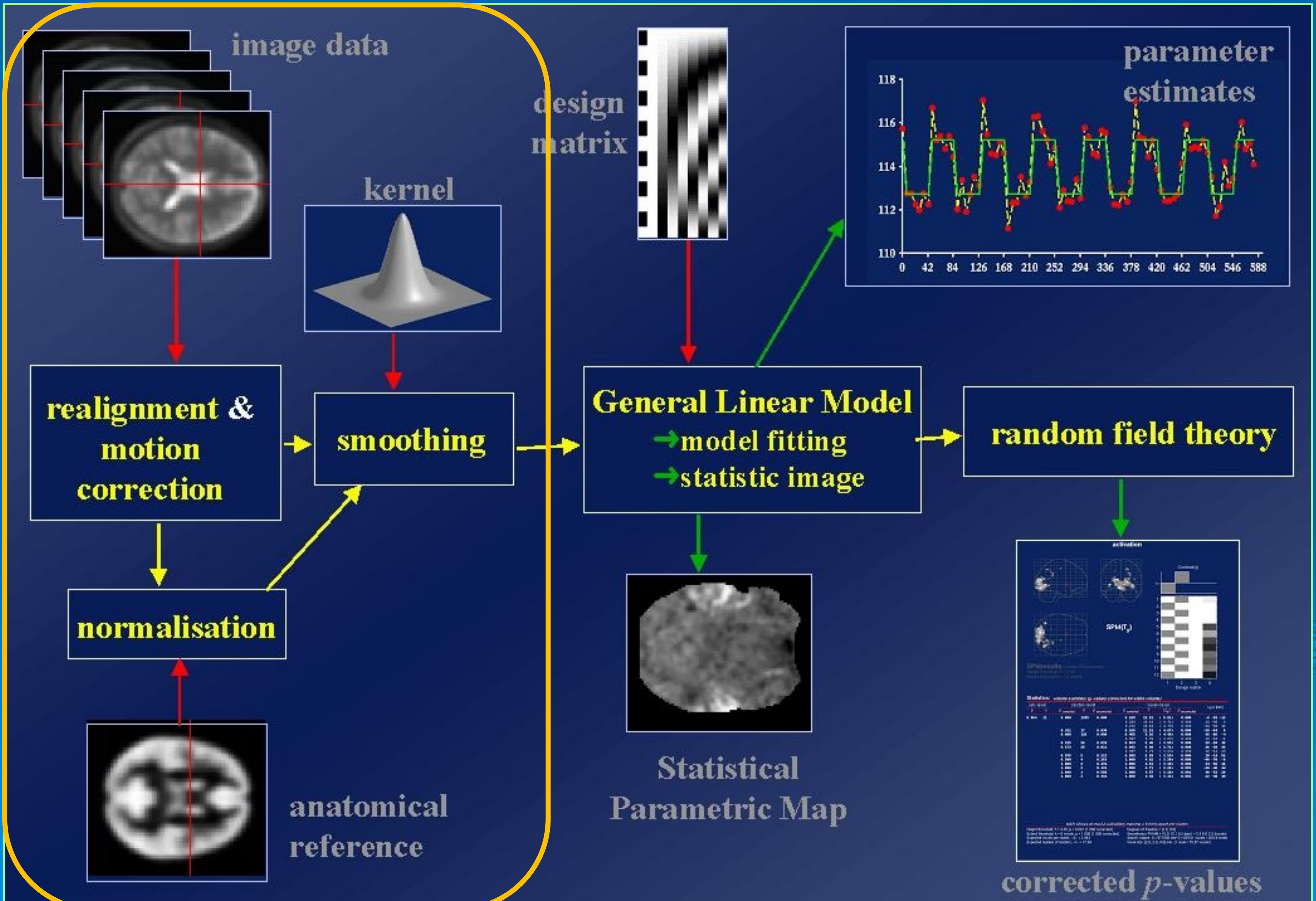
DATA ANALYSIS

GLM

General linear model

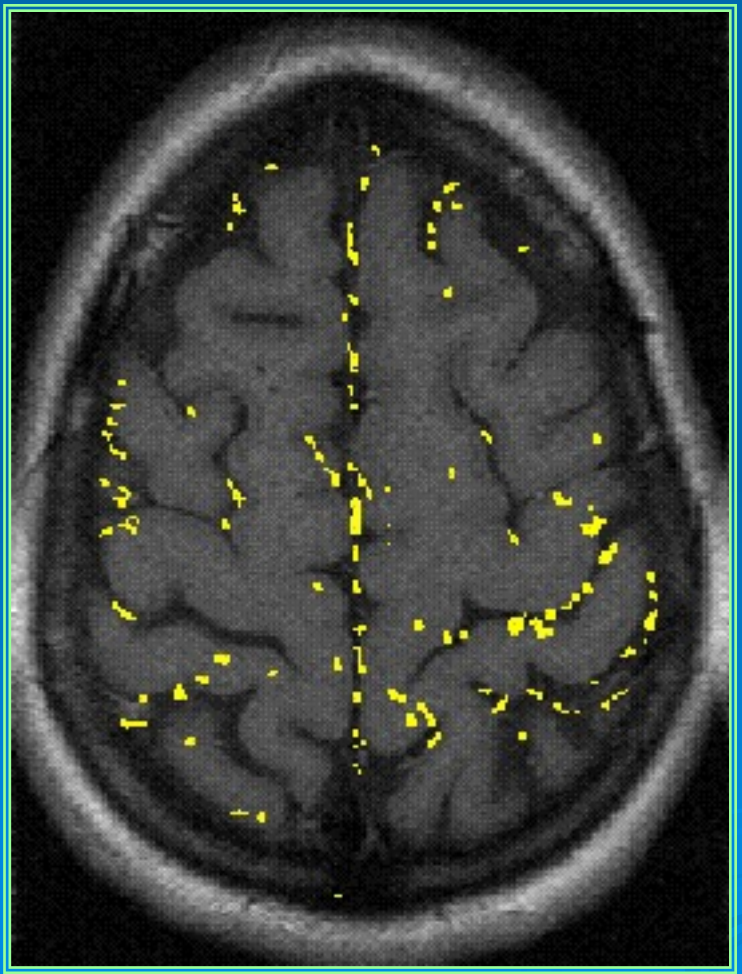
- **Standard GLM Analysis:**
  - Correlate model at each voxel separately
  - Measure residual noise variance
  - T-statistic = model fit / noise amplitude
  - Threshold T-stats and display map
- Signals of no interest (e.g. artifacts) can affect both activation strength and residual noise variance
- Use pre-processing to reduce/eliminate some of these effects

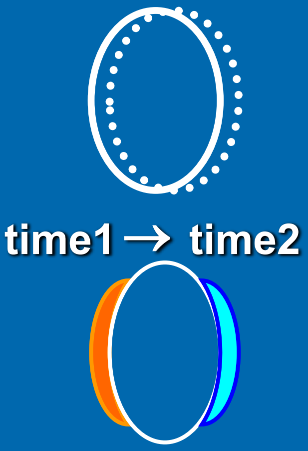
DATA ANALYSIS



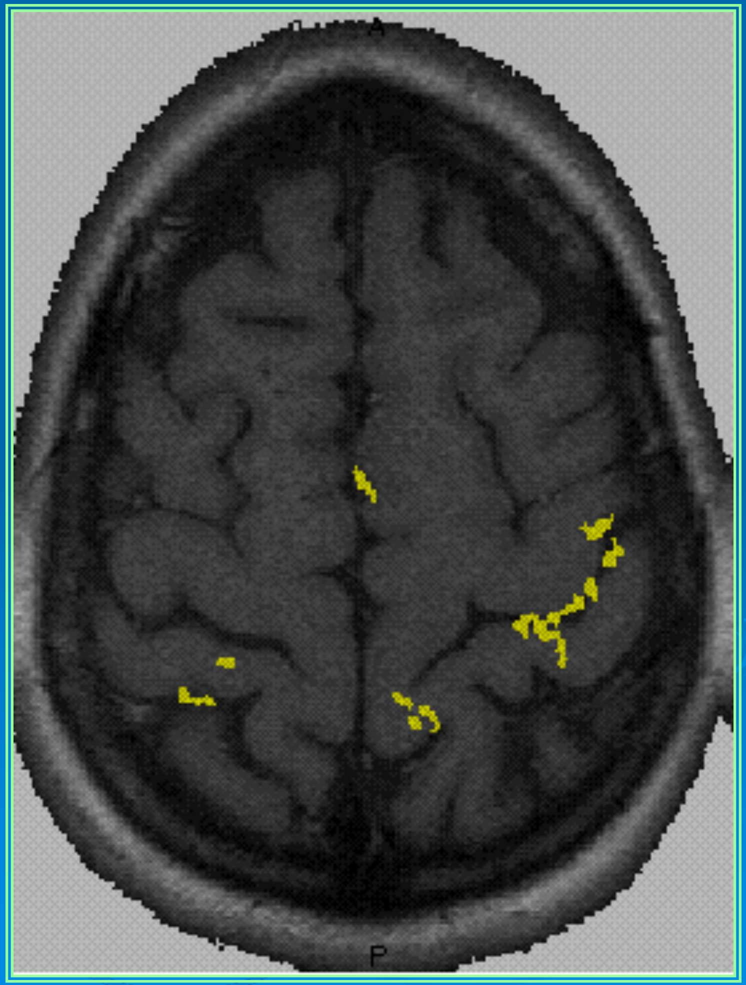
Head Motion: Main Artifact

before registration





after registration

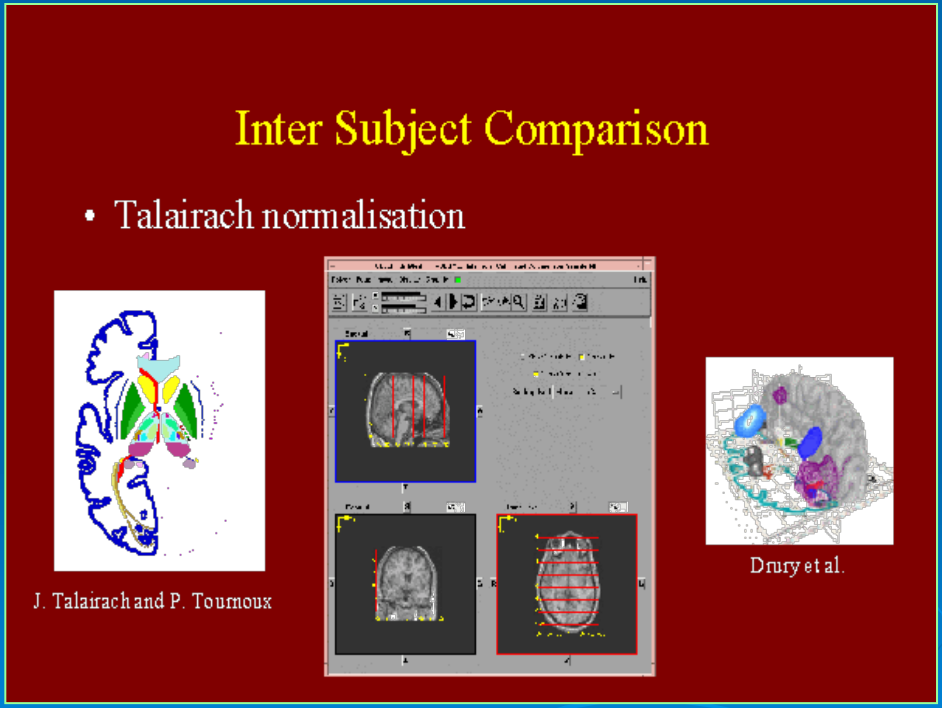


Normalization

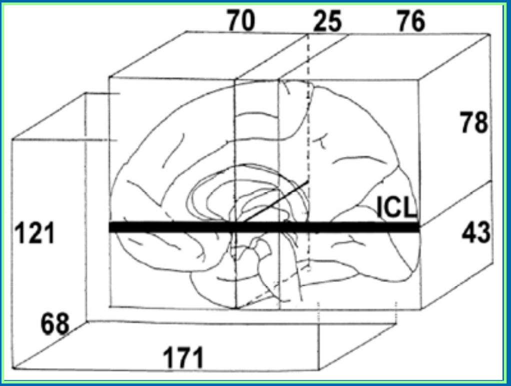
Spatial normalization refers to transforming images so that anatomy shown for all people is the same shape and size

No spatial normalization in clinical application

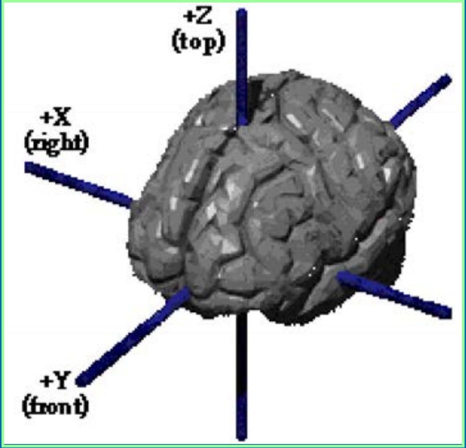
- Stereotactic surgery, radiation therapy
- In clinical application the true dimensions of the patient are necessary



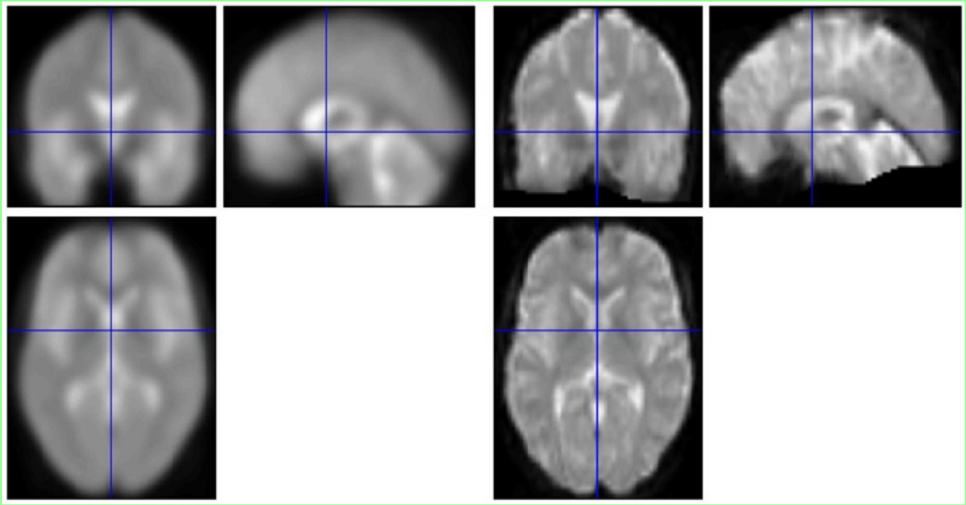
Normalization



Talairach Volume
(136 x 171 x 121 mm)



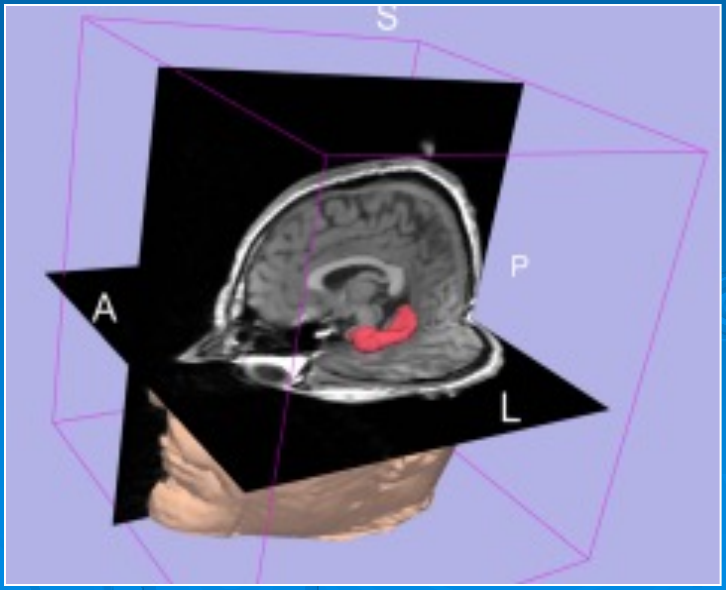
Talairach Coordinates



Template
ICBM152

The MNI Template
Montreal Neurological Institute

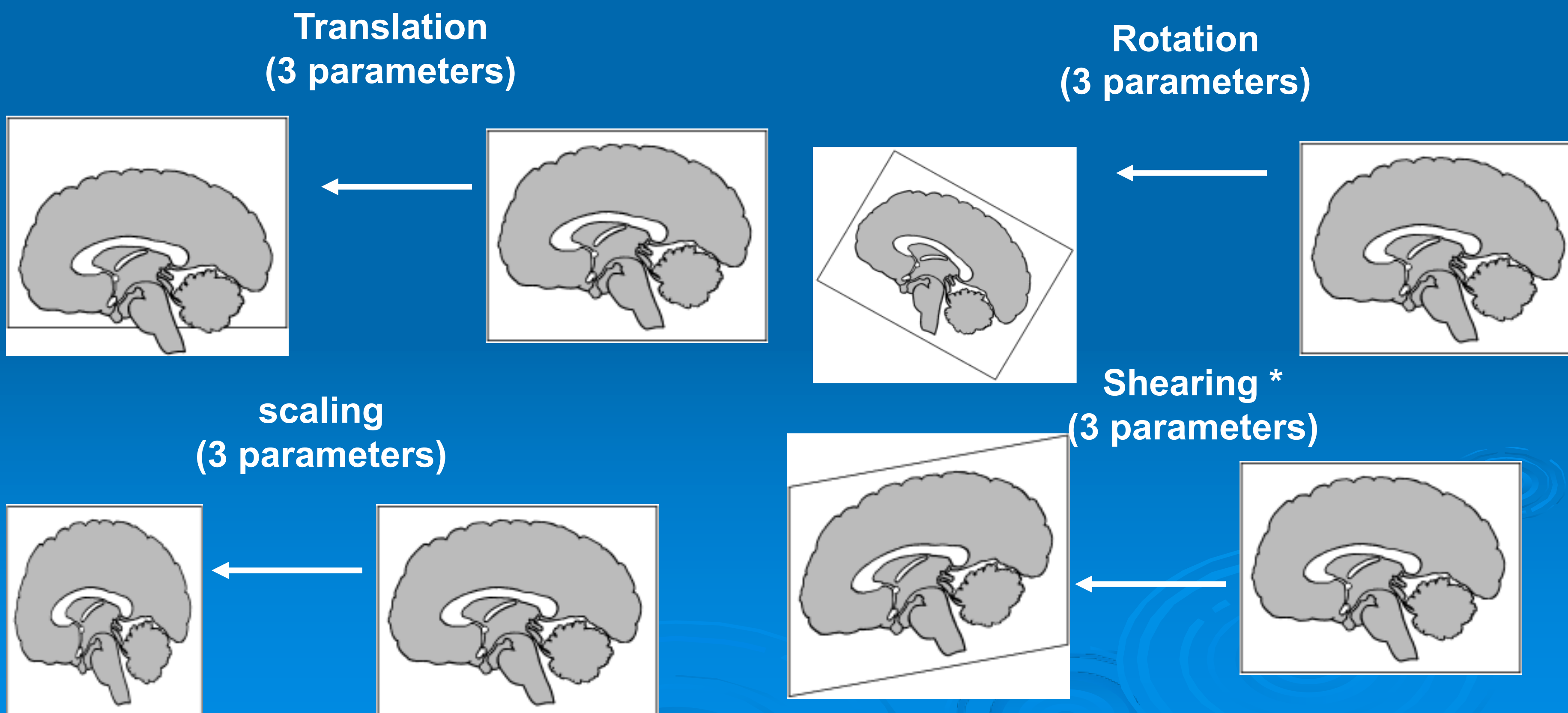
The current standard MNI template is the ICBM152 (International Consortium for Brain Mapping), which is the average of 152 normal MRI scans



AFFINE REGISTRATION

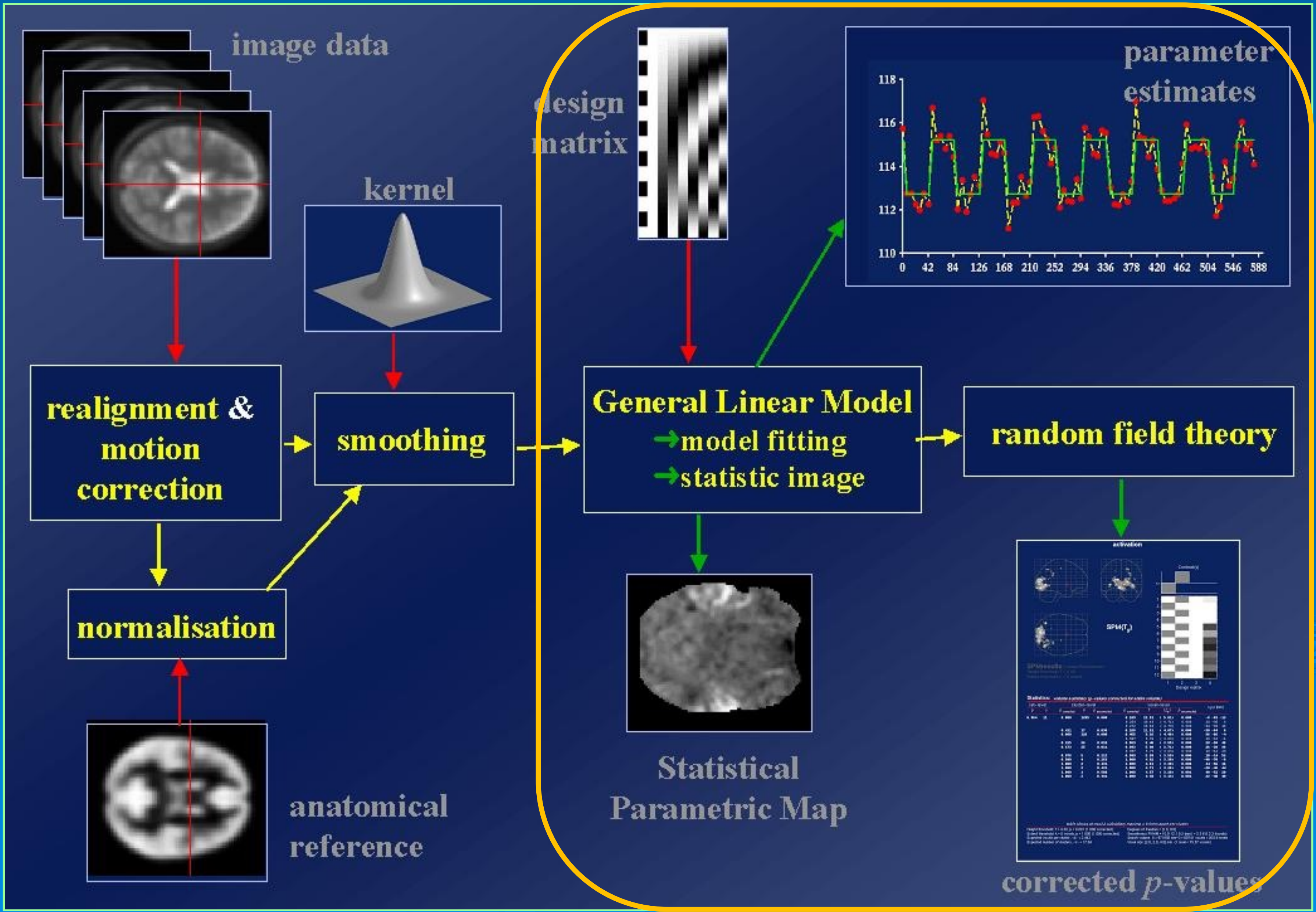
An affine transform can include rotation, scaling, shearing and translation

Rigid registration includes only rotation and translation



* Shearing slides one edge of an image along the X or Y axis, creating a parallelogram

DATA ANALYSIS



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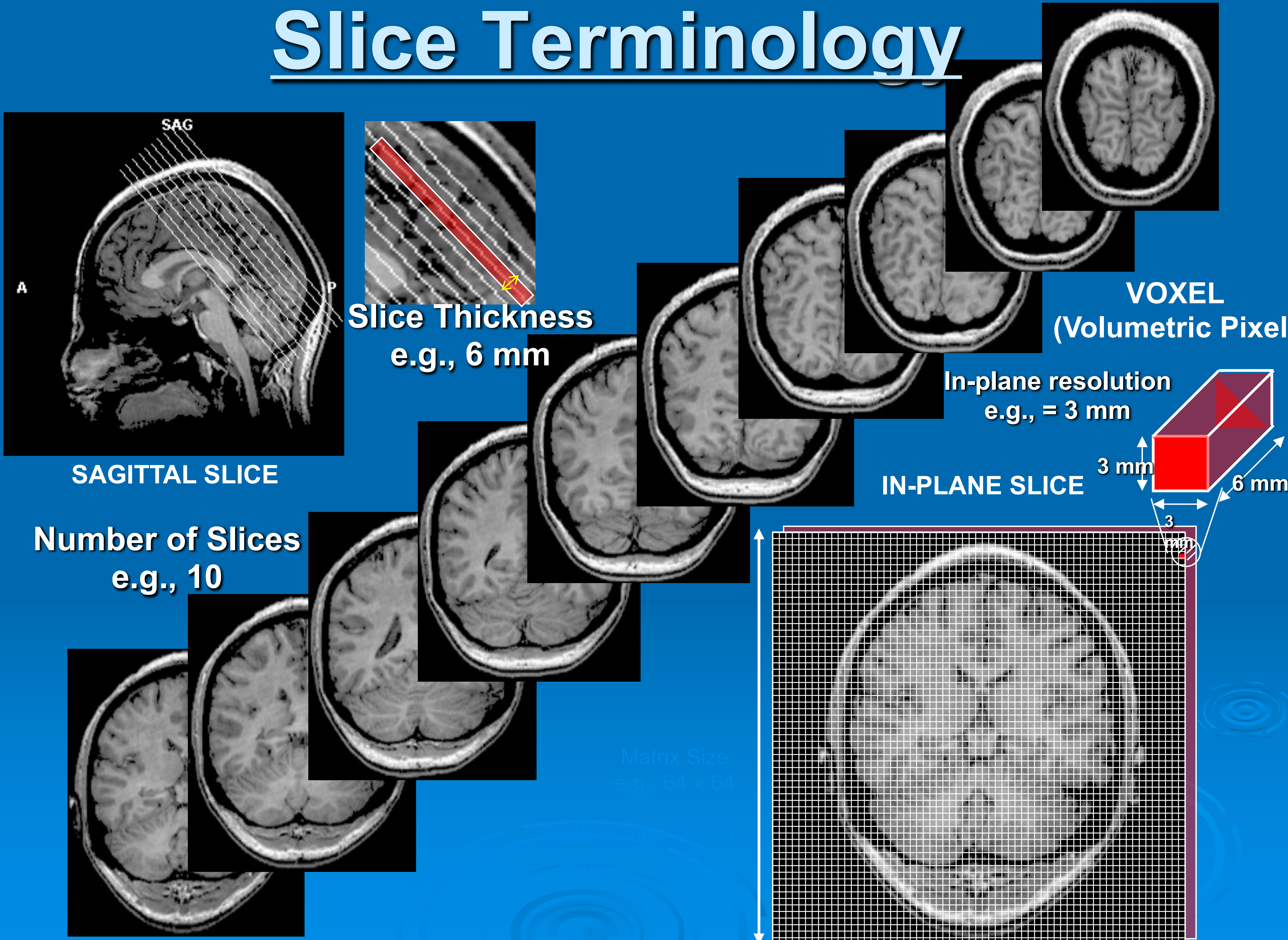
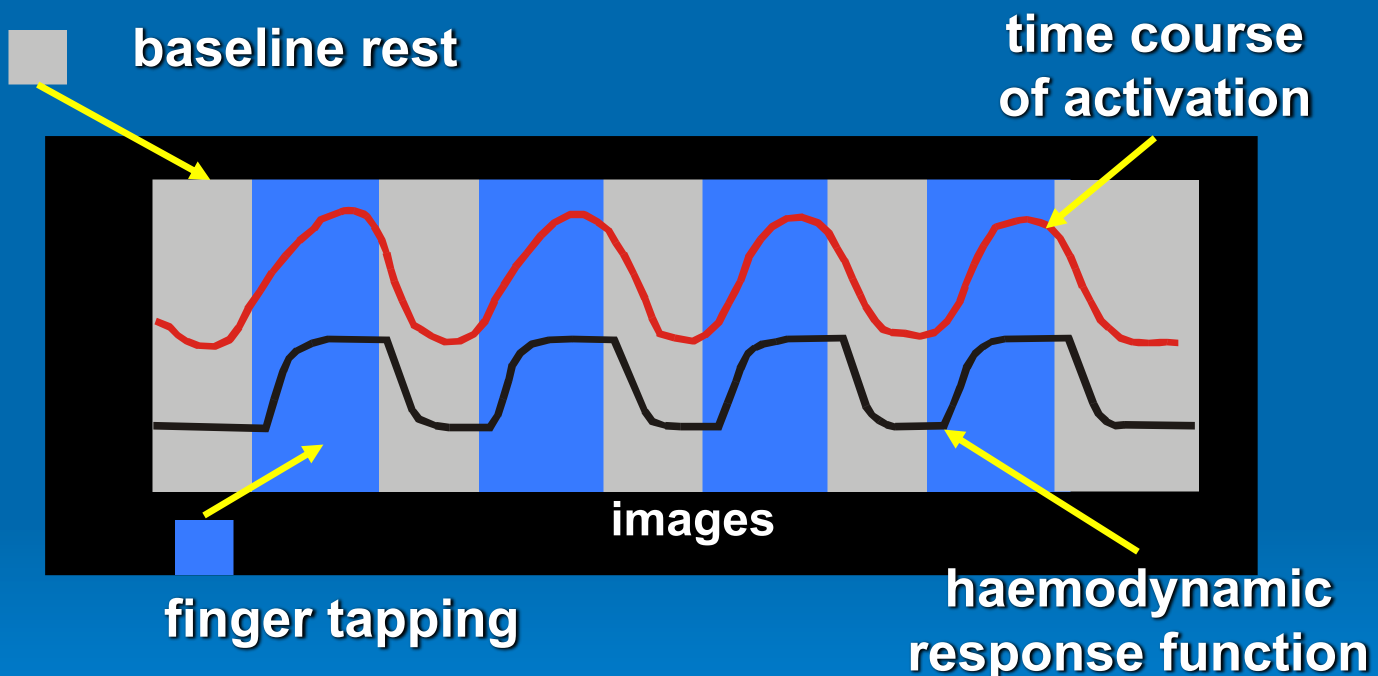
- Use pre-processing to reduce/eliminate some of these effects

Slice Terminology

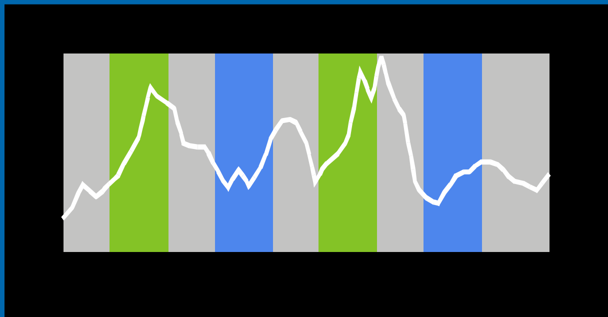


General Linear Model (GLM): Logic



Correlate model at each voxel separately

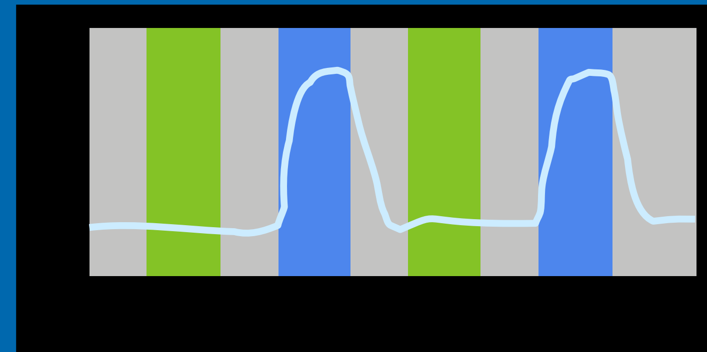
General Linear Model (GLM): Logic



fMRI signal

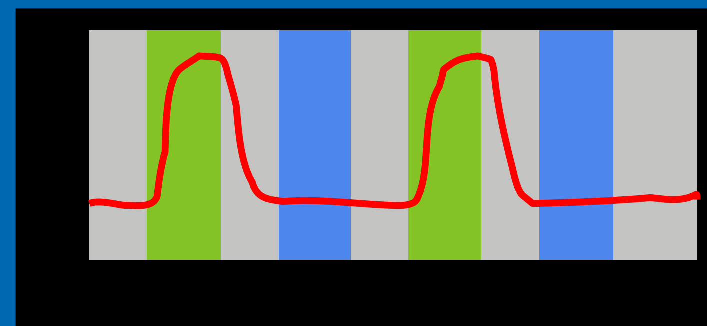
=

β_1 ×

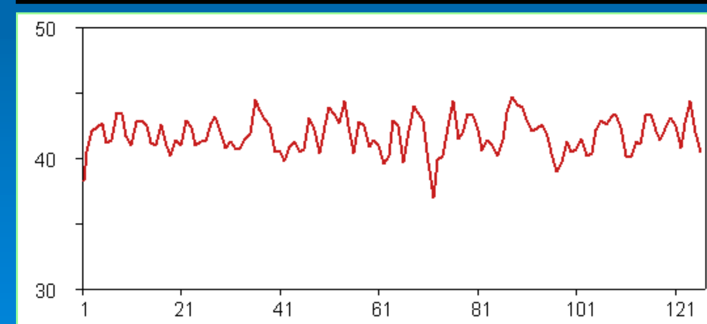


+

β_2 ×



+



Residuals Noise!

Parcel out variance in the voxel’s time course to the contributions of two predictors plus residual noise (what the predictors can’t account for).

Design Matrix

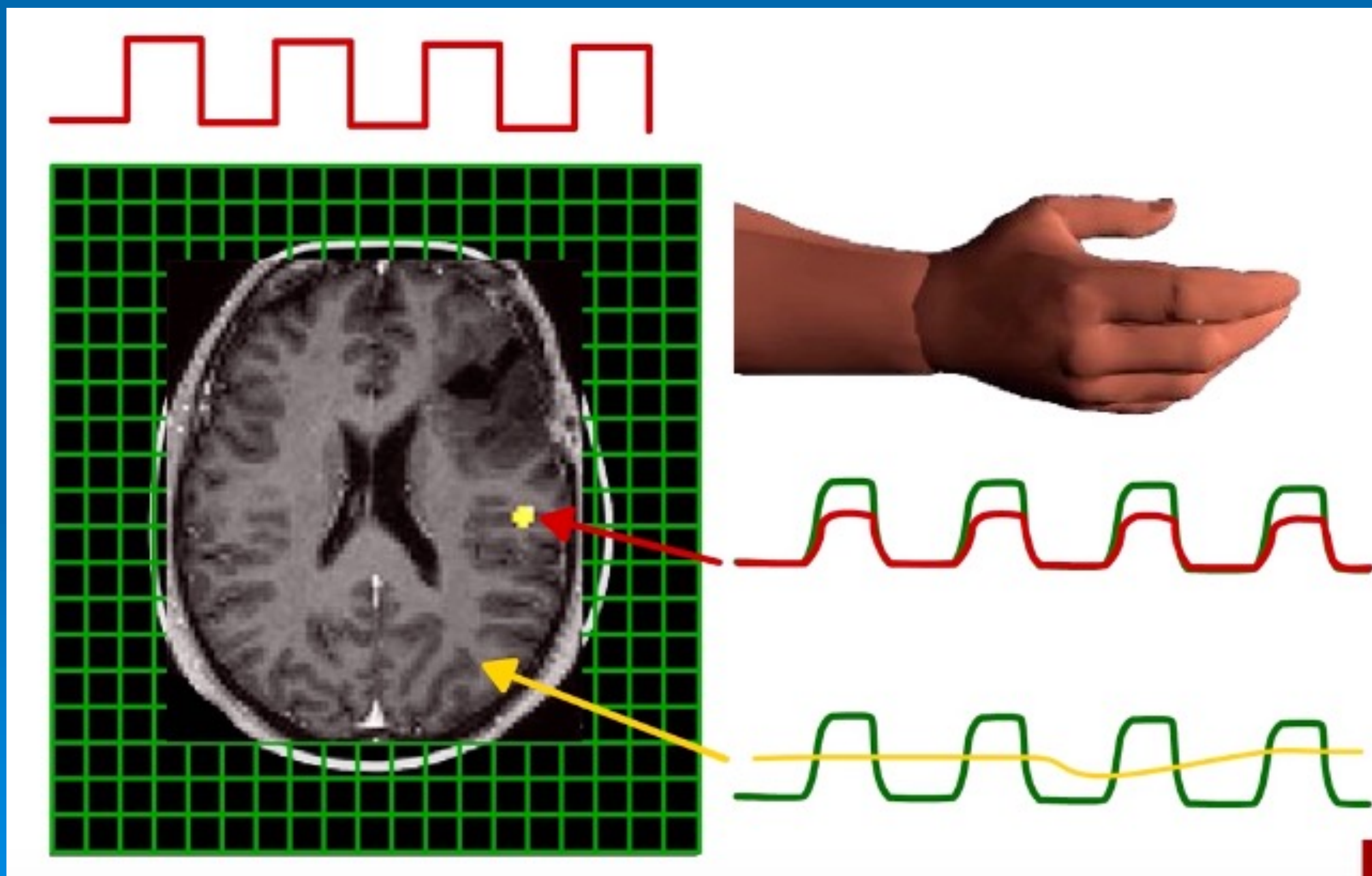
- Tapping right
- Tapping left

Adapted from Brain Voyager course slides

Table 8.1 List of Software Resources That Support fMRI Analysis

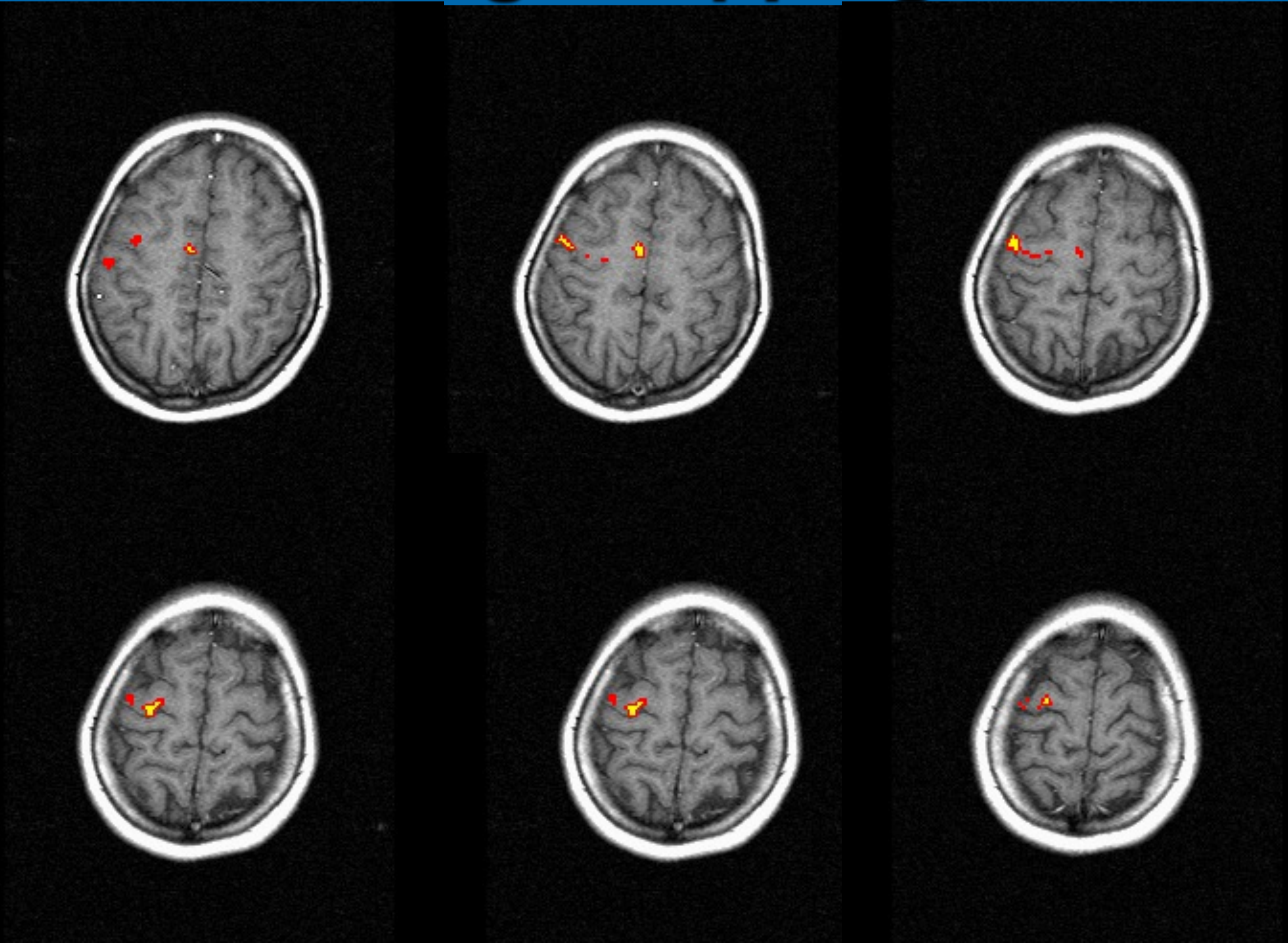
Name (in alphabetical order)	Web Site	Basic Method(s) Used for fMRI Analysis (most also include other tools)
Analysis of Functional NeuroImages (AFNI)	http://afni.nimh.nih.gov/afni/	GLM
BrainVoyager	http://www.brainvoyager.com/	GLM and ICA
Fiasco/FIAT	http://www.stat.cmu.edu/~fiasco/	GLM
FMRIB Software Library (FSL)	http://www.fmrib.ox.ac.uk/fsl/	GLM and ICA
FMRLAB	http://sccn.ucsd.edu/fmrlab/	ICA
FreeSurfer	http://surfer.nmr.mgh.harvard.edu/	Morphometric analysis
MEDx	http://www.medicalnumerics.com/products/medx/index.html	GLM and ICA
NIfTI	http://nifti.nimh.nih.gov/	Data format conversion
NITRC	http://www.nitrc.org/	A large source of neuroimaging tools
Statistical parametric mapping (SPM)	http://www.fil.ion.ucl.ac.uk/spm/	GLM
VoxBo	http://www.voxbo.org/index.php/Main_Page	GLM

fMRI display

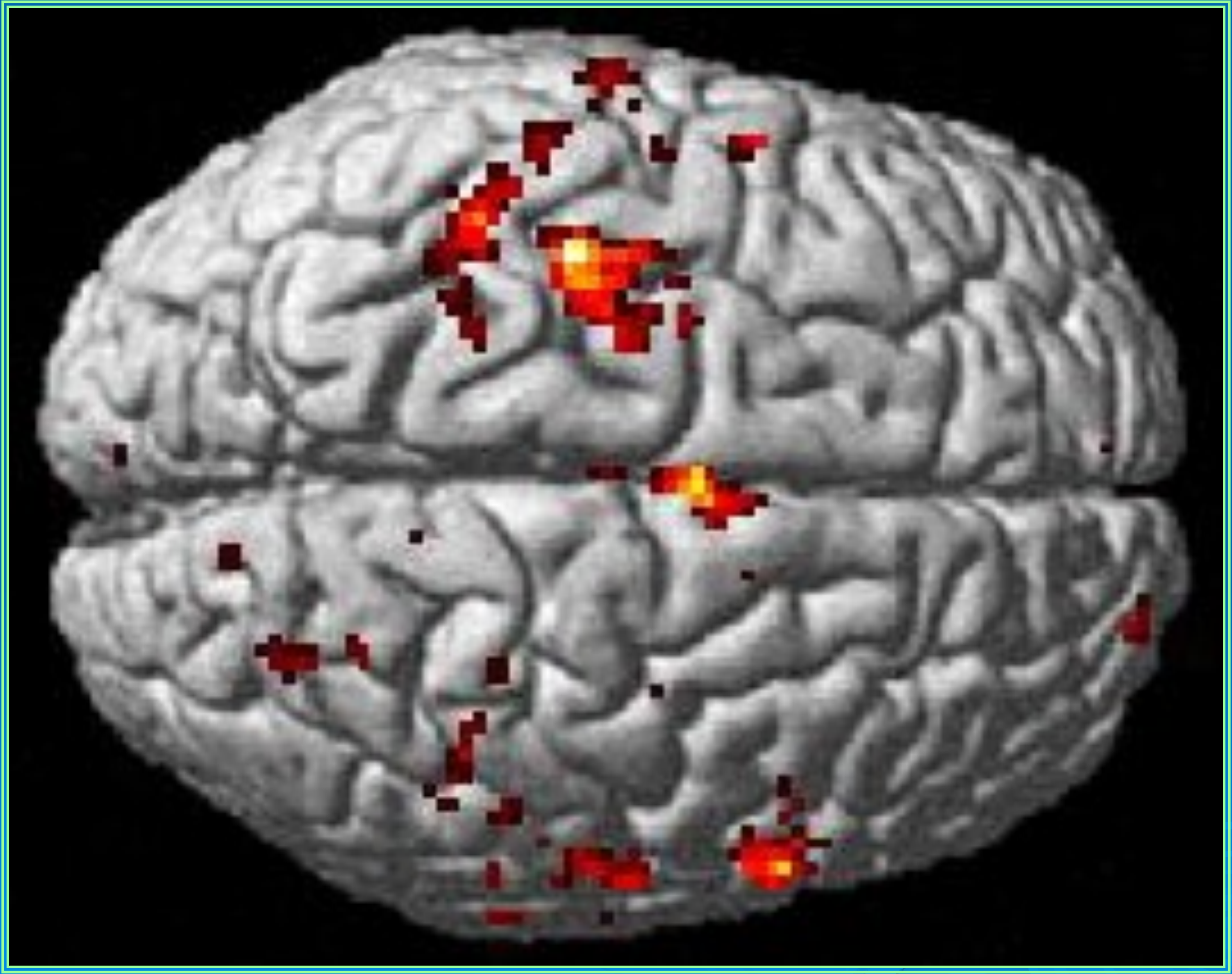


https://www.imaios.com/en/e-Courses/e-MRI/Functional-MRI/analysis-functional-mri-data

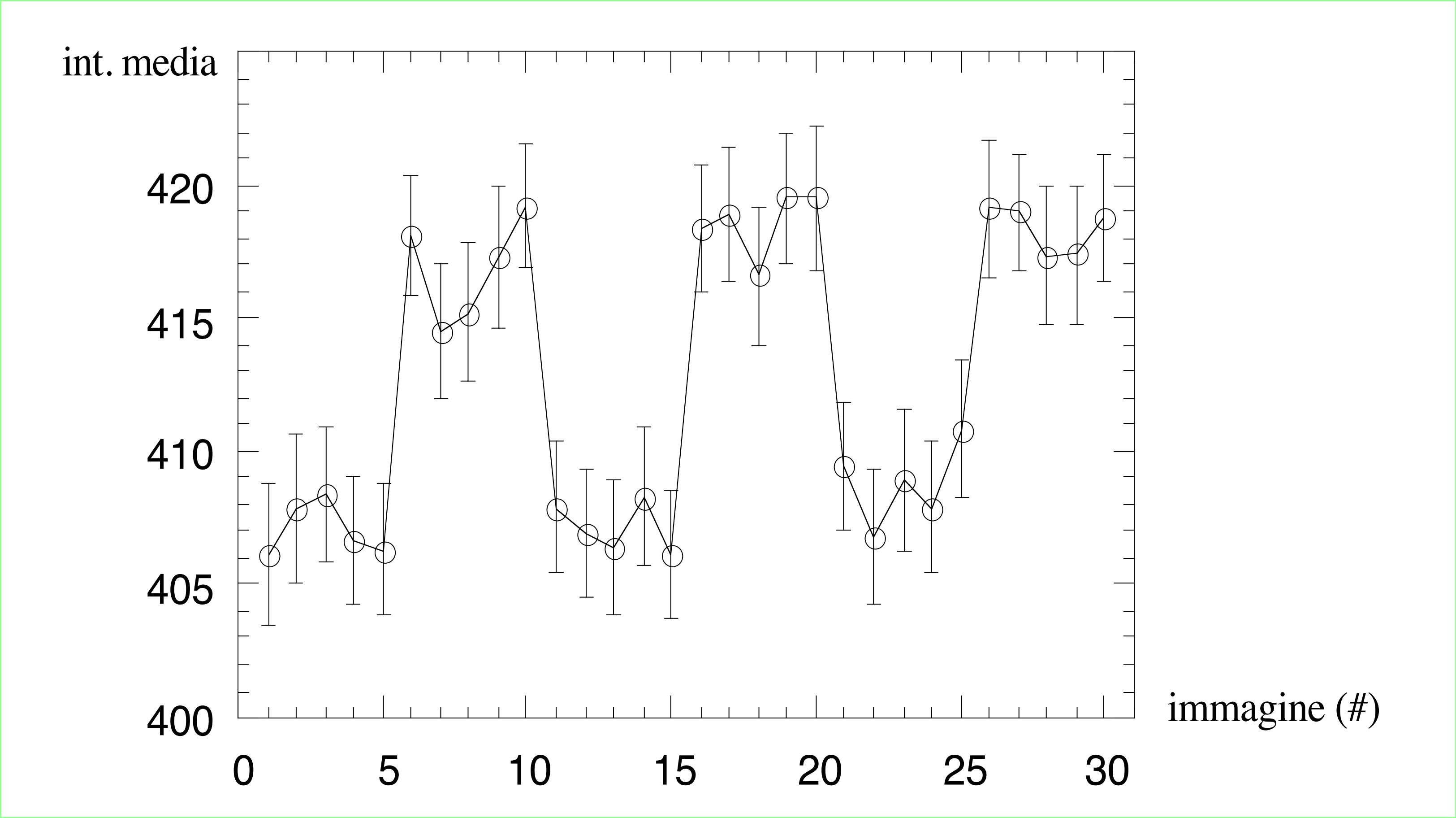
Finger tapping



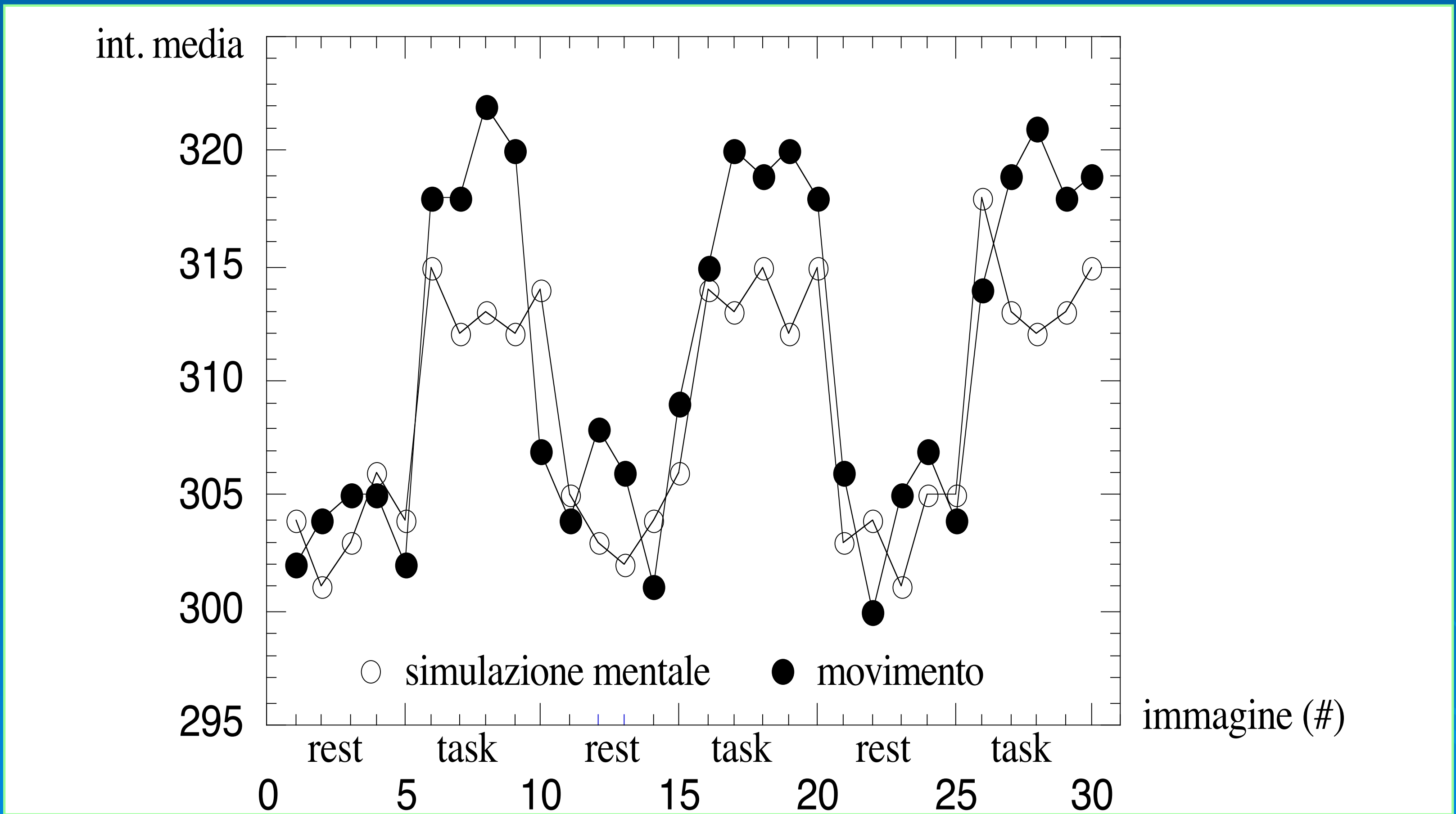
Finger tapping dx con comando acustico



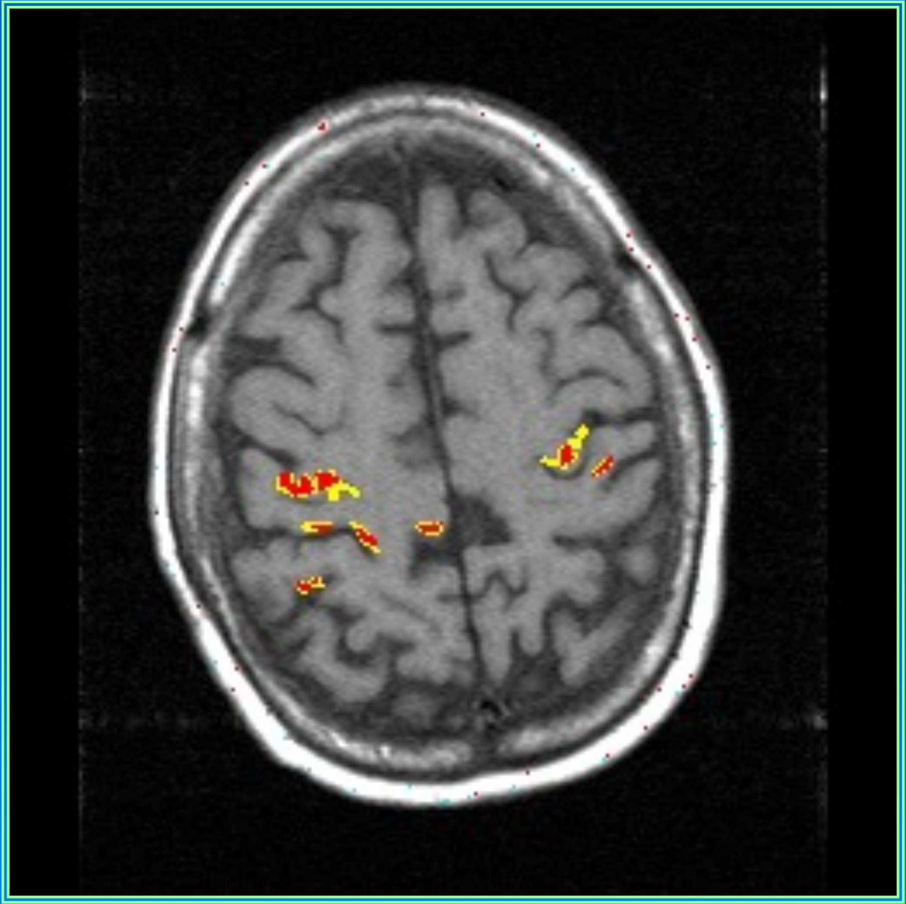
Experimental results



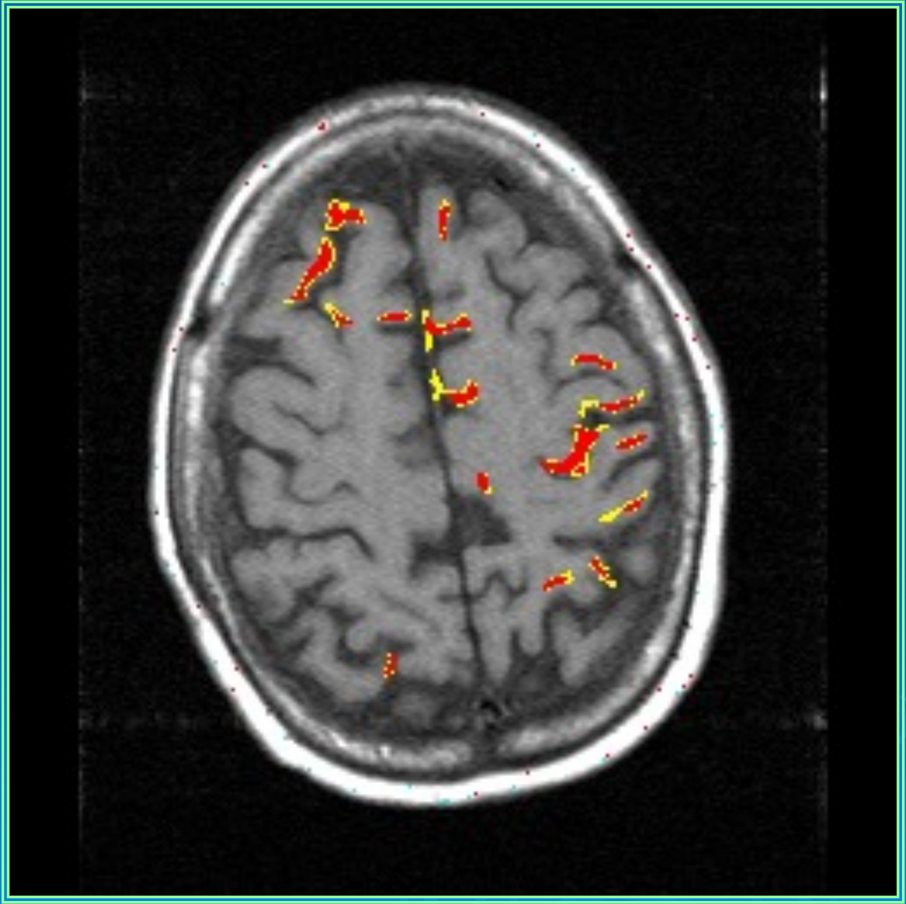
Task vs. imaginary task (finger tapping)



Finger tapping

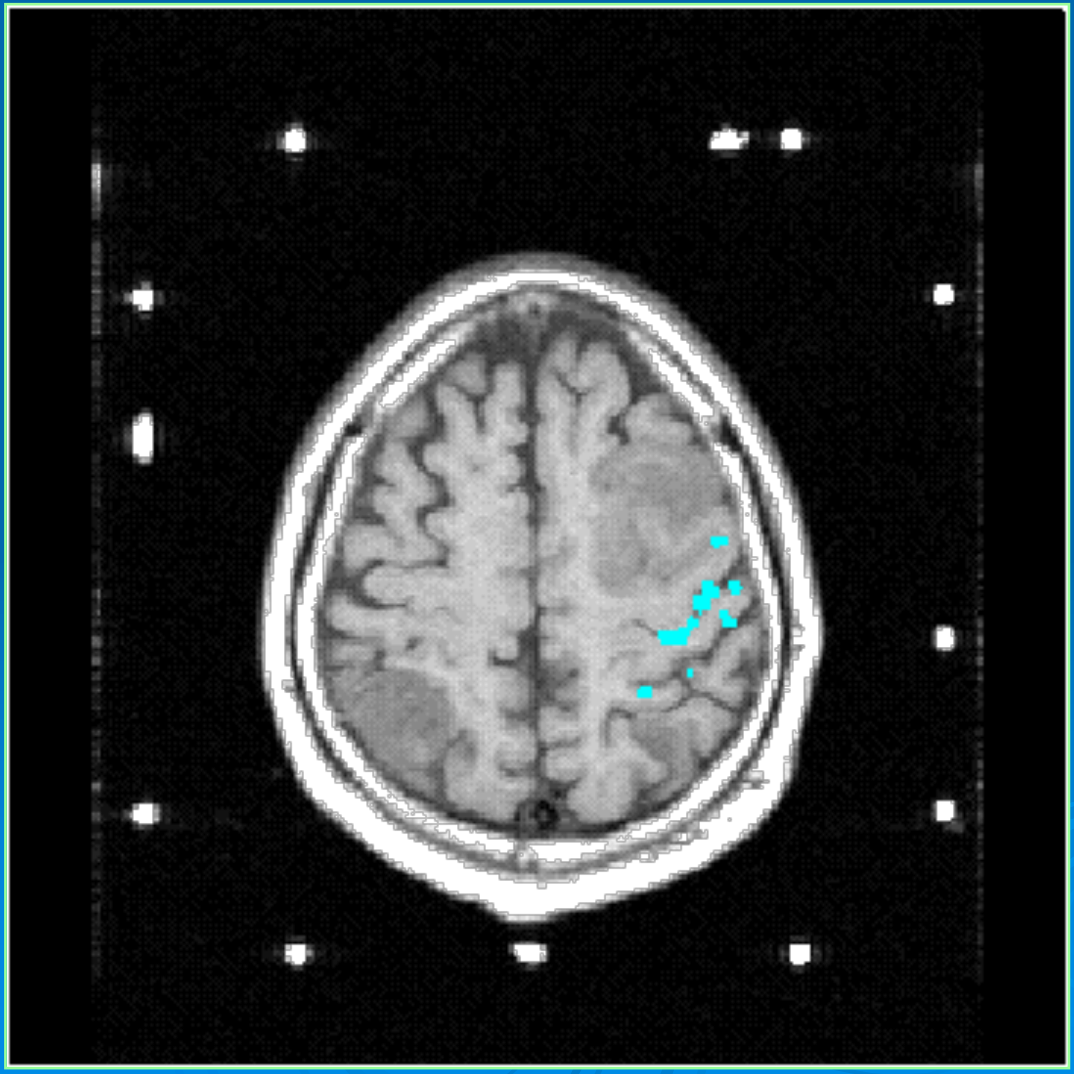


Left hand

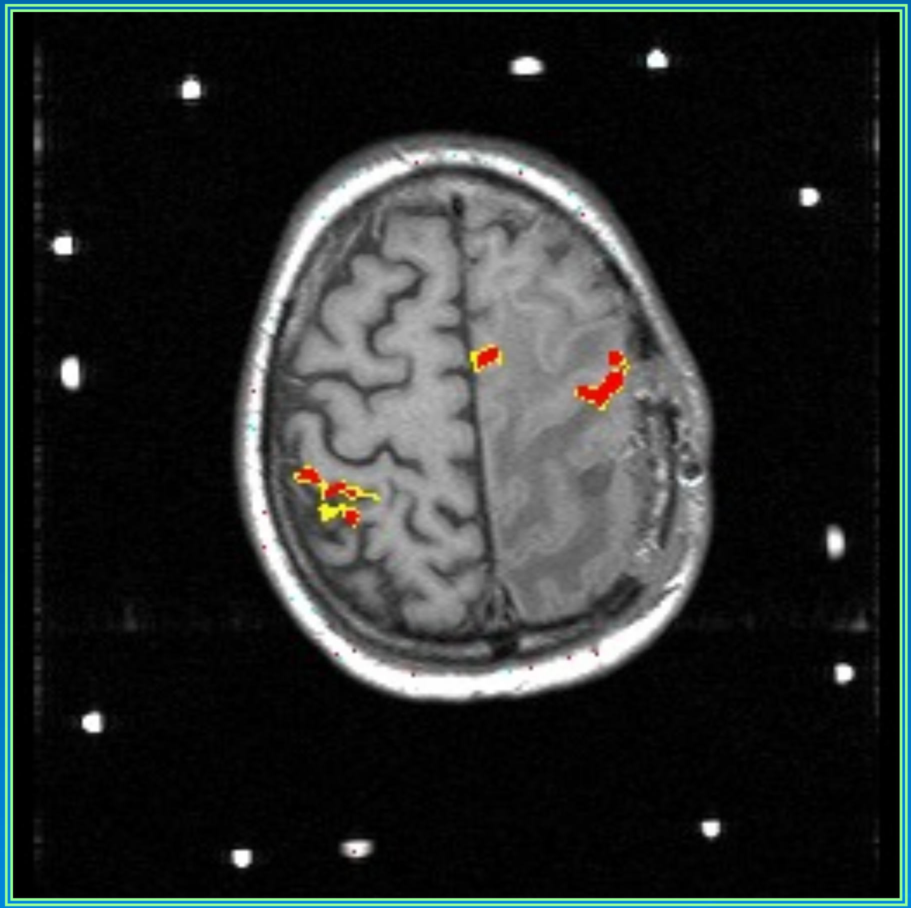


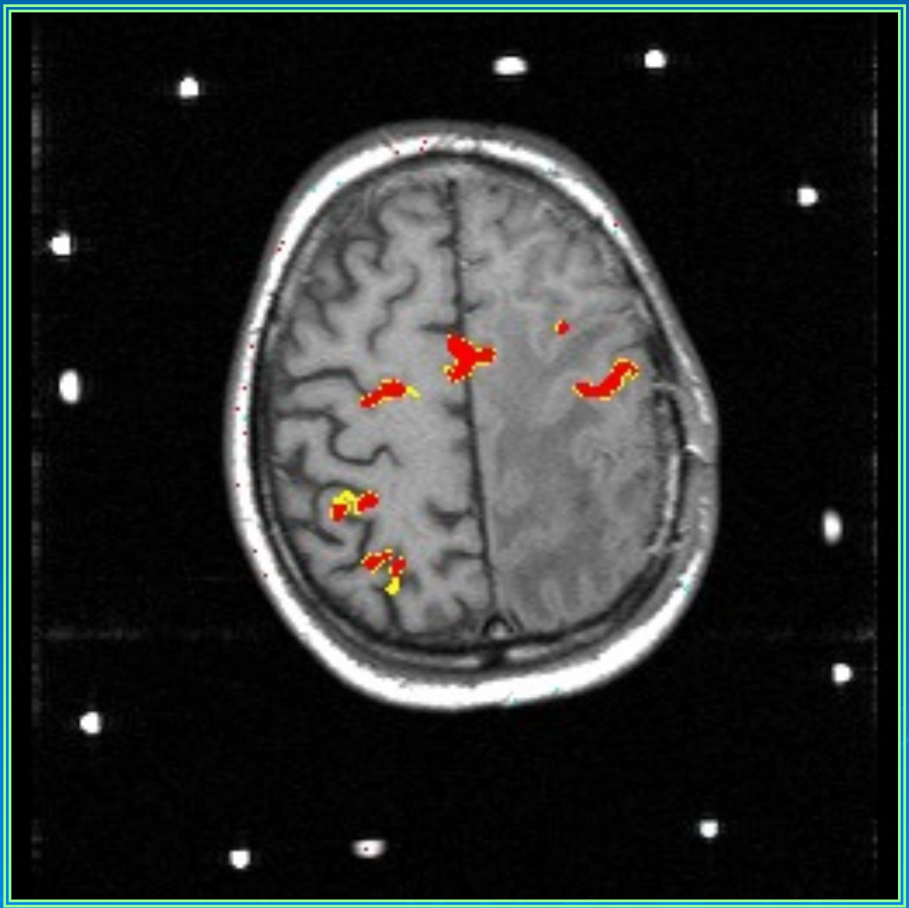
Right hand

Clinical applications: stereotactic surgery

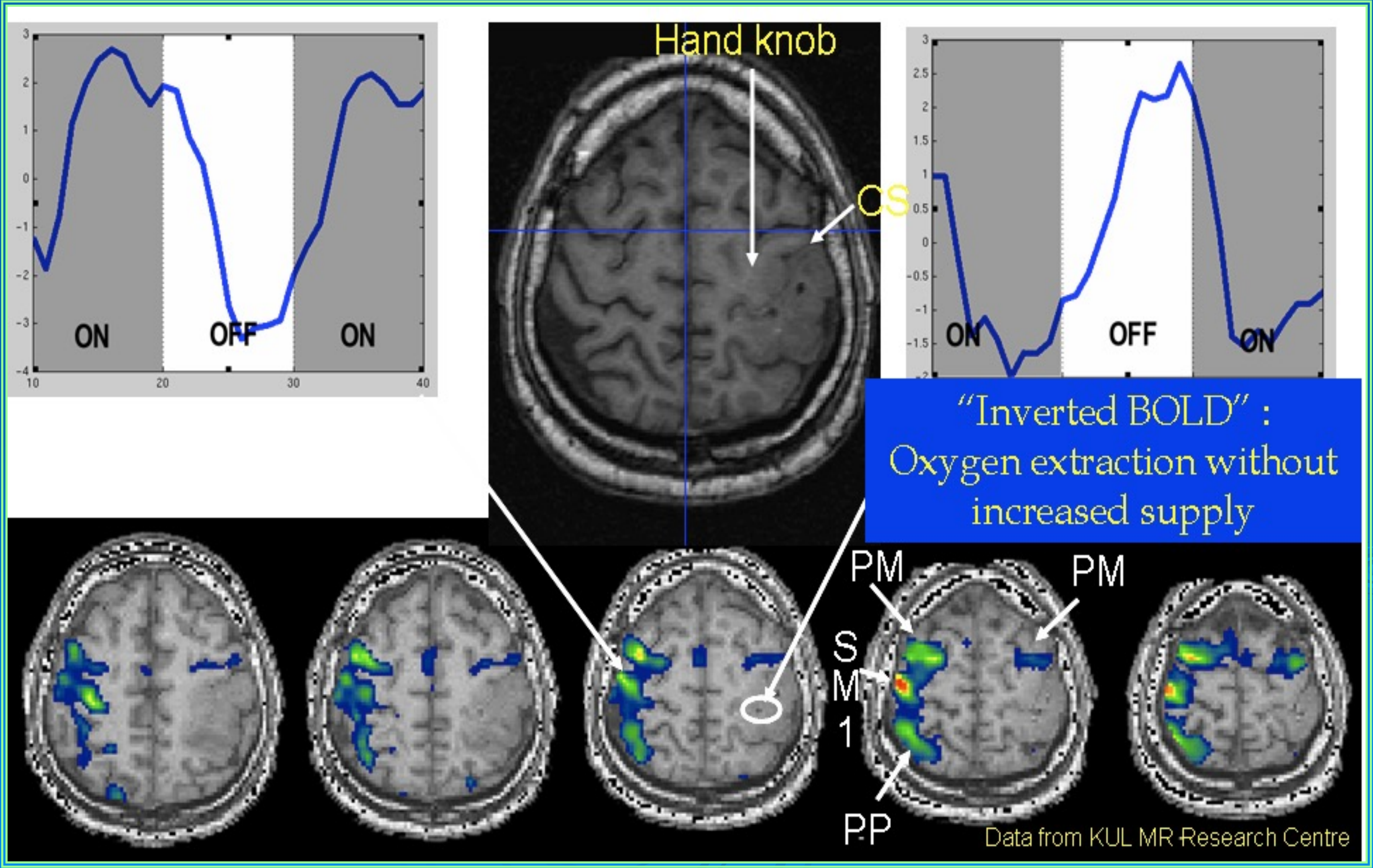


Clinical applications: stereotactic surgery





Inverted BOLD in tumor



The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2010

Willful Modulation of Brain Activity in Disorders of Consciousness

Martin M. Monti, Ph.D., Audrey Vanhaudenhuyse, M.Sc., Martin R. Coleman, Ph.D., Melanie Boly, M.D., John D. Pickard, F.R.C.S., F.Med.Sci., Luaba Tshibanda, M.D., Adrian M. Owen, Ph.D., and Steven Laureys, M.D., Ph.D.

- ✓ **In Cambridge, United Kingdom, and Liege, Belgium, we performed a study involving 54 patients with disorders of consciousness**
- ✓ **Technique was then developed to determine whether such tasks could be used to communicate yes-or-no answers to simple questions.**
- ✓ **Of the 54 patients enrolled in the study, 5 were able to willfully modulate their brain activity**

The NEW ENGLAND JOURNAL of MEDICINE

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Willful Modulation of Brain Activity in Disorders of Consciousness

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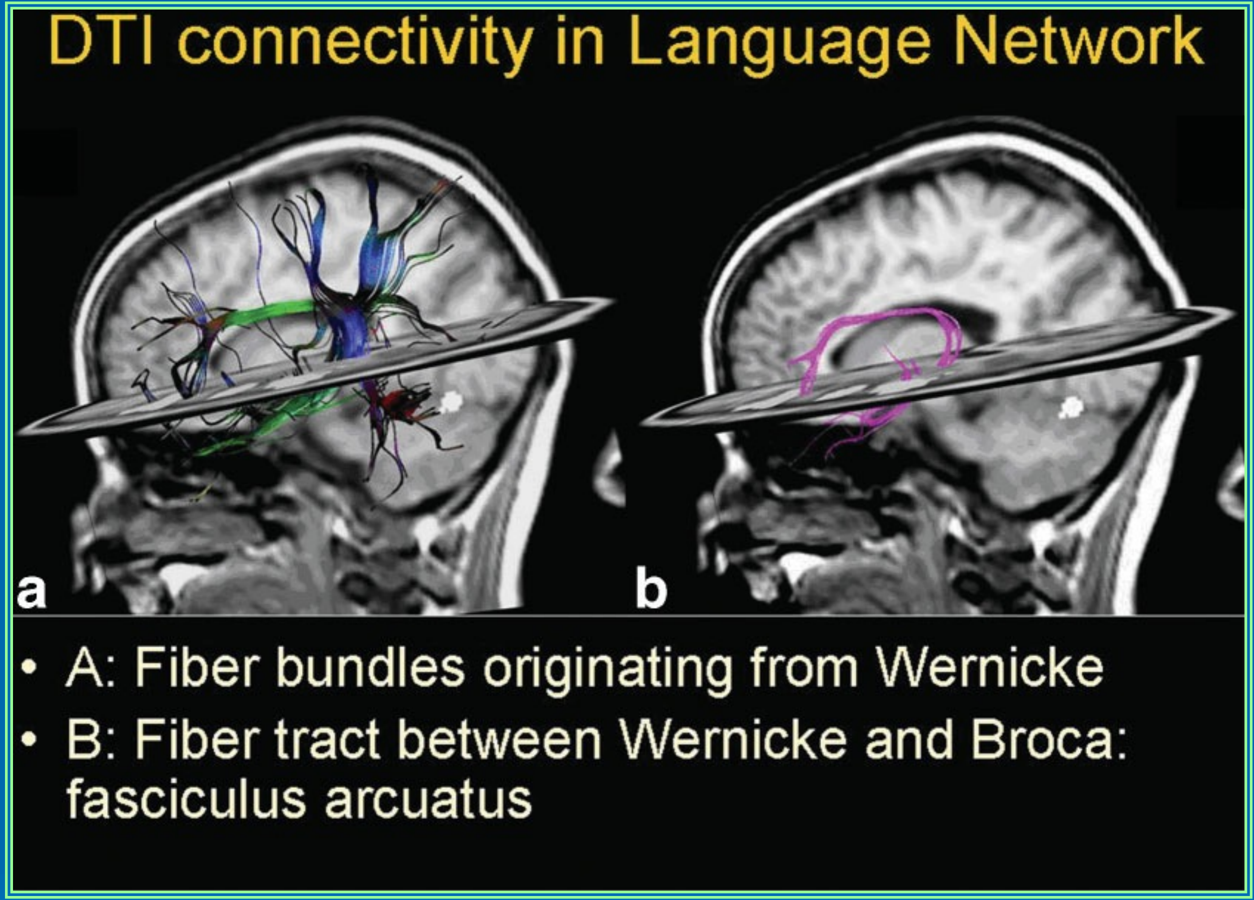
STATISTICAL ANALYSIS

Analyses were performed with the use of FSL software, version 4.1.[13] Data analysis included standard functional MRI preprocessing steps (functional MRI acquisition and preprocessing are described in the Supplementary Appendix). For each scan, a general linear model contrasting periods of active imagery with periods of rest was computed. All contrasts were limited to the brain locations within the supplementary motor area and the parahippocampal gyrus, as defined in the Harvard–Oxford Cortical Structural Atlas (available in FSL software), and a threshold was established, with gaussian random-fields theory, at a cluster-level z value of more than 2.3 (corrected $P<0.05$). The defined regions of interest were transformed from standard space (according to the criteria of the Montreal Neurological Institute) to fit each subject's structural image, with the use of a method involving 12 degrees of freedom.

$p<0.05$
the probability of the null hypothesis is 1/20

fMRI & DTI



a: Fiber bundles originating from a ROI corresponding to the activation site of Wernicke's area

- interconnected with the temporal pole, cerebellum, parietal lobe, perirolandic region, and frontal areas

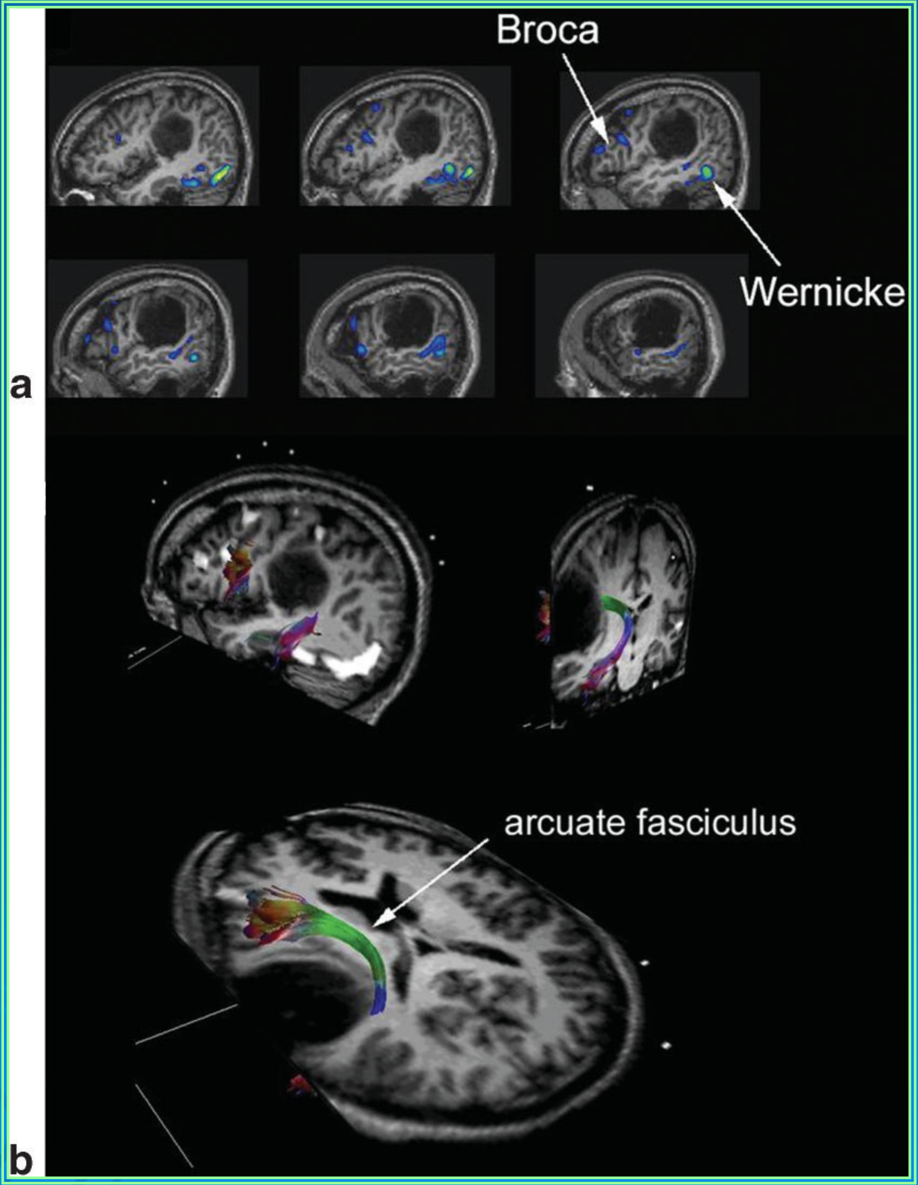
b: DTI fiber tracking between Wernicke's and Broca's regions.

MR imaging revealed a low-grade tumoral mass in the left supramarginal and angular gyri

fMRI & DTI

a) fMRI during a verbal fluency task depicts a left lateralized language, with Wernicke's area in the middle temporal gyrus and Broca in the inferior frontal gyrus. Both eloquent areas are some distance of the lesion.

b) Fiber-tracking depicting the arcuate bundle between Wernicke and Broca. The bundle seems to be displaced medially by the mass effect of the lesion and its middle part is adjacent to the tumor border.

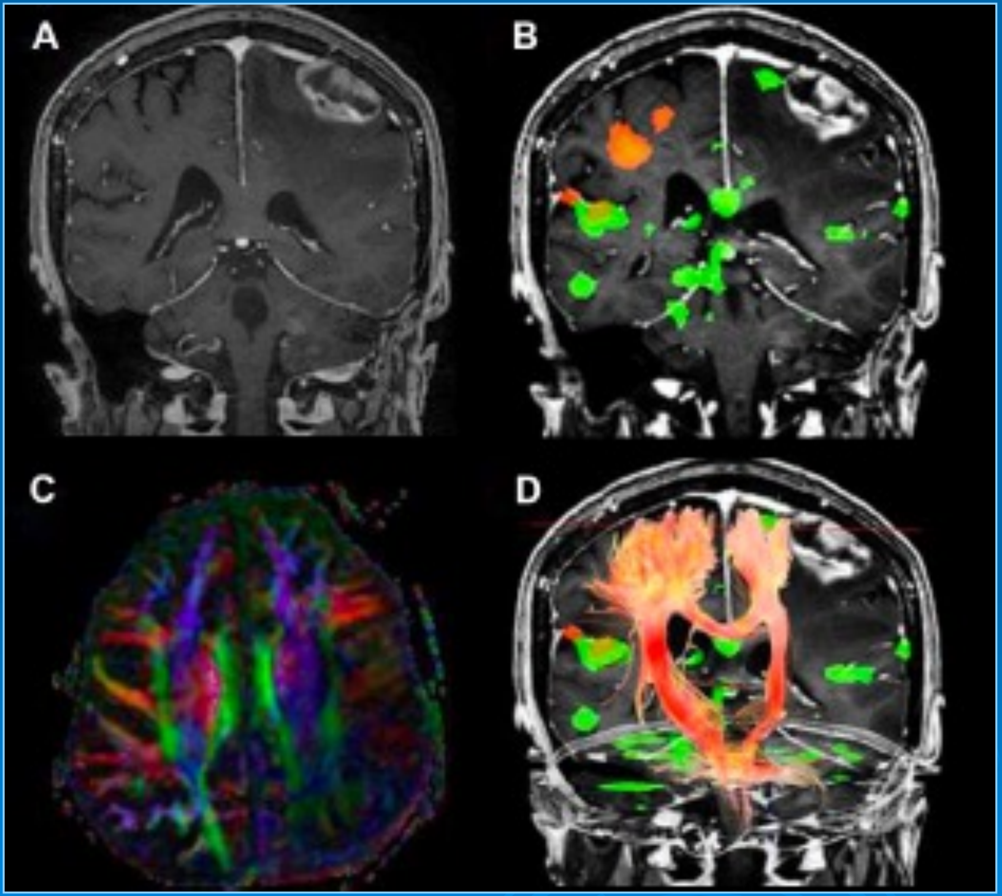


Clinical applications

Fusion of fMRI and tractography for surgical planning

(A) Gadolinium-enhanced image shows a melanoma metastasis with surrounding vasogenic edema

(B) fMRI shows the metastasis results in medial displacement of the motor activation area on the left
- **shown in green**

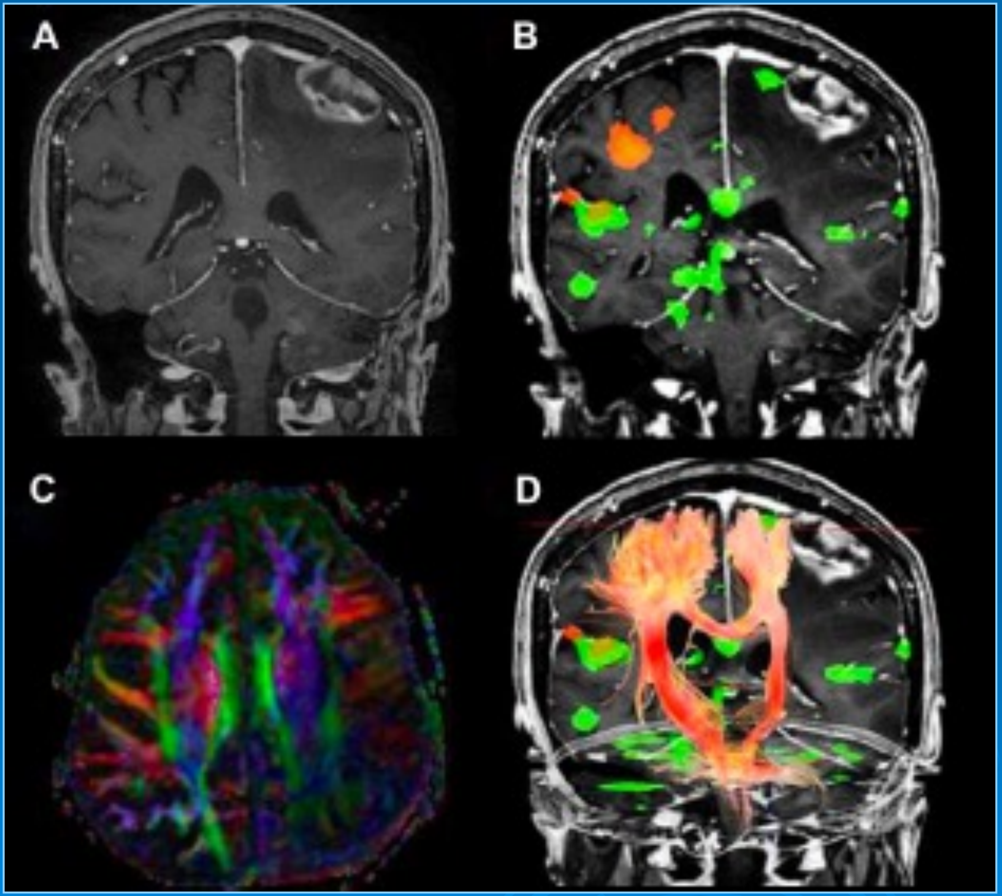


Lerner et al World Neurosurg. (2014) 82, 1/2:96-109

Clinical applications

Fusion of fMRI and tractography for surgical planning

C. FA map reveals less-robust anisotropy in the posterior left centrum semiovale and parietal subcortical white matter in the region of the tumor likely related to both displacement of fibers by the tumor and loss of anisotropy caused by vasogenic edema.

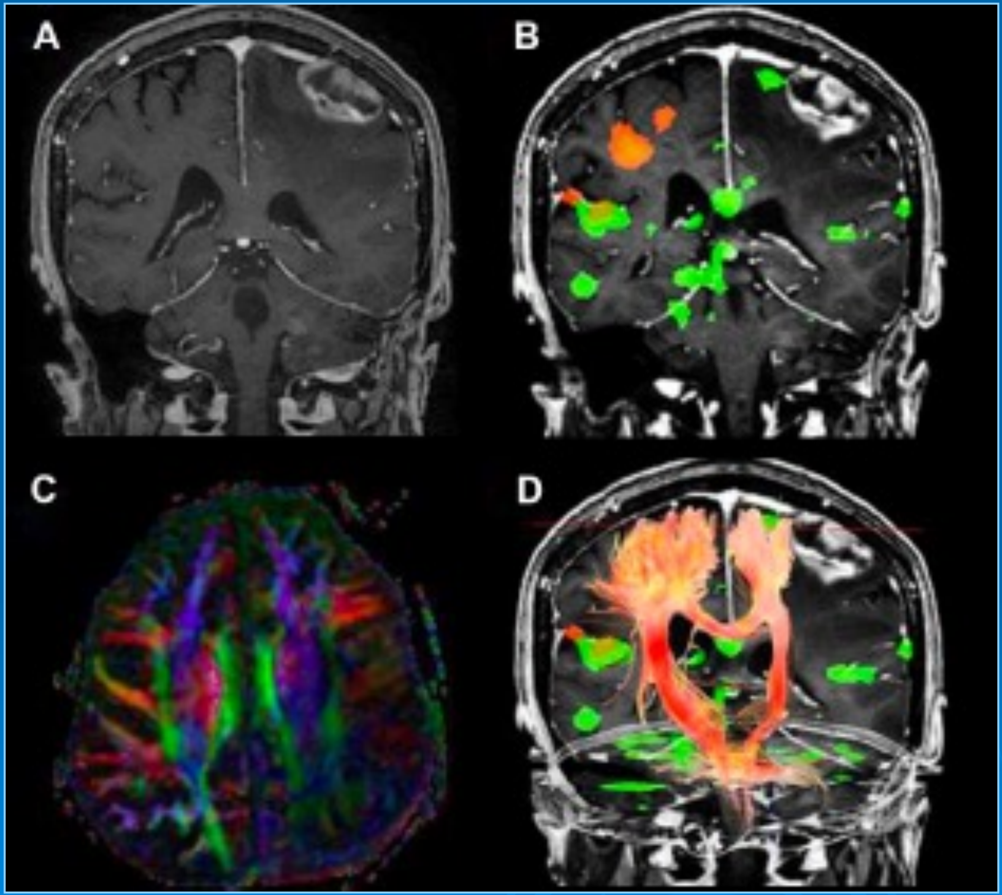


Lerner et al World Neurosurg. (2014) 82, 1/2:96-109

Clinical applications

Fusion of fMRI and tractography for surgical planning

D. **Tractography demonstrates displacement of the fiber tracts medially surrounding the area of motor activation.**



Lerner et al World Neurosurg. (2014) 82, 1/2:96-109