



LEIDS UNIVERSITAIR MEDISCH CENTRUM

MRI general introduction

Functional MRI (fMRI) data analysis overview

Serge A. Rombouts

Dept. Radiology, Leiden University Medical Center
Dept. Psychology, Leiden University
Leiden Institute for Brain and Cognition (LIBC)

Contact e-mail: s.a.r.b.rombouts@lumc.nl

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MRI:

Structural Imaging: grey matter and white matter

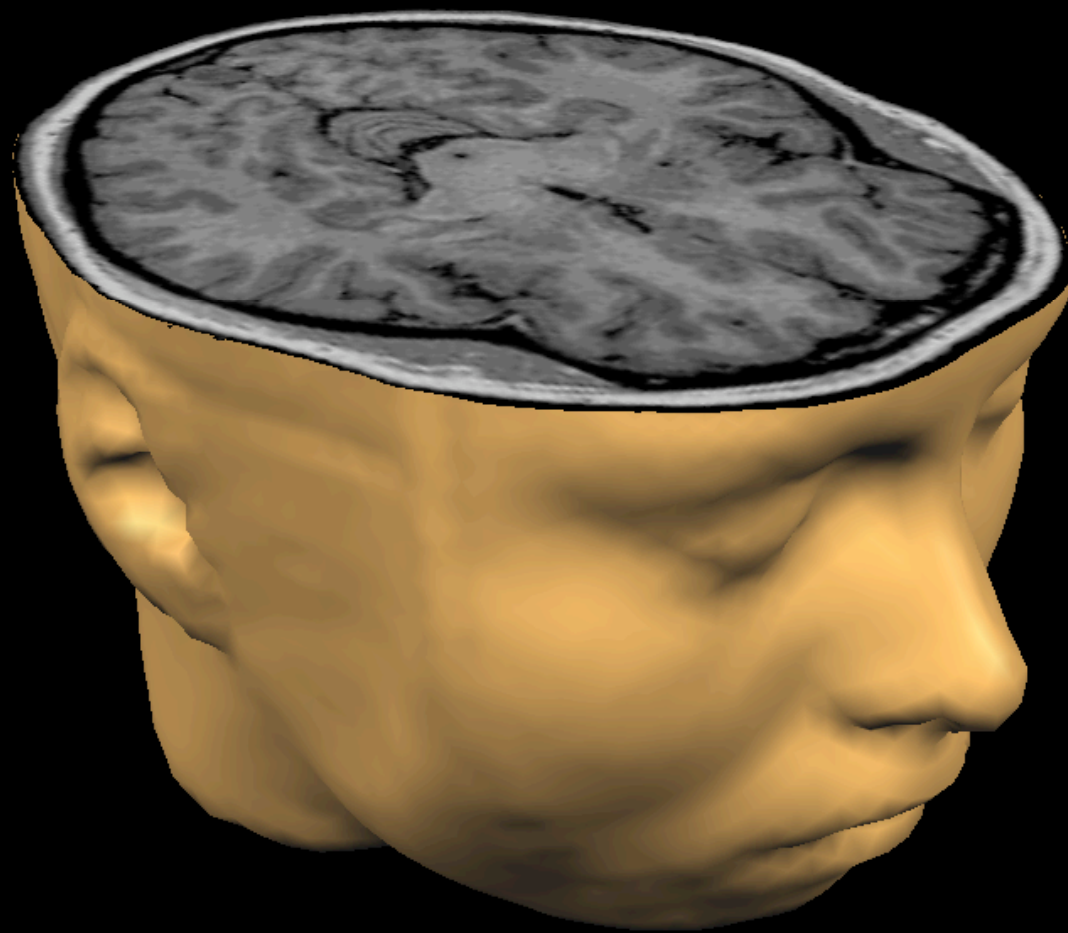
Functional MRI:

Brain Activation

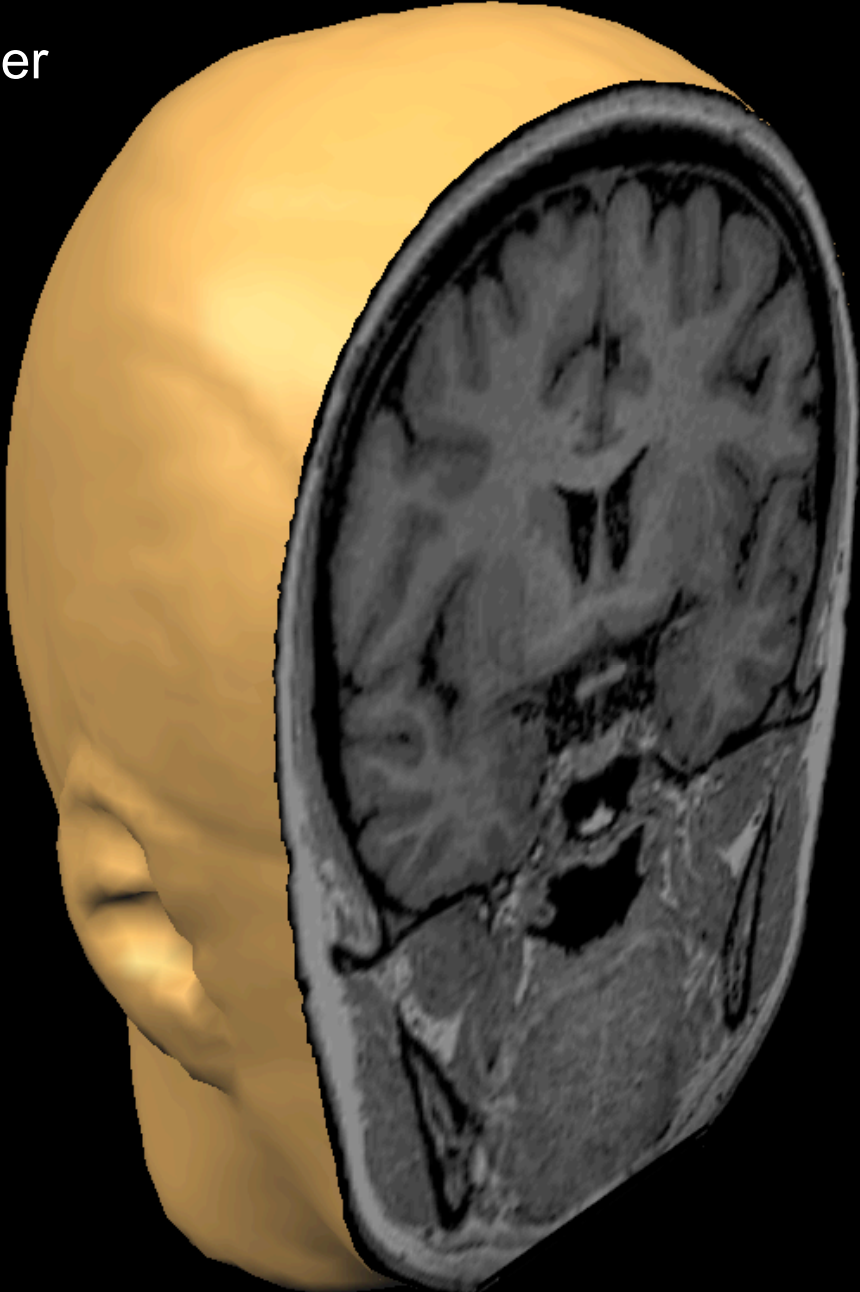
FMRI Data Analysis Overview



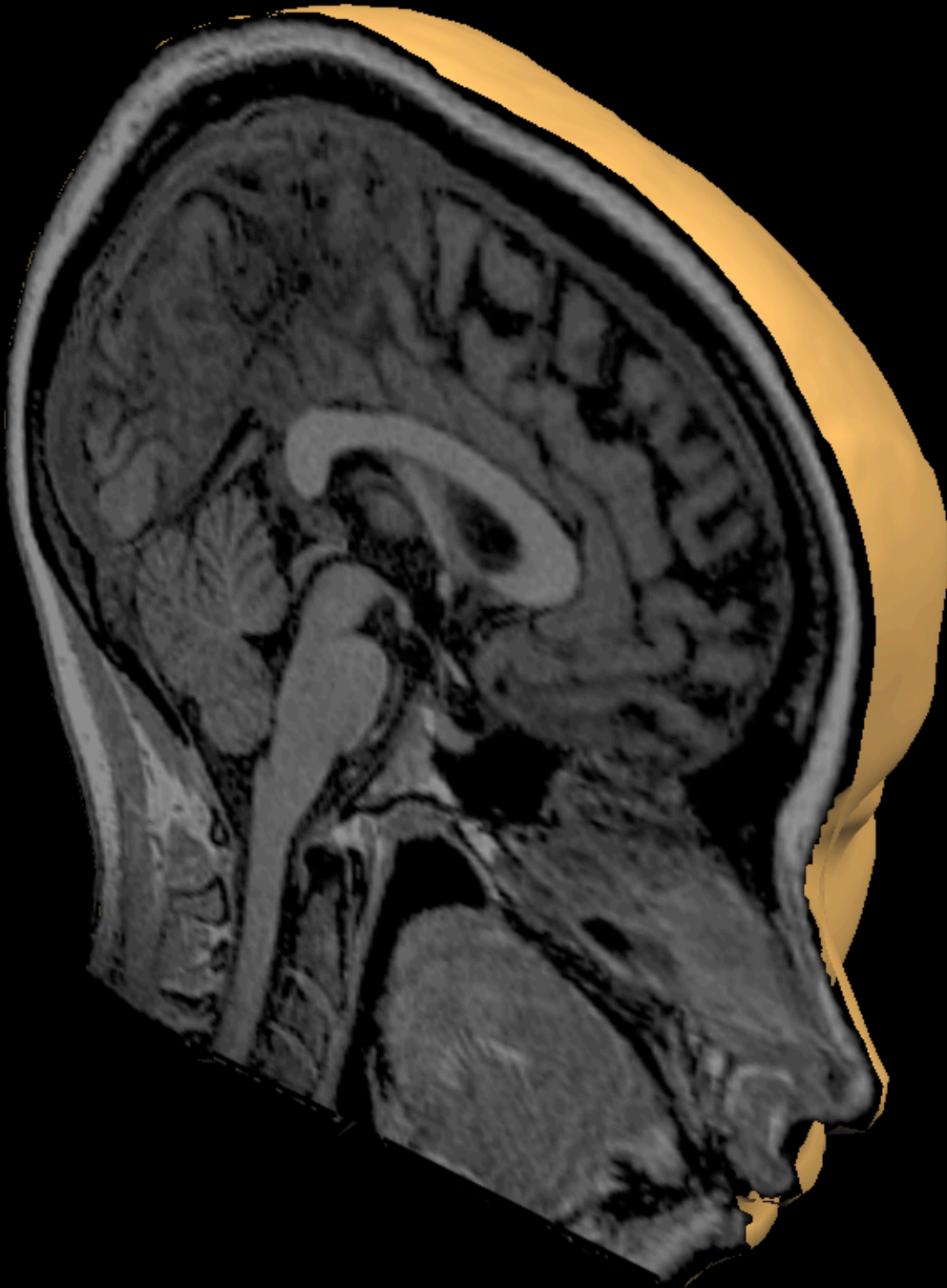
Created with Brain Voyager



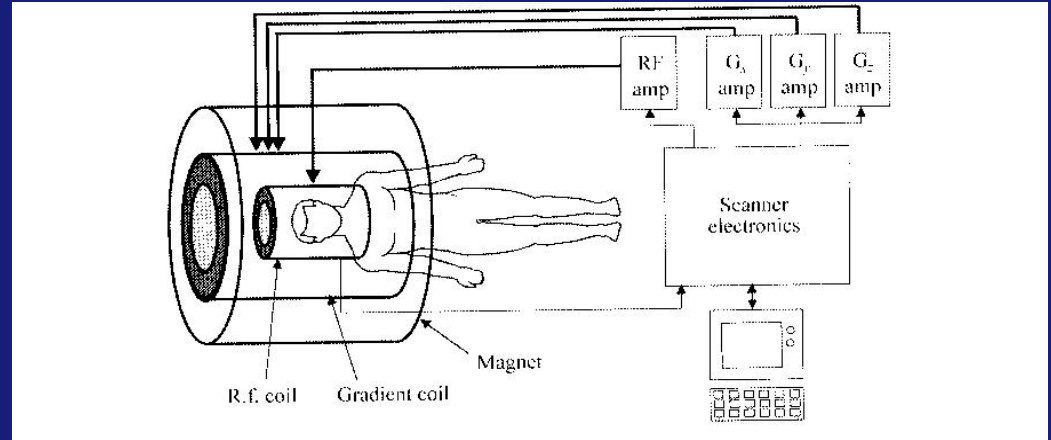
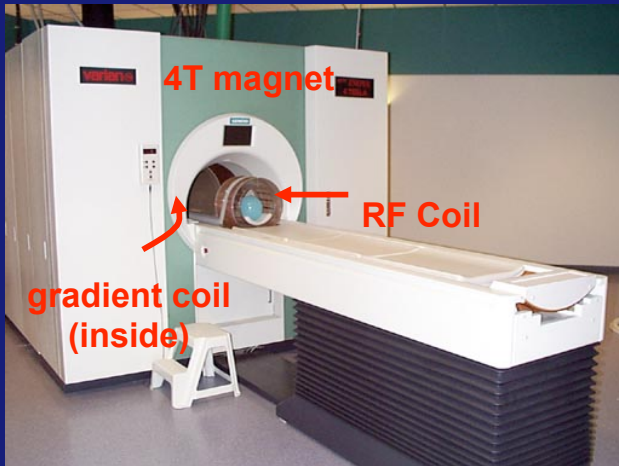
Created with Brain Voyager



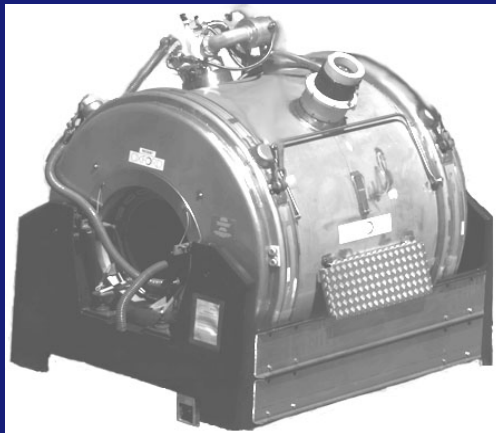
Created with Brain Voyager



Magnetic Resonance Imaging: imaging structures in the human body



Magnet



RF Coil

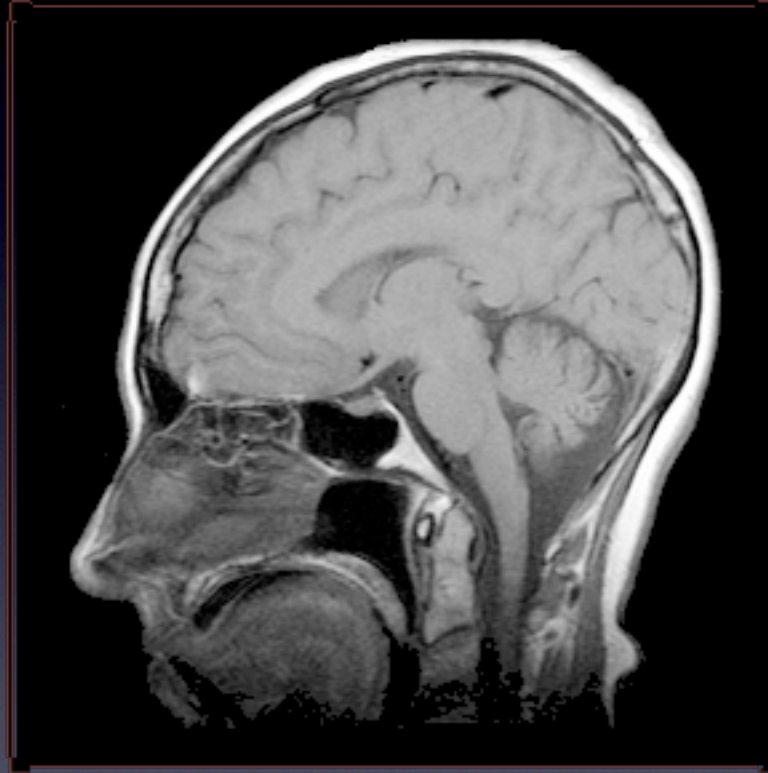


Source for Photos: Joe Gati



Source: http://www.simplyphysics.com/flying_objects.html

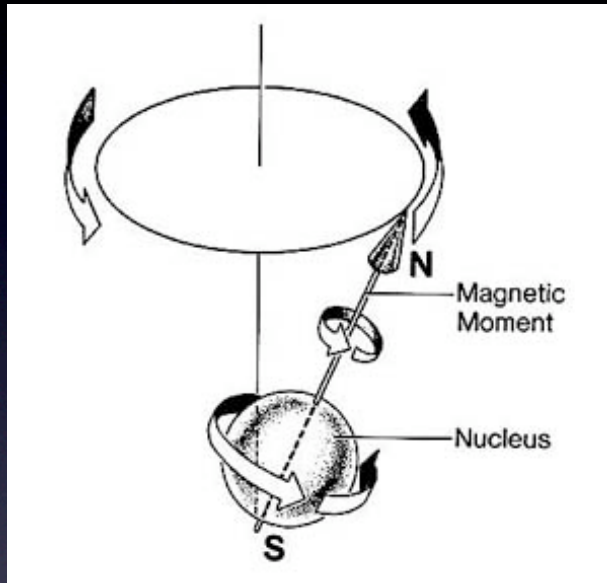
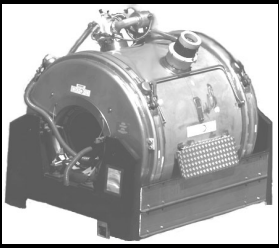
The Basics of MRI



Joseph P. Hornak, Ph.D.

<http://www.cis.rit.edu/htbooks/mri/>

Step 1: Put Subject in Big Magnet



Protons (hydrogen atoms) have “spins” (like tops). They have an orientation and a frequency.

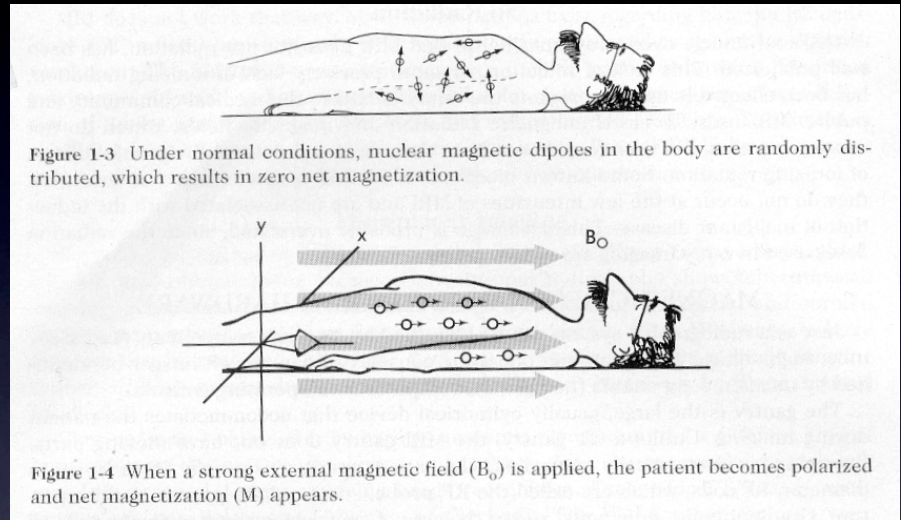
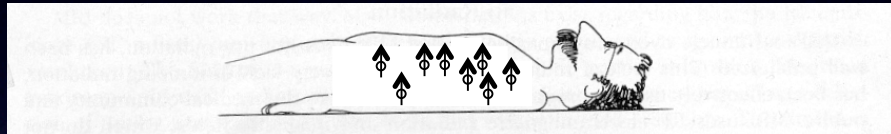
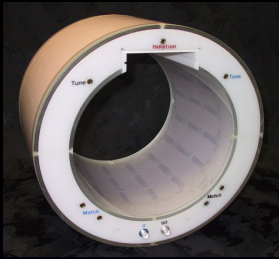


Figure 1-3 Under normal conditions, nuclear magnetic dipoles in the body are randomly distributed, which results in zero net magnetization.

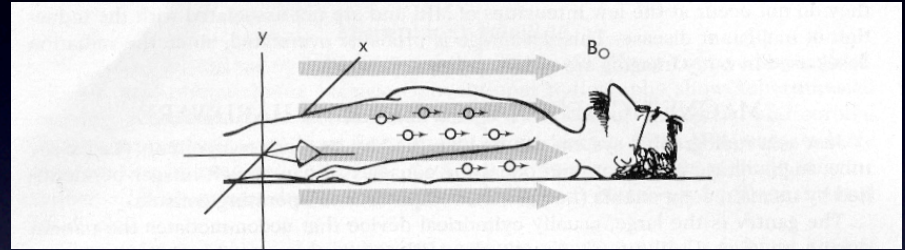
Figure 1-4 When a strong external magnetic field (B_0) is applied, the patient becomes polarized and net magnetization (M) appears.

When you put a material (like your subject) in an MRI scanner, some of the protons become oriented with the magnetic field.

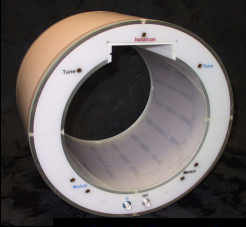
Step 2: Apply Radio Waves



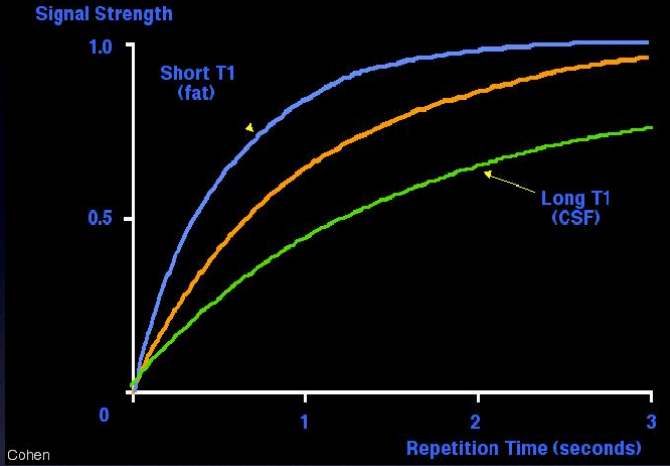
When you apply radio waves (RF pulse) at the appropriate frequency, you can change the orientation of the spins as the protons absorb energy.



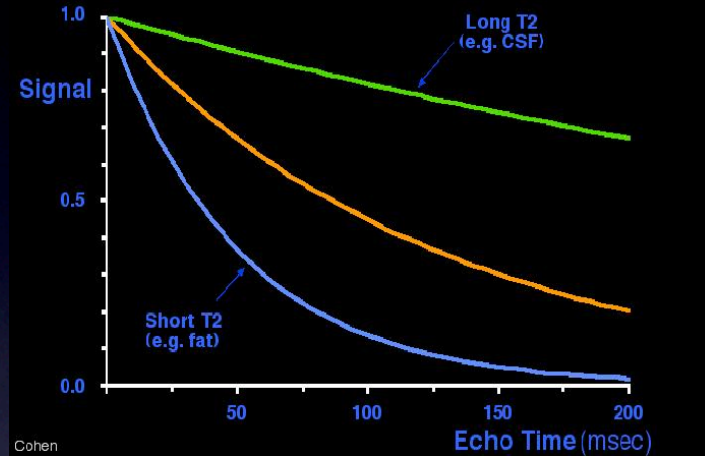
After you turn off the radio waves, as the protons return to their original orientations, they emit energy in the form of radio waves.



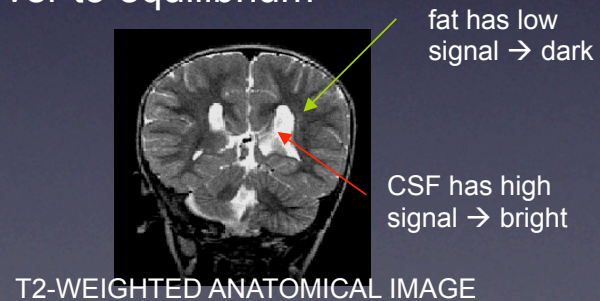
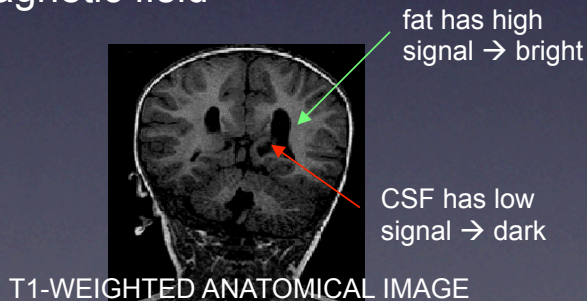
Step 3: Measure Radio Waves



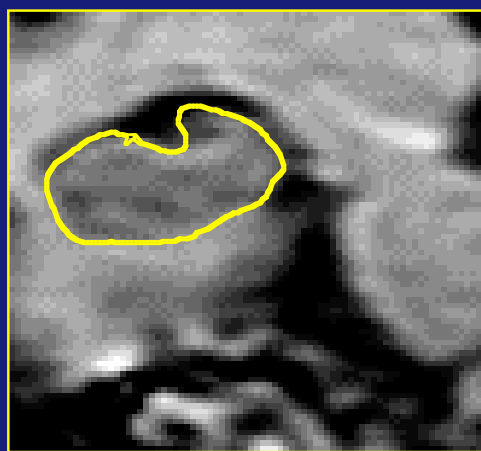
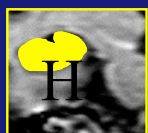
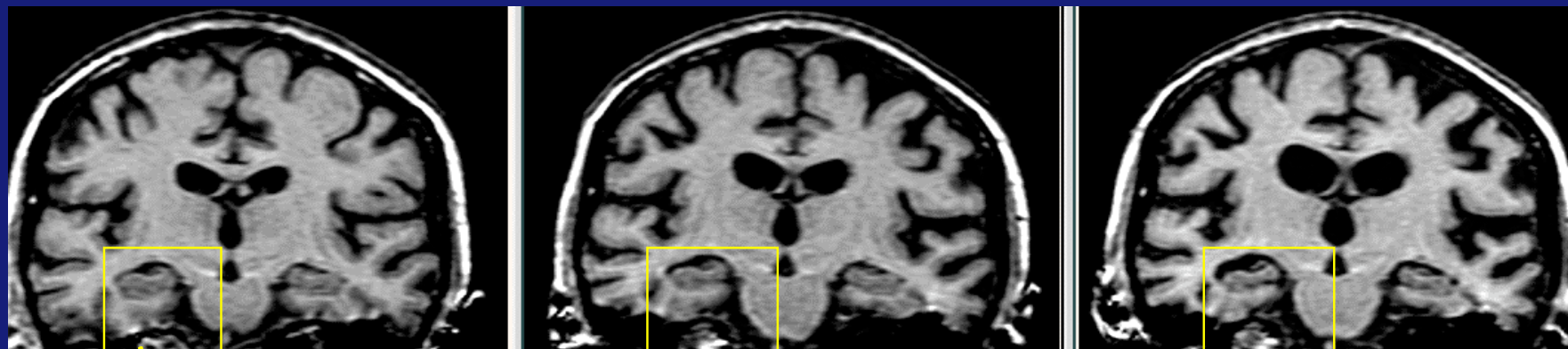
T1 measures how quickly the protons realign with the main magnetic field



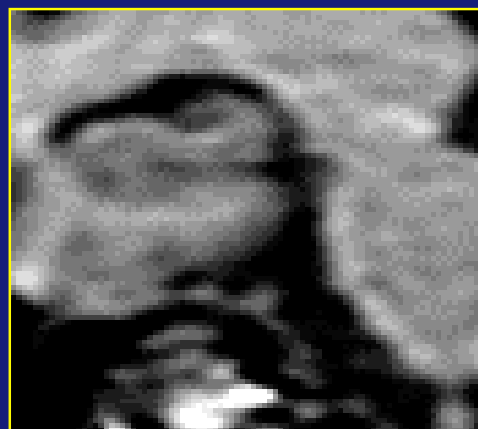
T2 measures how quickly the protons give off energy as they recover to equilibrium



Structural MRI: Alzheimer's disease



Time 0

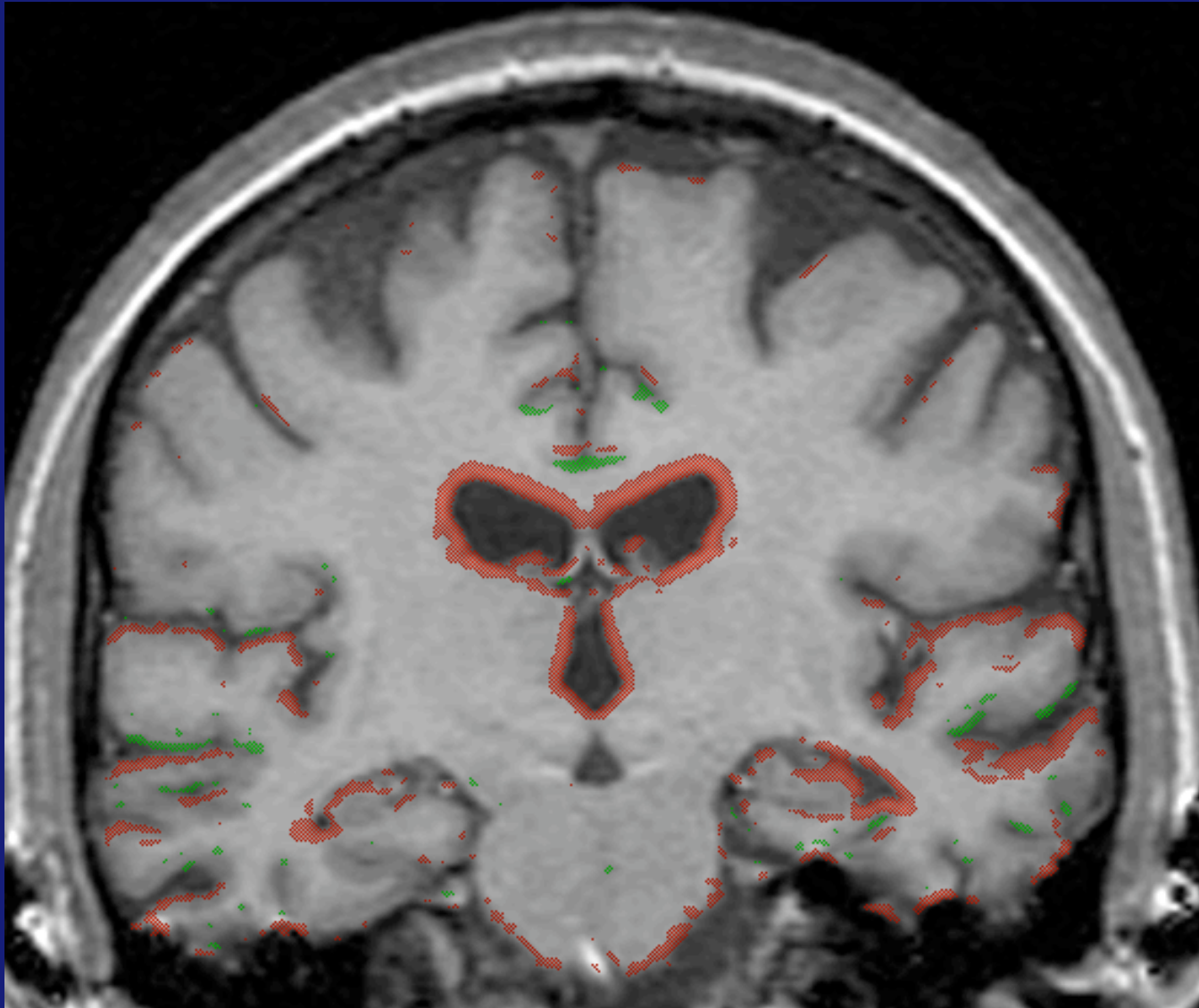


18months



36months

Red: widespread tissue loss in Alzheimer's disease



MRI

- Strong magnet
- Signal of hydrogen atoms
- Contrast in images caused by differences in:
 - hydrogen atom concentration
 - T1
 - T2

MRI:

Structural Imaging: grey matter and white matter

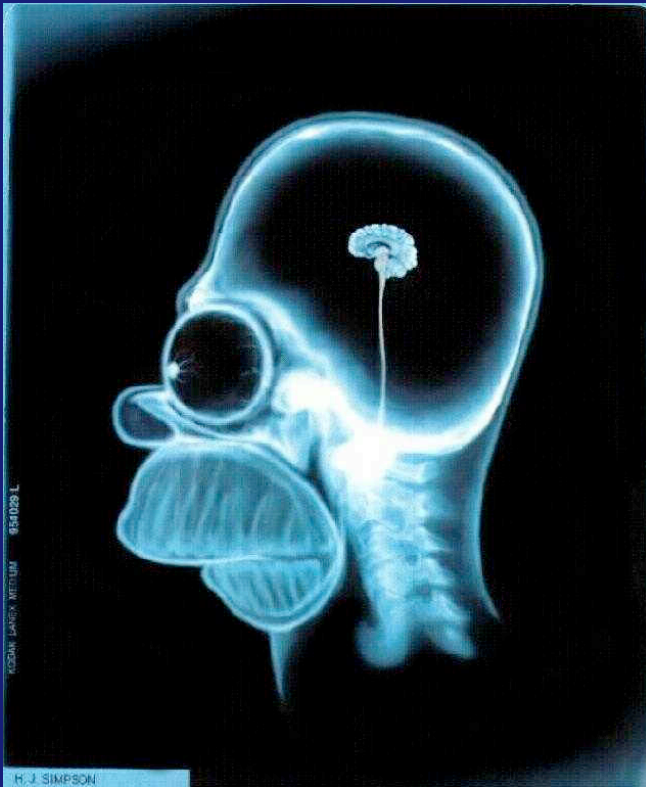
Functional MRI:

Brain Activation

- Experimental setup
 - The BOLD-effect
 - How to do an fMRI experiment
-
- Data Analysis

http://airto.loni.ucla.edu/BMCweb/BMC_BIOS/MarkCohen/Papers/TINS94/TINS.html

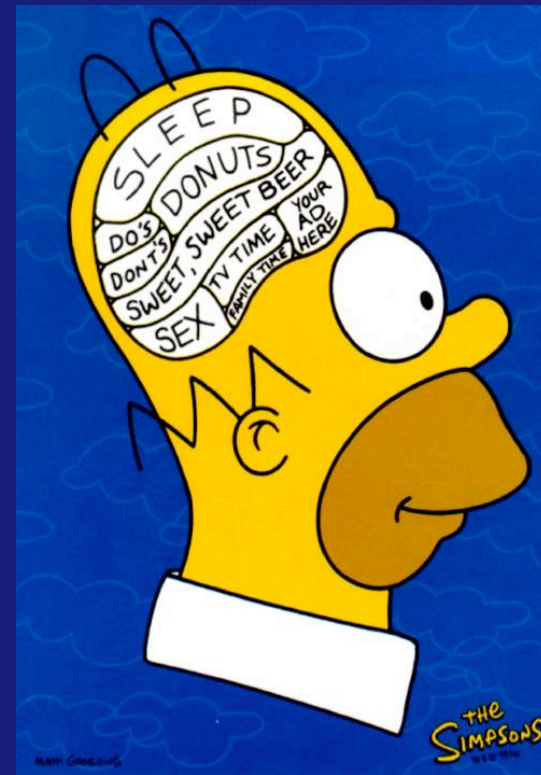
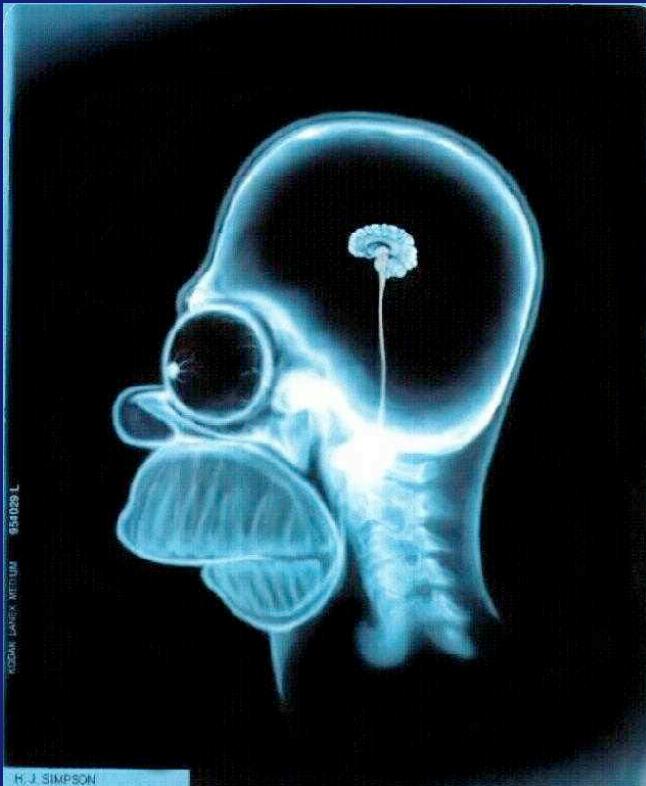
MRI studies brain anatomy.



From: http://defiant.ssc.uwo.ca/Jody_web/fmri4dummies.htm

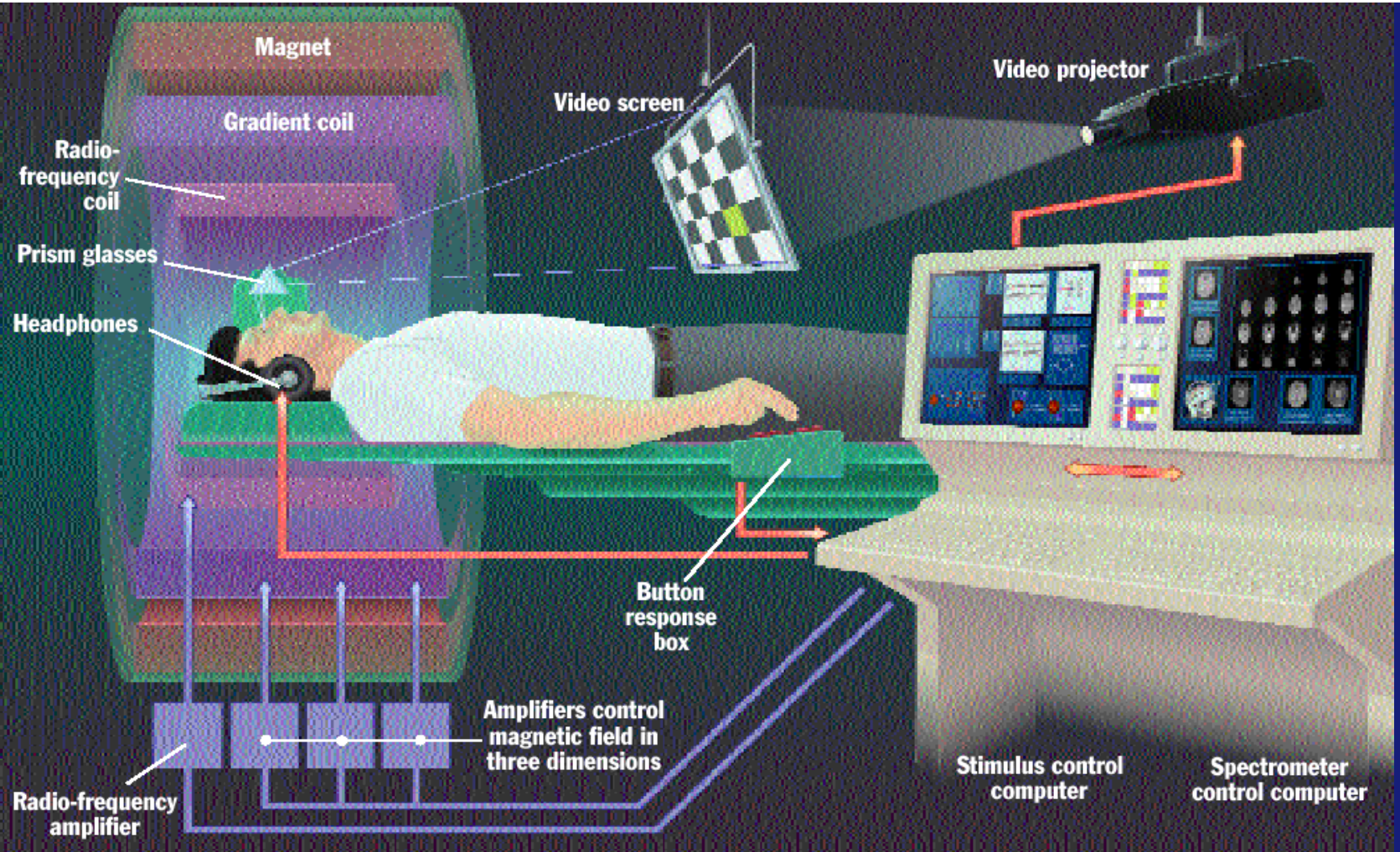
MRI studies brain anatomy.

Functional MRI (fMRI) studies brain function.



From: http://defiant.ssc.uwo.ca/Jody_web/fmri4dummies.htm

fMRI Setup

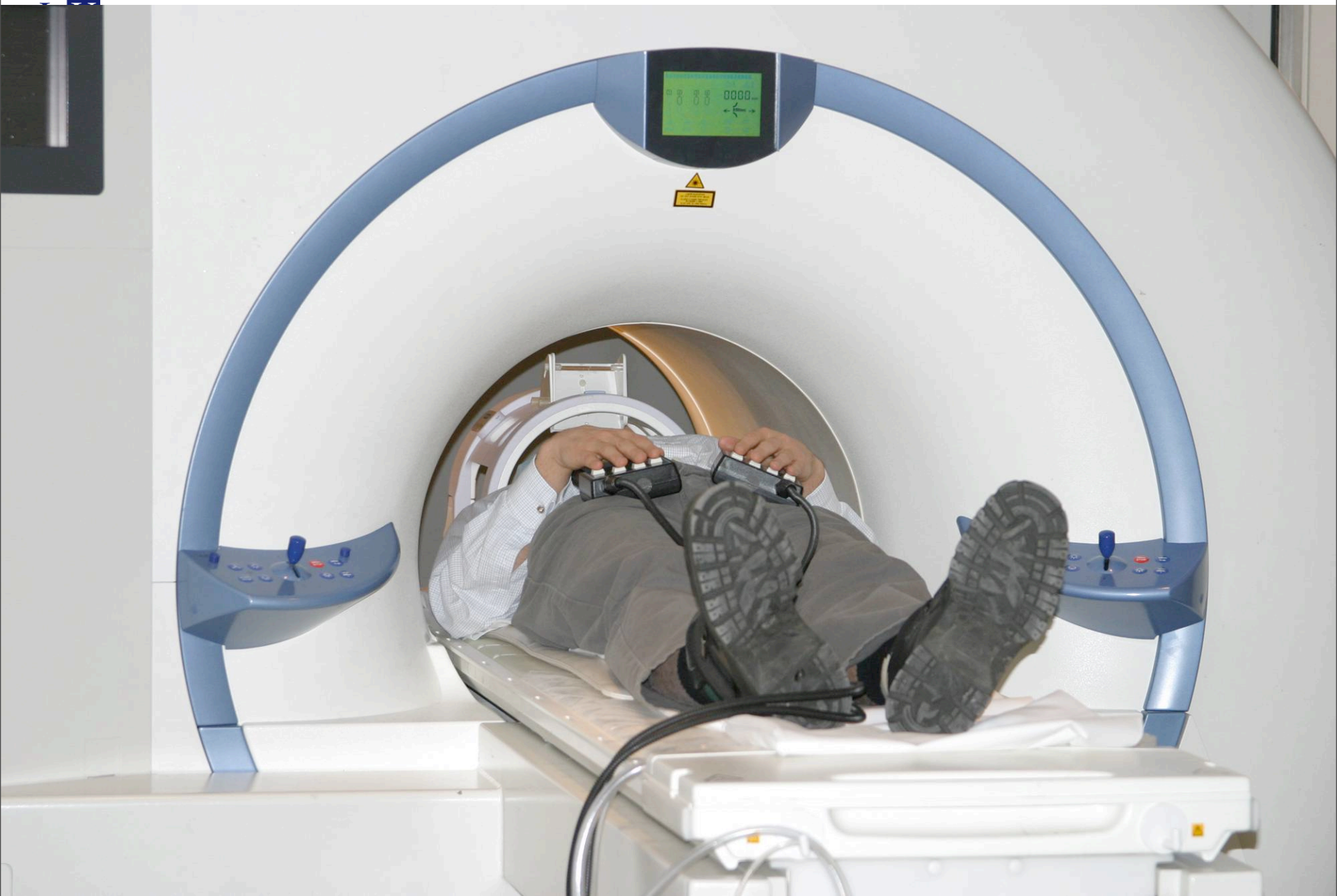


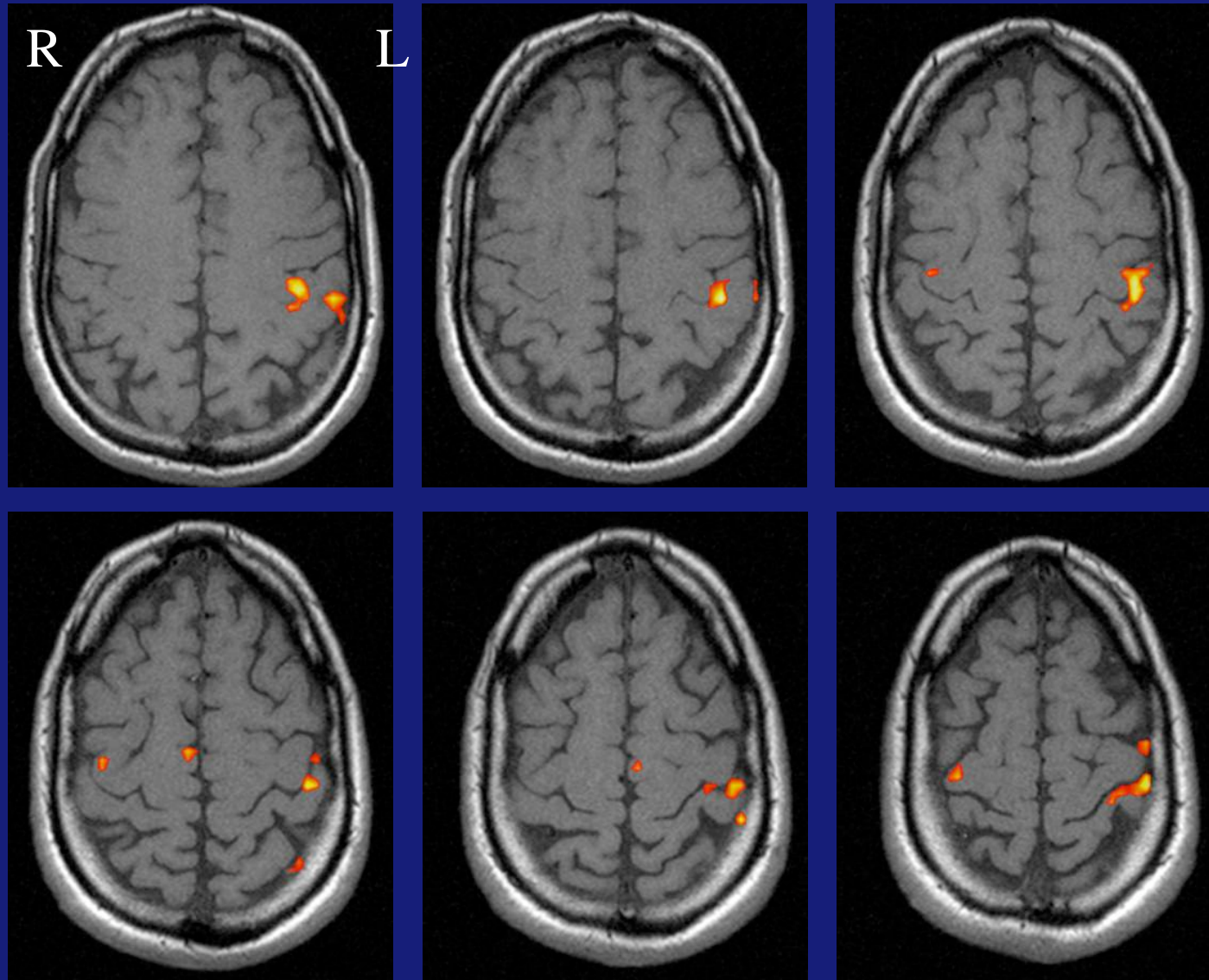


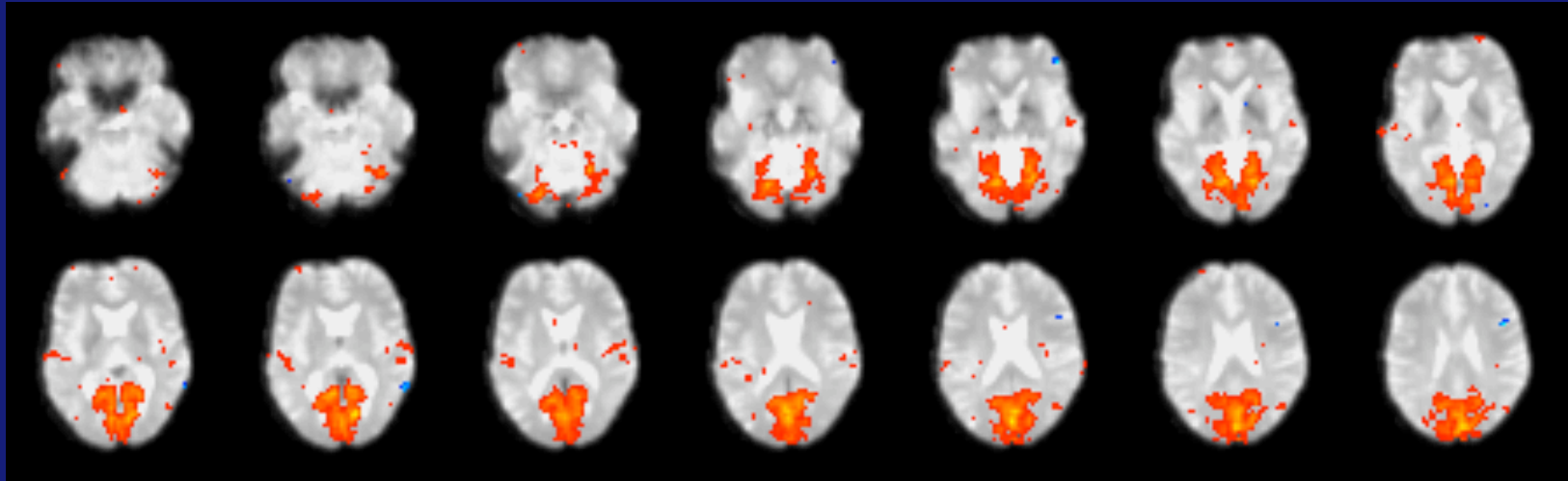
SIEMENS MAGNETOM

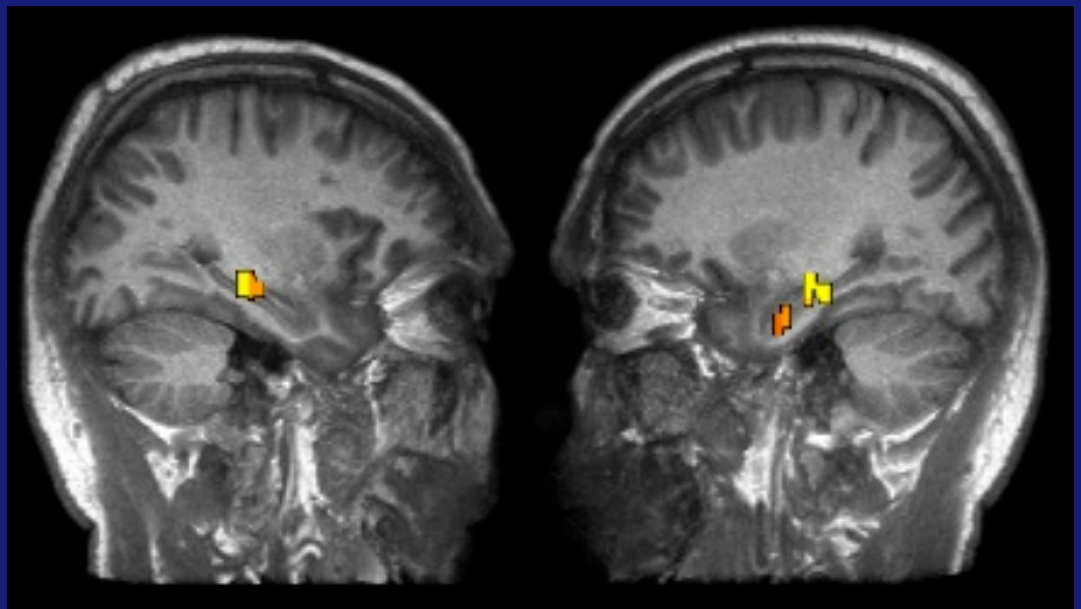
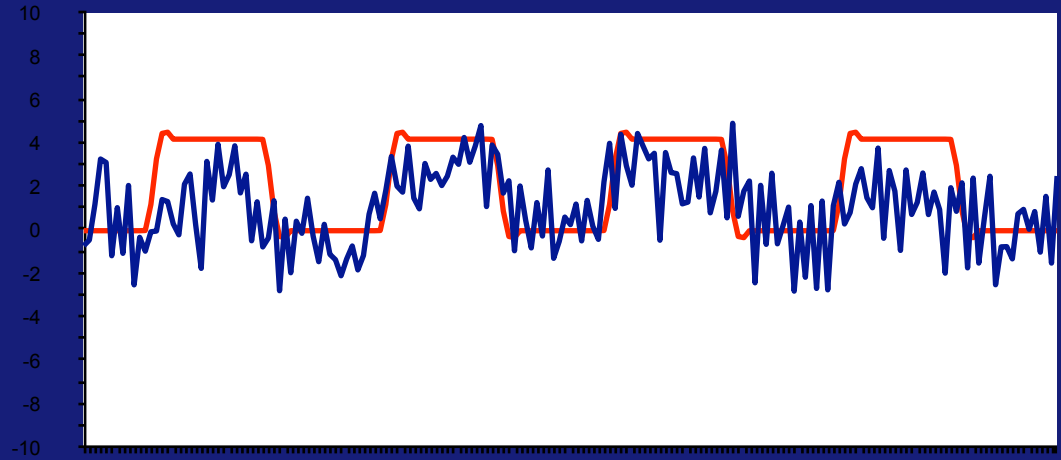
Sonata
Maestro Class



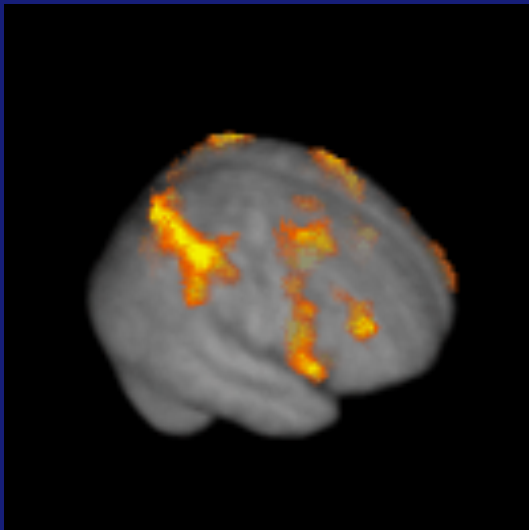




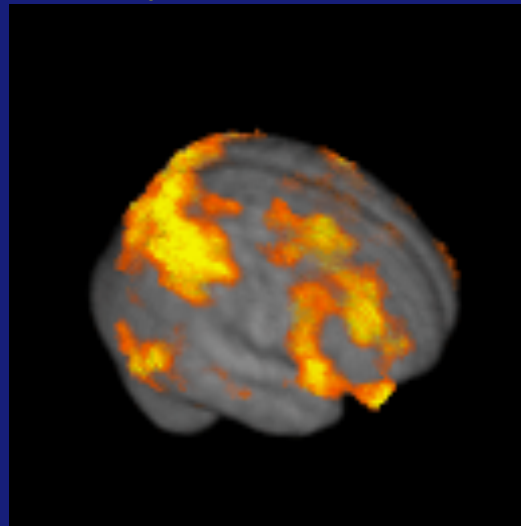




Working memory



Simple Working Memory

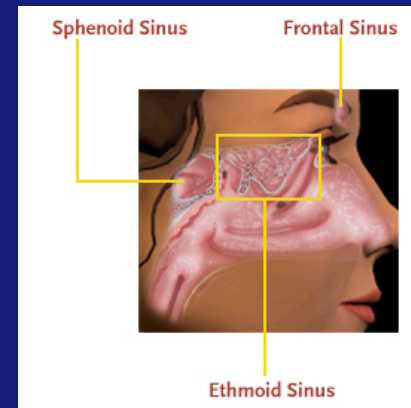
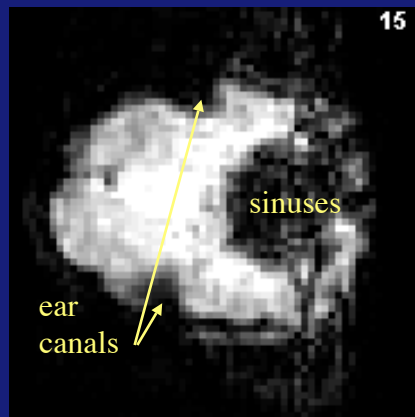
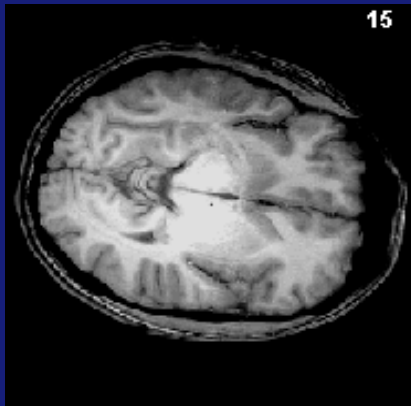


Increased Working Memory Load

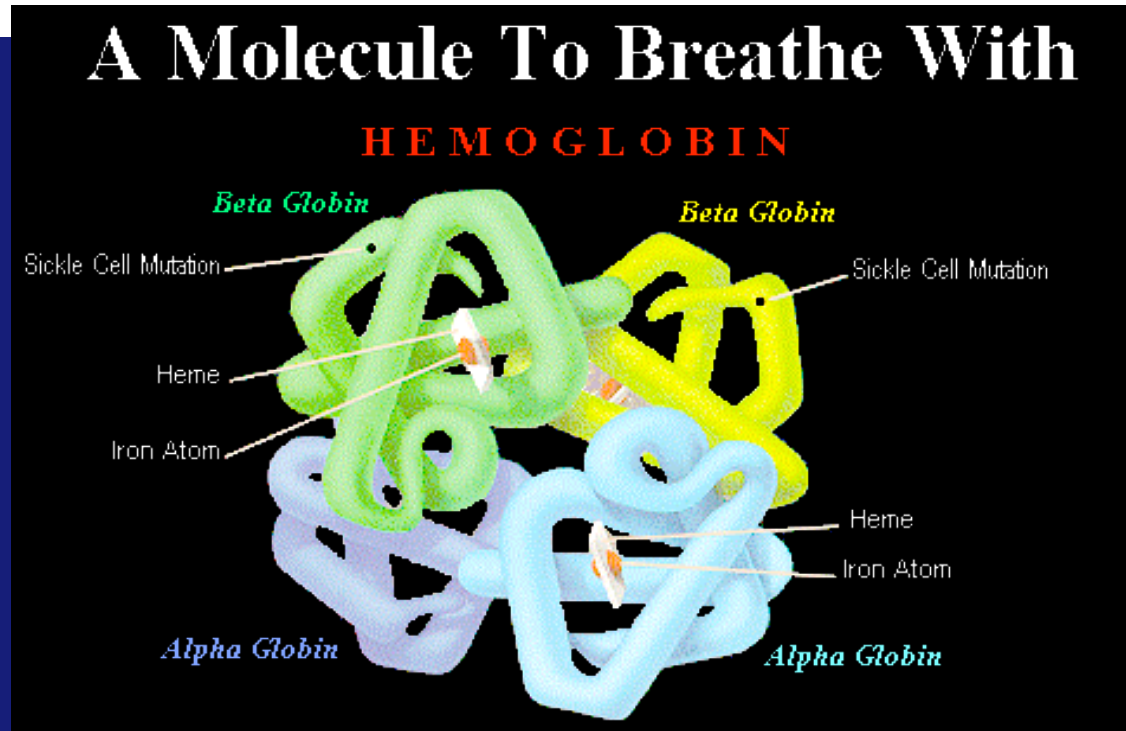
Remember: we have T1 and T2 images

We also have T2* weighted images: these are sensitive to local magnetic field inhomogeneities.

These T2* weighted images have artifacts near junctions between air and tissue: sinuses, ear canals



This is usually not so nice, but...



Hemoglobin (Hb):

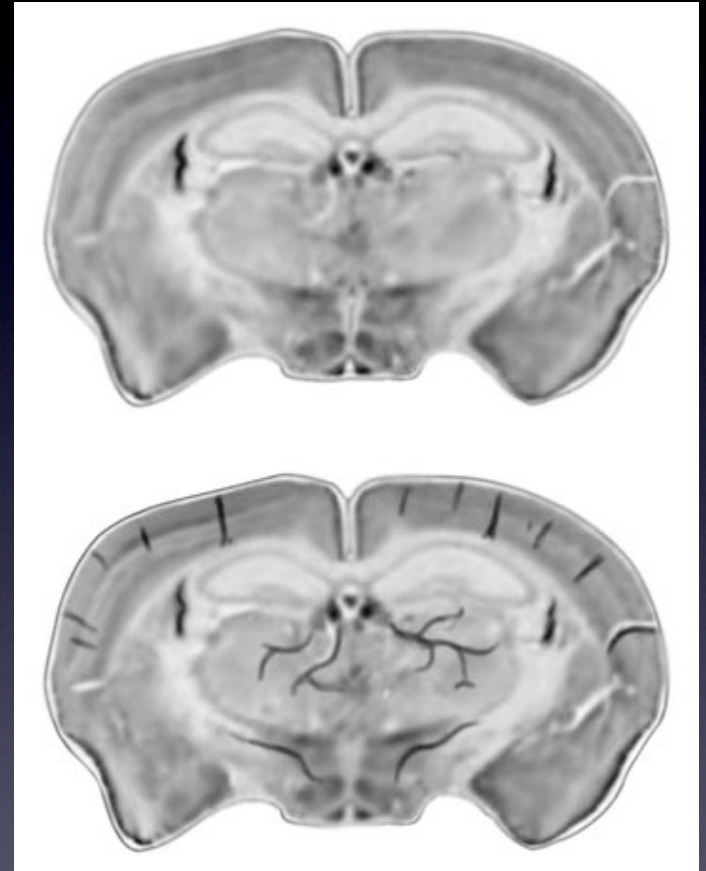
- four globin chains
- each globin chain contains a heme group
- at center of each heme group is an iron atom (Fe)
- each heme group can attach an oxygen atom (O_2)
- oxy-Hb (four O_2) is diamagnetic → no artifacts on T2* weighted images
- deoxy-Hb is paramagnetic → artifacts on T2* weighted images

Deoxygenated Blood → Signal Loss



Oxygenated blood?
No signal loss...

Deoxygenated blood?
Signal loss!!!

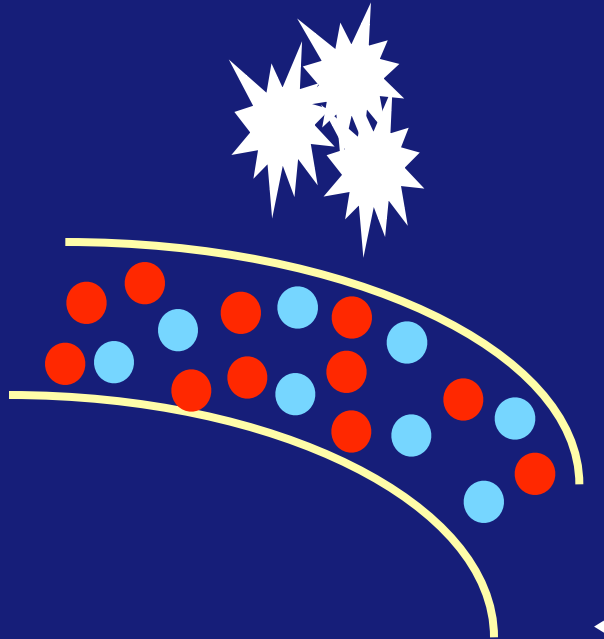


Images from Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

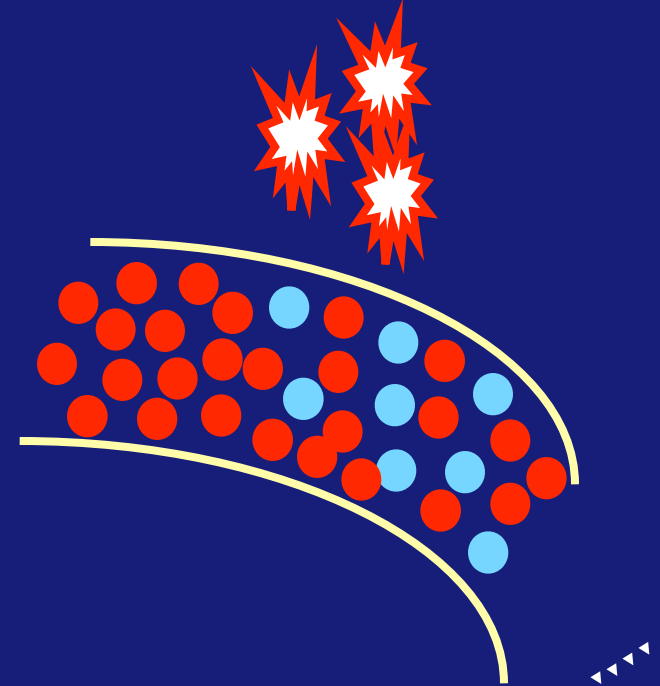
BOLD = Blood oxygenation level dependent

MRI: the BOLD effect

Rest



Neural Activation



- HbO_2 (oxyhemoglobin)
- Hb (deoxyhemoglobin)

“Oversupply” of $[\text{HbO}_2]$ \Rightarrow
Relative decrease of $[\text{Hb}]$

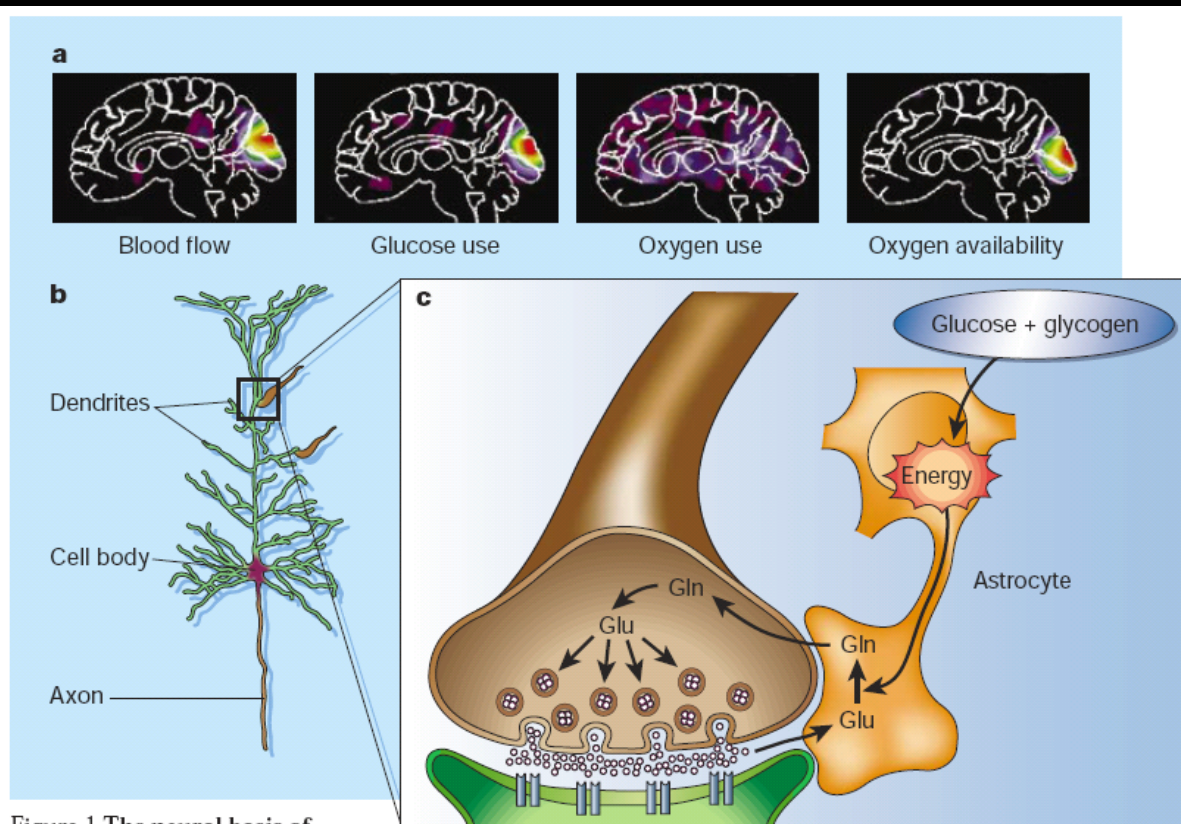
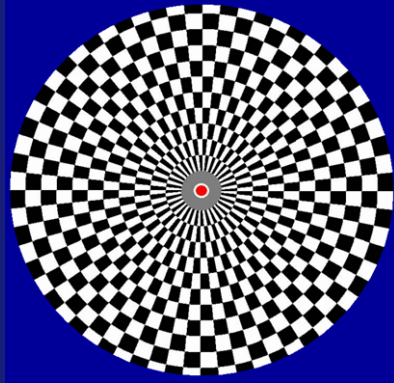


Figure 1 The neural basis of functional magnetic resonance imaging (fMRI). a, Viewing a stimulus such as a checkerboard produces marked changes in the areas of the brain that respond to visual stimuli, as seen in these positron-emission tomographic (PET) images. These changes include increases in glucose use and blood flow that are much greater than those in oxygen consumption. As a result there is an increase in the oxygen level in those areas (supply exceeds demand). PET is usually used to monitor blood flow. fMRI detects the changes in oxygen availability as a local change in the magnetic field. The resulting fMRI signal is a 'blood-oxygen-level-dependent' (BOLD) signal. b, As Logothetis *et al.*² show, these metabolic and circulatory changes are driven by electrical potentials arising from the input to, and information processing within, the dendrites of neurons. c, An attractive explanation for the BOLD signal invokes the preferential use of glycolysis in nearby non-neuronal cells (astrocytes) to handle an increase in the release of the neurotransmitter glutamate (Glu), which must be converted to glutamine (Gln) before it is returned to the neuron. Glycolysis consumes glucose to produce energy, but does not require oxygen.

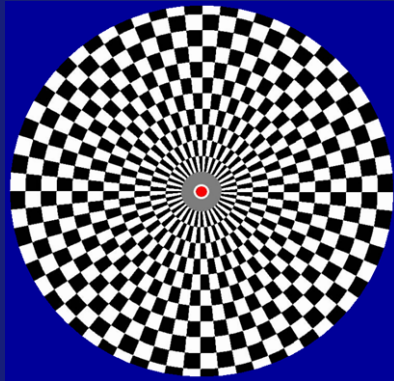
One of the first examples: fMRI Activation in the visual cortex



Flickering Checkerboard

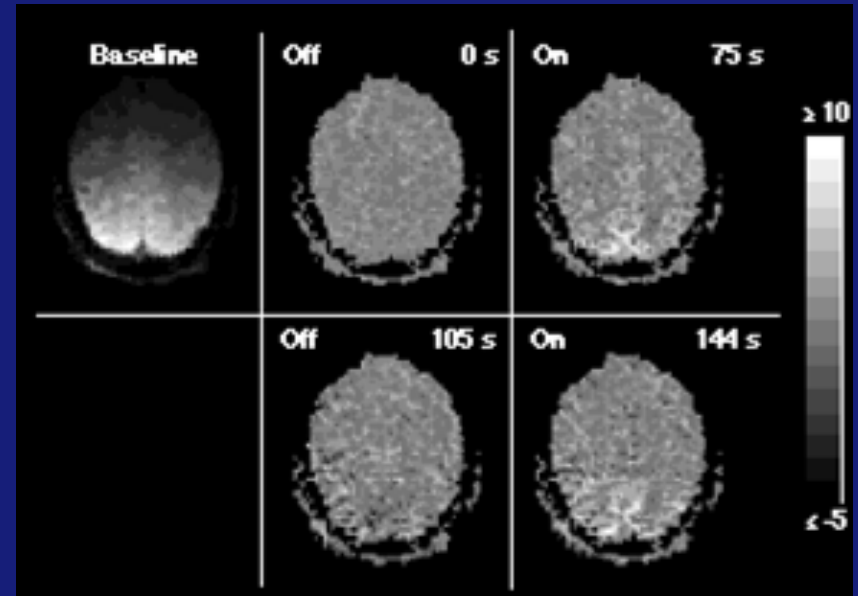
OFF (60 s) - ON (60 s) - OFF (60 s) - ON (60 s) - OFF (60 s)

One of the first examples: fMRI Activation in the visual cortex

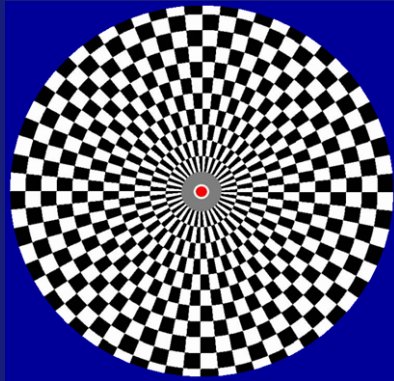


Flickering Checkerboard

OFF (60 s) - ON (60 s) - OFF (60 s) - ON (60 s) - OFF (60 s)

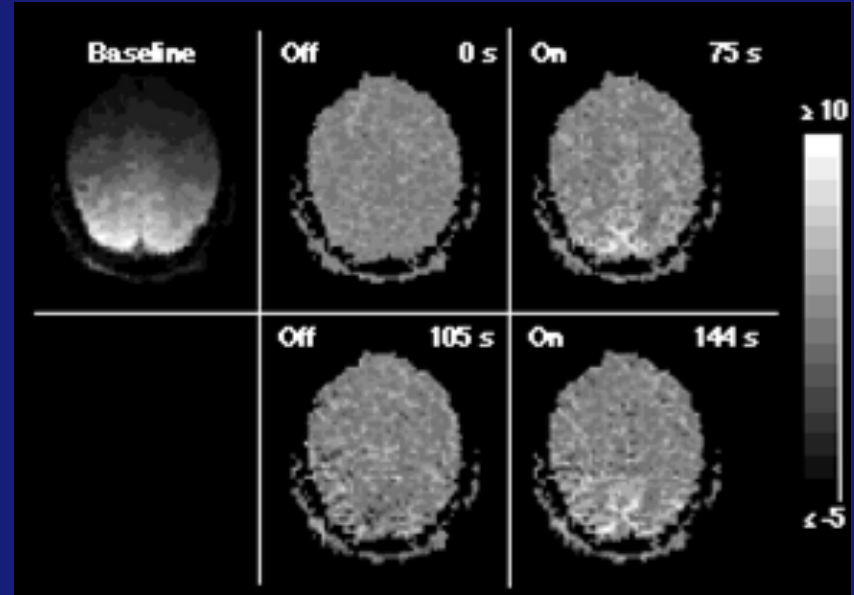


One of the first examples: fMRI Activation in the visual cortex

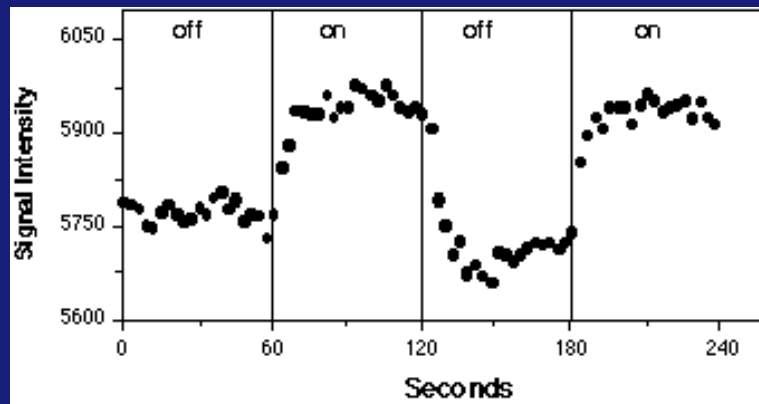


Flickering Checkerboard

OFF (60 s) - ON (60 s) - OFF (60 s) - ON (60 s) - OFF (60 s)



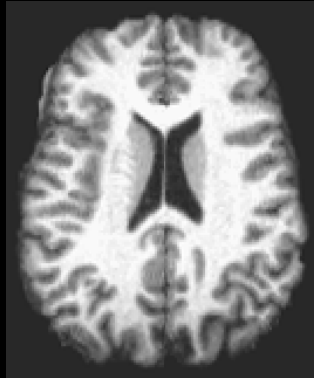
Brain
Activity



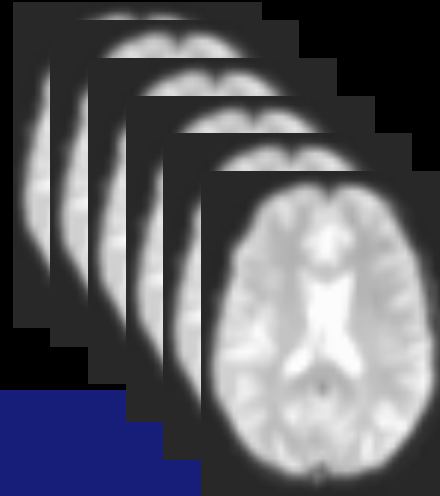
- Experimental setup
 - The BOLD-effect
 - **How to do an fMRI experiment**
-
- Data Analysis

- Make the MR sequence sensitive to BOLD: T2* weighted
- BOLD causes small signal changes ($\sim 0.1 - 3\%$) against thermal noise, physiological fluctuations, head motion, MR system instabilities \rightarrow we need many images to increase sensitivity \rightarrow Fast Scanning
- Reasonable / good spatial resolution
- **Typical fMRI experiment**
 - Single shot T2* echo planar imaging (EPI)
 - Spatial resolution 3–4 mm
 - TR: 2-4 seconds (20-40 slices)
 - $\sim 80 - 300$ whole brain scans ($\sim 4 - 15$ minutes)

MRI

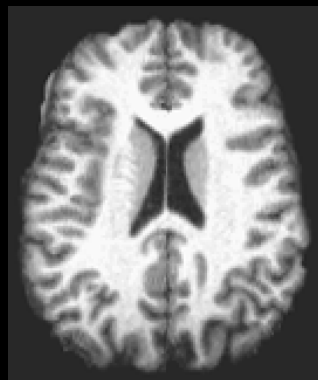


fMRI



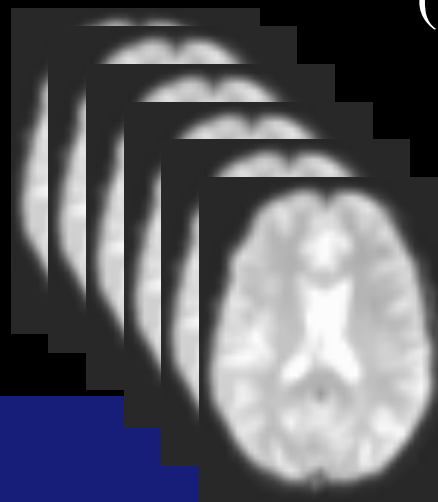
high resolution
(1 mm)

MRI



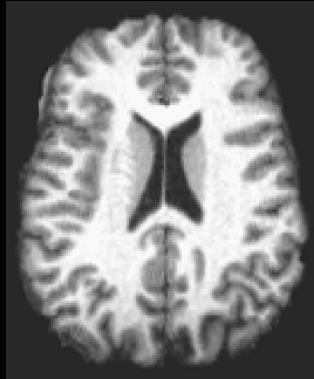
fMRI

low resolution
(~3 mm)



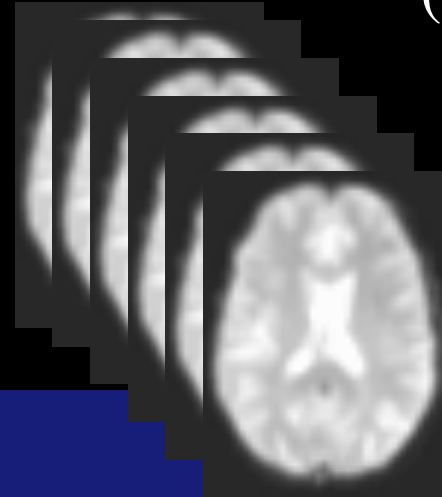
high resolution
(1 mm)

MRI



fMRI

low resolution
(~3 mm)



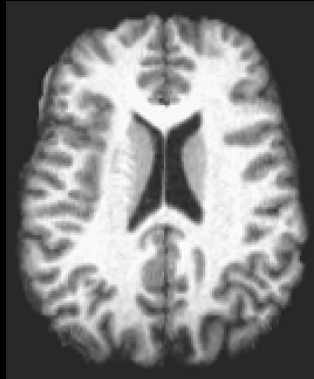
fMRI

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

↑ neural activity → ↑ blood oxygen → ↑ fMRI signal

high resolution
(1 mm)

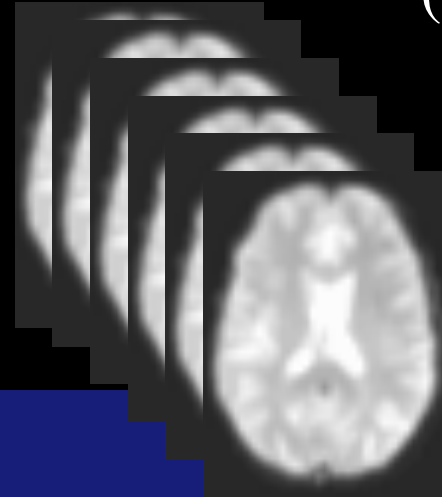
MRI



one image

fMRI

low resolution
(~3 mm)



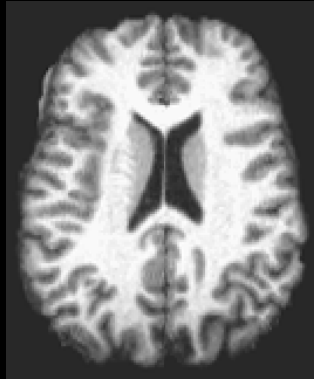
fMRI

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

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high resolution
(1 mm)

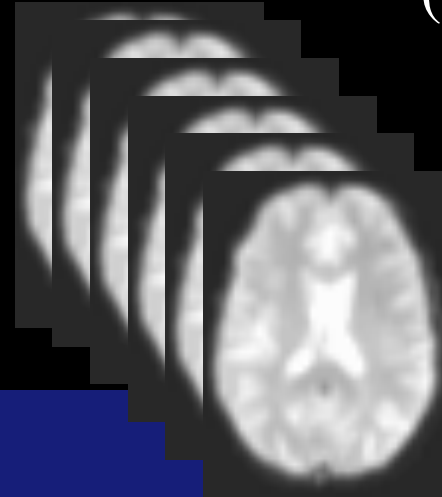
MRI



one image

fMRI

low resolution
(~3 mm)



many images
(e.g., every 2 sec for many minutes)

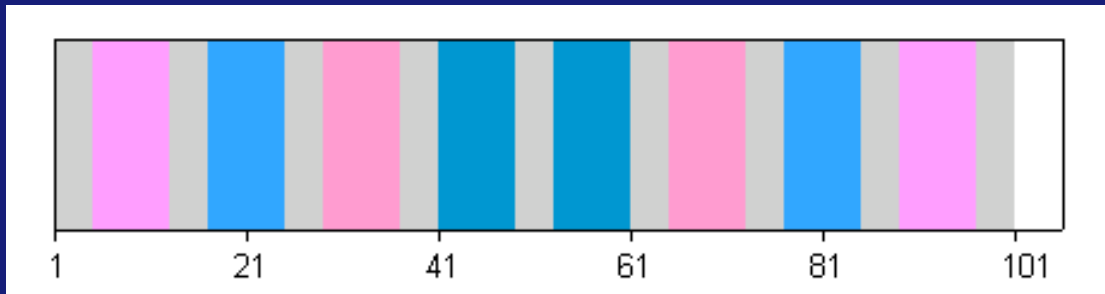
fMRI

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

↑ neural activity → ↑ blood oxygen → ↑ fMRI signal

You also need a paradigm

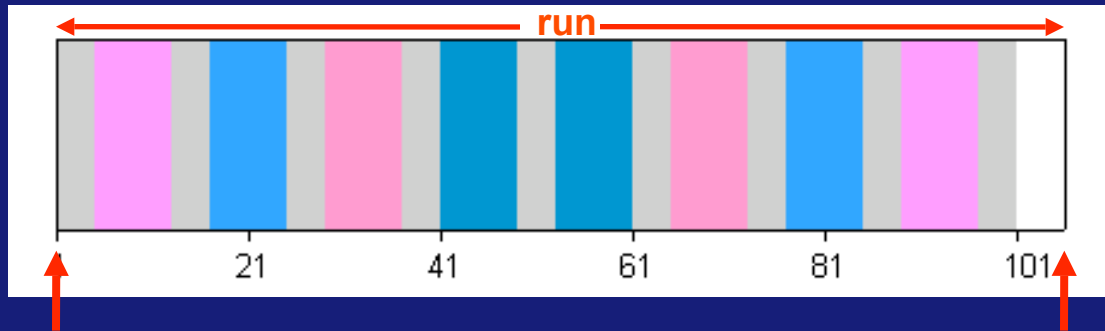
paradigm (jargon): the set of conditions and their order used in a particular fMRI session



Time 

You also need a paradigm

paradigm (jargon): the set of conditions and their order used in a particular fMRI session

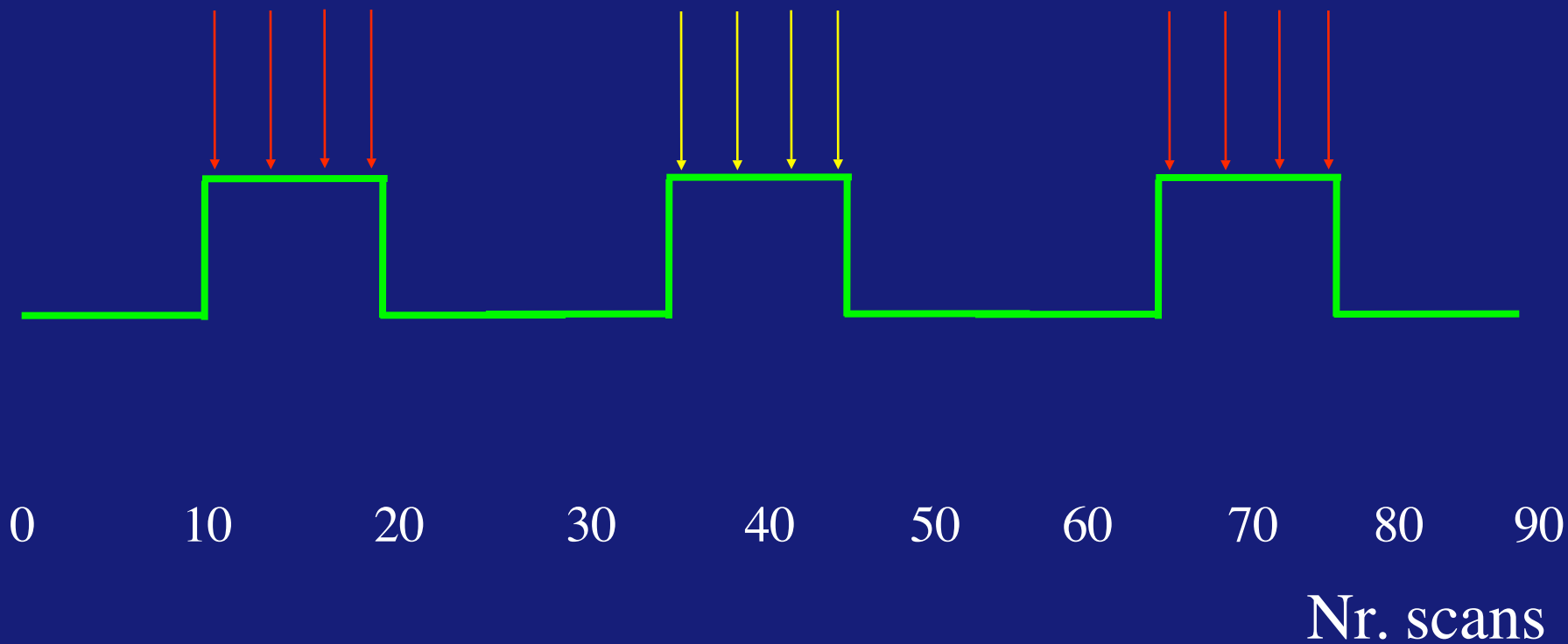


volume #1
(time = 0)

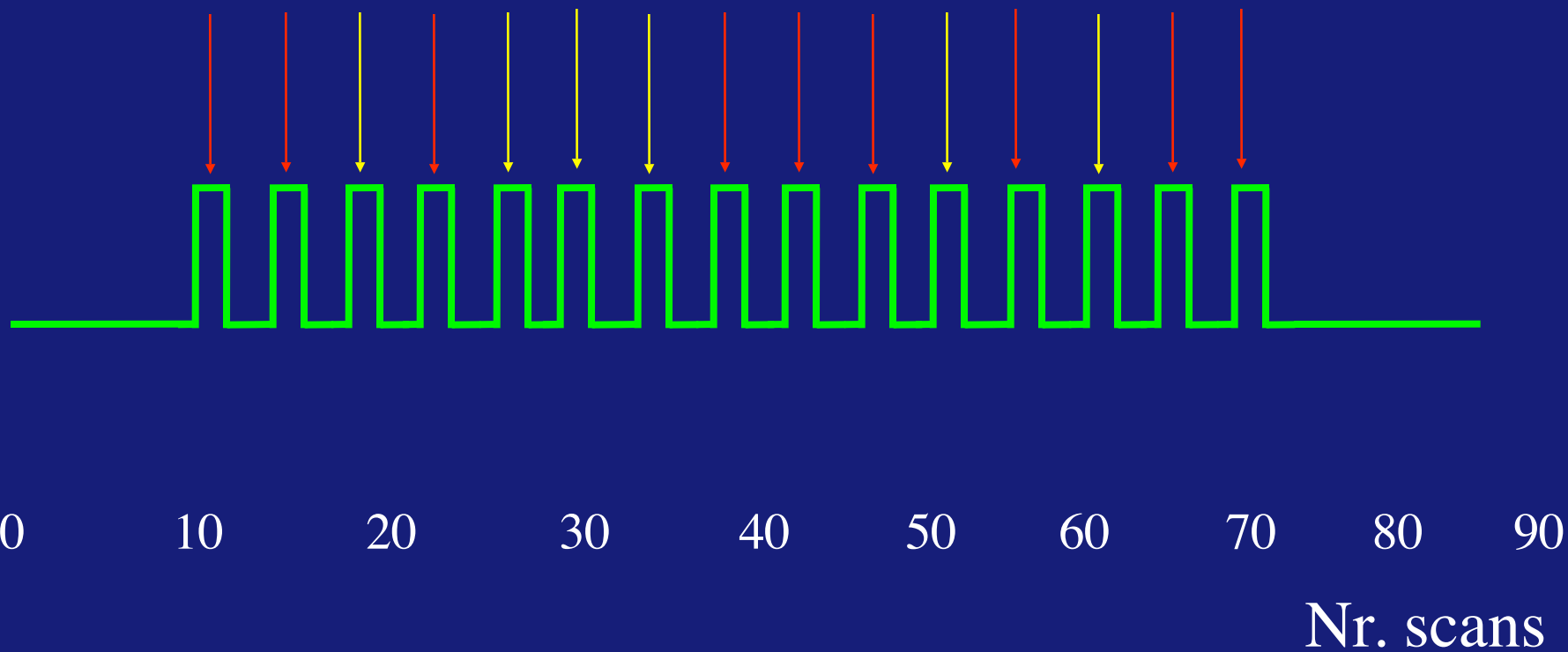
volume #105
(time = 105 vol x 2 sec/vol = 210 sec = 3:30)

Time

- Block designs
- Event Related designs



- Block designs
- **Event Related designs**



- *Advantages Event Related Designs (memory studies!!)*

- Randomisation (to prevent anticipation)
- Post-hoc classification

Correct response:

F F U F U F U U U F F U U F

Actual response:

F \dot{U} U F U F U \dot{F} U F F \dot{F} U F

False negative

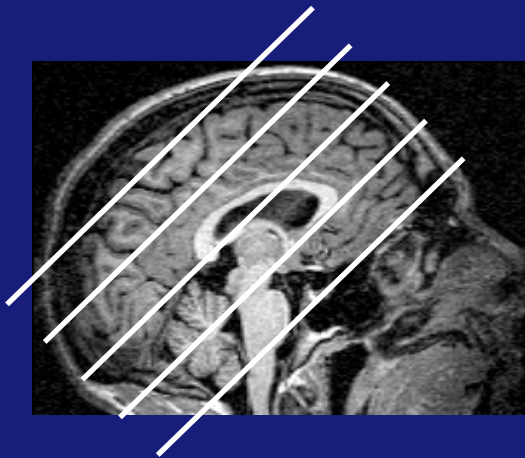
False positives

1) Prepare subject

- Consent form
- Safety screening
- Instructions

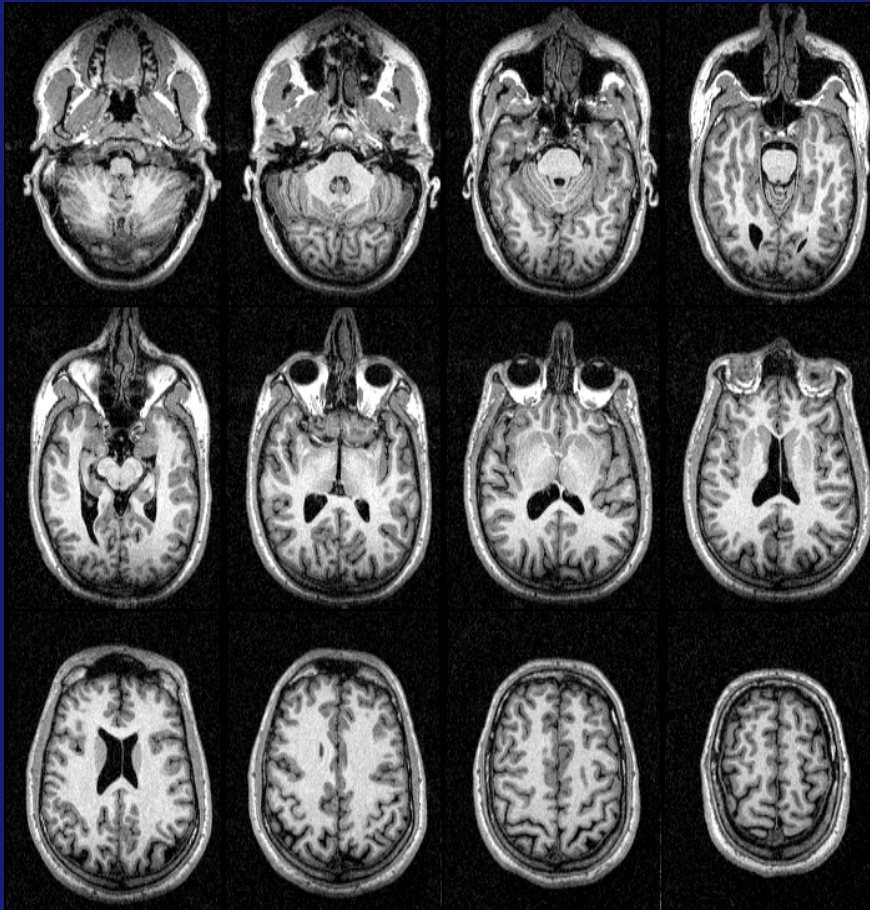
2) Scout images

Needed to plan your fMRI slices



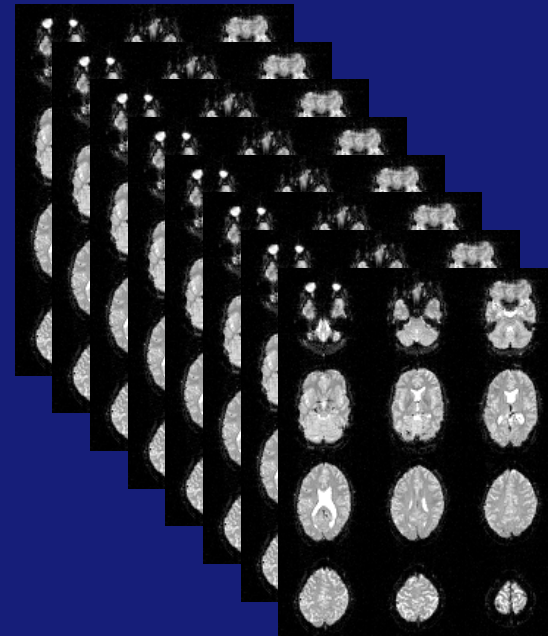
3) Get anatomical images

- high-resolution images (e.g., 1x1x1 mm)
- ~8 minutes



fMRI Experiment Stages: Functionals

- 4) Take functional (T2*) images while patient is performing your paradigm
- images are indirectly related to neural activity
 - usually low resolution images (3x3x3 mm)
 - sample many volumes (time points) (e.g., 1 volume every 2 seconds for 150 volumes = 300 sec = 5 minutes)



FMRI

- T2* weighted MR images are sensitive to local field inhomogeneities
- These inhomogeneities decrease in regions where the brain becomes more activated (more oxygen, causing more signal)
- For FMRI we need:
 - Many scans (and therefore fast scanning)
 - Reasonable spatial resolution
 - A paradigm

FMRI: Data Analysis Overview

Terminology

Analysis steps:

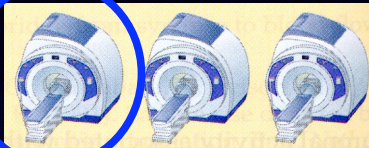
- Motion Correction
- Filtering: spatial and temporal
- General Linear Model: single subjects
- Averaging different subjects (group analysis):
registration to standard space

Terminology of fMRI

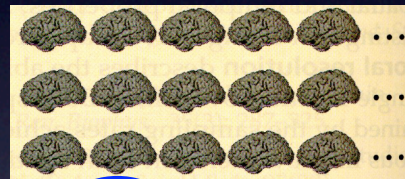
subjects



sessions



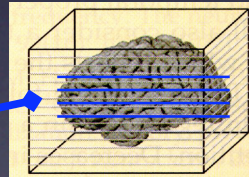
runs



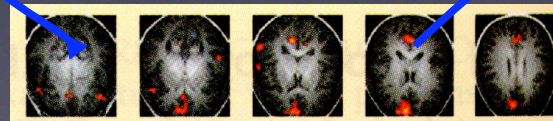
single run



volume



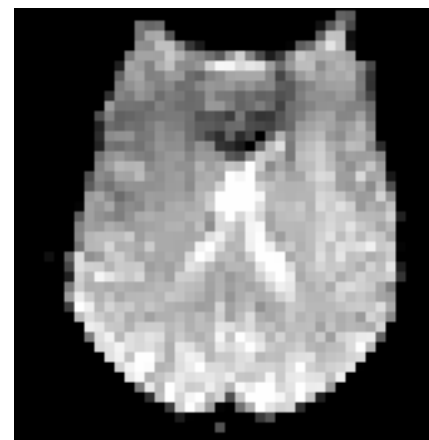
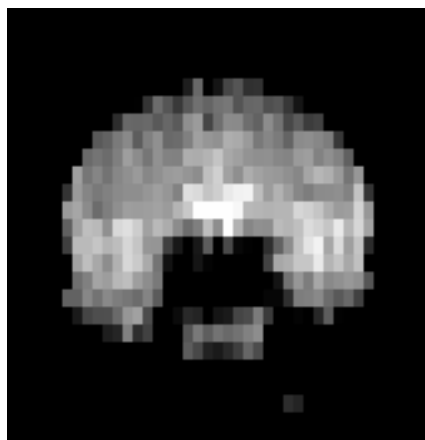
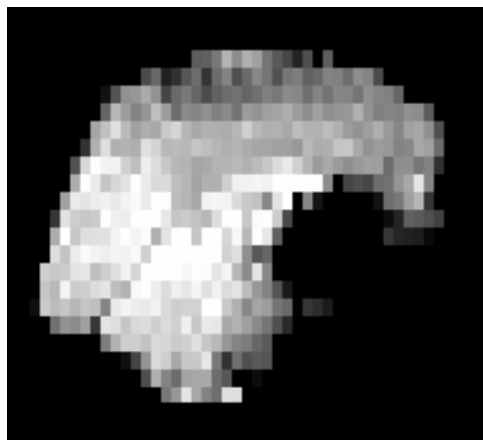
slices



voxel

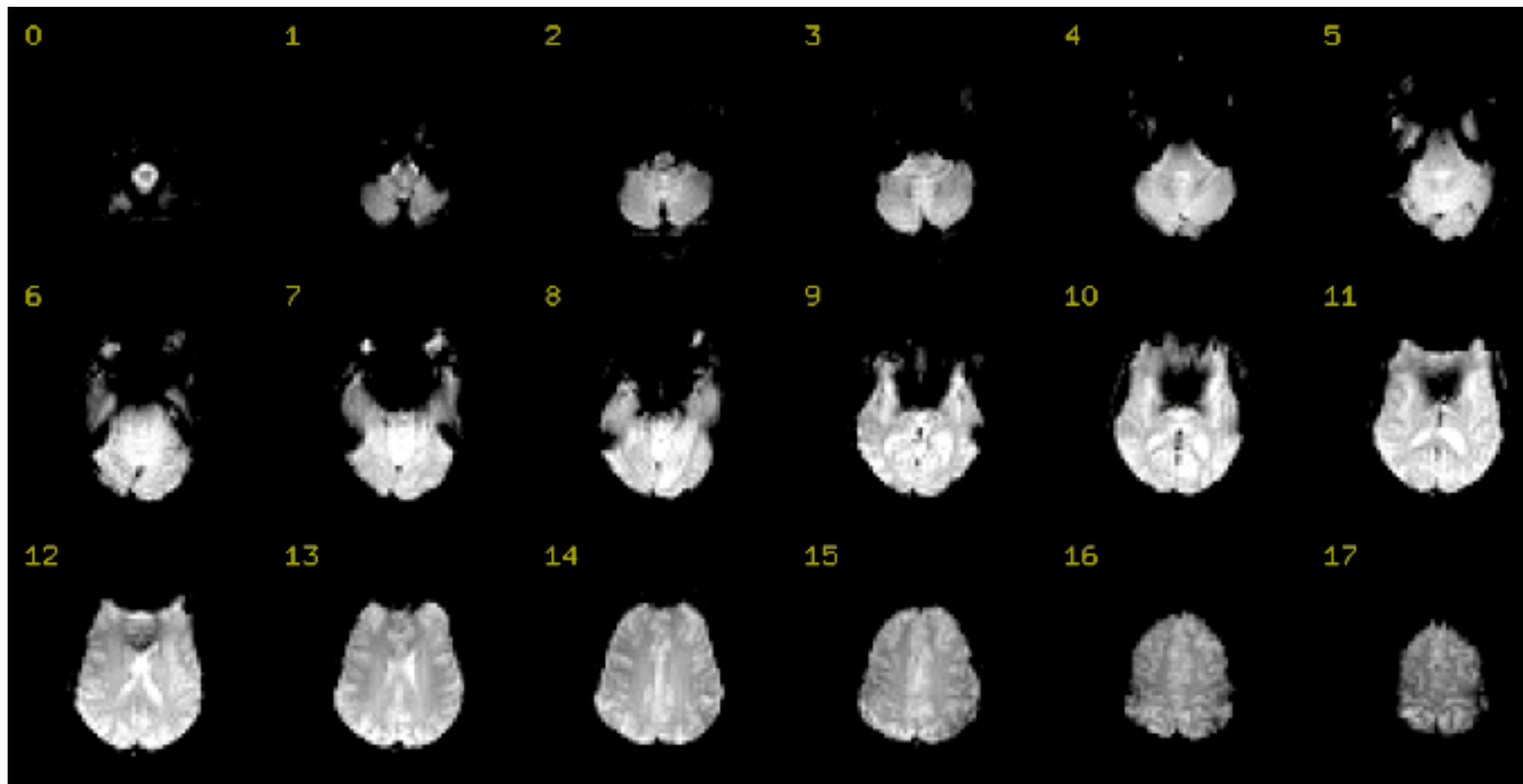


Images - Low Resolution FMRI



- A sequence of low resolution T2*-weighted volumes are taken during the FMRI experiment
- For example, 200 volumes, 1 taken every 3 secs
- A single FMRI volume is shown here in *orthogonal view*

Images - Low Resolution FMRI



The same FMRI volume is shown here in *lightbox* view

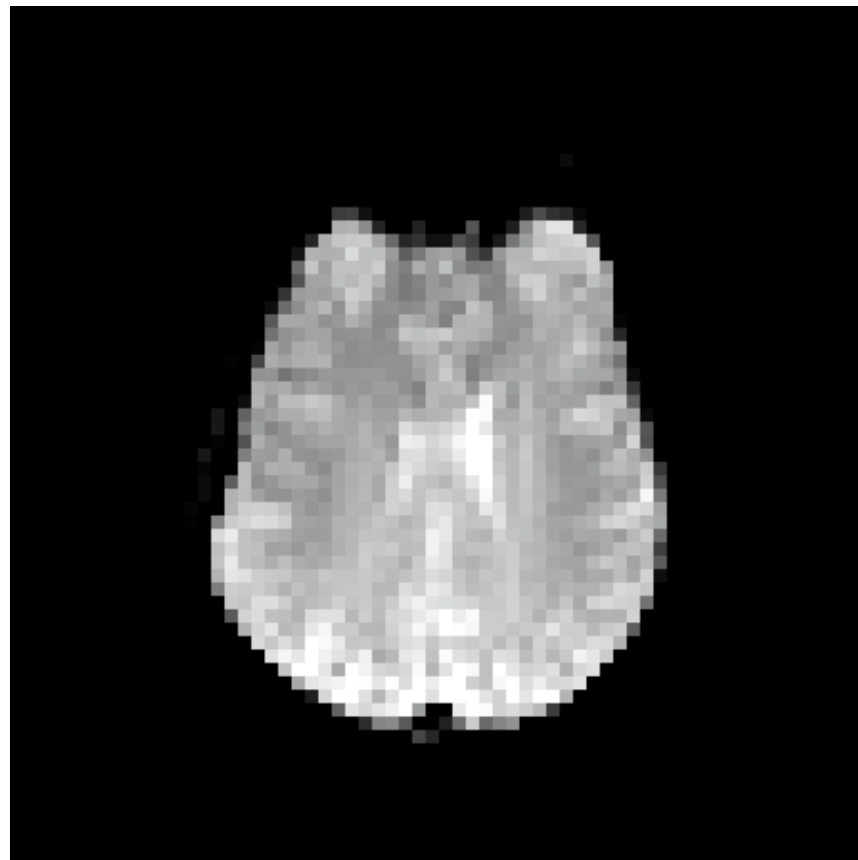


Images - Low Resolution FMRI

The whole time series - a single slice taken from
each volume



Images - Low Resolution FMRI

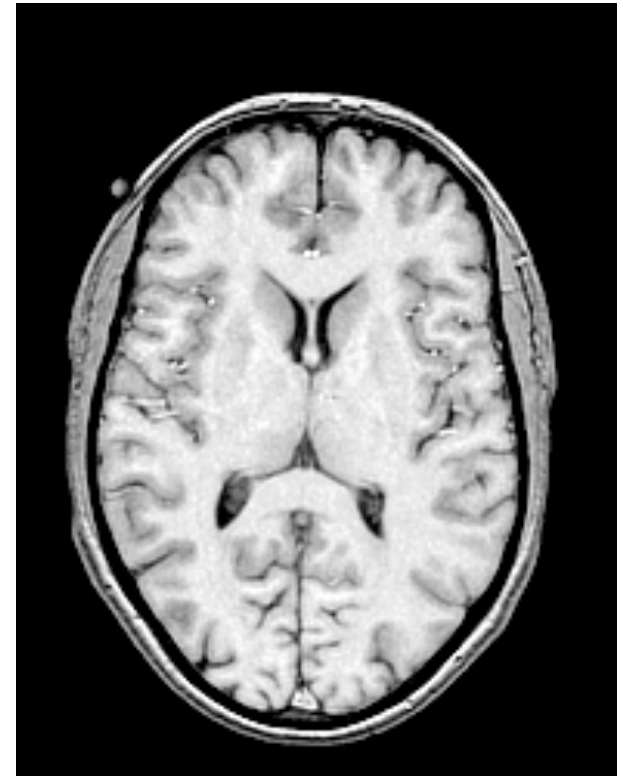


The whole time series - a single slice taken from each volume



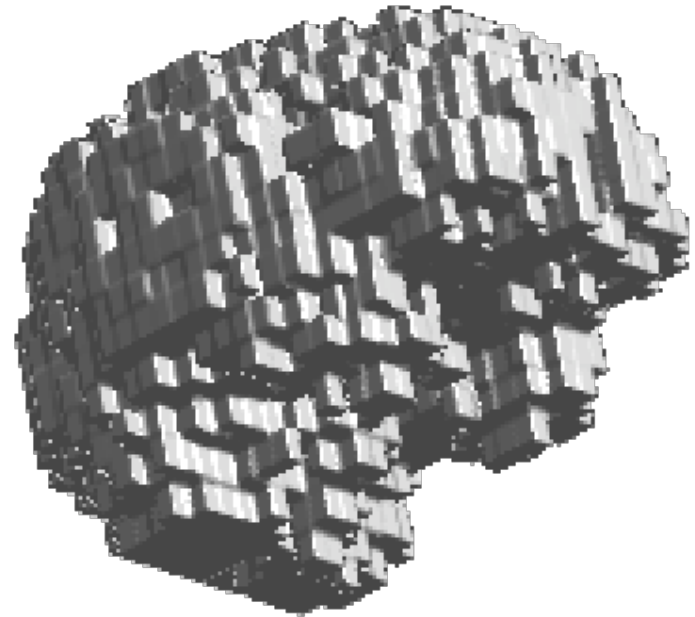
Images - High Resolution MRI

- A single high-resolution T1-weighted image is taken
- Used, for example, to map activations onto
- Also as an accuracy aid in subject-subject or subject-standard EPI registration





Images - High Resolution MRI

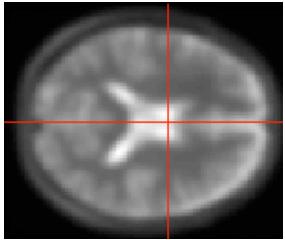


Compare high-resolution voxels with low-resolution

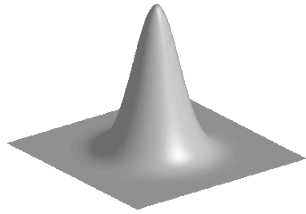


FMRI Analysis Overview

fMRI time-series



Motion
Correction

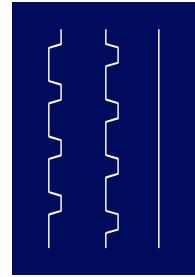


Filtering

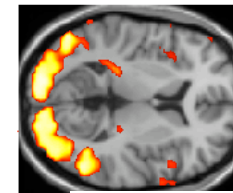
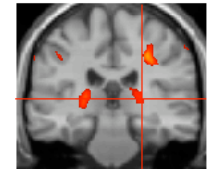
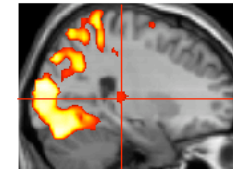
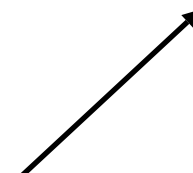
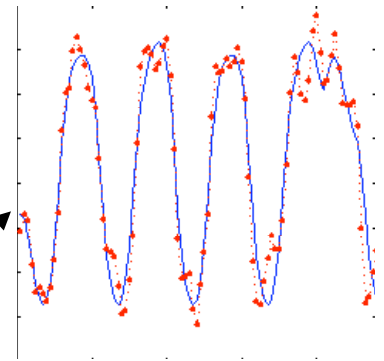


General Linear Model

Design matrix



Parameter Estimates



FMRI: Data Analysis Overview

Terminology

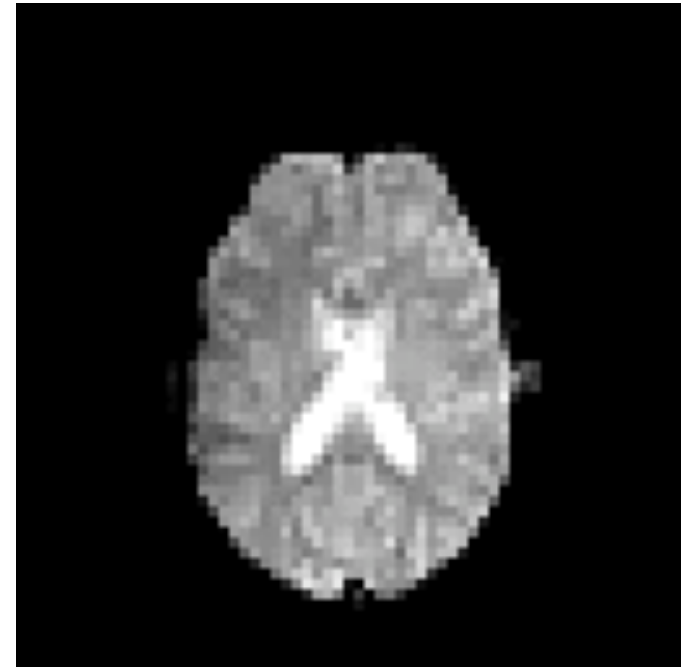
Analysis steps:

- Motion Correction
- Filtering: spatial and temporal
- General Linear Model: single subjects
- Averaging different subjects (group analysis):
registration to standard space



Motion Correction: Why?

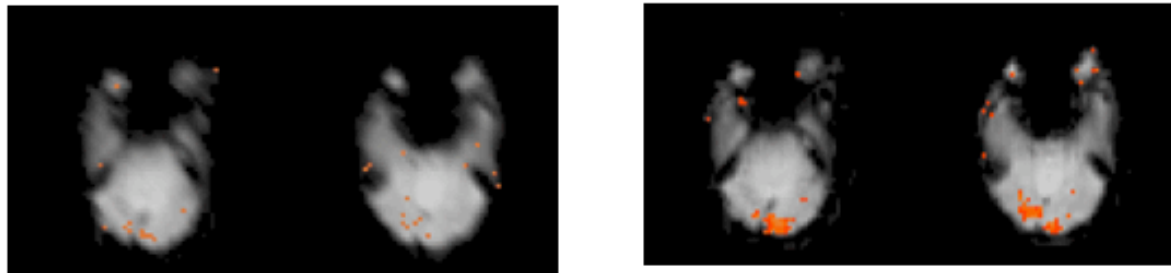
- People move in the scanner
- Even with padding around the head there is still some motion
- Through time each voxel should be located at a consistent anatomical point
- Motion correction realigns to a common reference



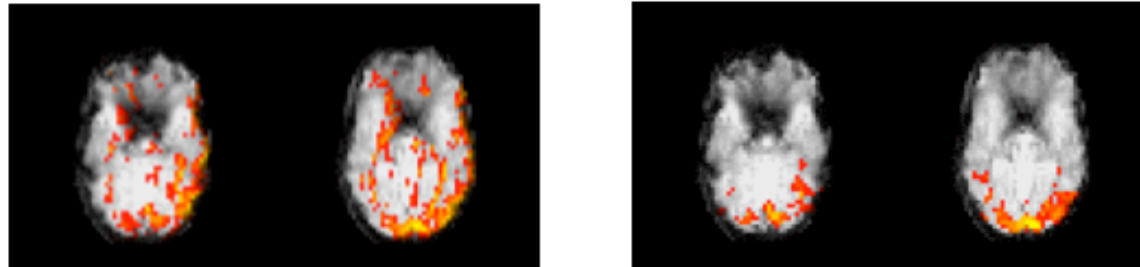


Effect of Motion Correction

Uncorrelated Motion



Stimulus Correlated Motion



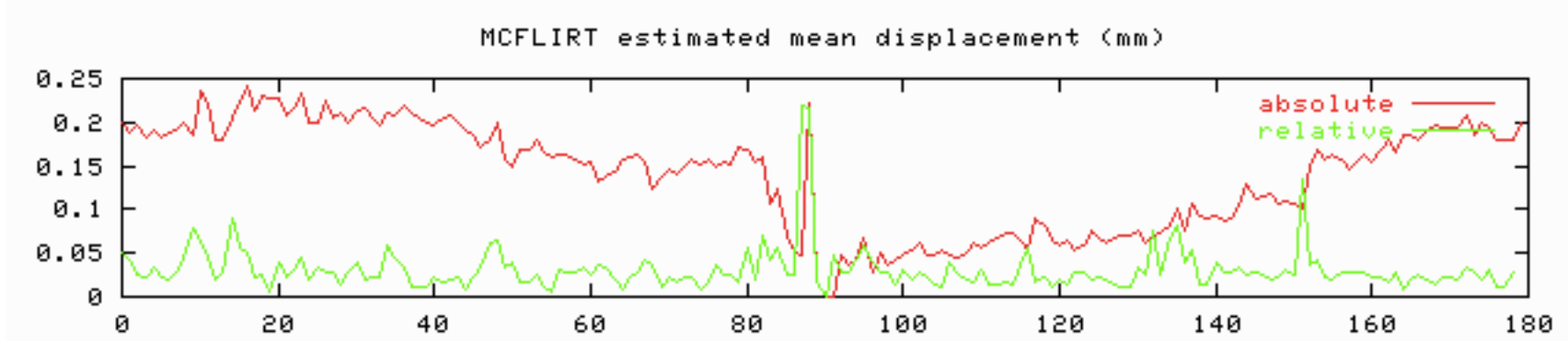
Without MC

With MC



Motion Parameter Output

Summary of total motion (**relative** and **absolute**)



Note that large jumps are more serious than slower drifts, especially in the relative motion plot

FMRI: Data Analysis Overview

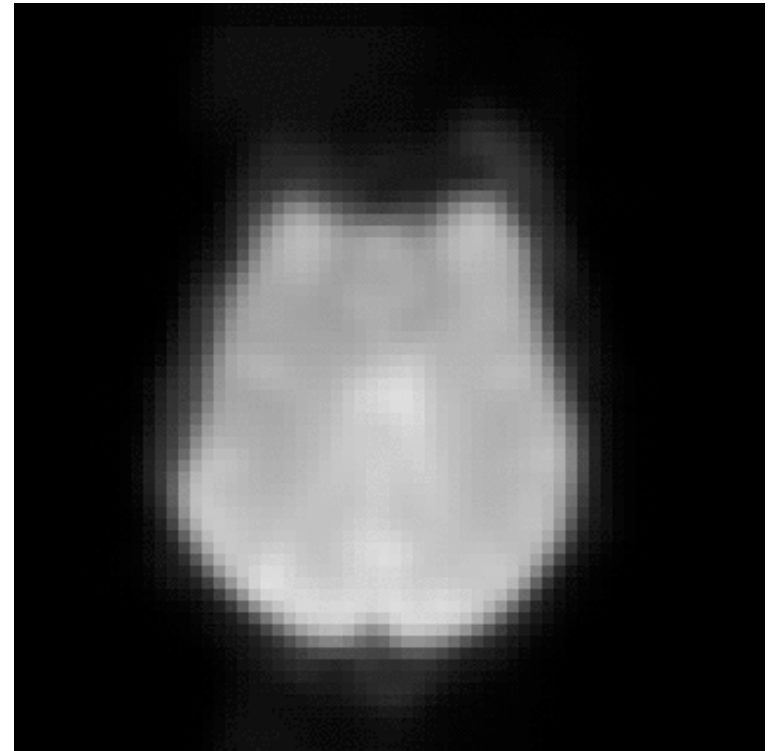
Terminology

Analysis steps:

- Motion Correction
- Filtering: spatial and temporal
- General Linear Model: single subjects
- Averaging different subjects (group analysis):
registration to standard space



Spatial Filtering

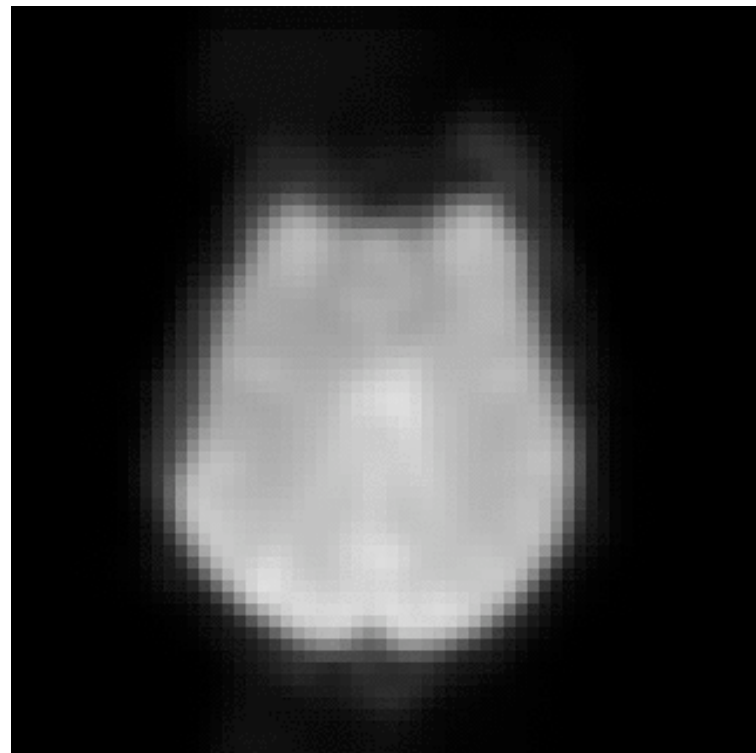




Spatial Filtering

Why do it?

Increases signal to noise ratio if
size of the blurring is less
than size of activation

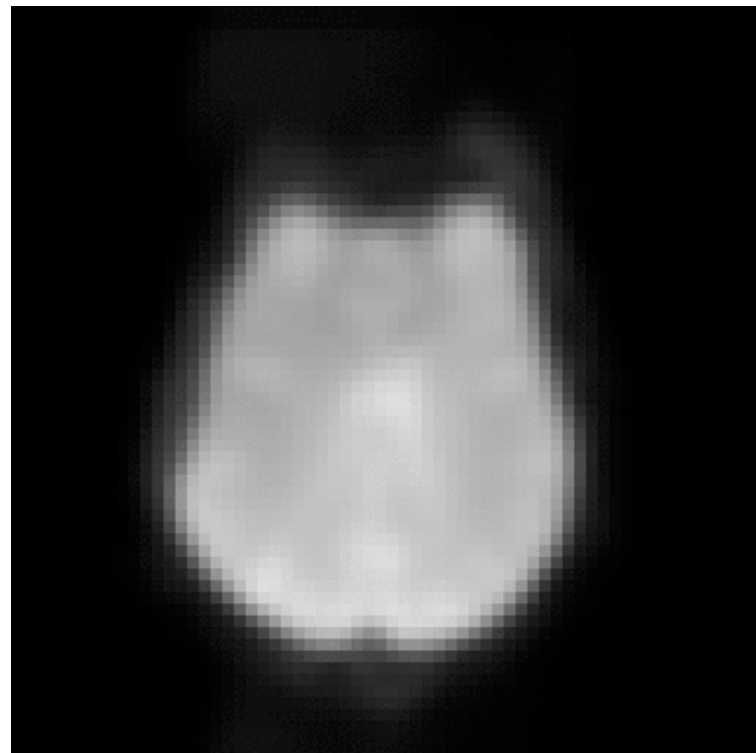




Spatial Filtering

Why do it?

Increases signal to noise ratio if size of the blurring is less than size of activation



However:

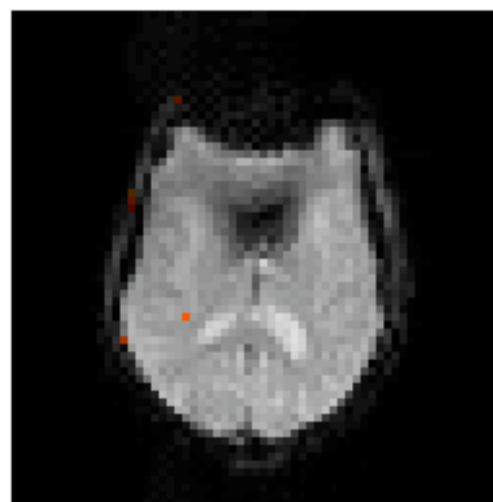
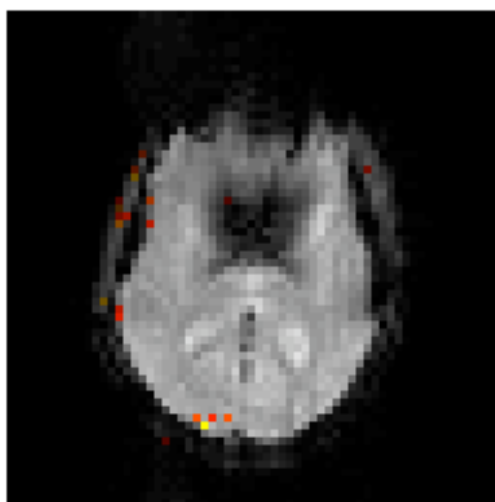
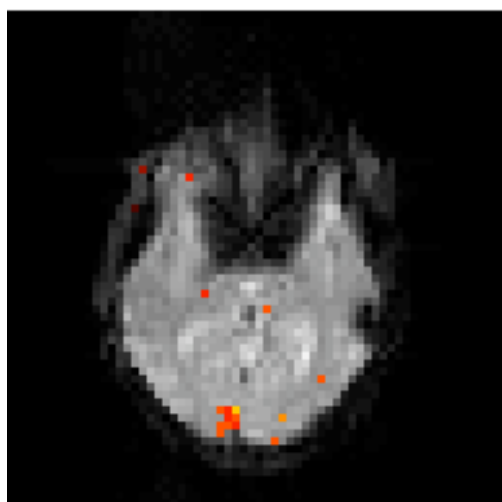
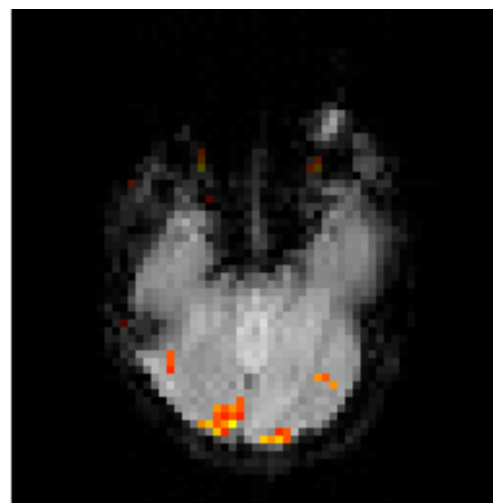
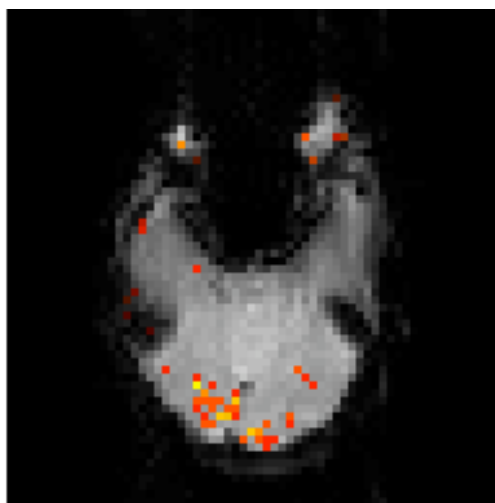
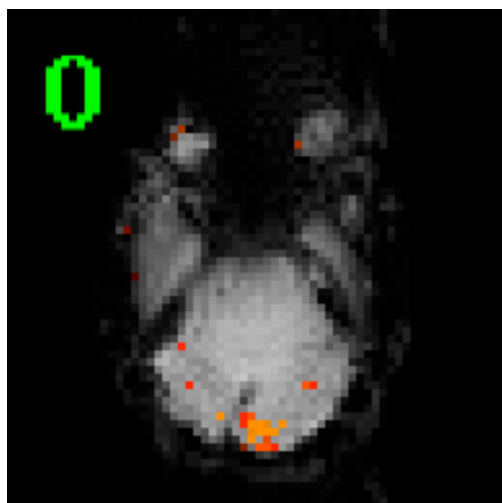
- Reduces small activation areas



Spatial Filtering: Results at Different FWHM



Spatial Filtering: Results at Different FWHM

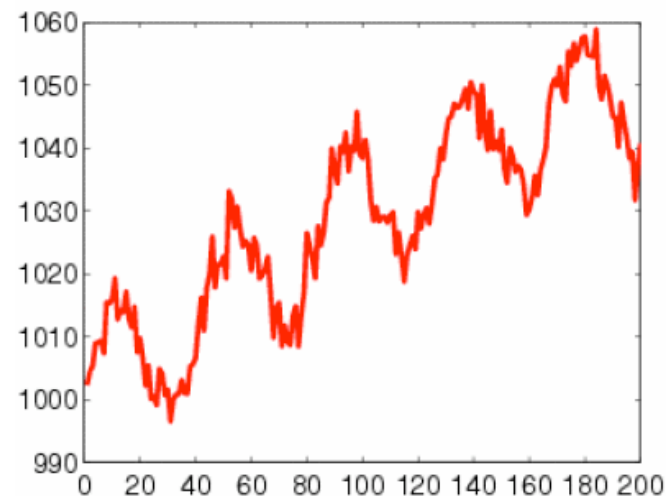




Temporal Filtering: Why?

- Time series from each voxel contains low frequency drifts and high frequency noise
- Drifts are scanner-related and physiological (cardiac cycle, breathing etc)
- Both high and low frequency noise hide activation

Raw Signal



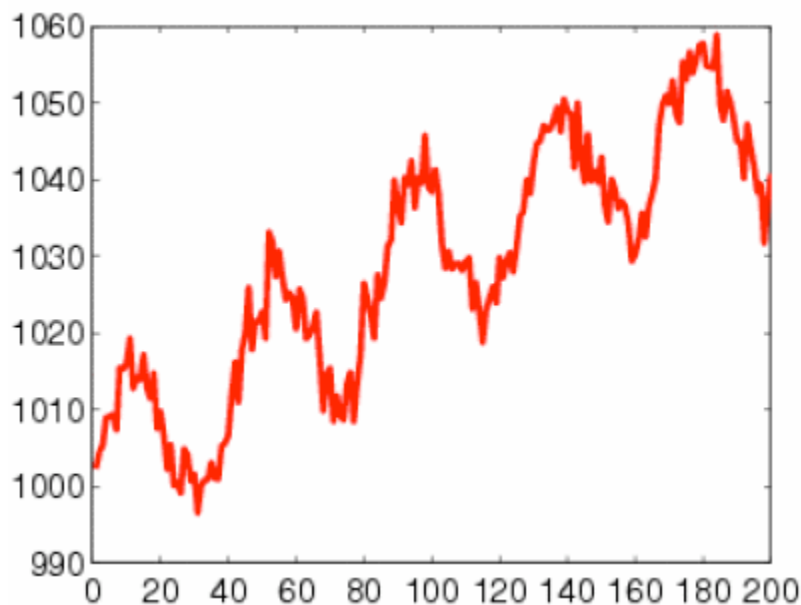
What is temporal filtering?

- Removal of high frequencies, low frequencies or both, without removing signal of interest

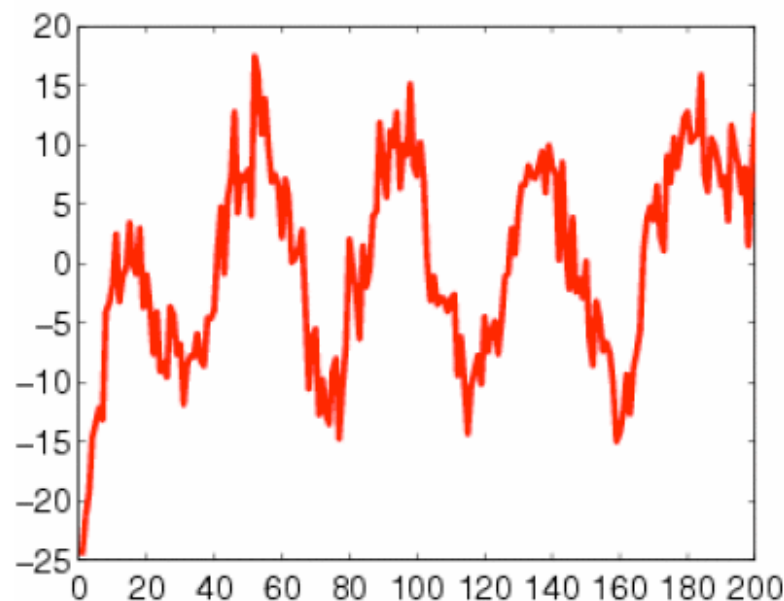


Temporal Filtering: Highpass

Raw Signal



Highpass Filtered

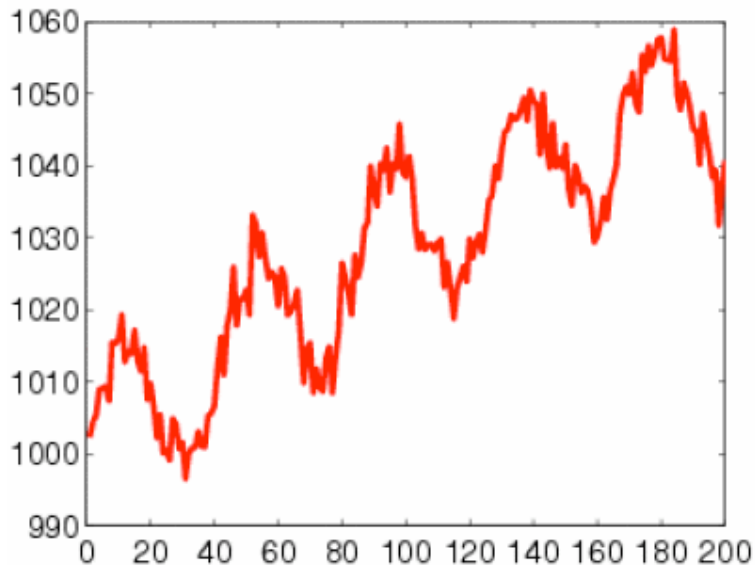


Removes low frequency signals, including linear trend

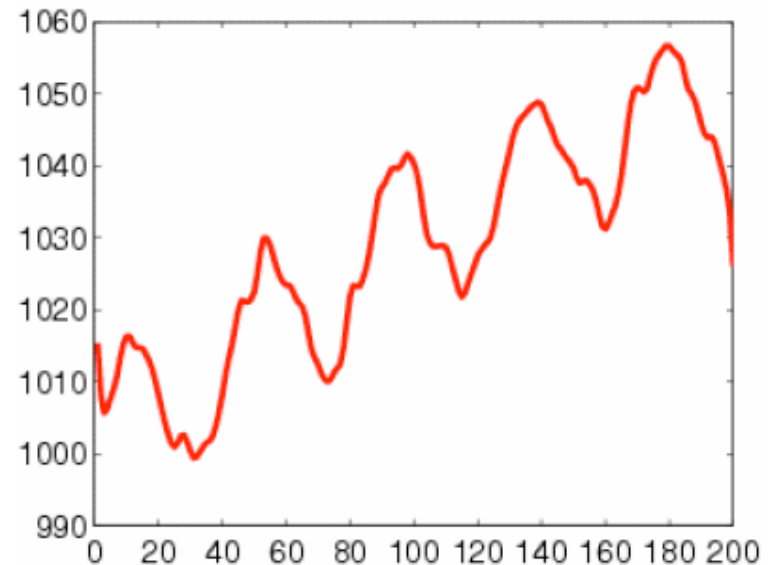


Temporal Filtering: Lowpass

Raw Signal



Lowpass Filtered

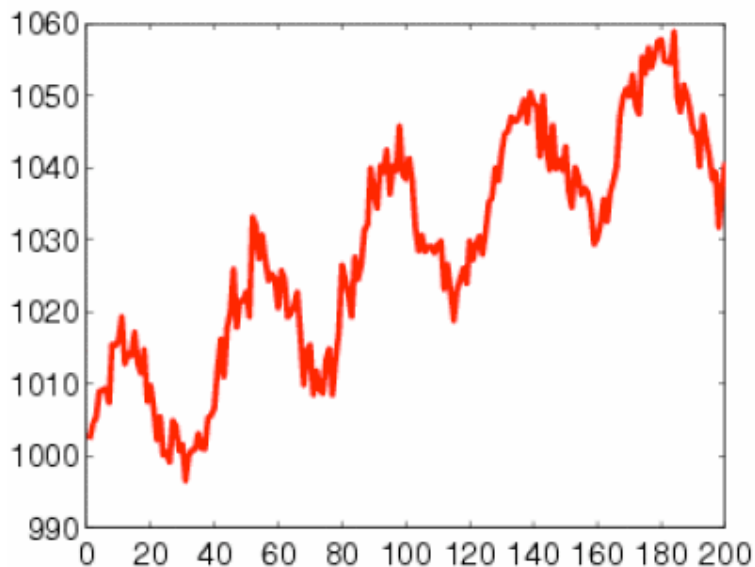


Removes high frequency noise

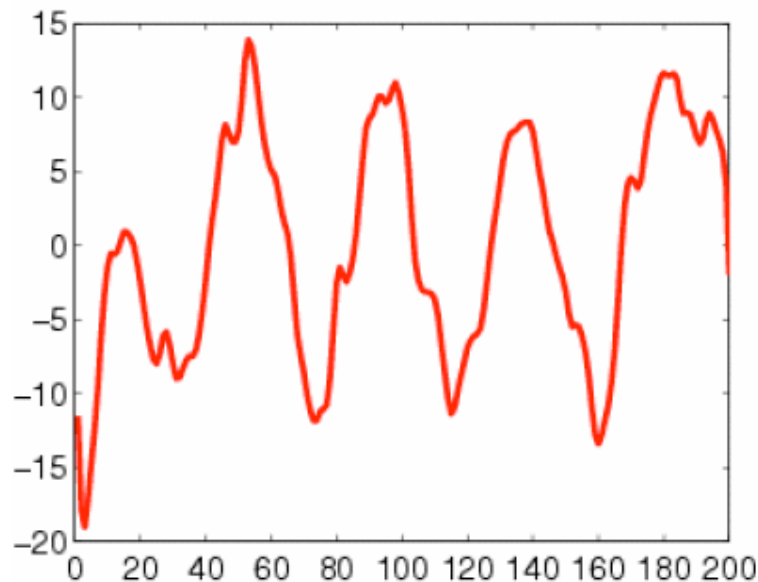


Temporal Filtering: Bandpass

Raw Signal



Bandpass Filtered

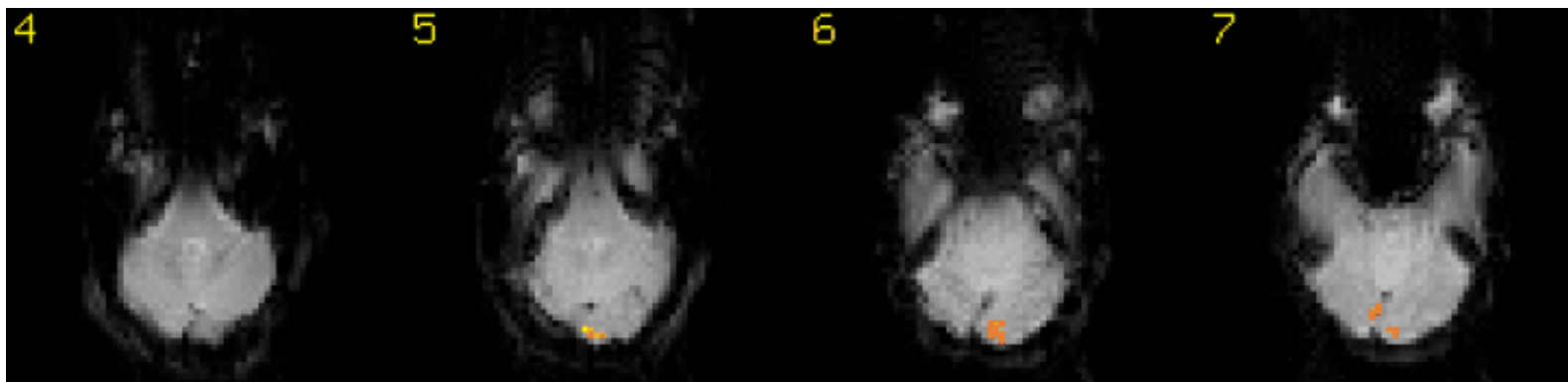


- Combination of lowpass and highpass filters
- Removes high frequency noise and low frequency drifts

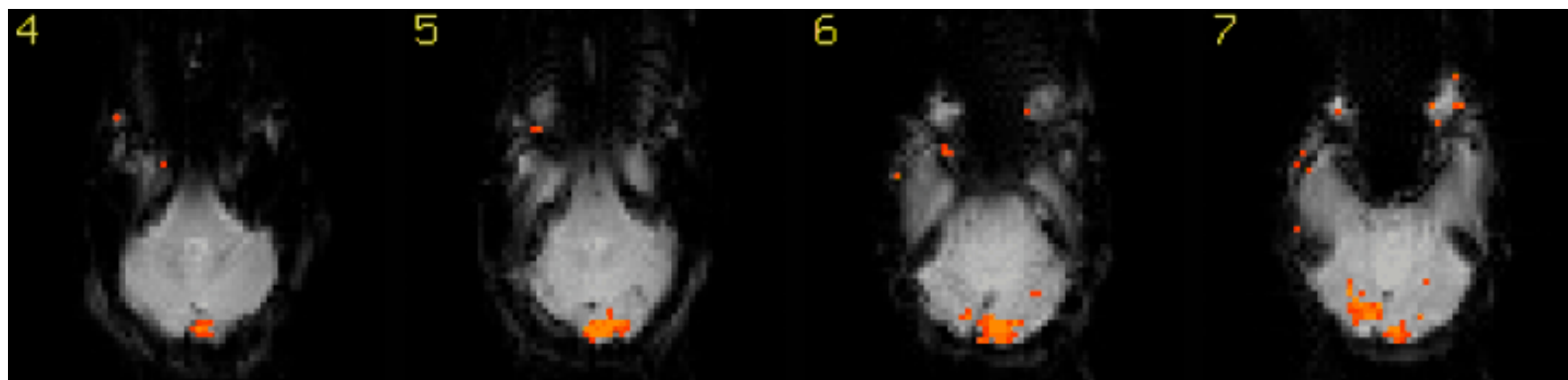


Effect of Temporal Filtering

No Temporal Filtering



Temporal Filtering



FMRI: Data Analysis Overview

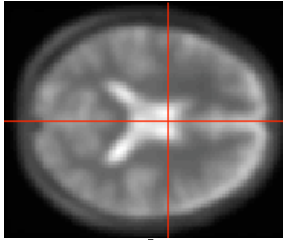
Terminology

Analysis steps:

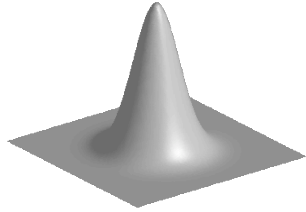
- Motion Correction
- Filtering: spatial and temporal
- General Linear Model: single subjects
- Averaging different subjects (group analysis): registration to standard space

FMRI Analysis Overview

fMRI time-series

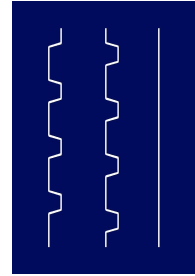


Motion
Correction



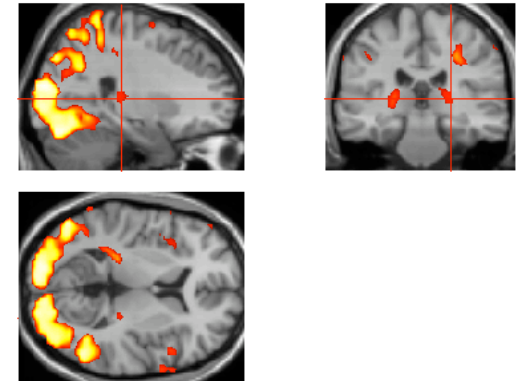
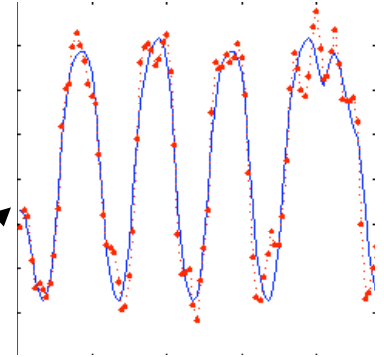
Filtering

Design matrix



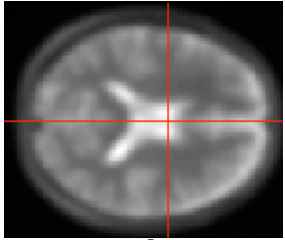
General Linear Model

Parameter Estimates

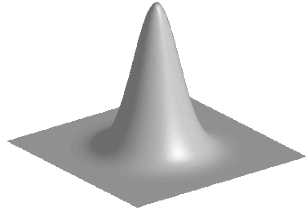


FMRI Analysis Overview

fMRI time-series

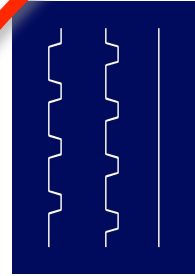


Motion
Correction



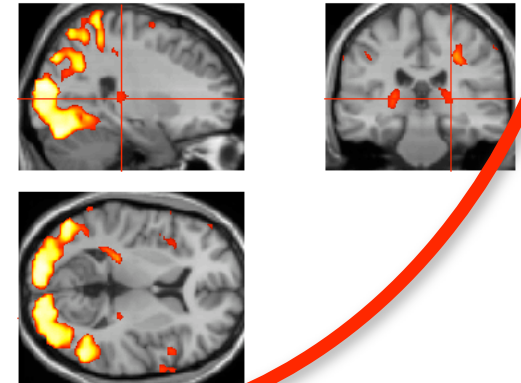
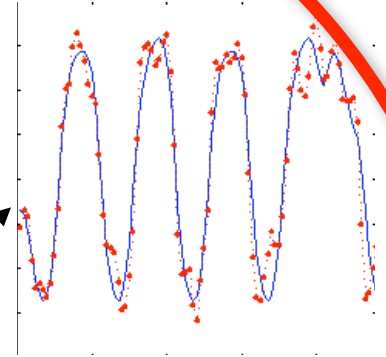
Filtering

Design matrix



General Linear Model

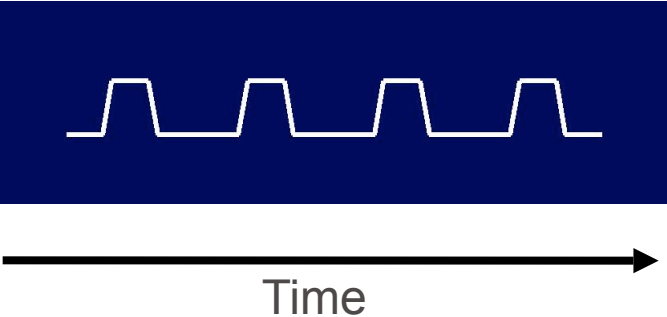
Parameter Estimates





A Simple Model

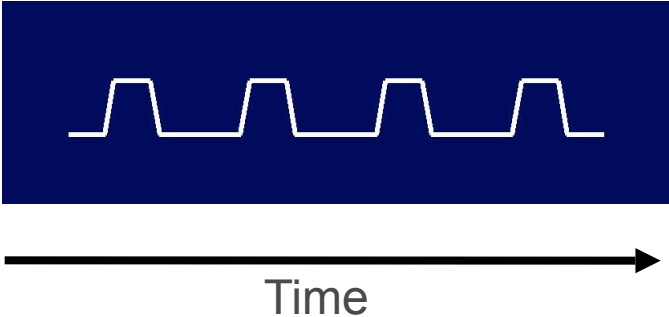
If I have a stimulus that looks this



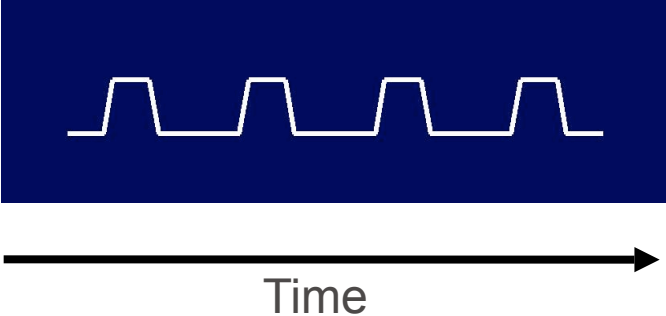


A Simple Model

If I have a stimulus that looks this



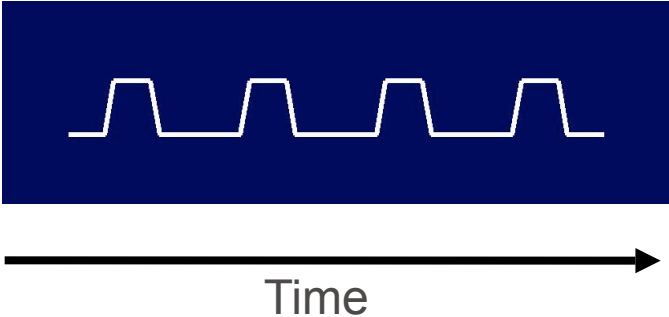
then I predict that a voxel that responds to a flashing chequerboard, looks like this



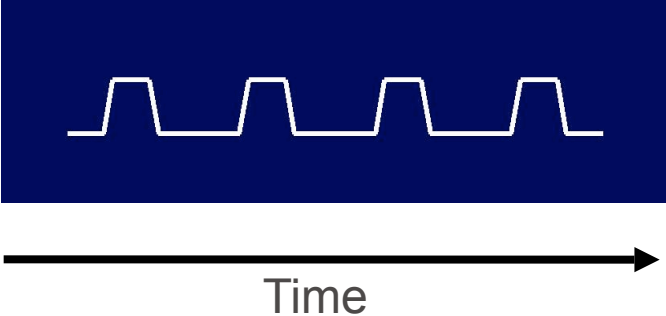


A Simple Model

If I have a stimulus that looks this

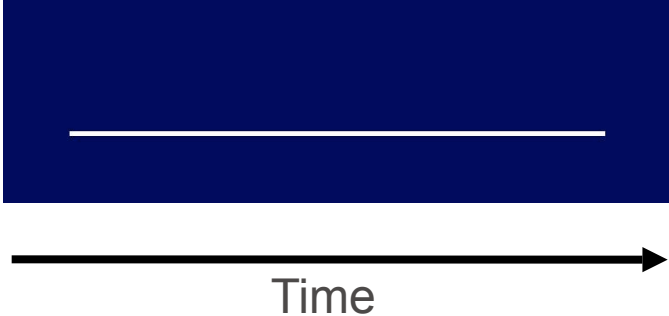


then I predict that a voxel that responds to a flashing chequerboard, looks like this



and

a voxel that just doesn't care, looks like this





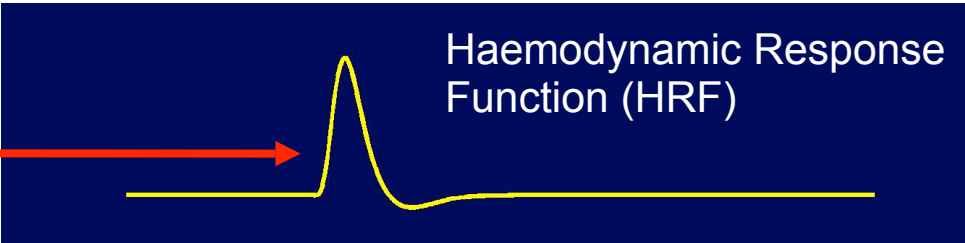
Can we think of a better model?

- The model should embody our belief about what happens with the signal.

We know (from experiment) that a stimulus looking like this



Will elicit a BOLD signal change looking like this



Time



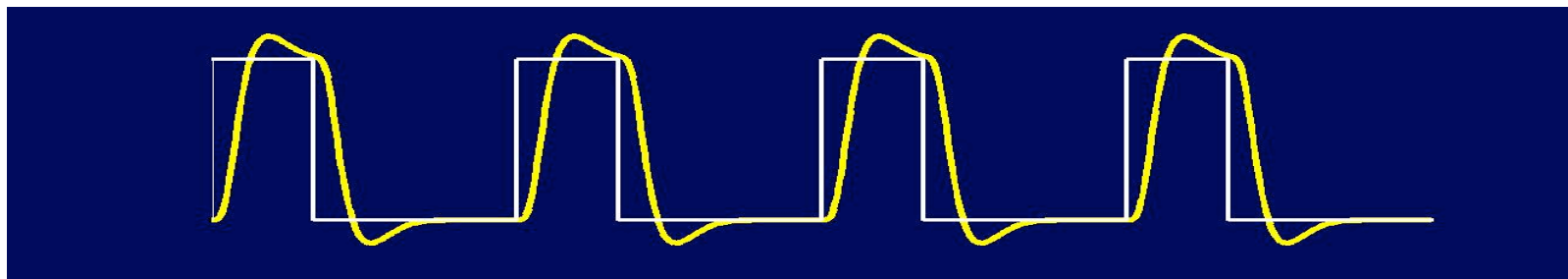
Predicted Response

The process can be modelled by **convolving** the activity curve with a "haemodynamic response function" or HRF



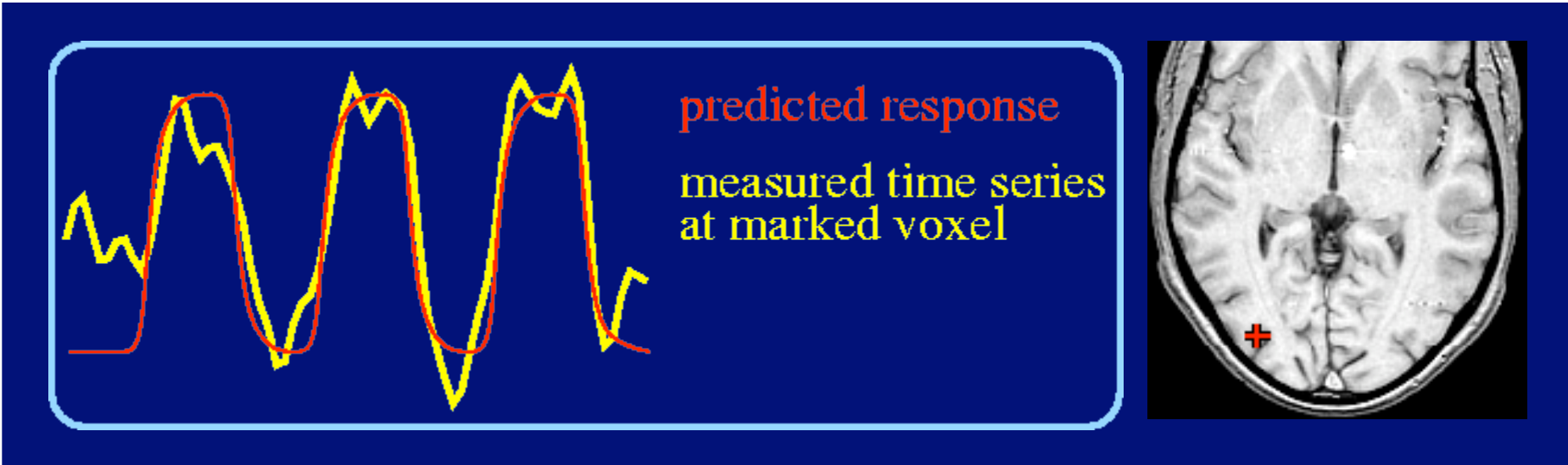
HRF

Predicted neural activity



Predicted response

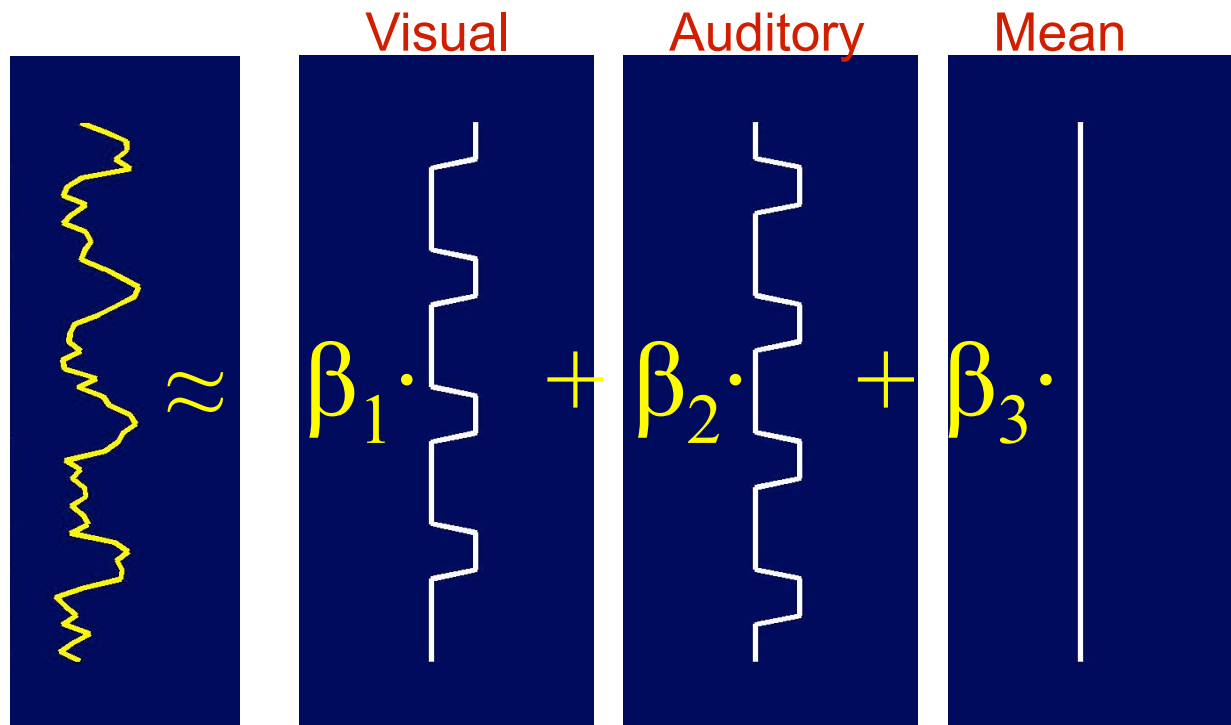
Modelling the Response



- Model the stimulus-induced change in BOLD signal (predicted response)
- Find which voxels have time series that match that predicted response
- A good match implies brain activation related to the stimulus

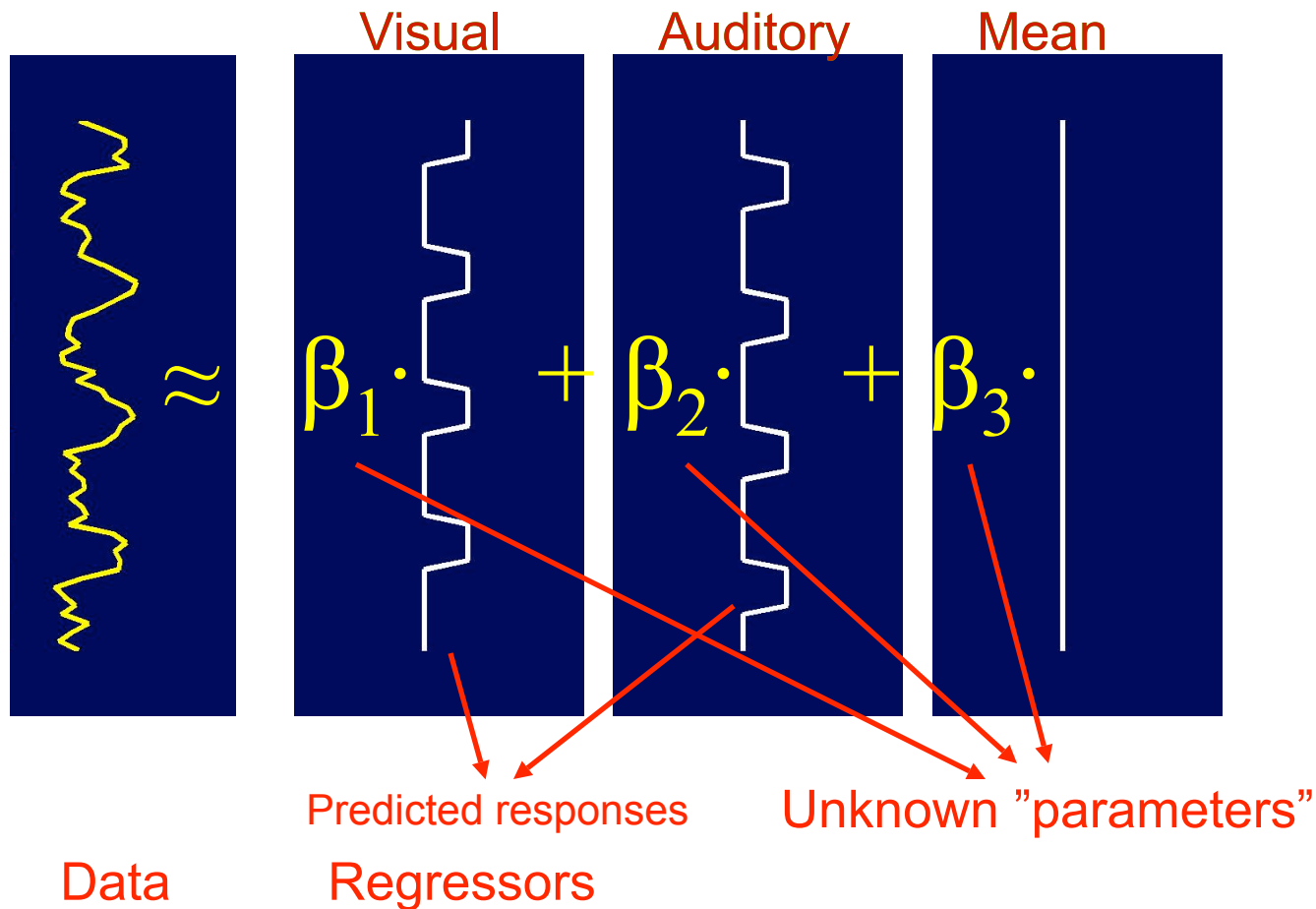


Linear Combinations of Predicted Responses





Linear Combinations of Predicted Responses

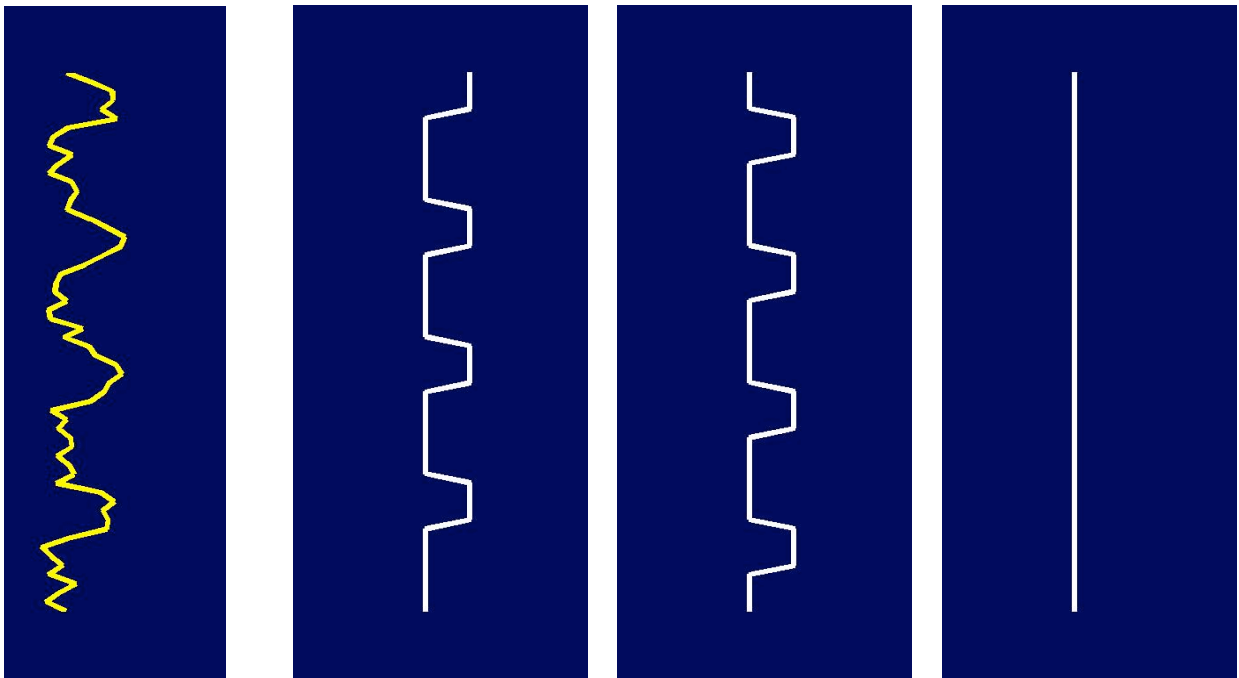




Estimation:

Finding the "best" parameter values

- The estimation entails finding the parameter values such that the linear combination "best" fits the data.

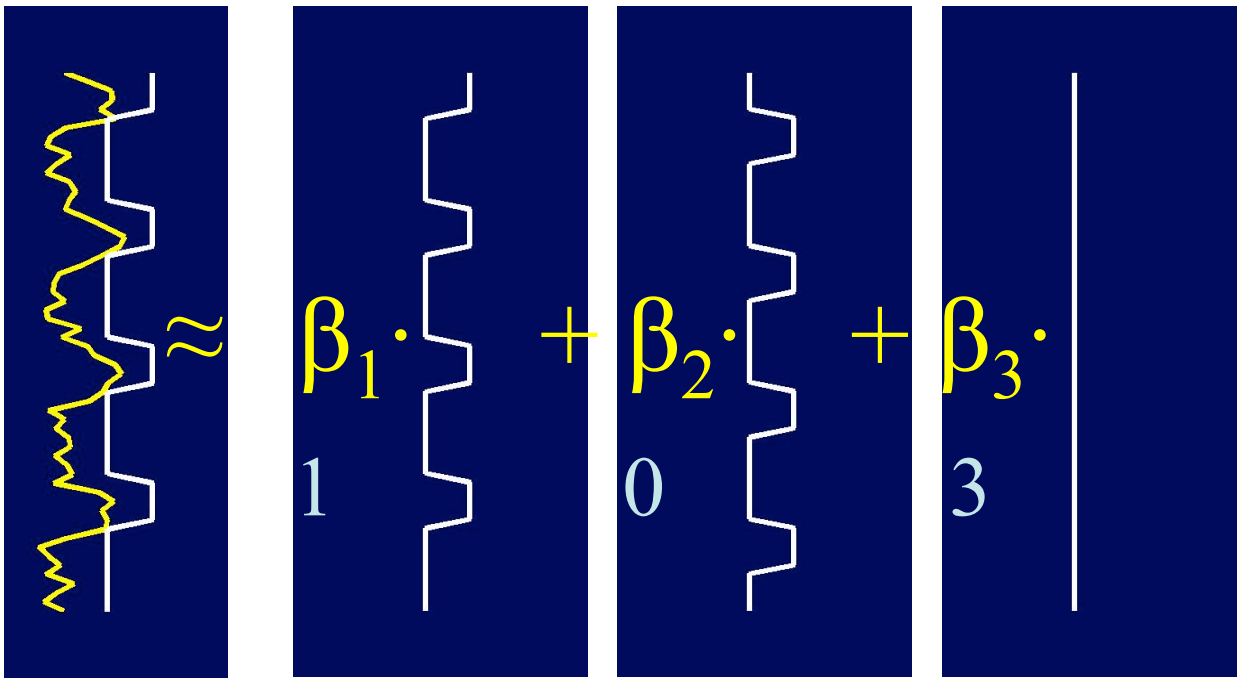




Estimation:

Finding the "best" parameter values

- The estimation entails finding the parameter values such that the linear combination "best" fits the data.

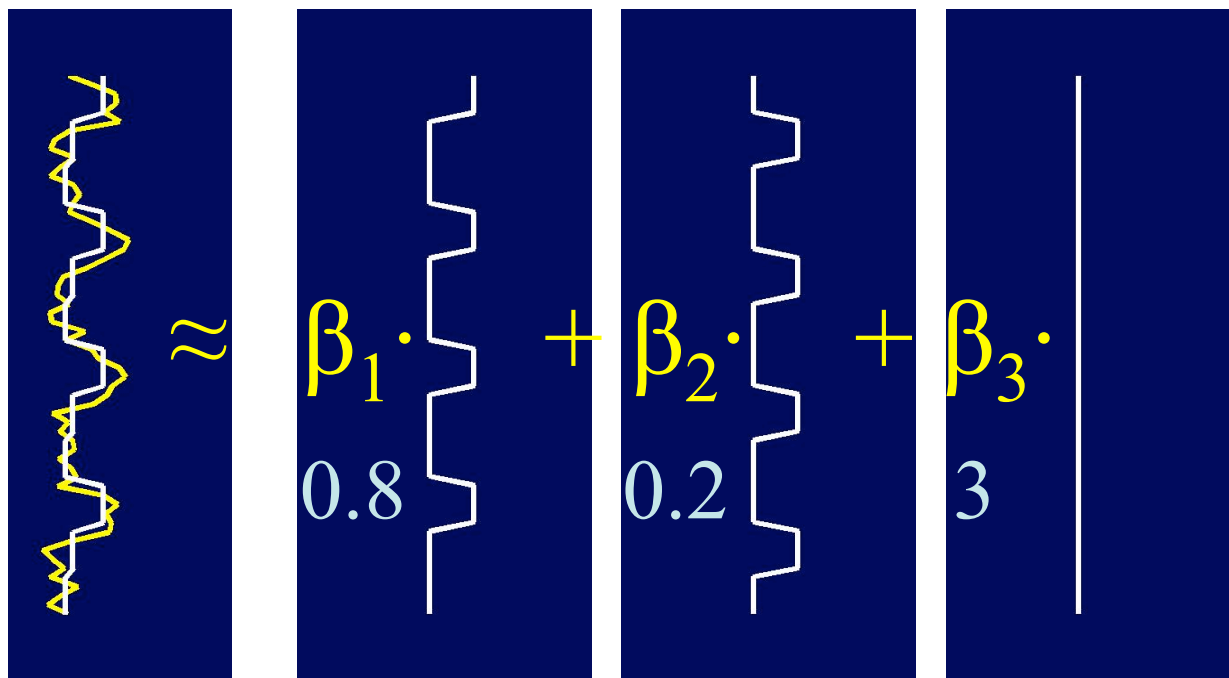


Bad fit



The Estimation: Finding the "best" parameter values

- The estimation entails finding the parameter values such that the linear combination "best" fits the data.



Good fit

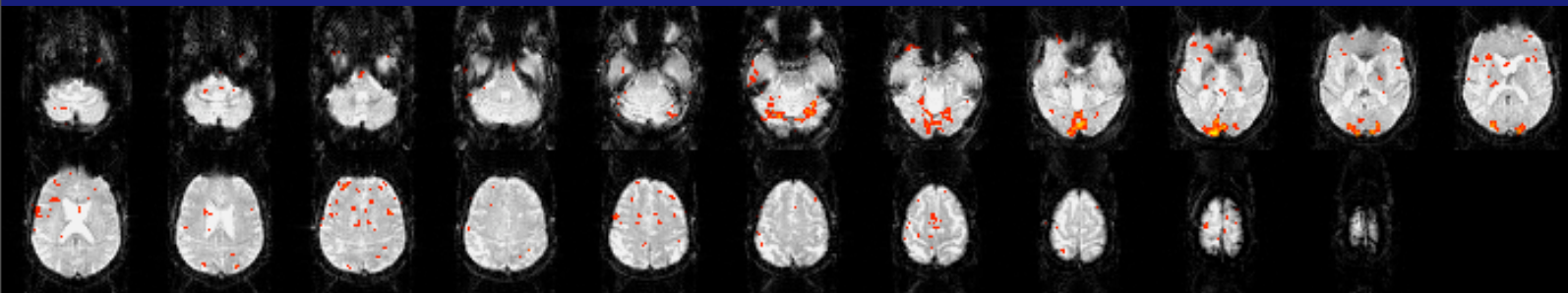
FMRI: Data Analysis Overview

Terminology

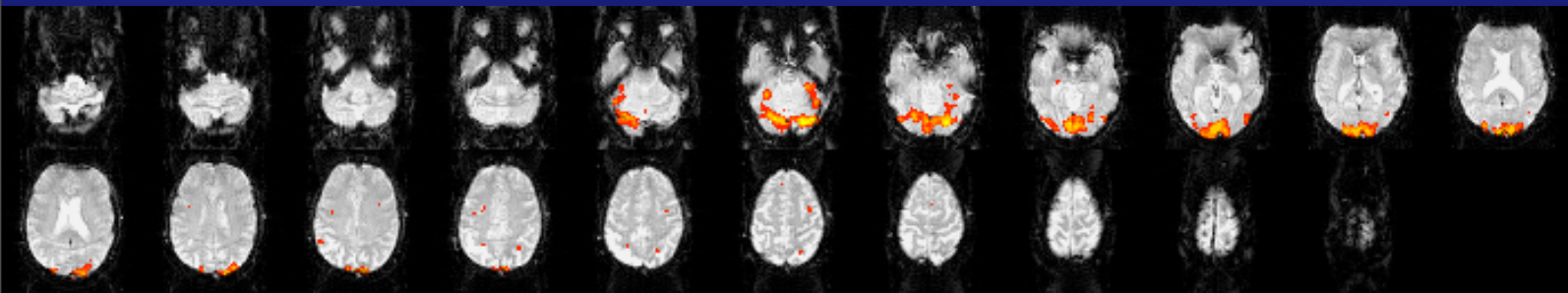
Analysis steps:

- Motion Correction
- Filtering: spatial and temporal
- General Linear Model: single subjects
- Averaging different subjects (group analysis): registration to standard space

1. Analyse each patient's data
2. Combine all these results into one group average and perform group statistics

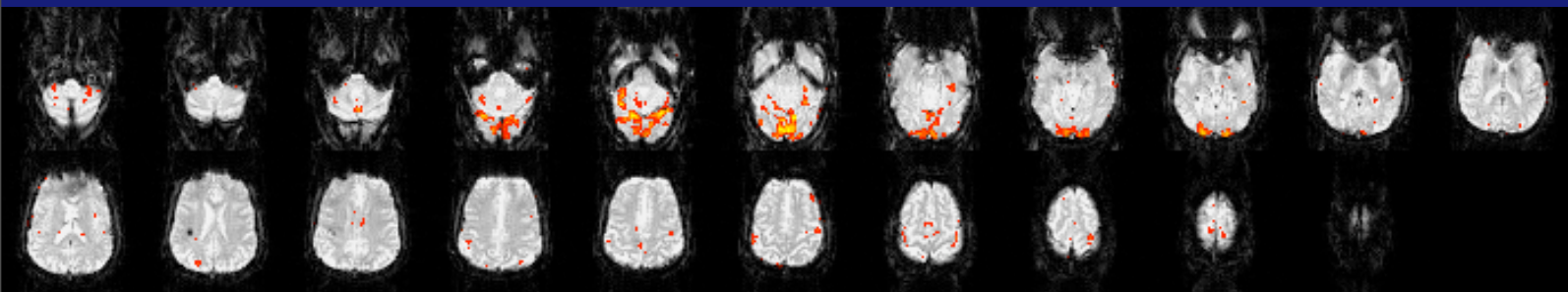


Patient 1



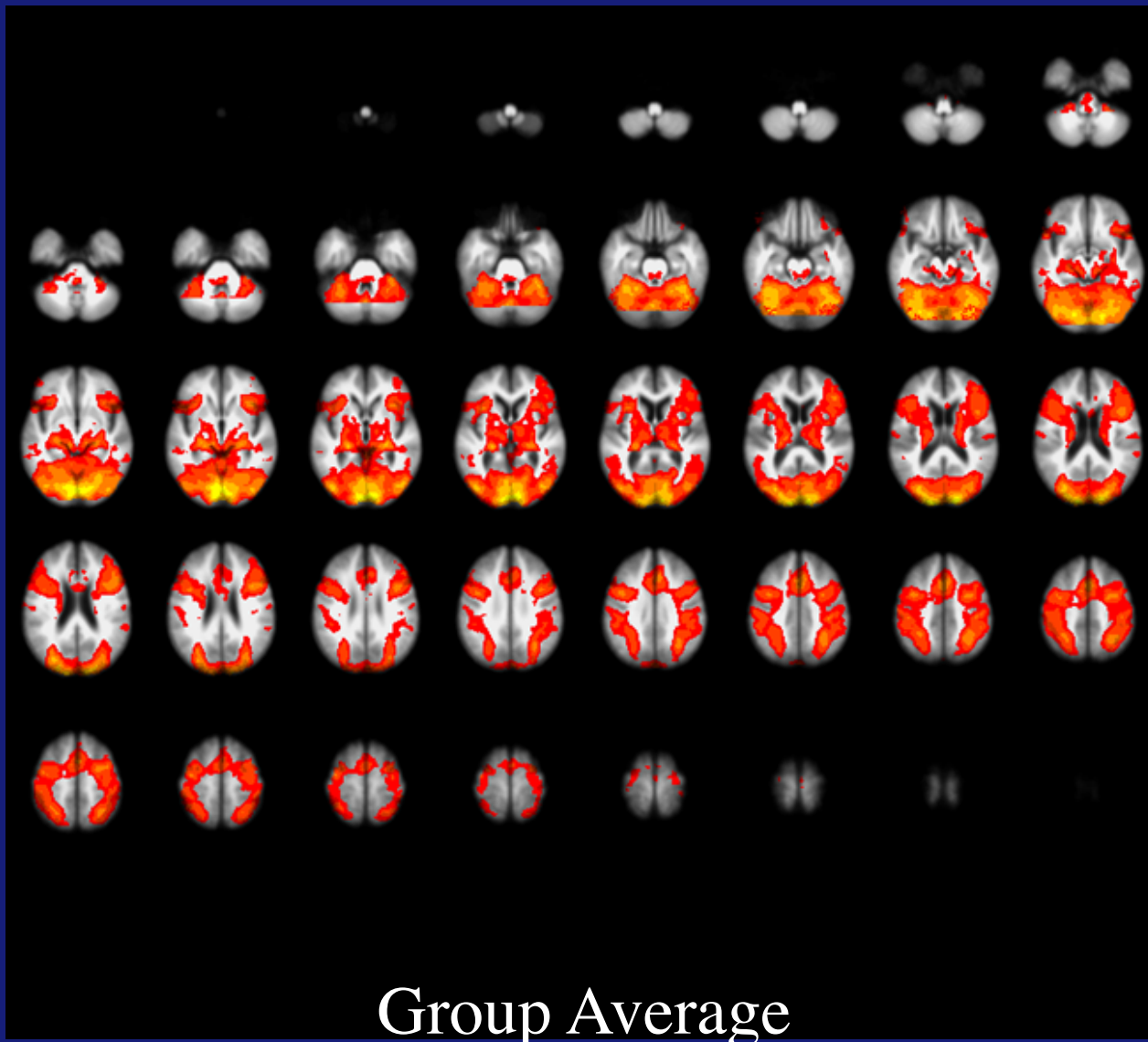
Patient 2

·
·
·
·
·



Patient 40

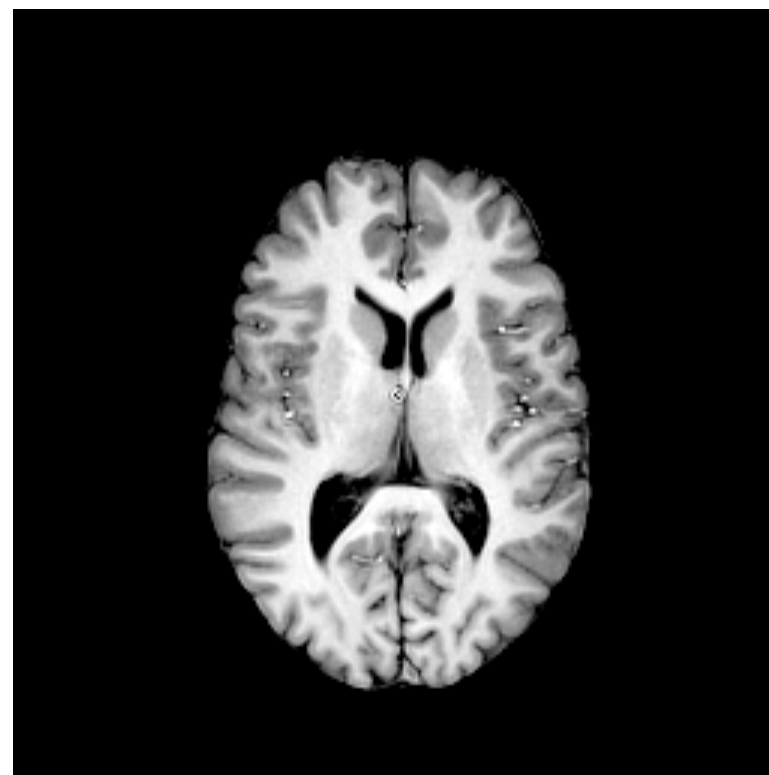
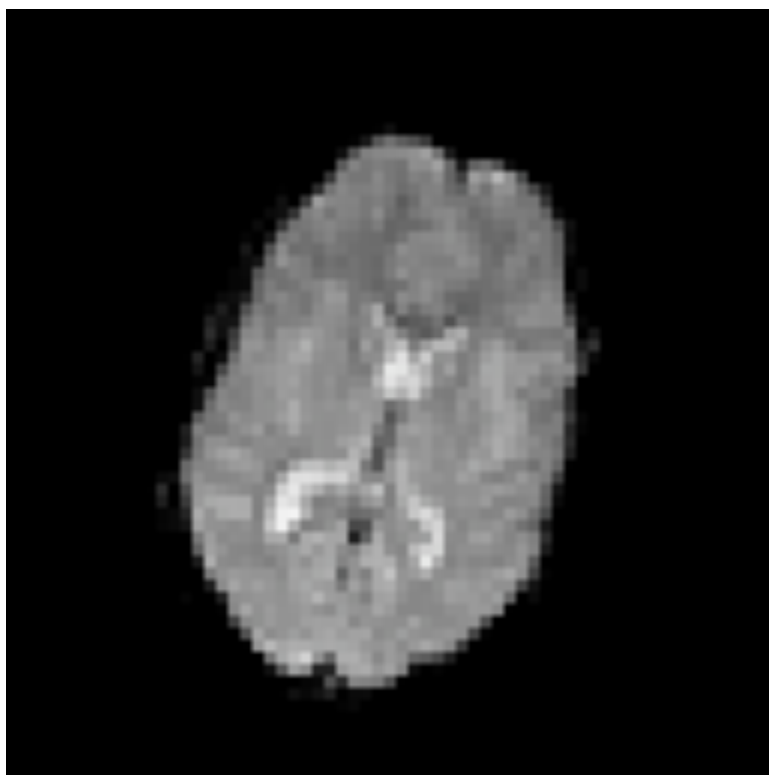
Higher level analysis (group statistics)





For group averaging we need to register all images to a common (standard) space

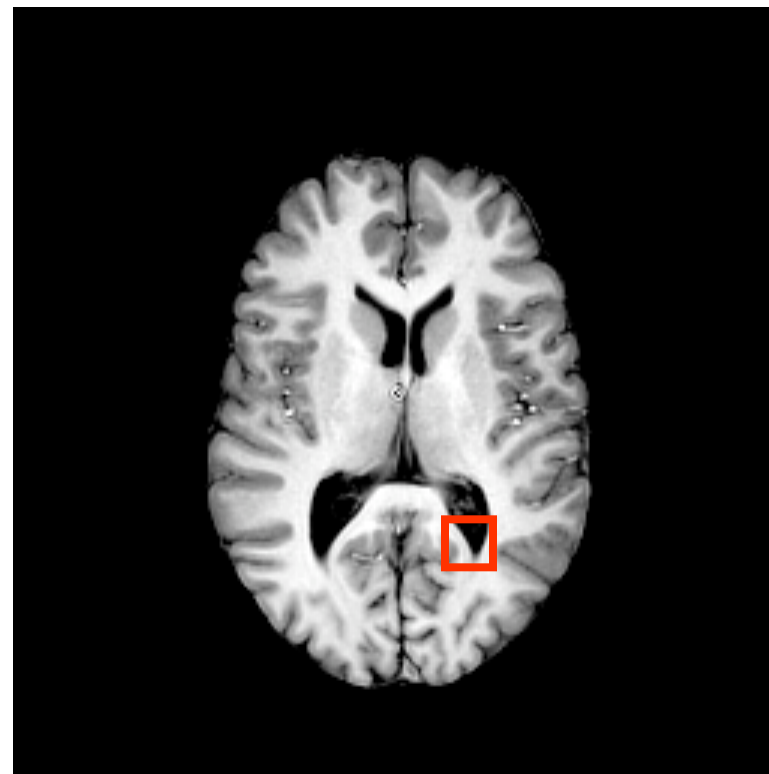
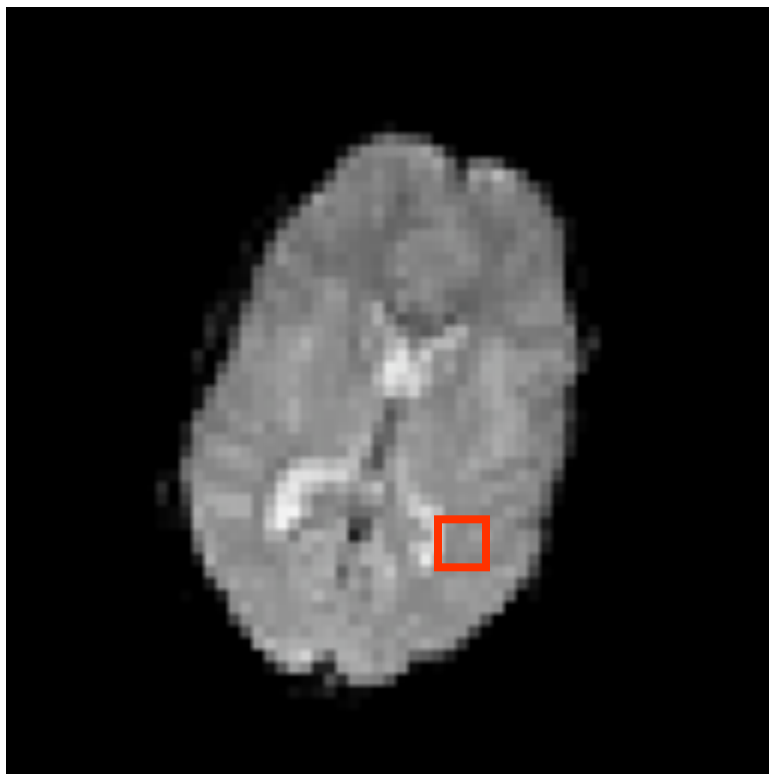
What is Registration?





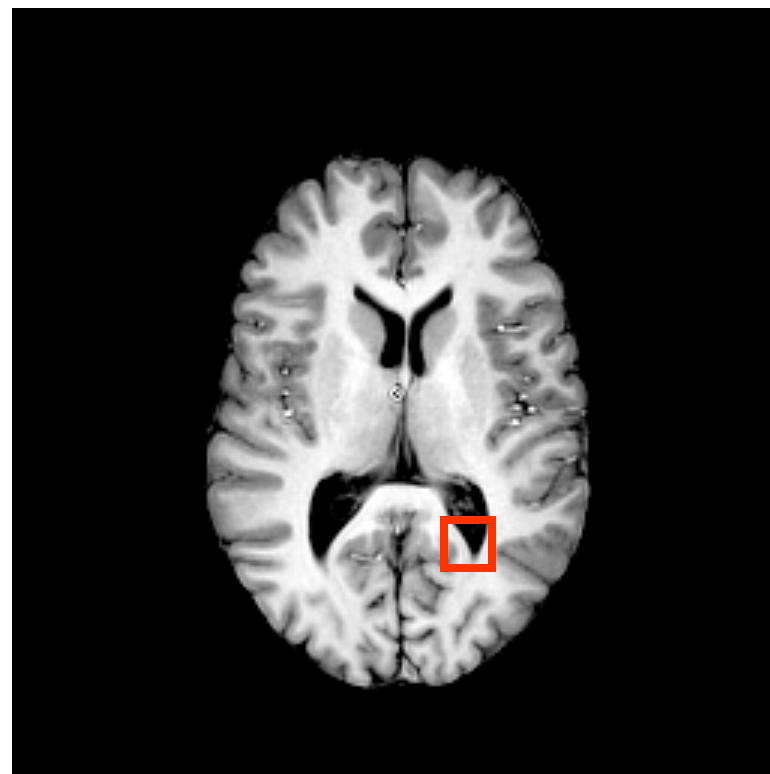
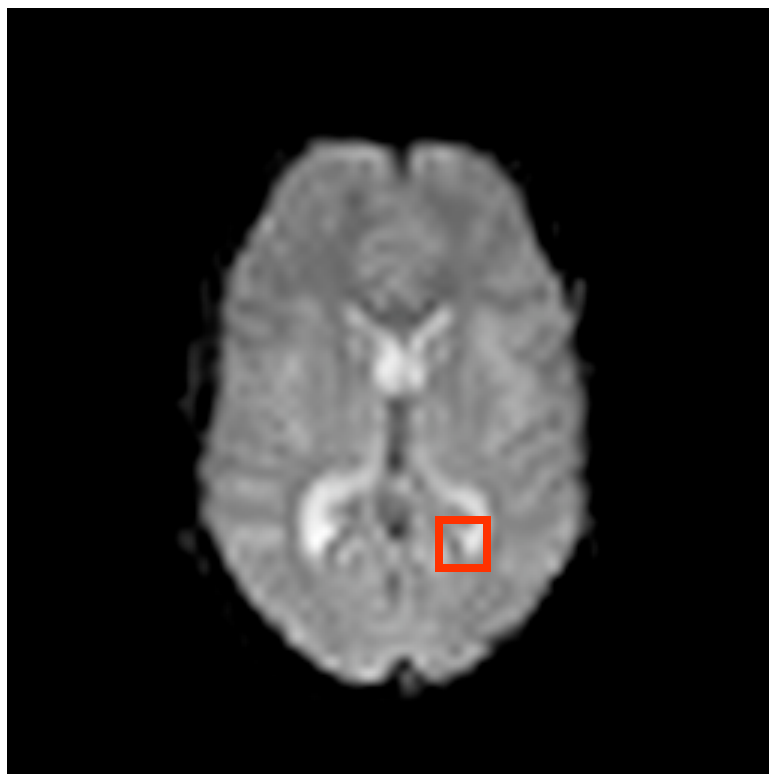
For group averaging we need to register all images to a common (standard) space

What is Registration?





What is Registration?



Voxel location = anatomical location
with accurate intensity values



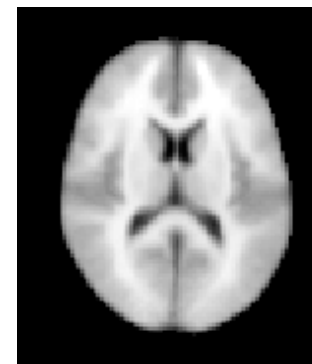
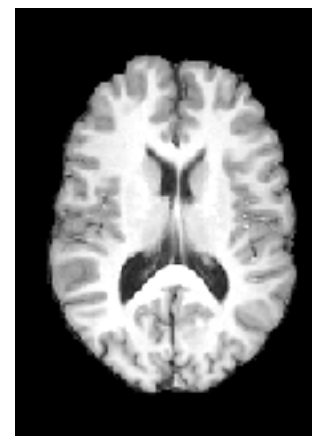
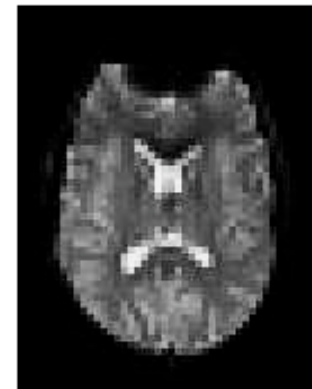
Two Stage Registration

Stage 1: EPI to structural image

- same anatomy
- different contrast/modality
- 6 or 7 DOF transformation is sufficient

Stage 2: Structural to template

- different anatomy
- same contrast/modality
- 12 DOF for average templates
(*e.g.* MNI152)



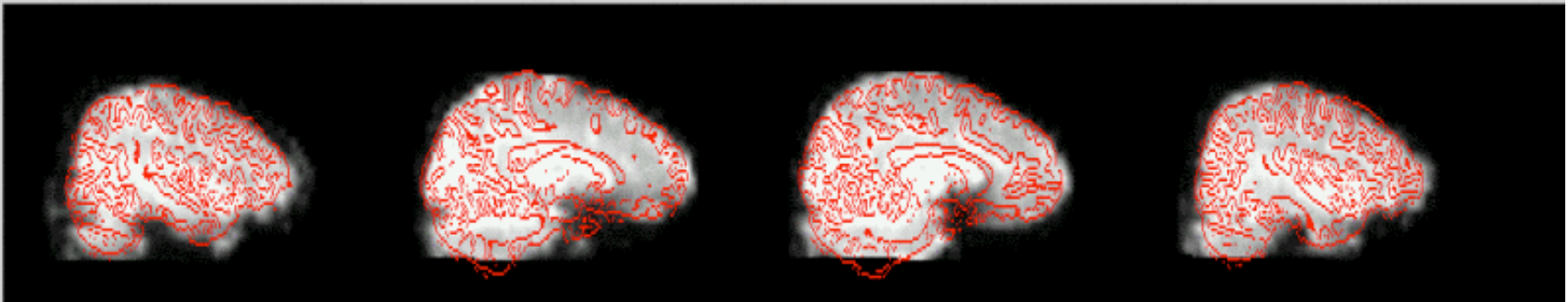


FLIRT within FEAT

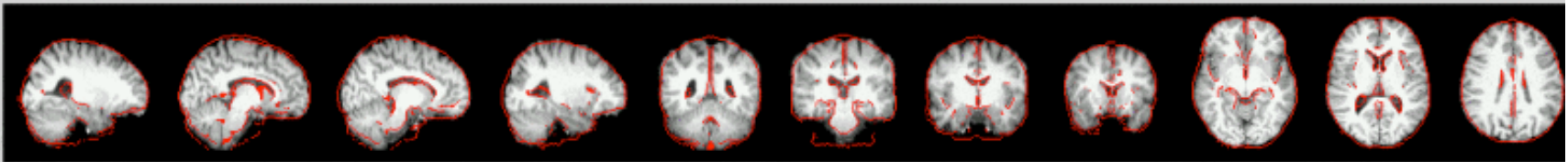
FEAT Registration Report

for FEAT session [/usr/fs3/steve/COURSE/feeds3.0/results/fmri.feats](#)
Thu Sep 19 16:30:47 BST 2002

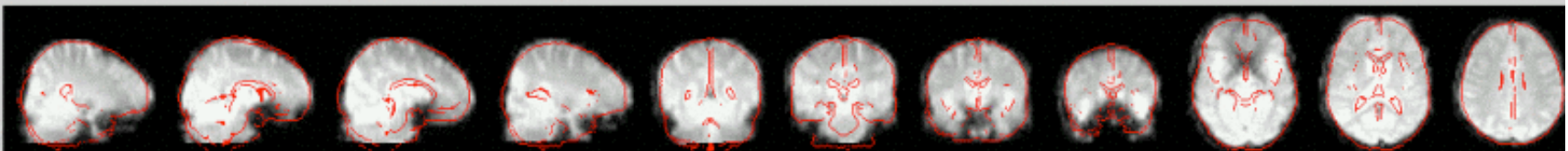
Registration of example_func (underlying image) to highres (red lines)



Registration of highres (underlying image) to standard (red lines)

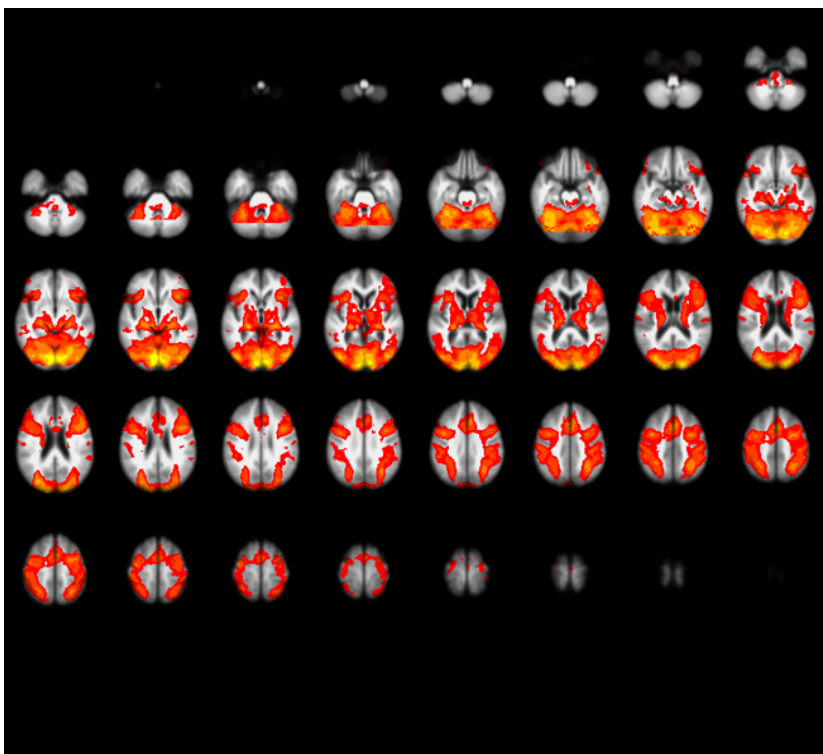


Registration of example_func (underlying image) to standard (red lines)





Group data: statistical thresholding



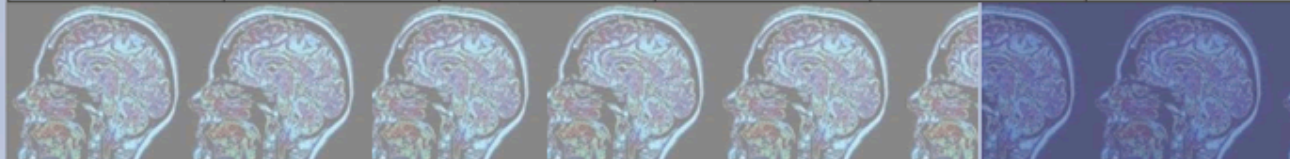
For each voxel: is the average beta (across subjects) greater than zero?

Thanks to

- FSL group (course slides)
- Meike Grol
- Ab Mooijaart



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VACANCIES

VACANCIES

👉 PhD student / Assistent in opleiding (F/M) (1.0 fte)

Leiden University:

- Institute for Psychological Research: Clinical Psychology Unit
- Leiden Institute for Brain and Cognition (LIBC)

Vacancy number: 8-032

The Clinical Psychology unit seeks applicants for a (paid) position as PhD student (promovendus) from the 1st of September 2008. This is a fixed term position (4 years), involving 90% research time and 10% teaching.

Project description:

Title: *Prefrontal emotion regulation in social anxiety disorder.*

This fMRI project investigates the prefrontal regulation of emotions and social-emotional behavior in relation to social anxiety. There is increasing evidence that social anxiety disorder (SAD) is associated with a failure in the prefrontal regulation of emotions and social behavior. The present project investigates the involvement of frontal and limbic structures as well as their connectivity during emotion regulation tasks in patients with SAD, such as prefrontal inhibition and social approach-avoidance tasks. Moreover, the effects of social stress and stress hormones on prefrontal emotion regulation will be investigated in healthy subjects and patients with SAD (see also vacancy nr 8-031 for a related PhD project).

This PhD-project will be imbedded in the sub-program "Stress regulation, Cognition and Psychopathology" of the Clinical Psychology Unit, and is financially supported by a NWO VIDI grant awarded to Dr. K. Roelofs for her project: "The Psychoneuroendocrinology of Social Anxiety: An Emotion Regulation Approach."

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