Instrumentation for Medical Imaging

IV - Magnetic Resonance Imaging (MRI)
Ressonância magnética, ressonância magnética funcional e neurofeedback

Bruno Direito - migueldireito@gmail.com
(IBILI piso1 gab.77)
João Pereira - joaoandrefpereira@gmail.com

- Background
- NMR signal (*overview/reminder*)
    - Relaxation (longitudinal and transverse)
    - Contrast
- functional image
    - BOLD
- project BrainTrain
    - Neurofeedback (*rt-fMRI-NF*)
        - ROI
        - connectivity (presented by Joao Pereira)

Short Bio

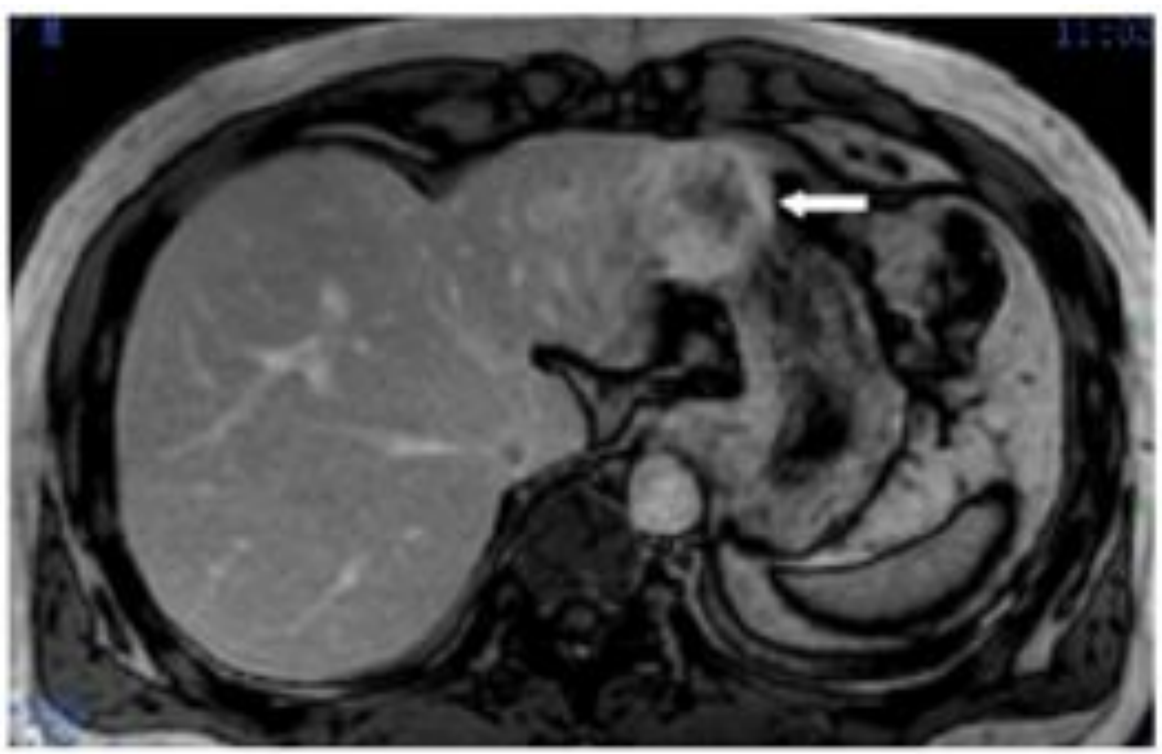
(2013-today) Post-doc with the Visual Neuroscience Lab at IBILI | Faculty of Medicine of the University of Coimbra Project: *"**BrainTrain**"*
(2008-2013) PhD degree in Information Science and Technology | Faculty of Science and Technology of the University of Coimbra Thesis: "*Development of classification methods for real-time seizure prediction*"
(2007-2008) M.Sc. degree in Biomedical engineering | Faculty of Science and Technology of the University of Coimbra
(2002-2007) Licentiate degree in Biomedical engineering | Faculty of Science and Technology of the University of Coimbra

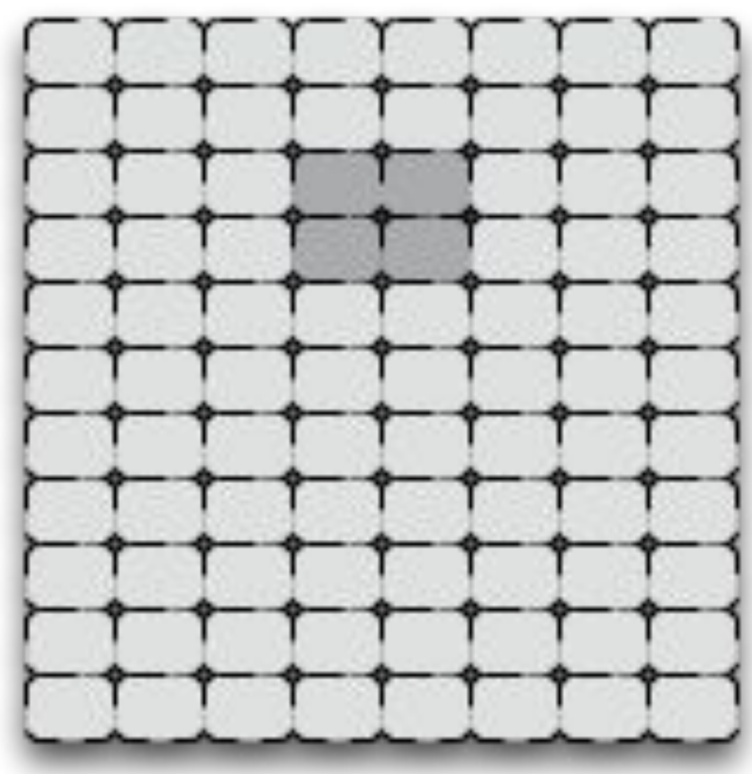
Overview

A 46-year-old male with hepatocellular carcinoma of the left lobe of liver. Contrast enhanced MR image shows a periphery enhanced mass invading the stomach and mimicking a gastric subepithelial mass (http://qims.amegroups.com/article/viewFile/1317/1773/4537)

Contrast resolution

Spatial resolution

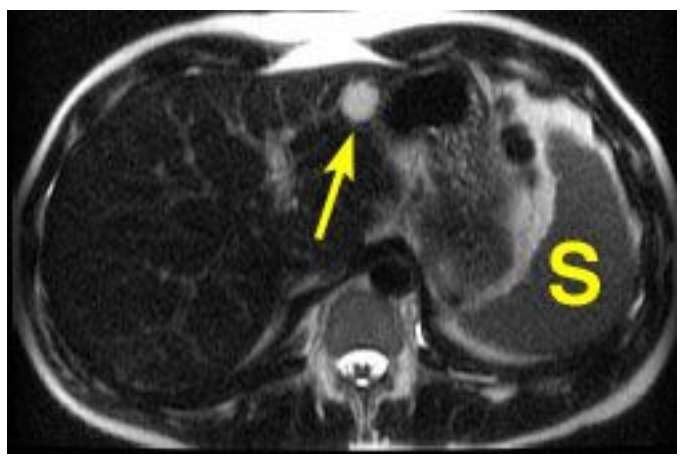


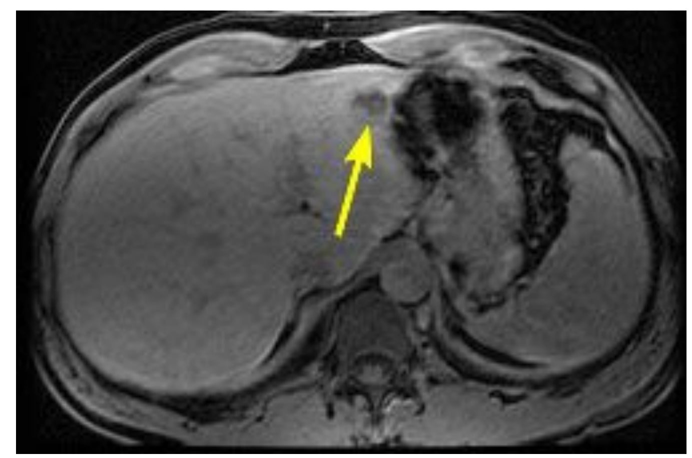


Overview

- We can change the nature of the image, changing specific parameters of MRI to improve the *contrast resolution* and *spatial resolution* of the image

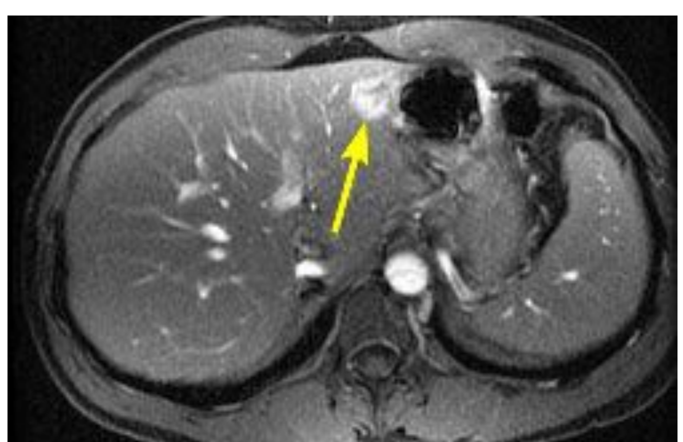
T2-weighted image





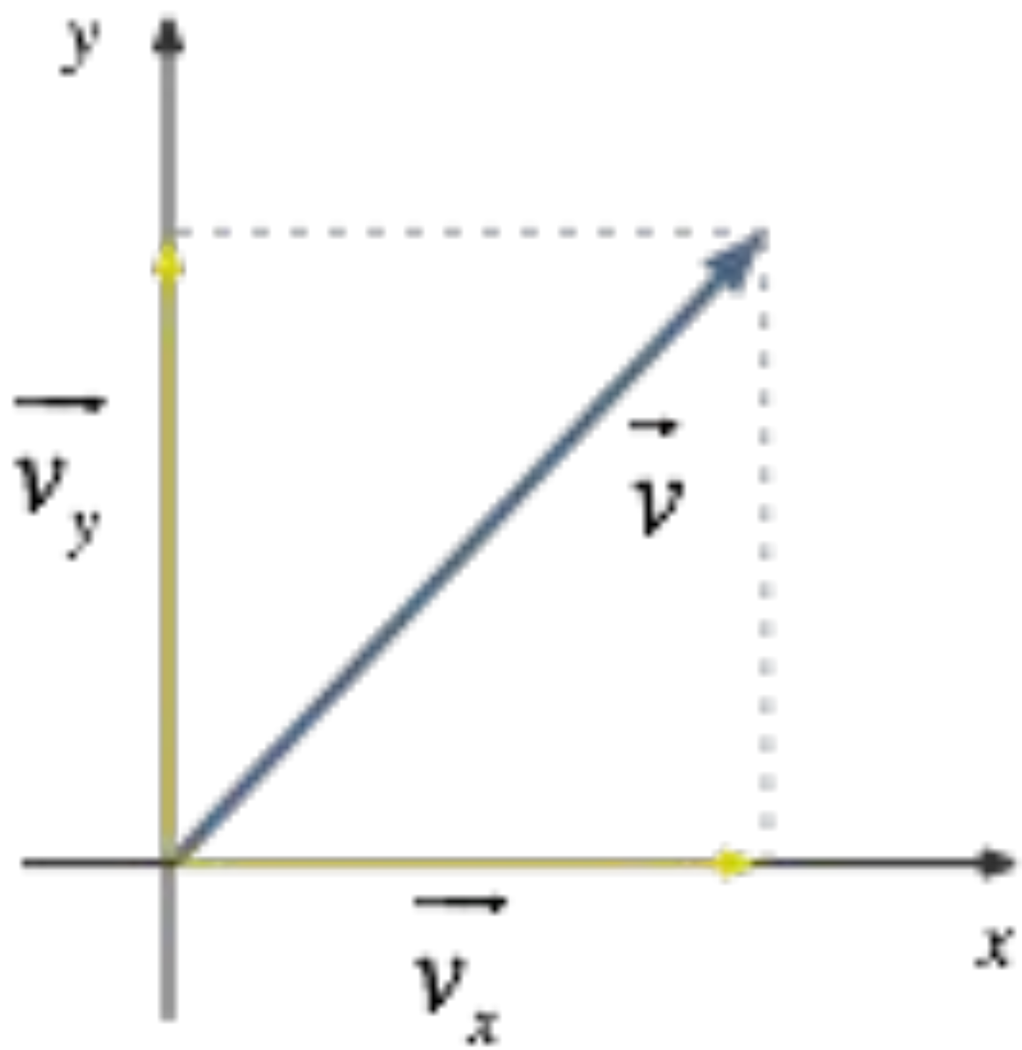
Un-enhanced T1-weighted

w/ contrast agent



Remember

Vector *amplitude* and *direction*
Vector decomposition into components (longitudinal and transverse)



Magnetic susceptibility is a natural property of all tissues

- Measure of how magnetised the tissue becomes when it is placed in a strong magnetic field (*depends on the arrangement of electrons in the tissue*)

- *Diamagnetic* materials have a very weak susceptibility

 - Produces an internal field in the opposite direction to the applied field. *Most body tissues are diamagnetic*

- *Paramagnetic* materials have a stronger susceptibility and produce a field in the same direction as the main field

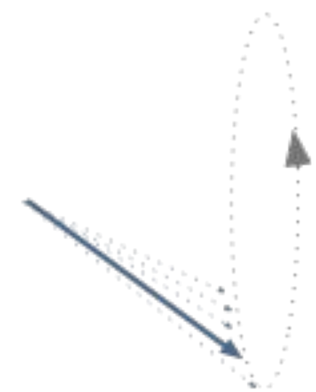
 - examples include gadolinium (used as an MR contrast agent), deoxy-haemoglobin and met-haemoglobin.

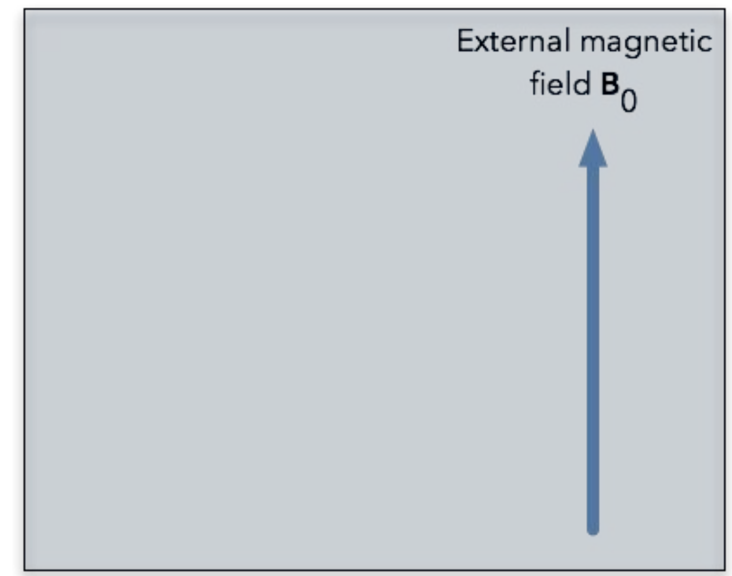
- *Superparamagnetic*

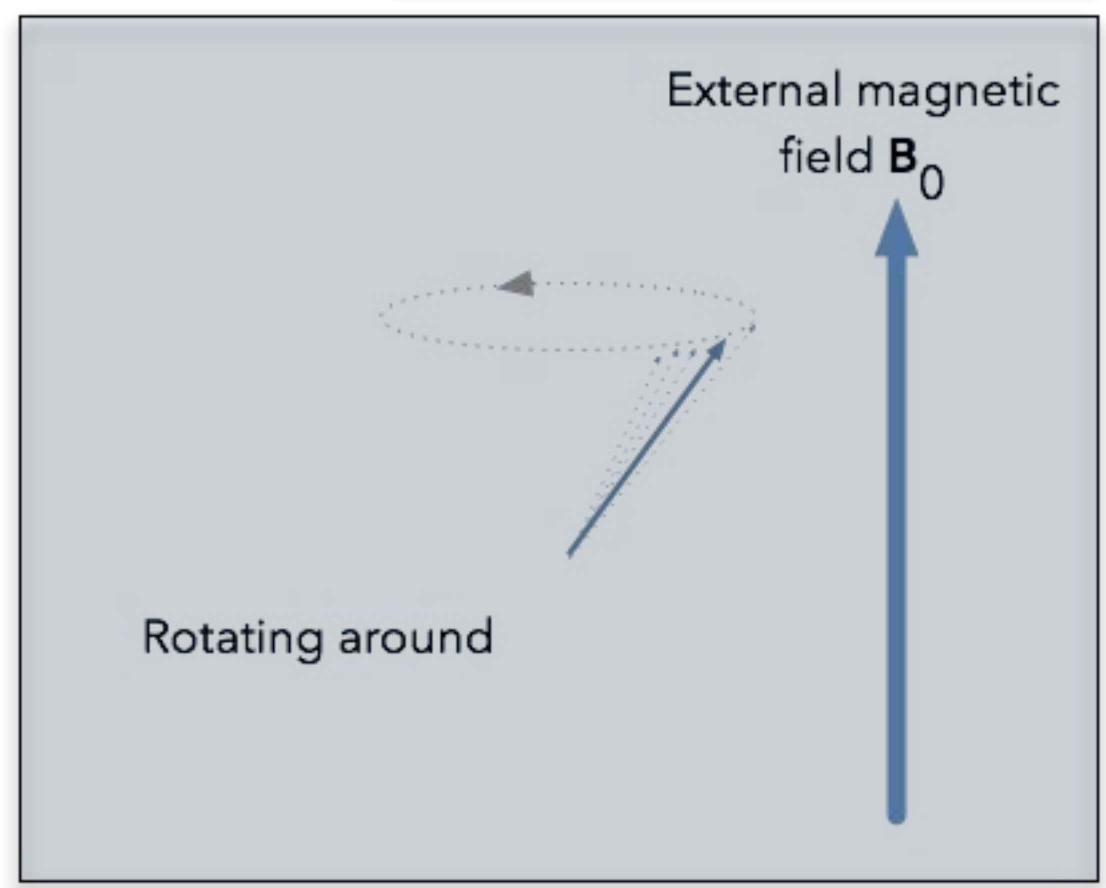
- *Ferromagnetic*

Generating the NMR signal

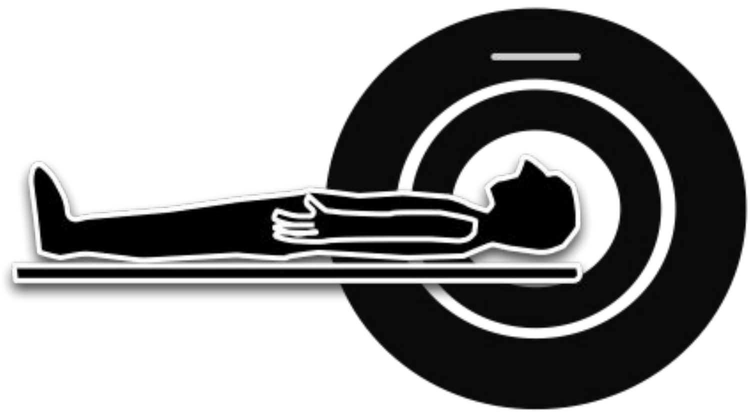
- What would happen if an external magnetic B_0 field was applied to this particle?
  - We would *probably* expect an alignment with B_0
  - Reality, because of the *spin angular momentum*, it will rotate around B_0
    - Precession

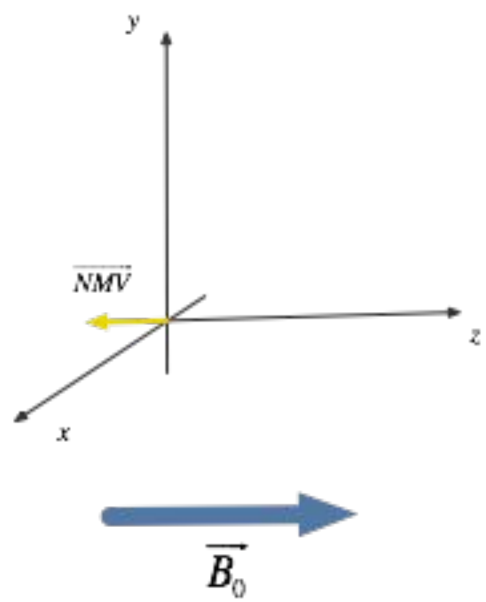


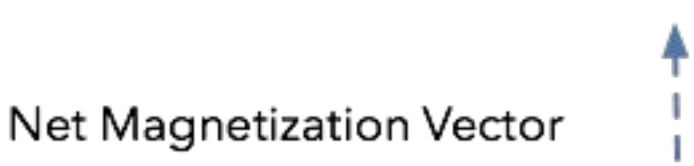




Generating the NMR signal



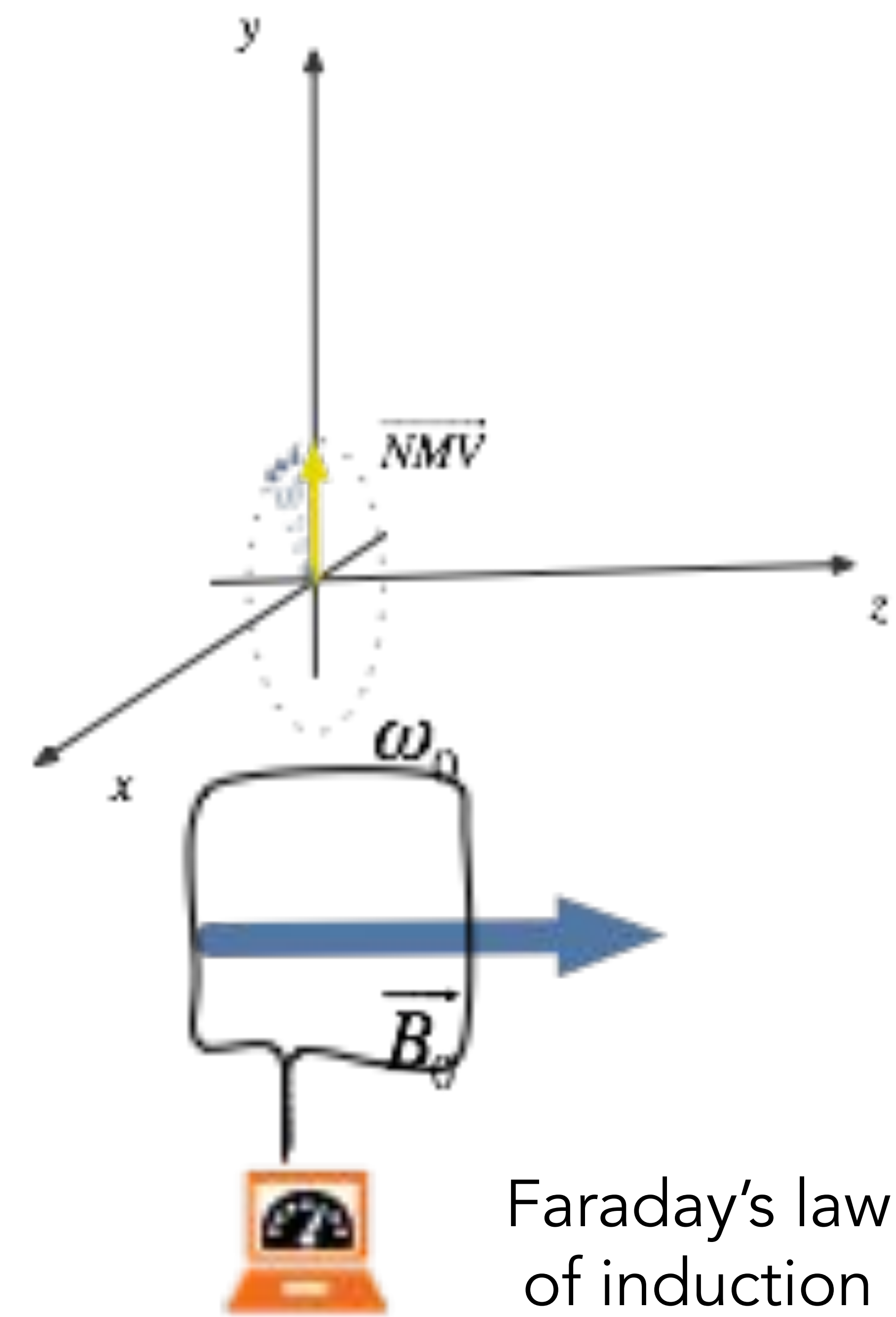




- We have a NMV, antiparallel to B_0
  - we cannot detect it along the same direction of B_0 because of B_0 strength
- What we want to do is to *change the orientation of the NMV*
  - *perpendicular* to the B_0
- Is it static (e.g. always pointing to the y-axis) ?

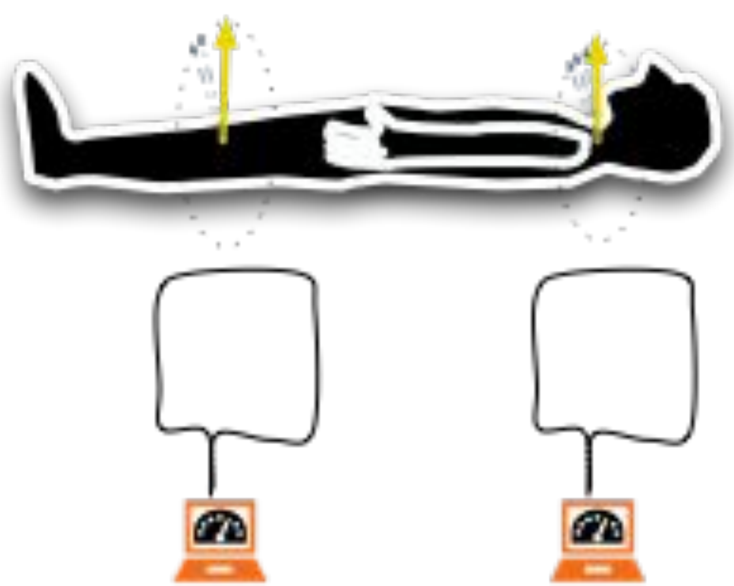
Generating the NMR signal

- Longitudinal
  - 'canceled', i.e. sum of all individuals is ~0
- Transverse
  - static?
  - If we have some coherent phase, the NMV is *rotating / precessing!* around z-axis/B_0
    - Larmor freq.
  - Now the NMV can be detected!



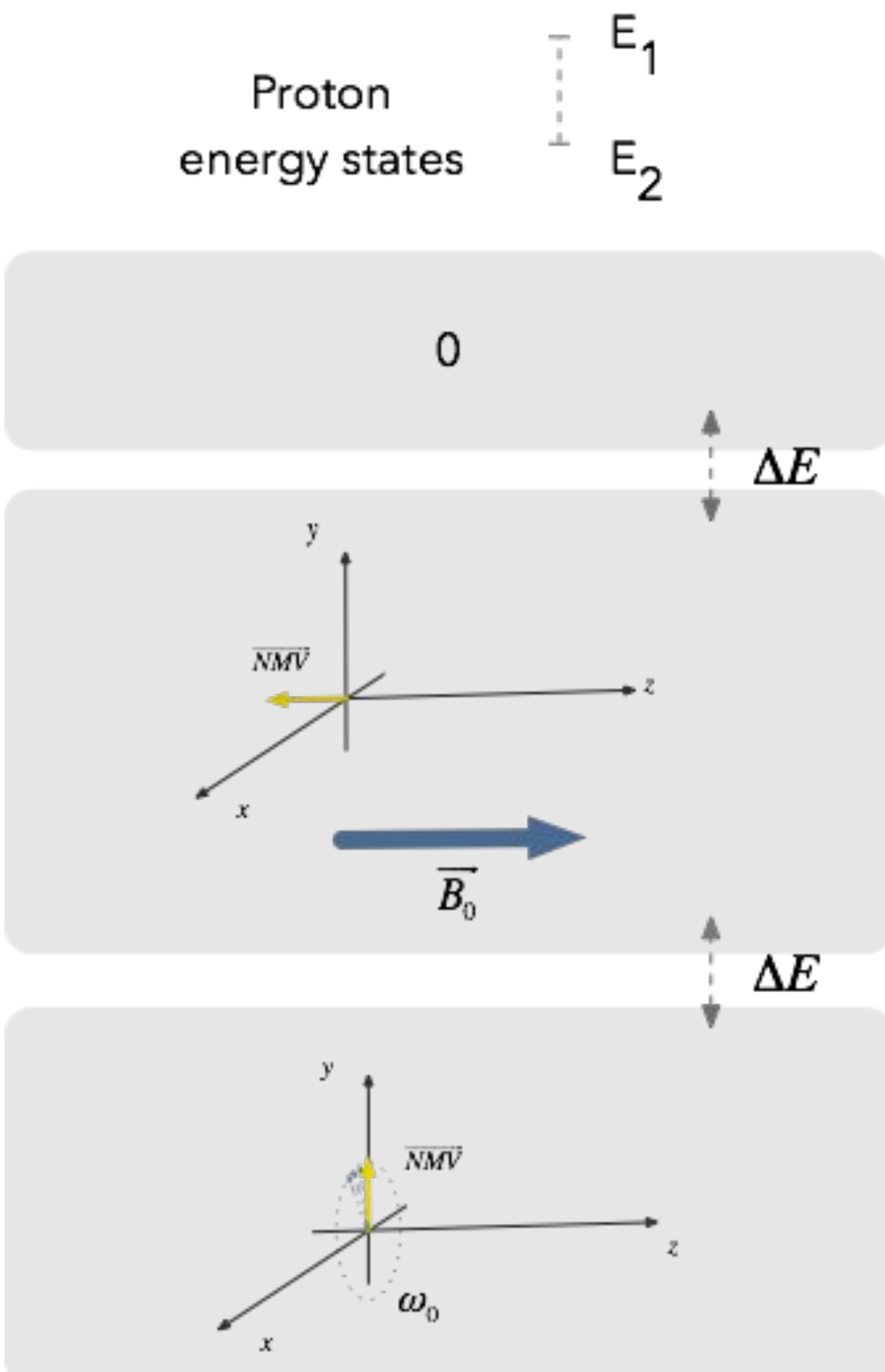
Faraday's law of induction

Generating the NMR signal



- Transverse
  - NMV is *rotating* around z-axis/B_0
    - Larmor freq.
  - The electrical induction (voltage generation) is proportional to the NMV
    - Signal Intensity (as a measure of transverse magnetization)
  - Different location with different NMV (transverse)

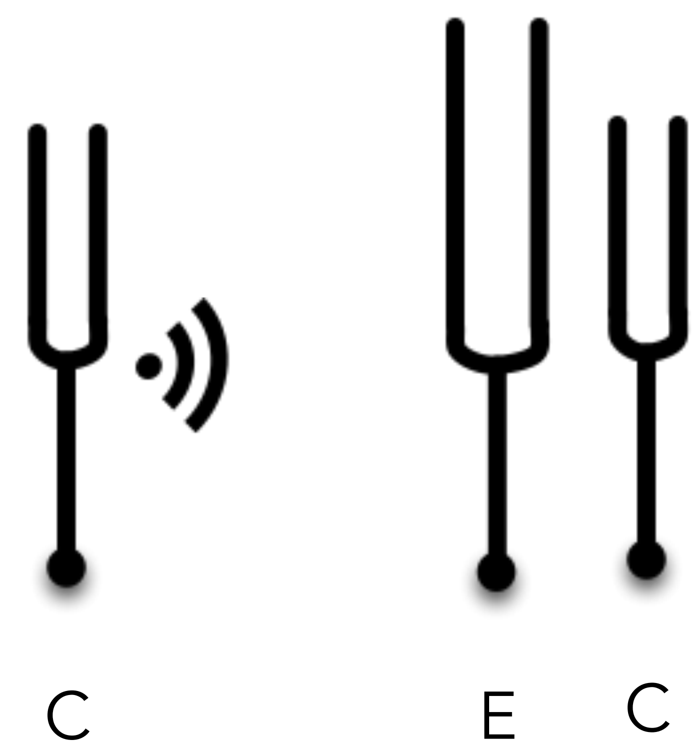
Generating the NMR signal



- How do we do this?
    - We need an additional 'system'
        - to get enough energy to provoke a change in NMV orientation

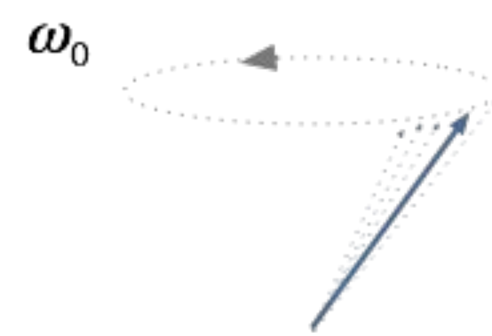
Generating the NMR signal

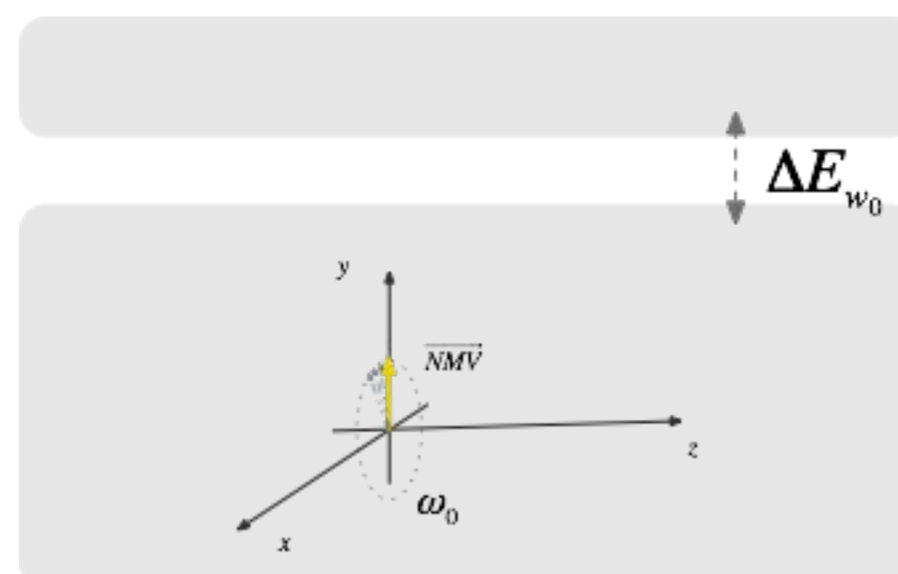
- Explore a feature named Resonance
    - Let us consider tuning forks (C or Dó and E or Mi)
    - If we hit the first C (on the left) it will start to oscillate/vibrate and the second C (on the right) will start to oscillate and the E will not!
        - due to the natural frequency at which the tuning fork oscillates
            - there is an efficient transfer of energy between both C's
            - with the E tuning fork we don't have the same freq. and do not observe resonance



Generating the NMR signal

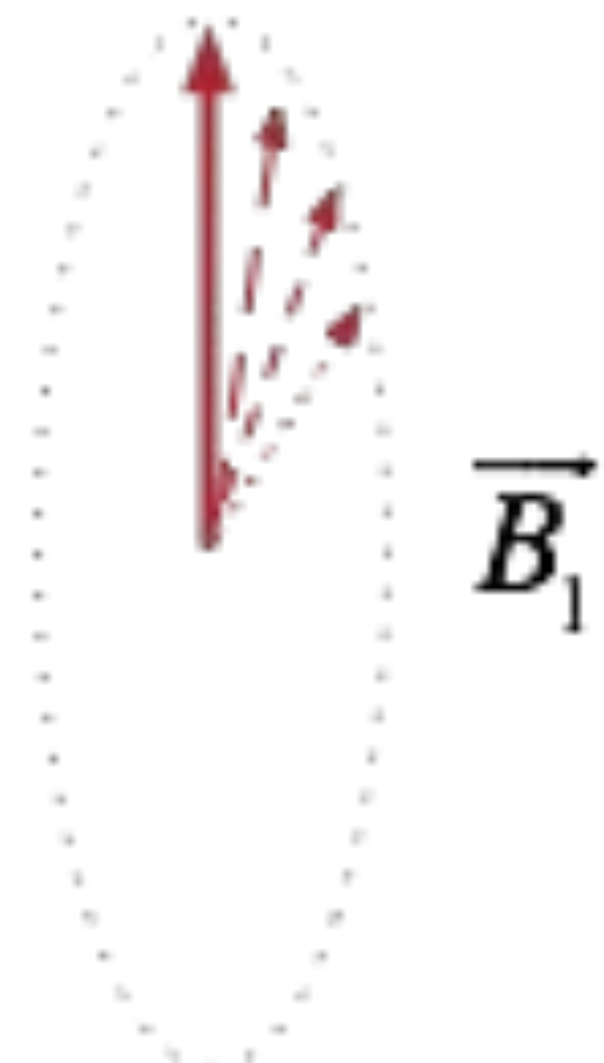
- Resonance in NMR
  - Precession, with frequency w_0, computed using the Larmor equation
  - If we apply energy in the system at this specific frequency
    - we should have an efficient transfer of energy to the system





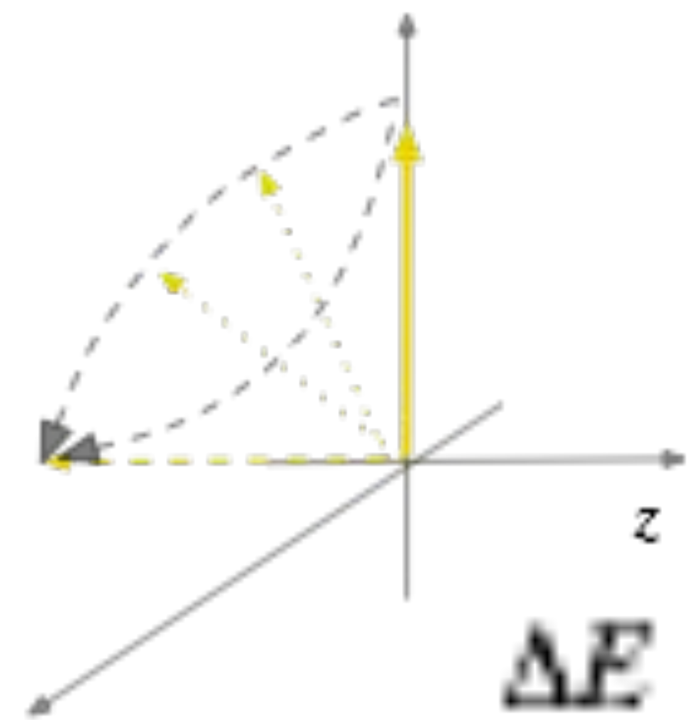
Generating the NMR signal

- Larmor equation
  - Frequency of rotation is around 64MHz (B_0=1.5T)
- B_1 is applied at this freq.
  - Also known as RF pulse
    - range of MHz
    - pulse (on-off)



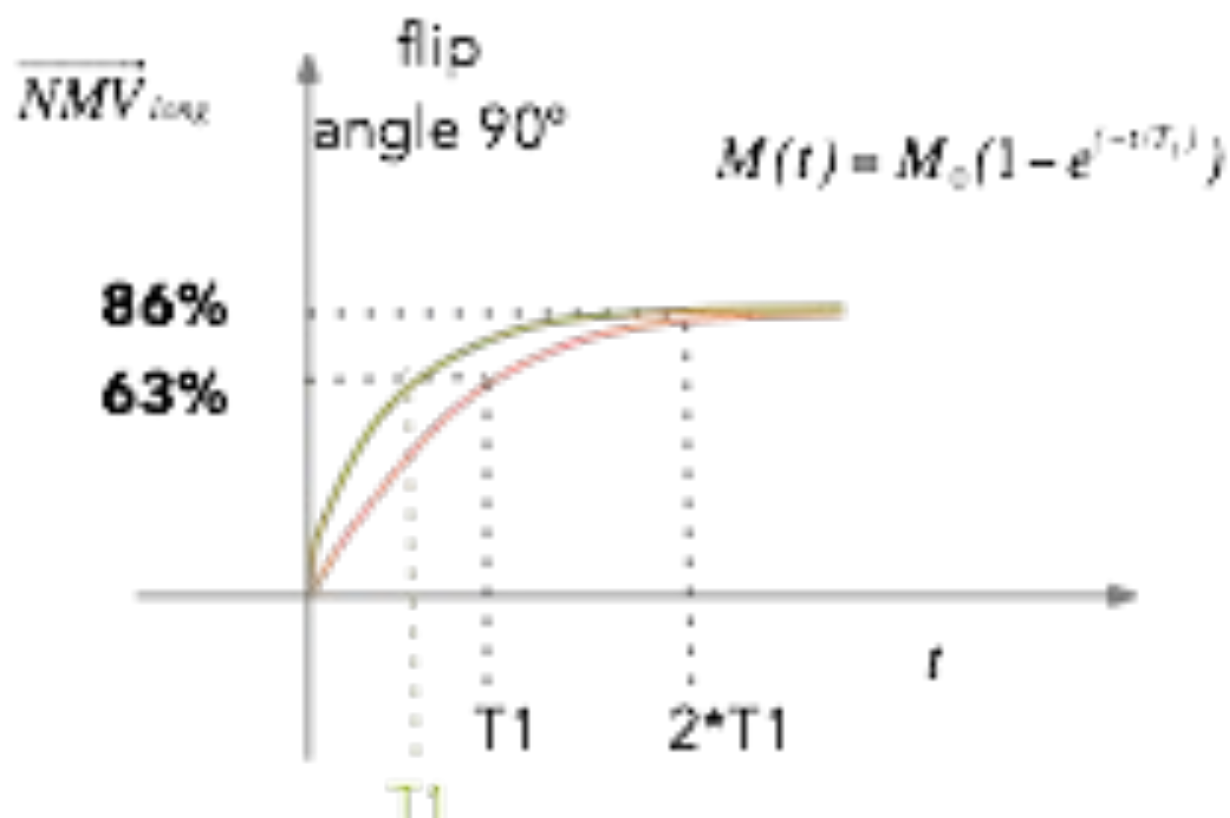
Relaxation

- Let us assume that B_1 is removed
  - Evolves to the lowest possible energy state
  - end up in the resting state
    - release of energy
      - where does it goes?
  - Let's look at each part separately - longitudinal and transversal



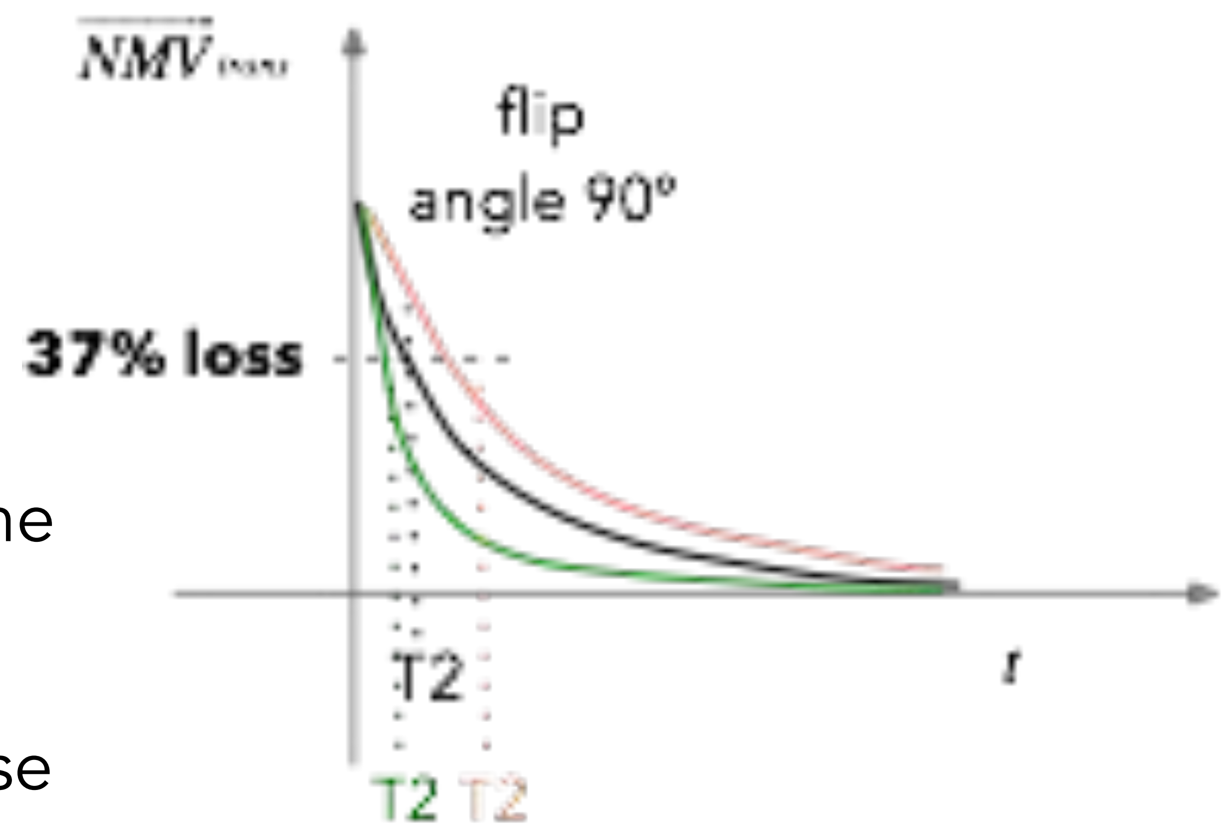
Longitudinal relaxation

- Longitudinal magnetisation
- a.k.a. spin-lattice relaxation
  - *lattice* - unrelated system elements
  - T1 increases with αB_0
    - 63% of baseline longitudinal magnetisation



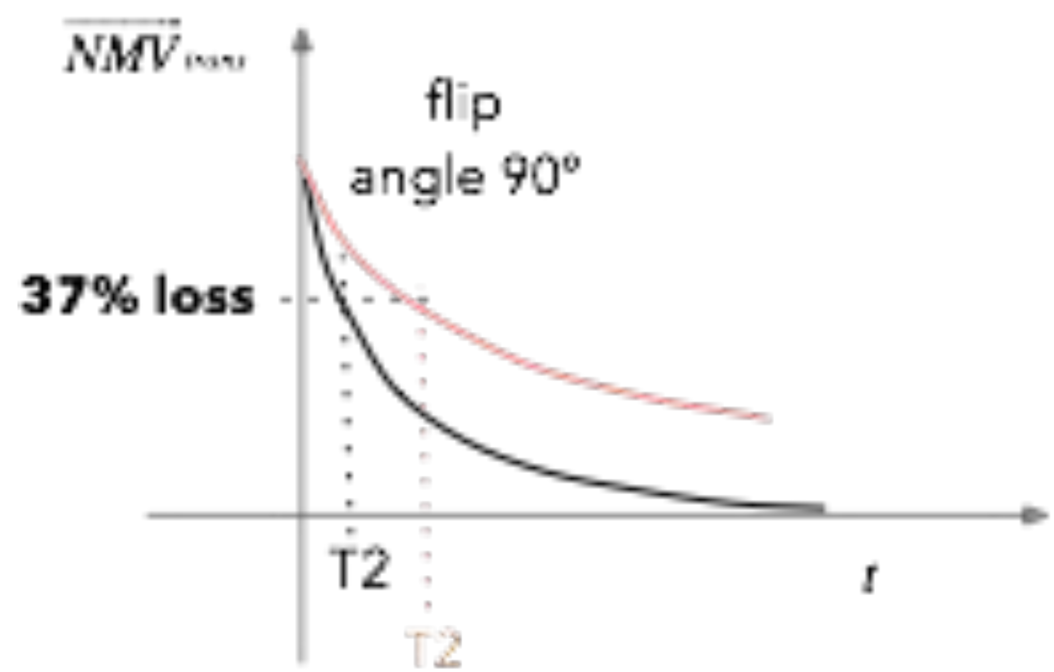
Transverse relaxation

- Transverse magnetisation
  - exponencial decay, max when flip angle is 90º
  - how can we measure it?
  - the exponencial is described by a time constant called T2
    - amount of time that it takes to loose 37%
    - varies from tissue to tissue



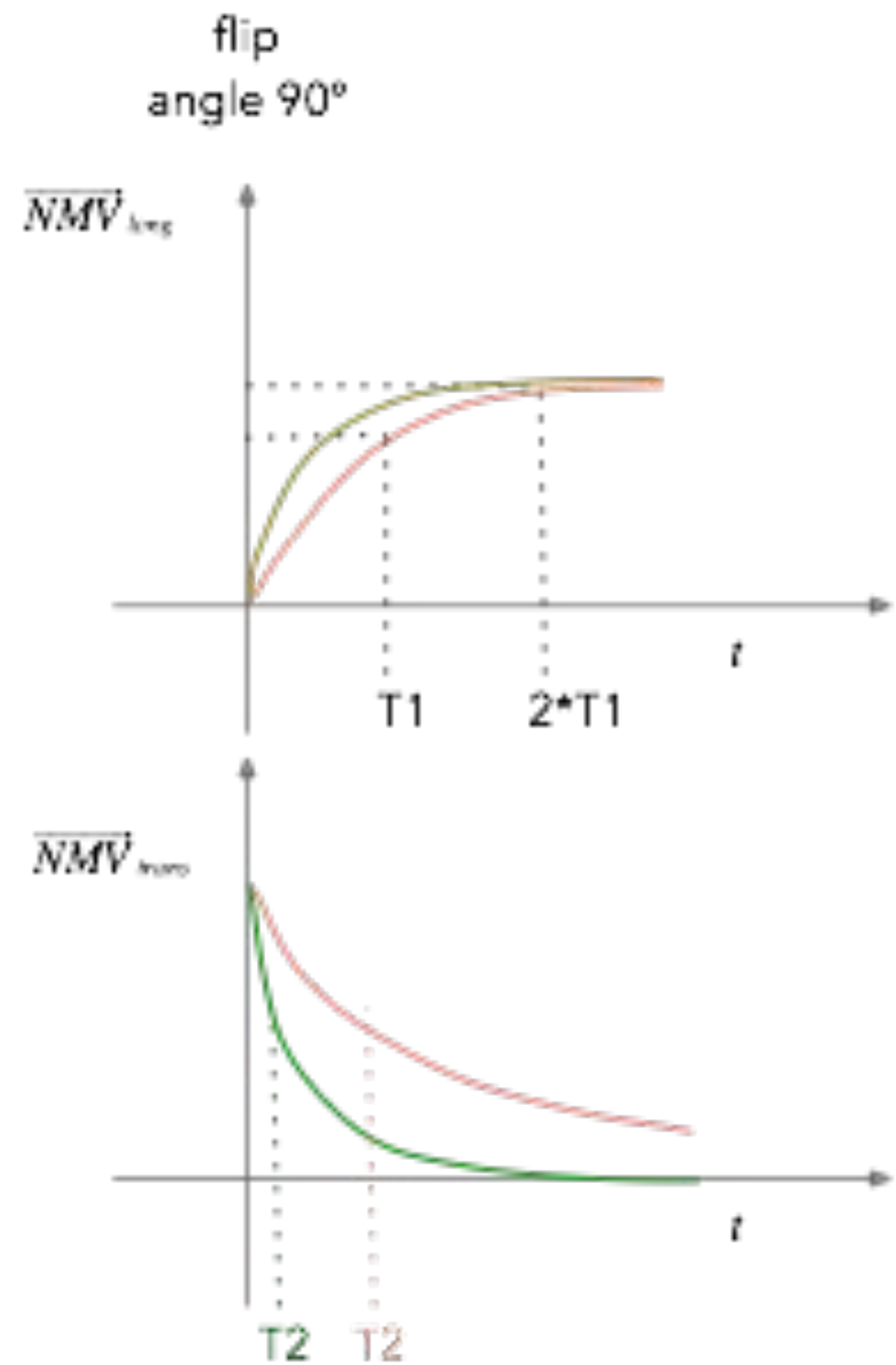
Transverse relaxation

- Energy transfer
  - from spins (in higher energy state) to other spins
    - a.k.a. Spin-Spin relaxation
  - process depends of energy exchange between spins
- Example
  - (pink) e.g. CSF - longer T2
    - probability of energy exchange occurring is lower - spins are "far apart"



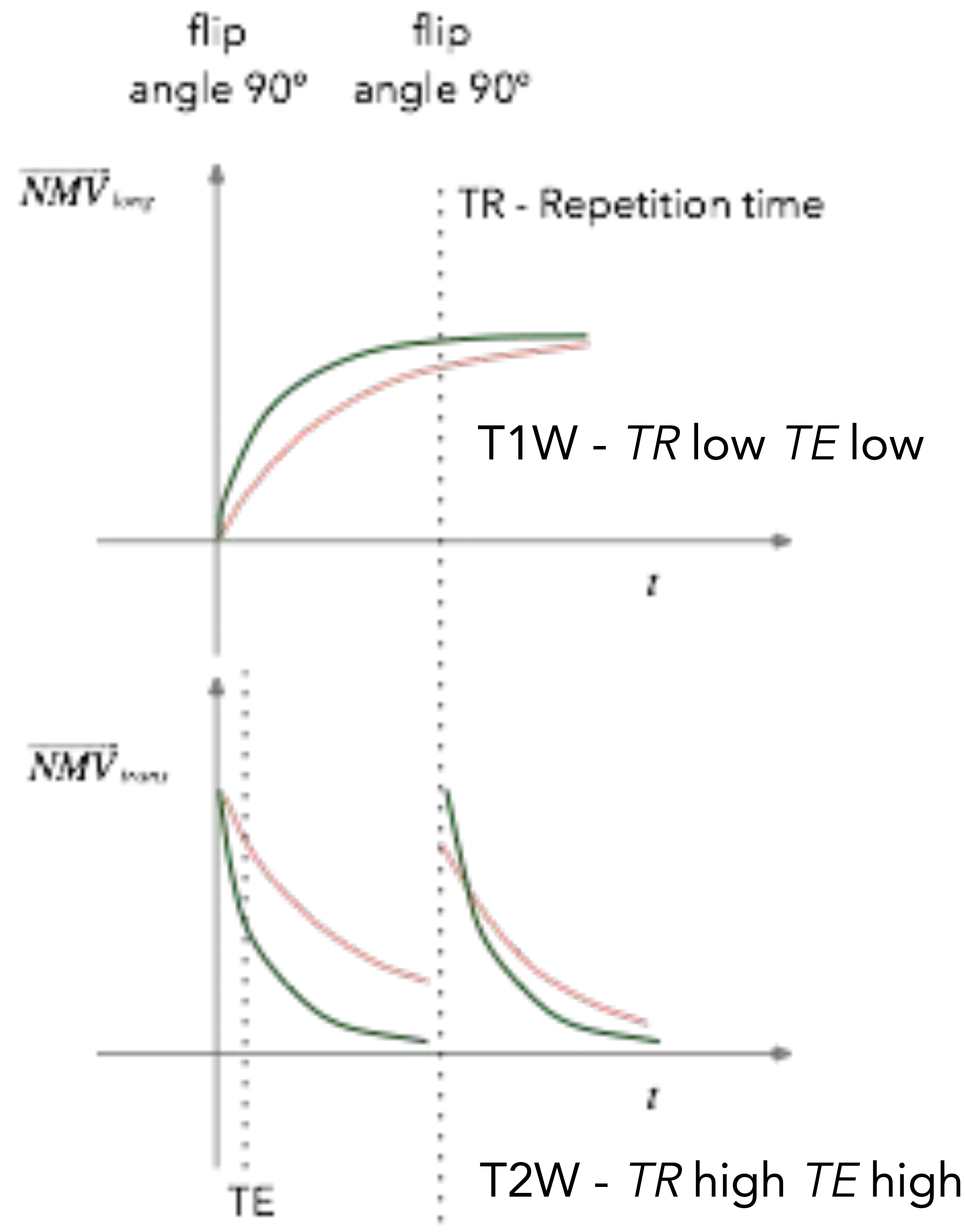
Contrast

- contrast -
  - Let us look closer at the transverse/longitudinal magnetisation

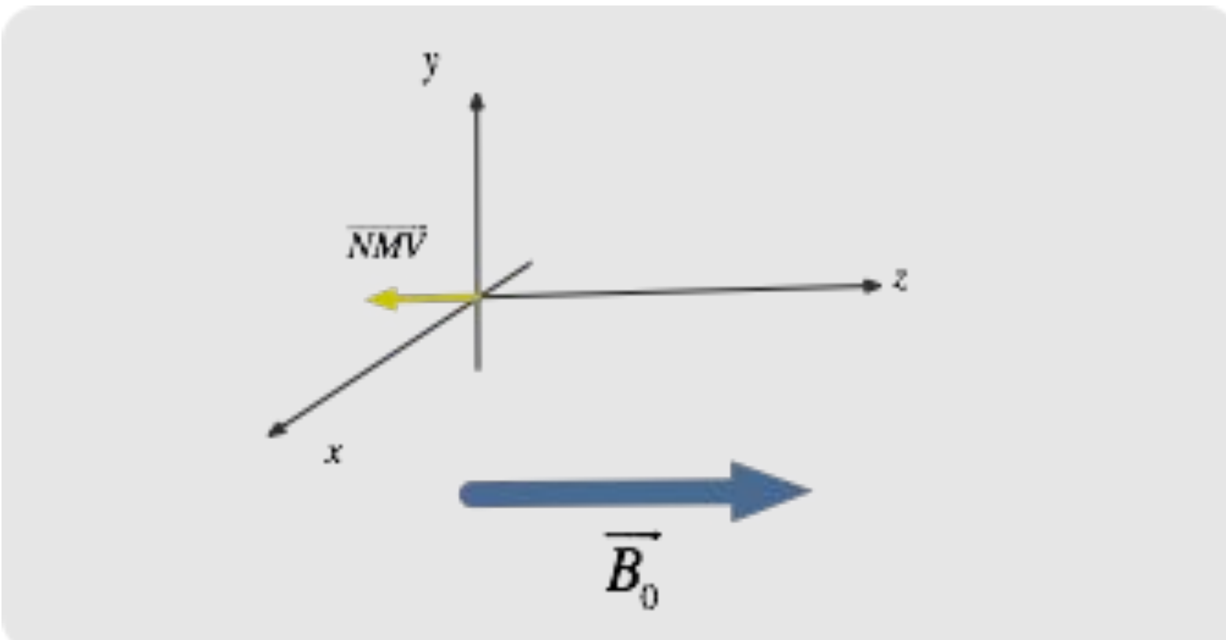


Contrast

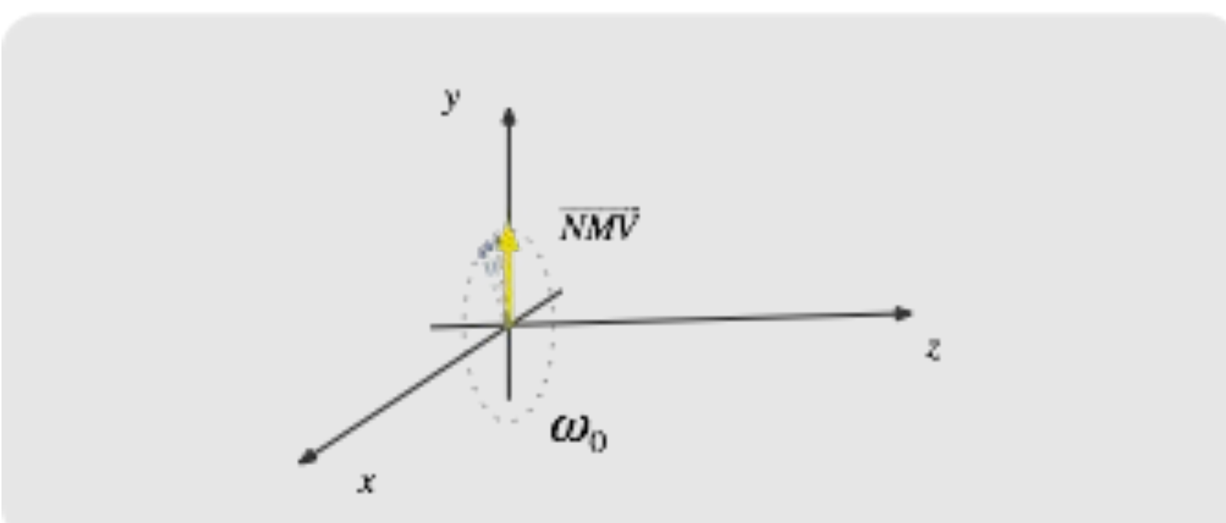
- contrast - transverse/longitudinal magnetisation
- Add a RF pulse TR after the first and look at the NMV components
- image with T1 contribution to the SI,
- image with the T2 contibution



Magnetic susceptibility



unfortunately, B0 is not exactly the same throughout the entire body

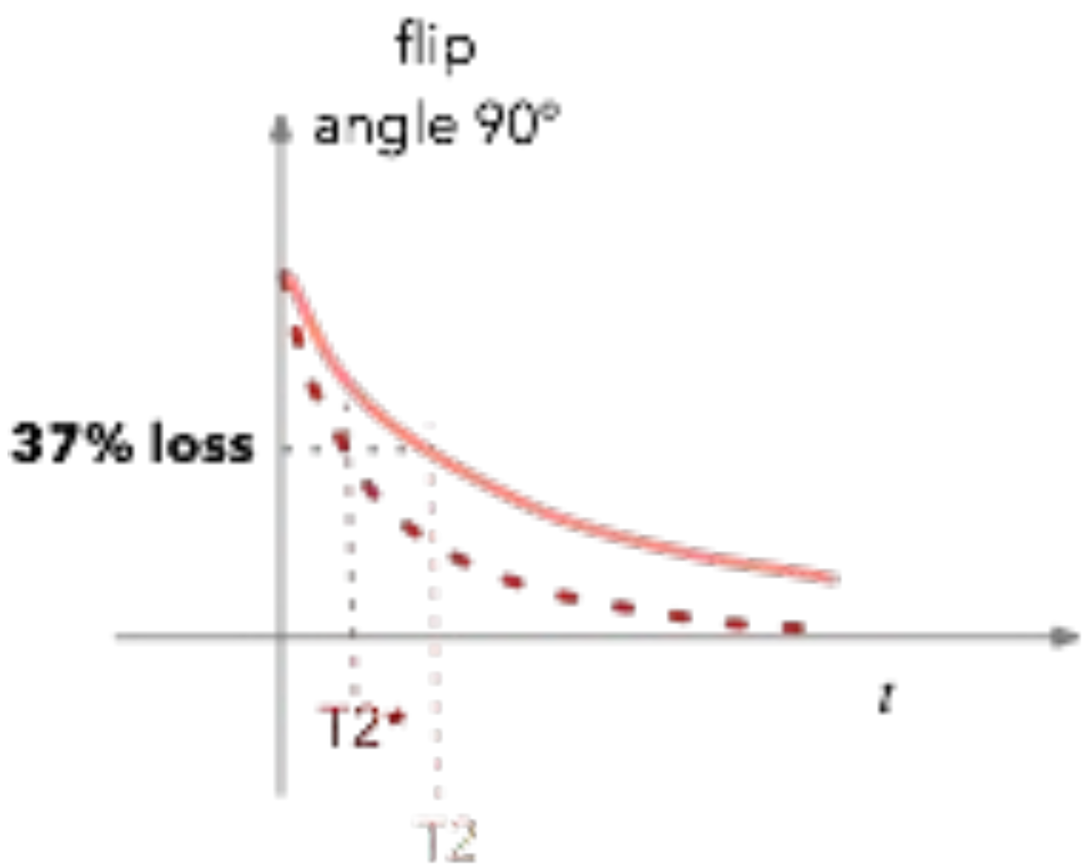


interaction of tissues with the applied magnetic field B0 causes point-to point variability - local amount of magnetic field (X)

$$\omega = \gamma(B_0 + X)$$

freq determined by the B0

Magnetic susceptibility

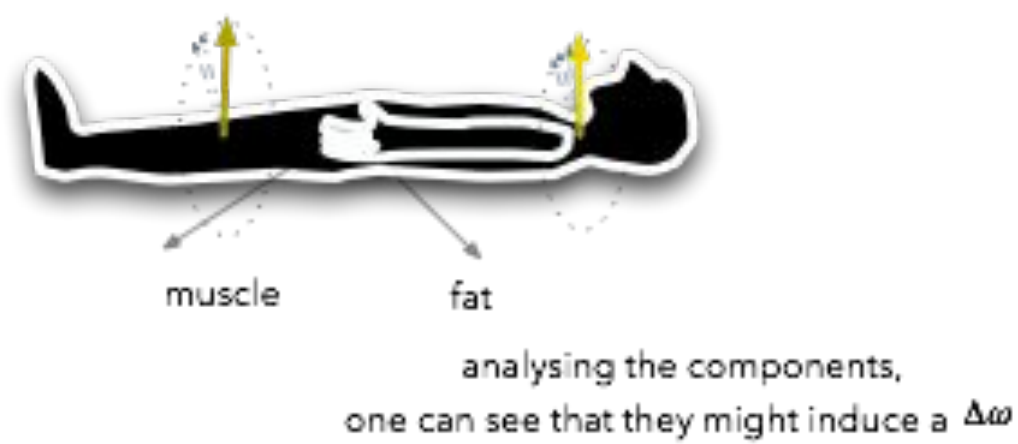


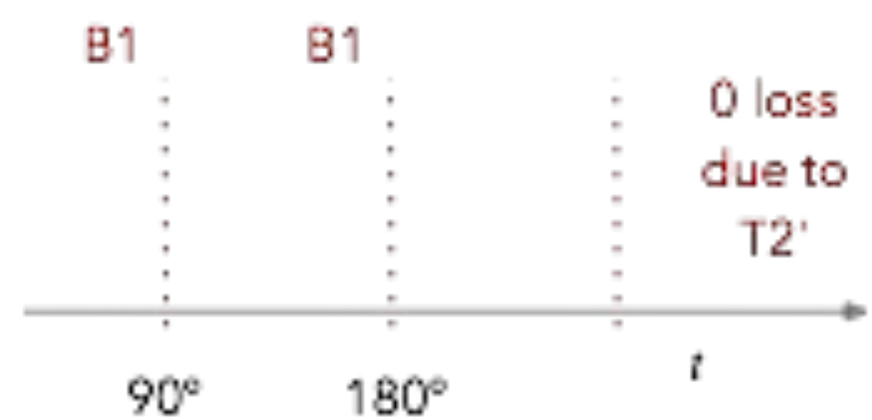
- Interaction of tissues in the magnetic field B0 causes point-to-point variability
  - local amount of magnetic field (X)
    - two neighbour spins experience two different magnetic field,
    - precess at different rates $\Delta\omega$
    - de-phase faster
- Real-life relaxation - T2*

$$\omega = \gamma(B_0 + T_2')$$

Spin Echo

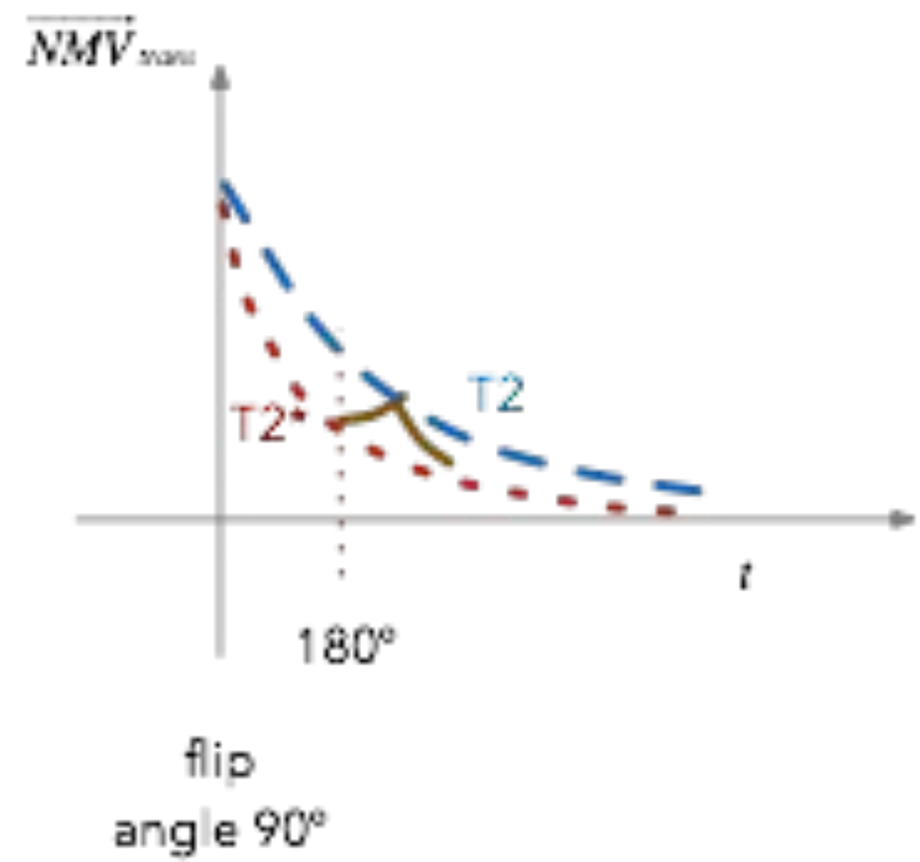
- de-phasing faster due to magnetic susceptibility
  - can we correct it?
  - Spin-echo
    - loss and recovery of signal





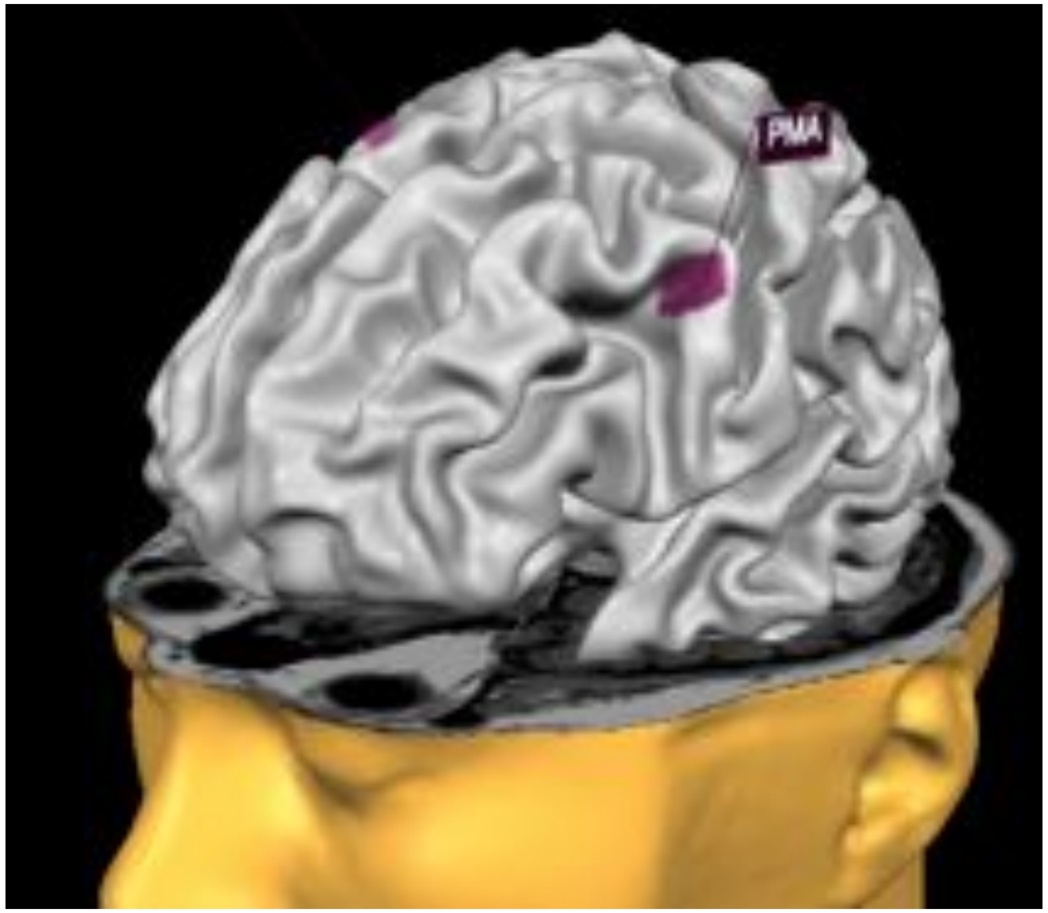
Spin Echo

- Loss and recovery of signal intensity
  - Allows to recover the T2 curve based on the 90 and 180° pulses



functional MRI

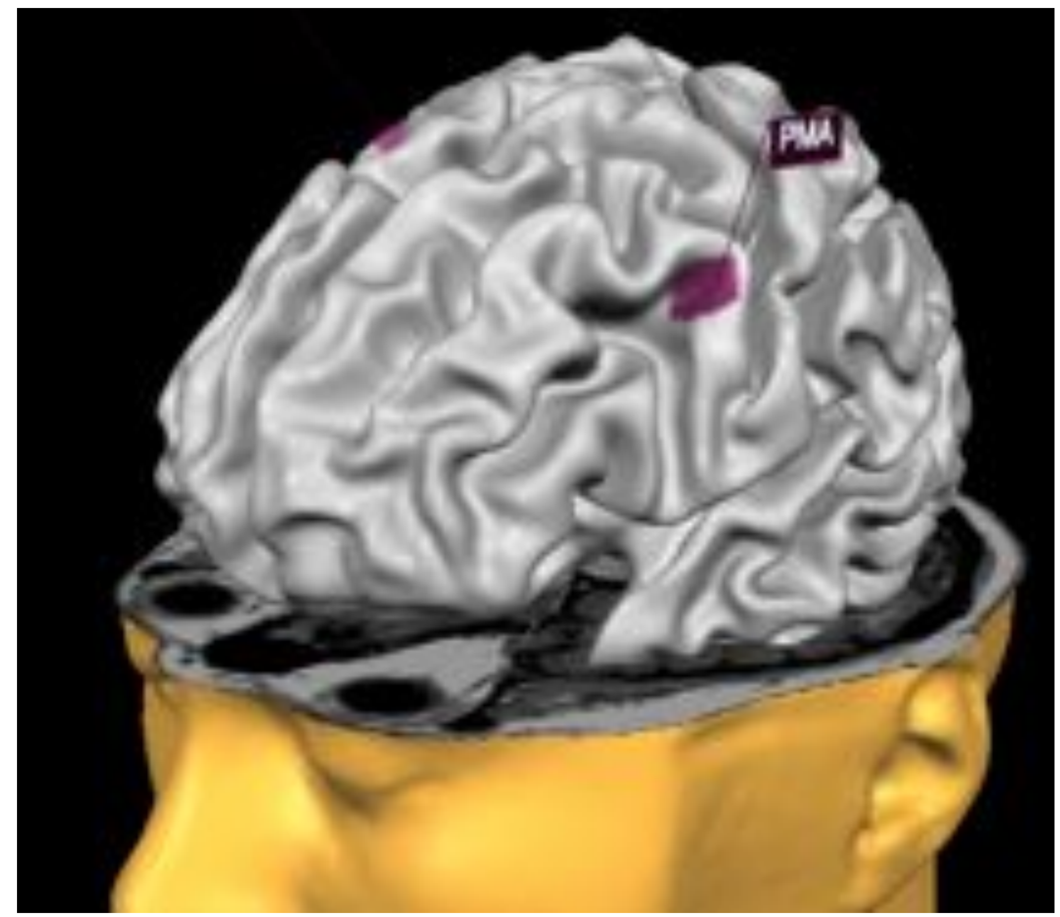
- How can we use this to study the brain function?



Brainvoyager Tutor

functional MRI - background

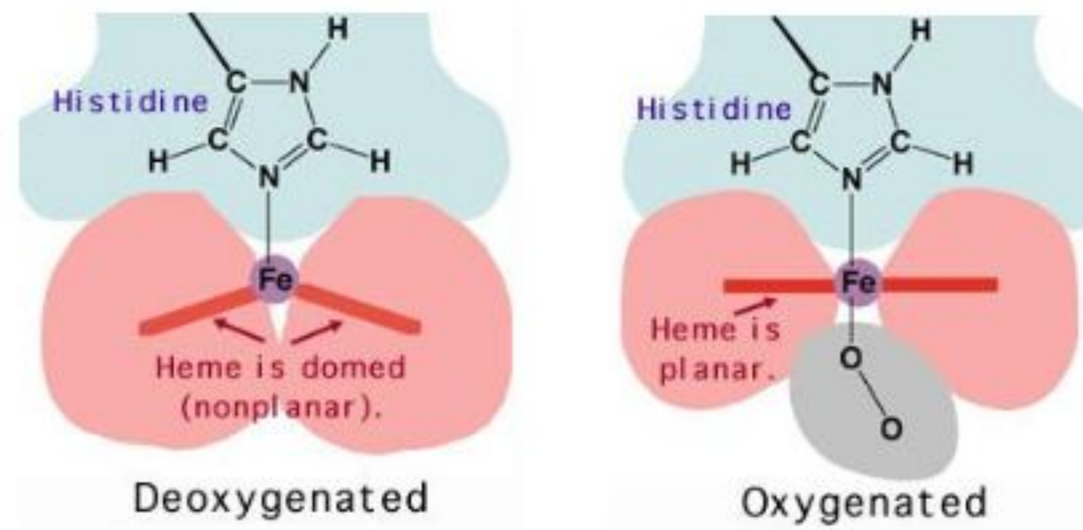
- Pre-operative tool (e.g. Epilepsy studies)
- The brain is *functionally* sub-specialized
  - brain regions related to/engaged specific tasks
  - increase in neuronal activity in these regions
    - the neurons require additional amount of metabolic substrates - vascular response
    - oxygen is delivered to cells bonded to *haemoglobin*



Brainvoyager Tutor

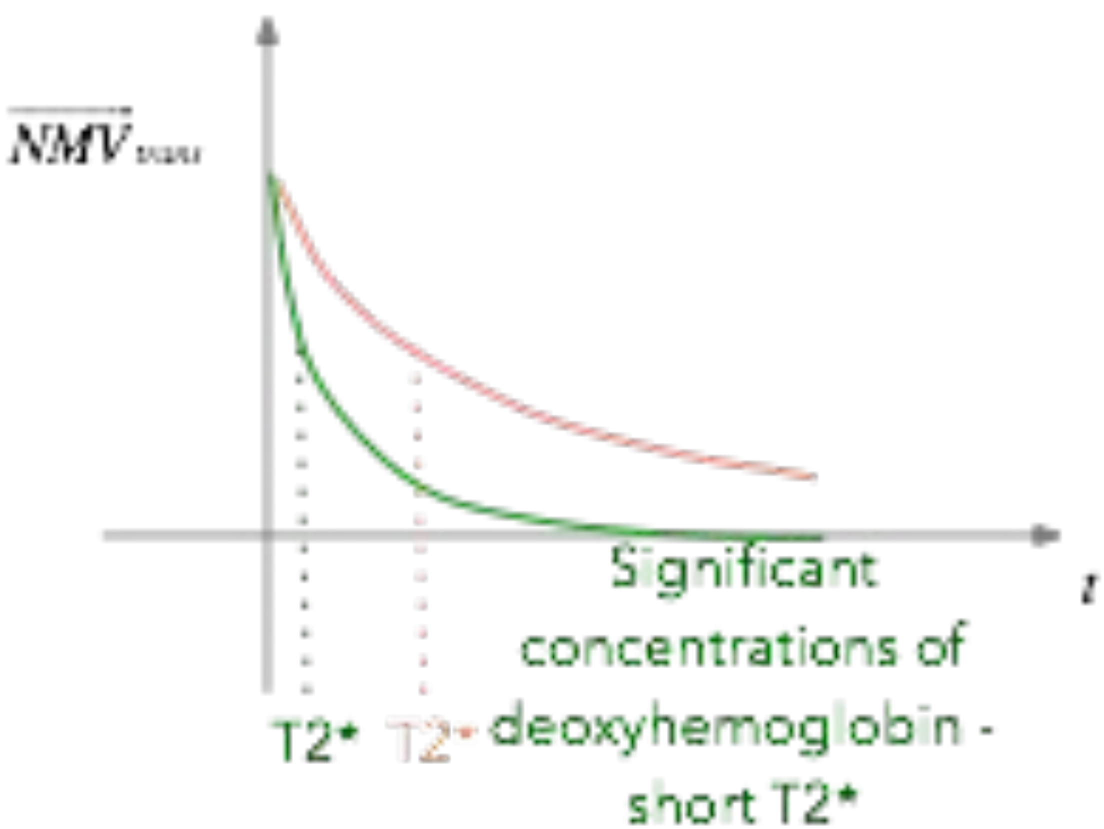
functional MRI - background

- Oxygenated haemoglobin is diamagnetic
    - elements that have a very weak susceptibility
- Deoxygenated haemoglobin is paramagnetic
    - have a stronger susceptibility



Paramagnetic **Diamagnetic**

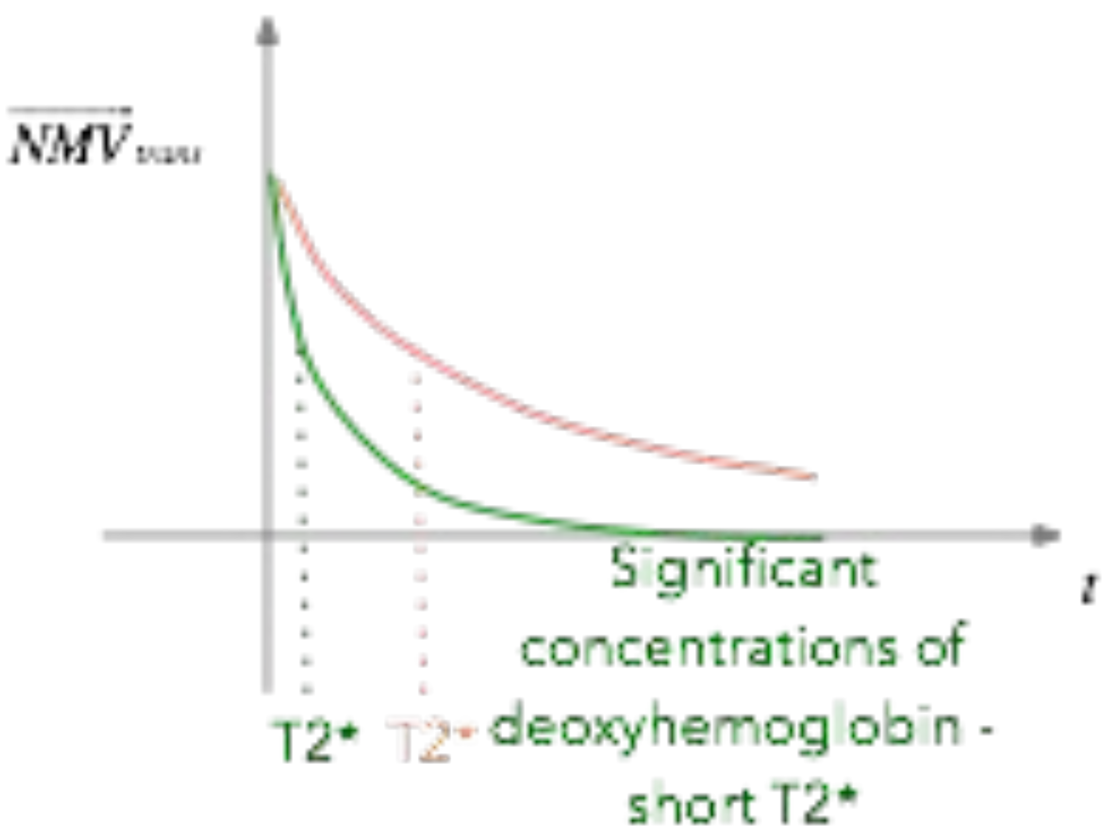
functional - BOLD



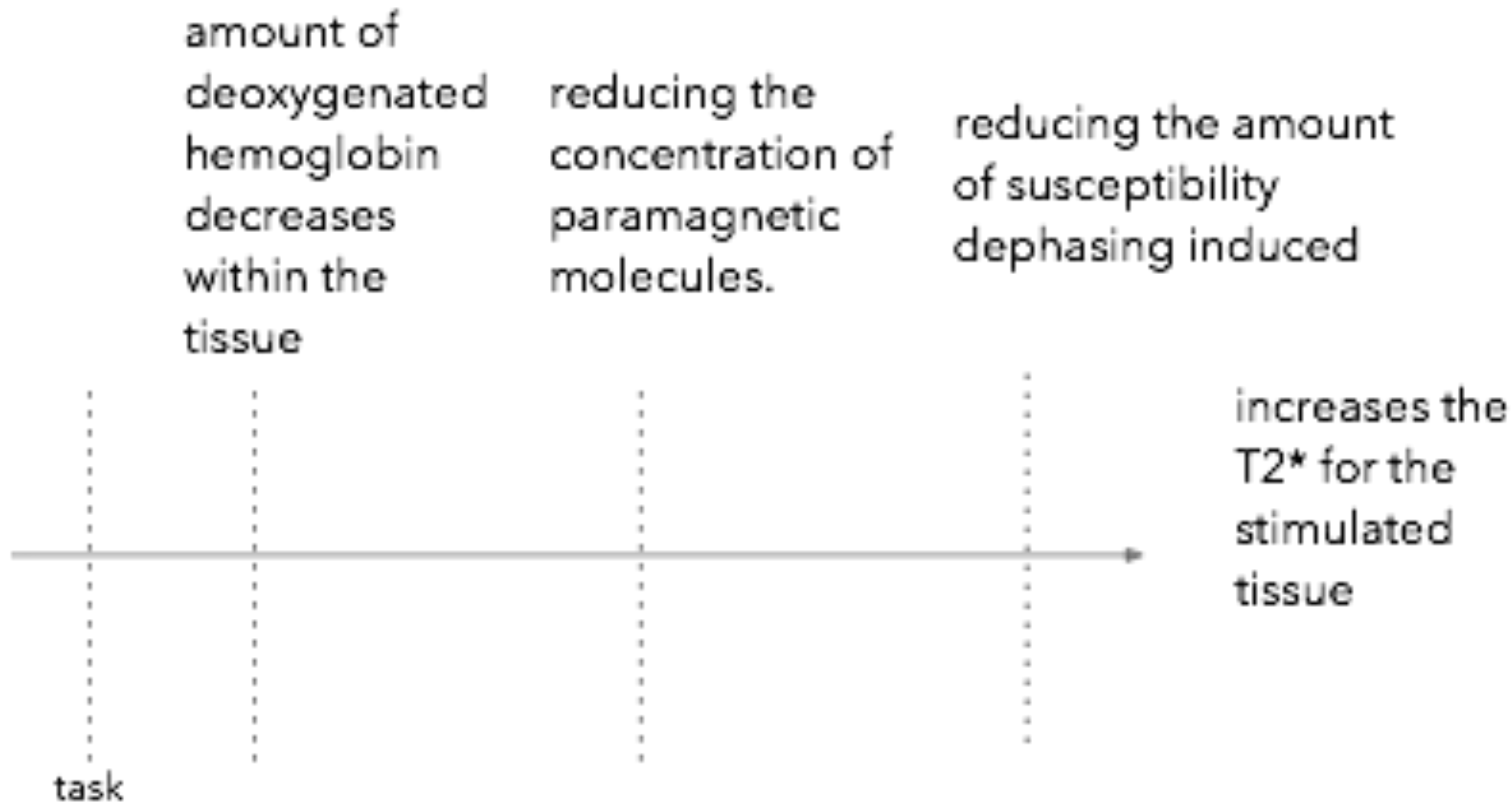
Significant concentrations of deoxygenated hemoglobin shorten the *T2** relaxation time of the tissue

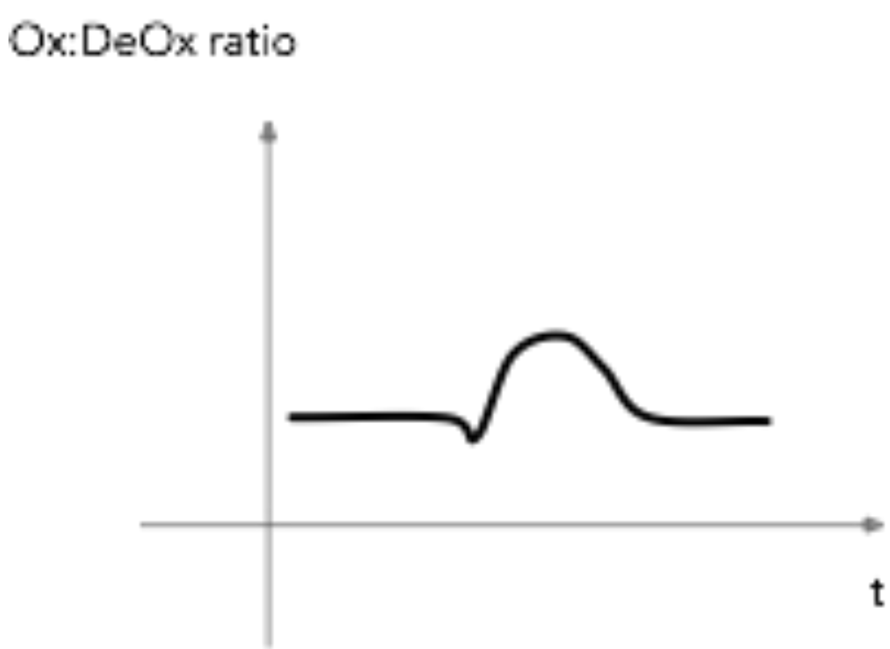
- decrease in SI compared to tissue with oxygenated haemoglobin.

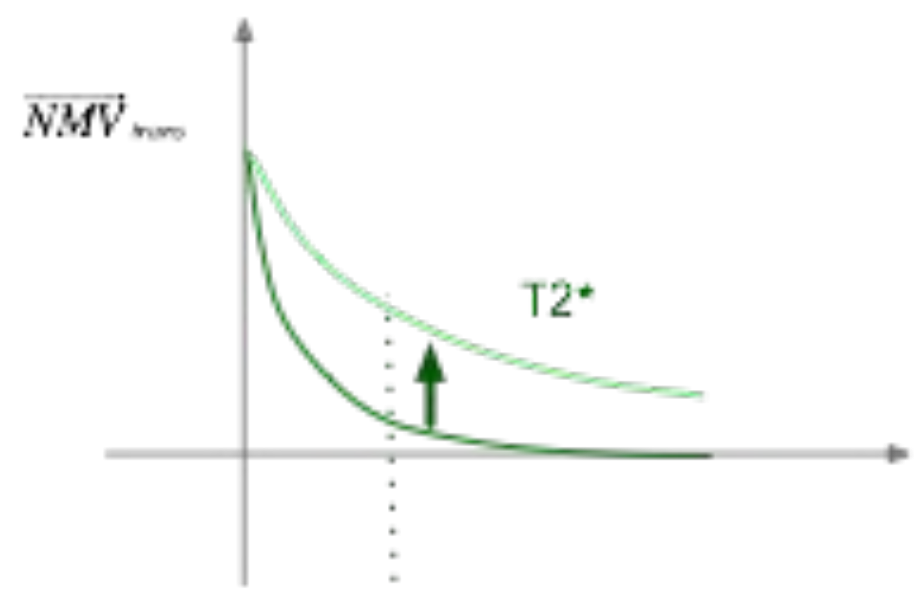
functional - blood-oxygenation-level-dependent effect or BOLD effect



Let us assume that **stimulated tissue** - e.g. brain cortex engaged in a task -undergoes an **increase in blood flow** with an increased delivery of oxygenated haemoglobin



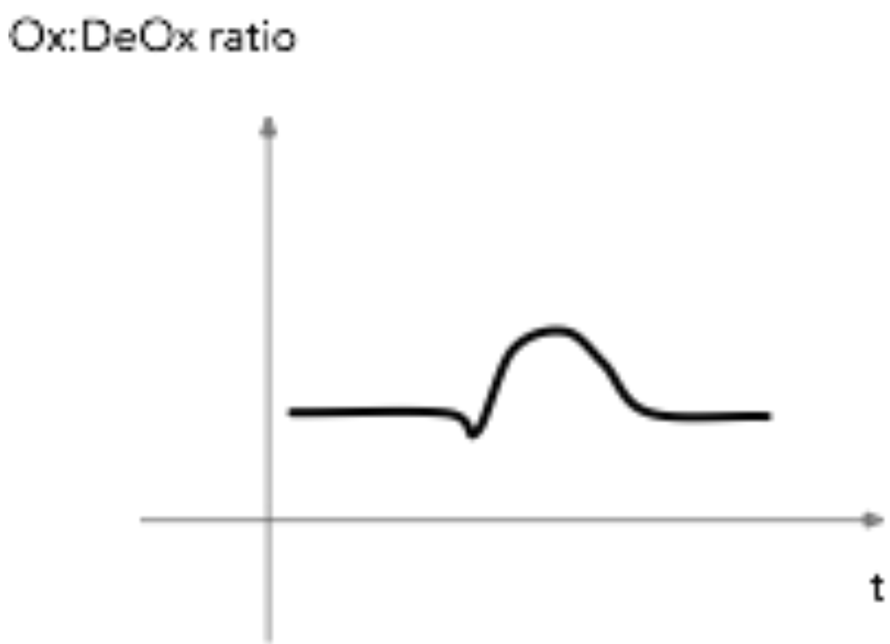




Haemodynamic response function

functional MRI

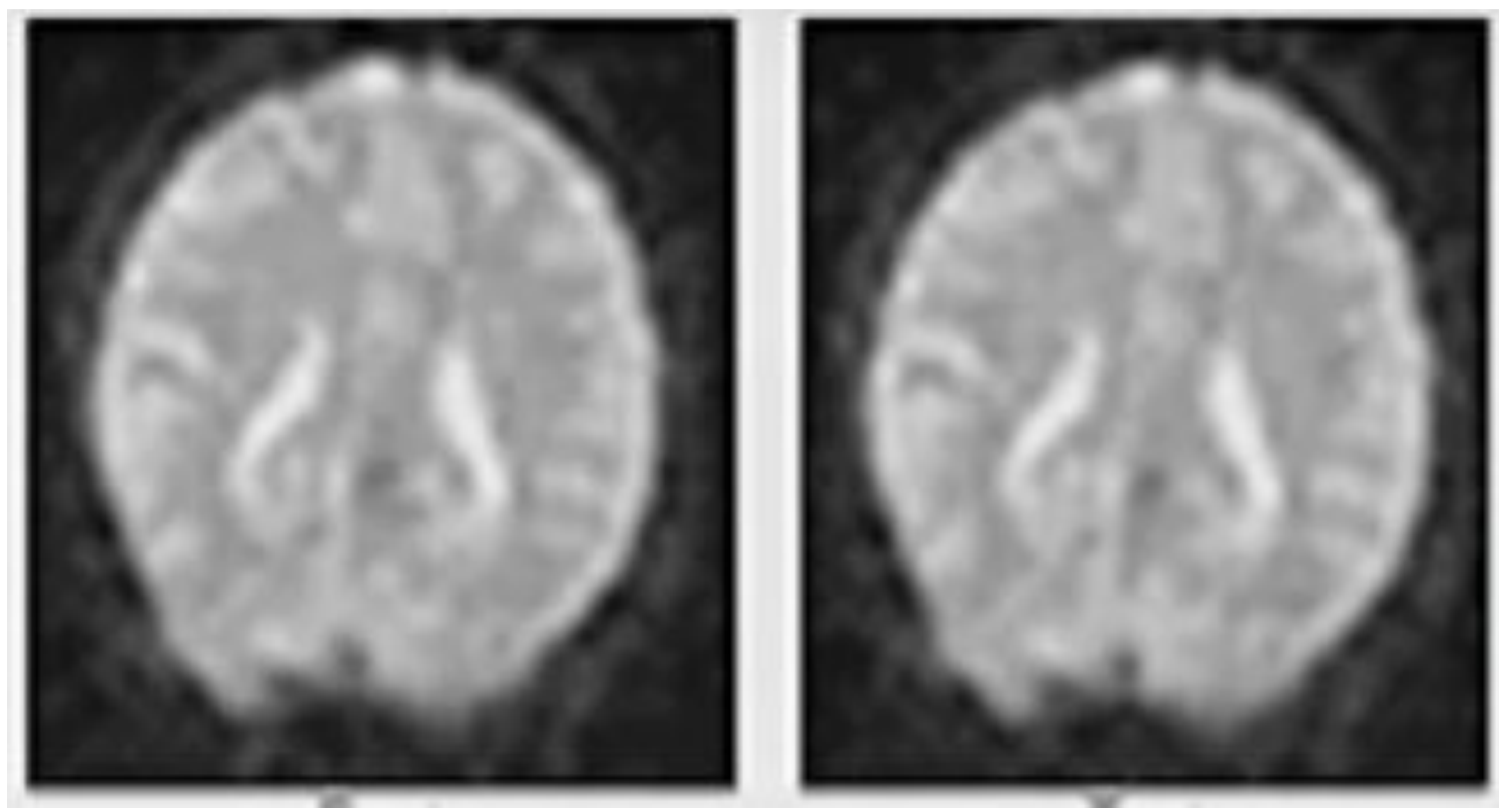
- How can we get an image based on this information?



- If enough resolution (contrast), we could determine which voxels change during task performance
  - delay after the beginning
  - very small signal change (2 to 3 % variation)

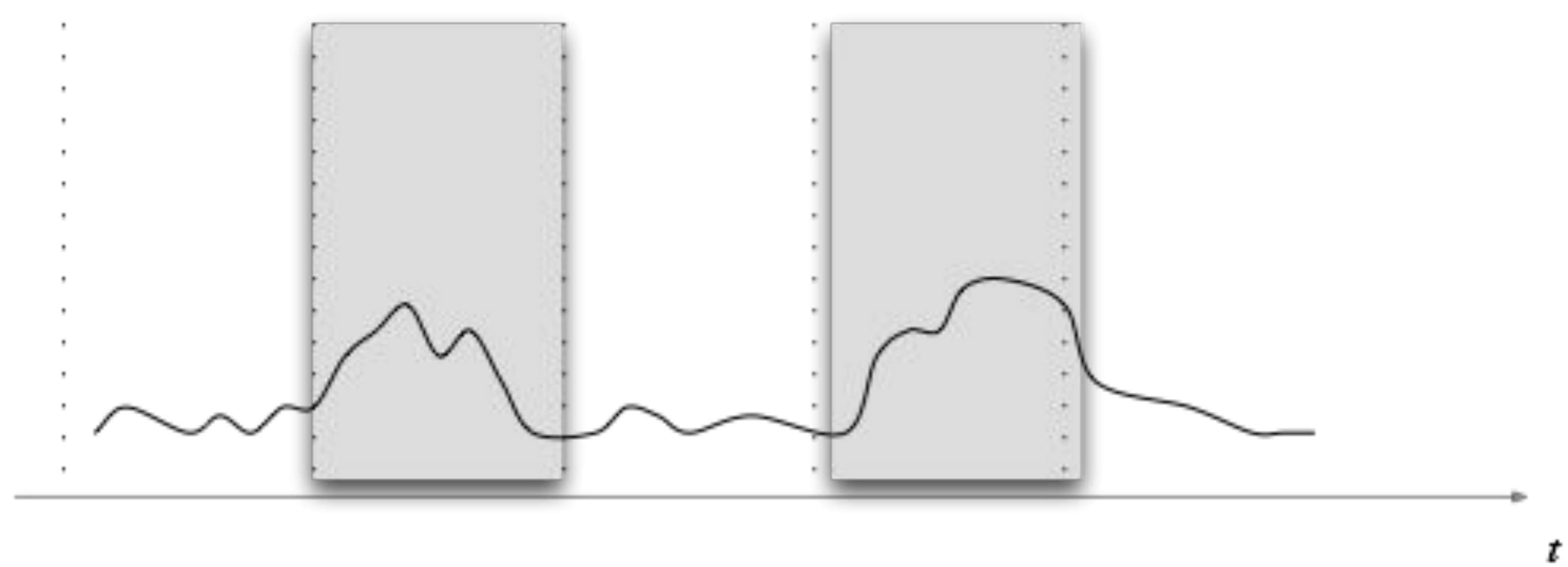
fMRI data

difference between two fMRI images



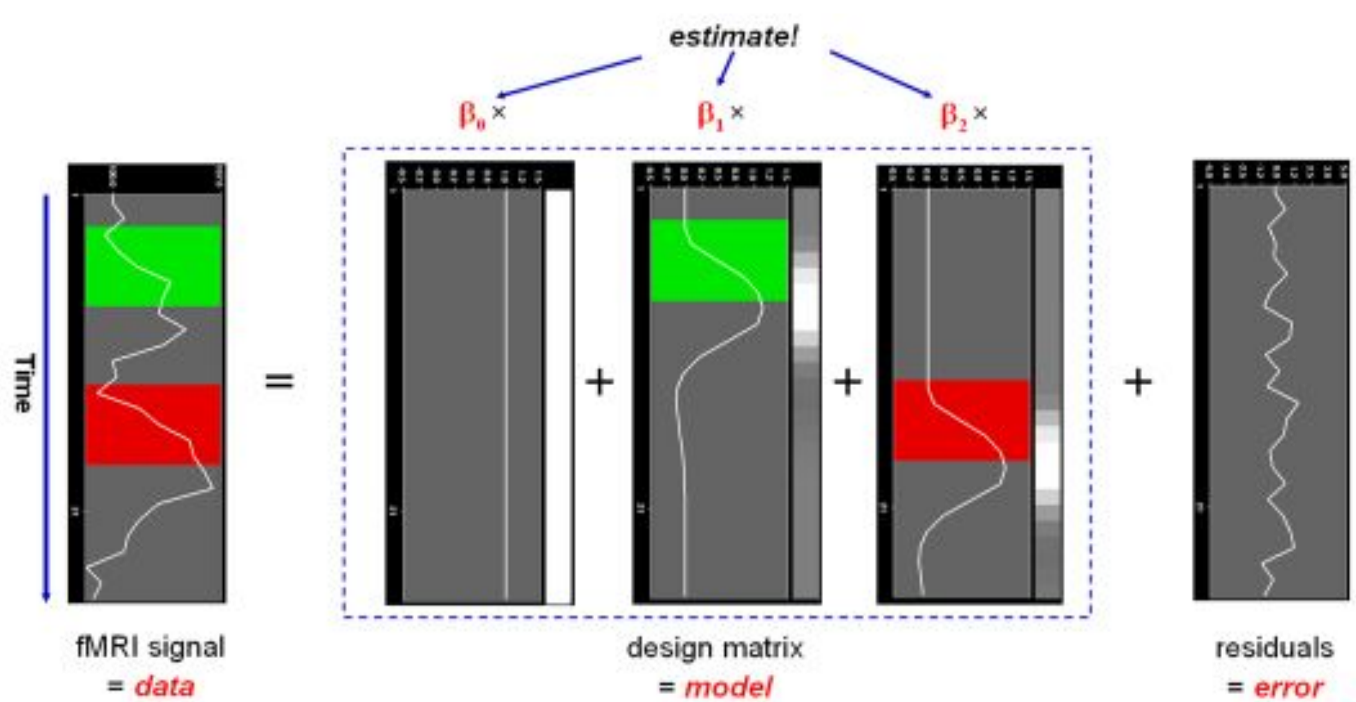
functional MRI

- The typical approach is to perform a large series of measurements in the presence and absence of the stimulus and subtract the images
  - increasing statistical significance



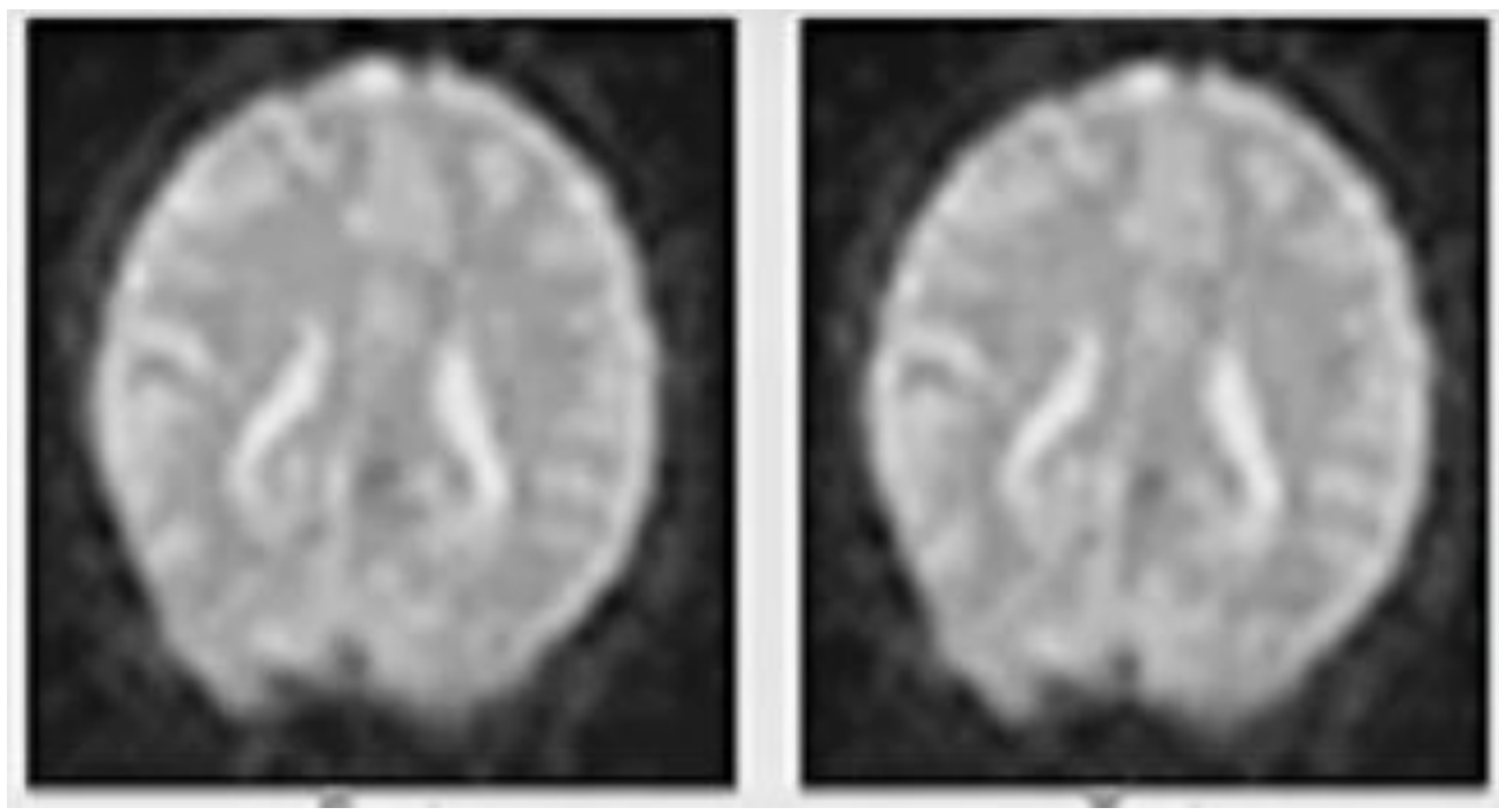
General Linear Model

- Statistical framework
  - Simplest case: baseline and condition
  - but we can go further and use different conditions



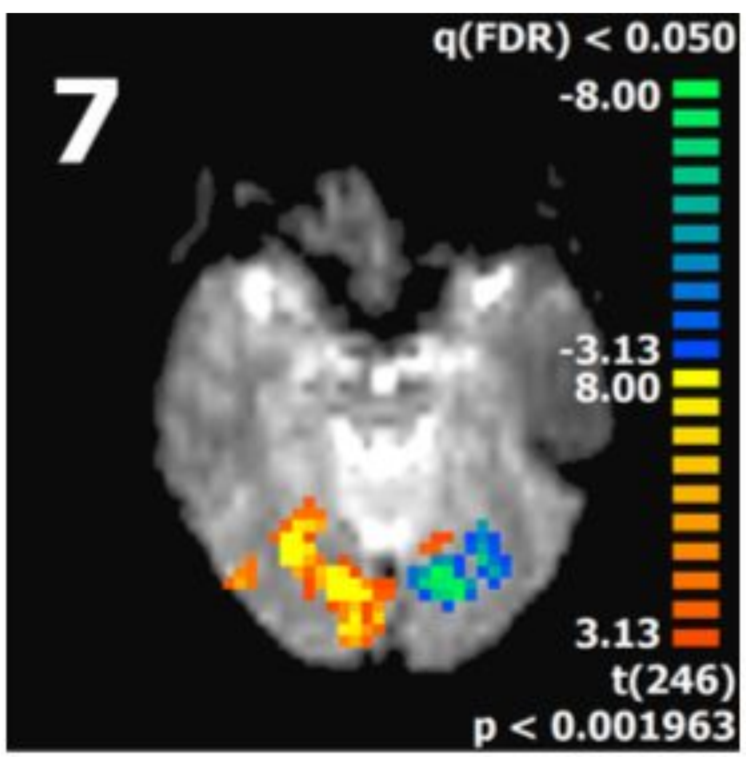
fMRI statistical map

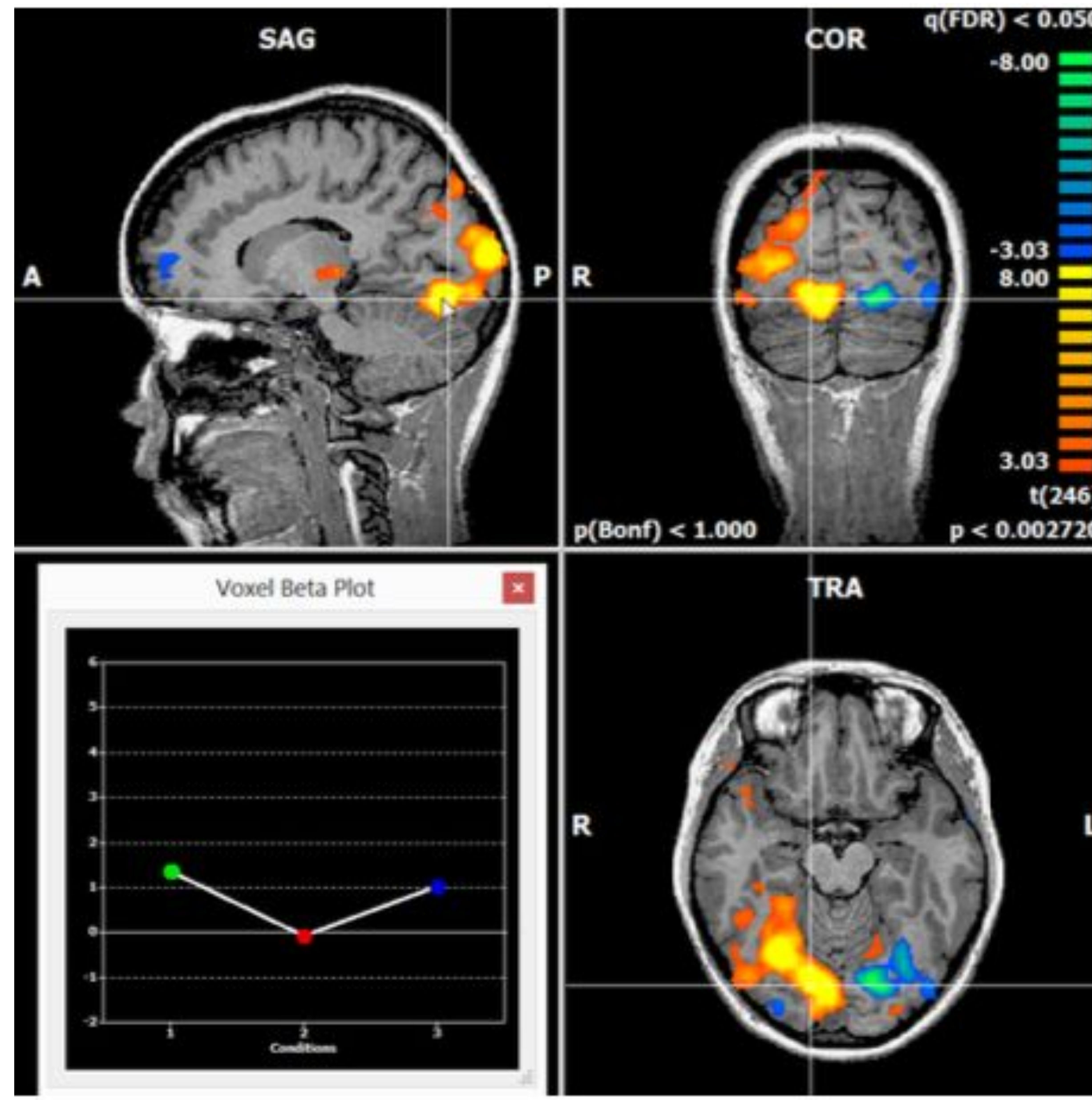
difference between two fMRI images



fMRI statistical map

2D and 3D statistical map based on GLM contrast condition>baseline



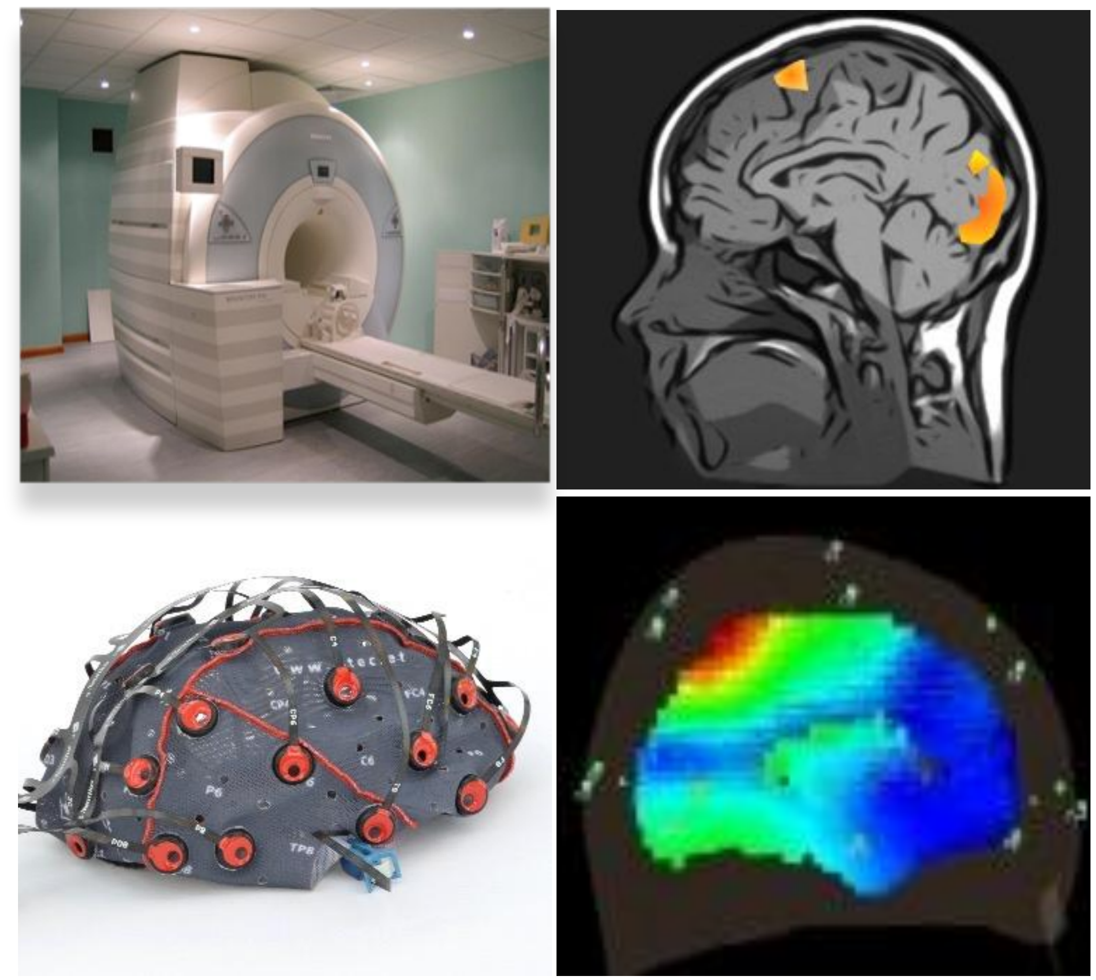


Questions?

Project *Braintrain*

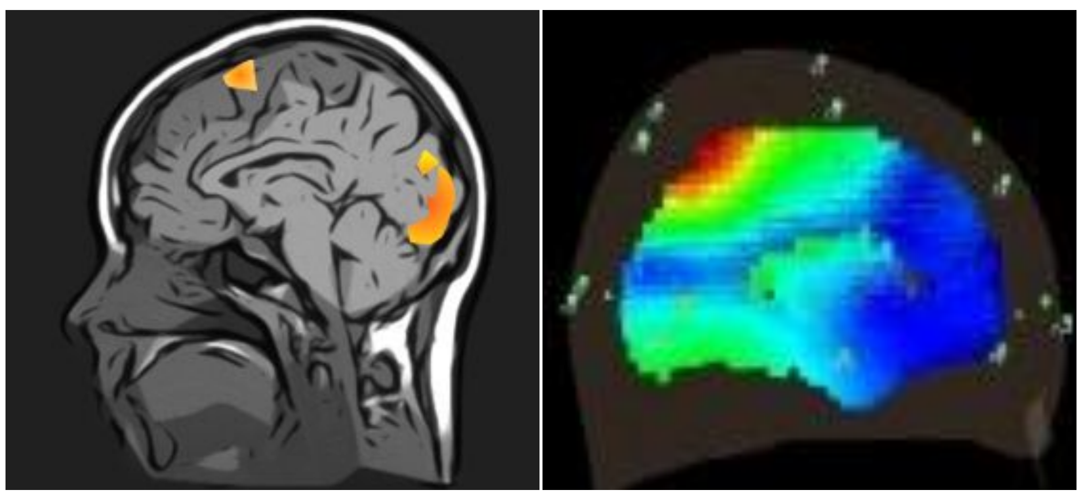
Background

- Developments in neuroimaging
  - Information about areas previously unavailable to other imaging techniques
    - *Direct* access to brain function
    - Identification of *neural correlates*/functional networks



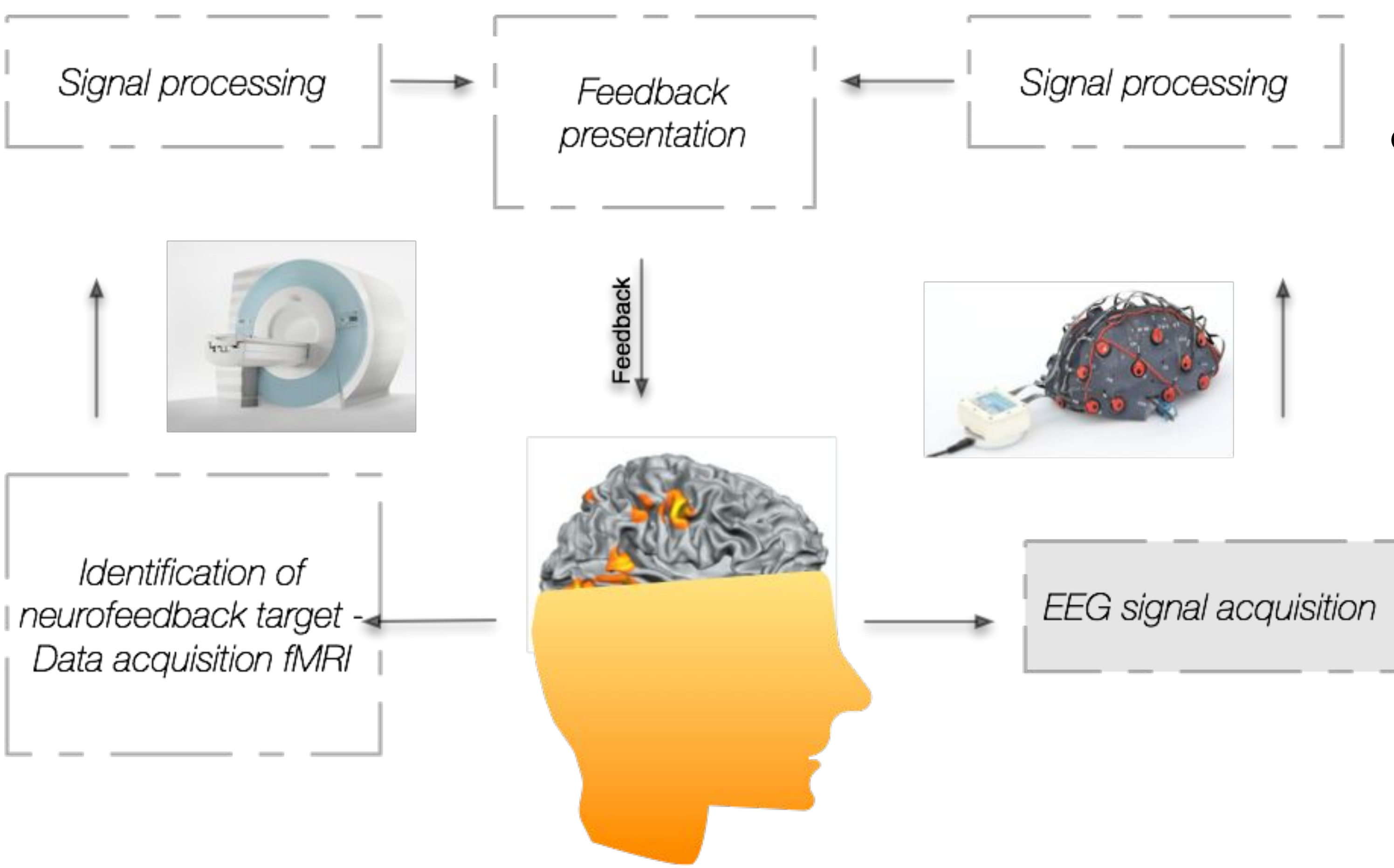
Magnetic Resonance Imaging (MRI) Scanner and Electroencephalography (EEG)

Background



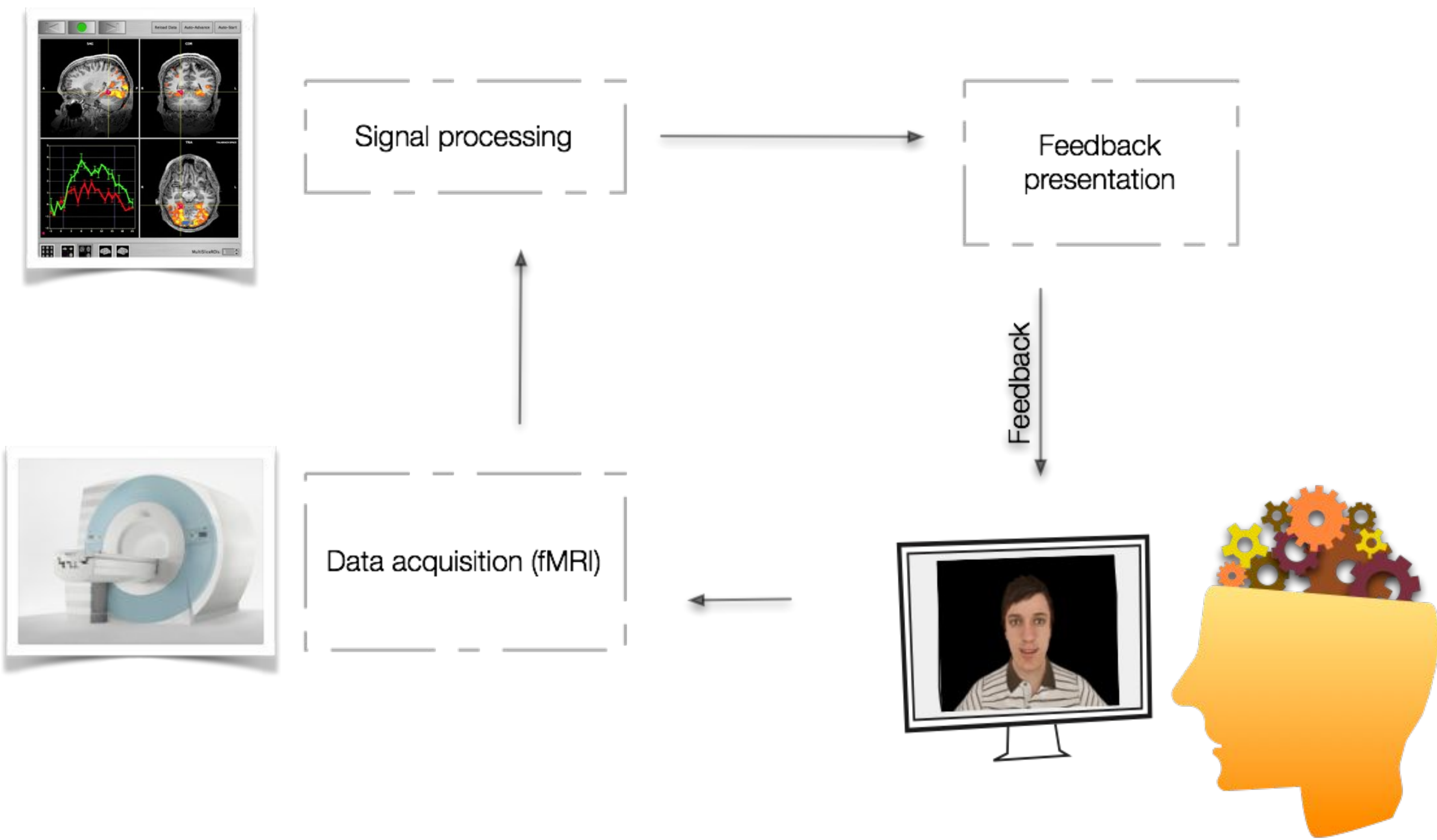
- Unique view to understanding brain dysfunctions
- Comparison between control and clinical groups
  - Access to the mechanisms involved
  - Creation/development of interventional tools/applications
    - Direct/personalised intervention on the dysfunctional mechanisms

Neurofeedback and Brain-Computer Interfaces



- Uses information from neuroimaging in (pseudo) real-time
    - Allows to present this information to the participant
    - The participant can *regulate his own brain activity*

rt-fMRI Neurofeedback

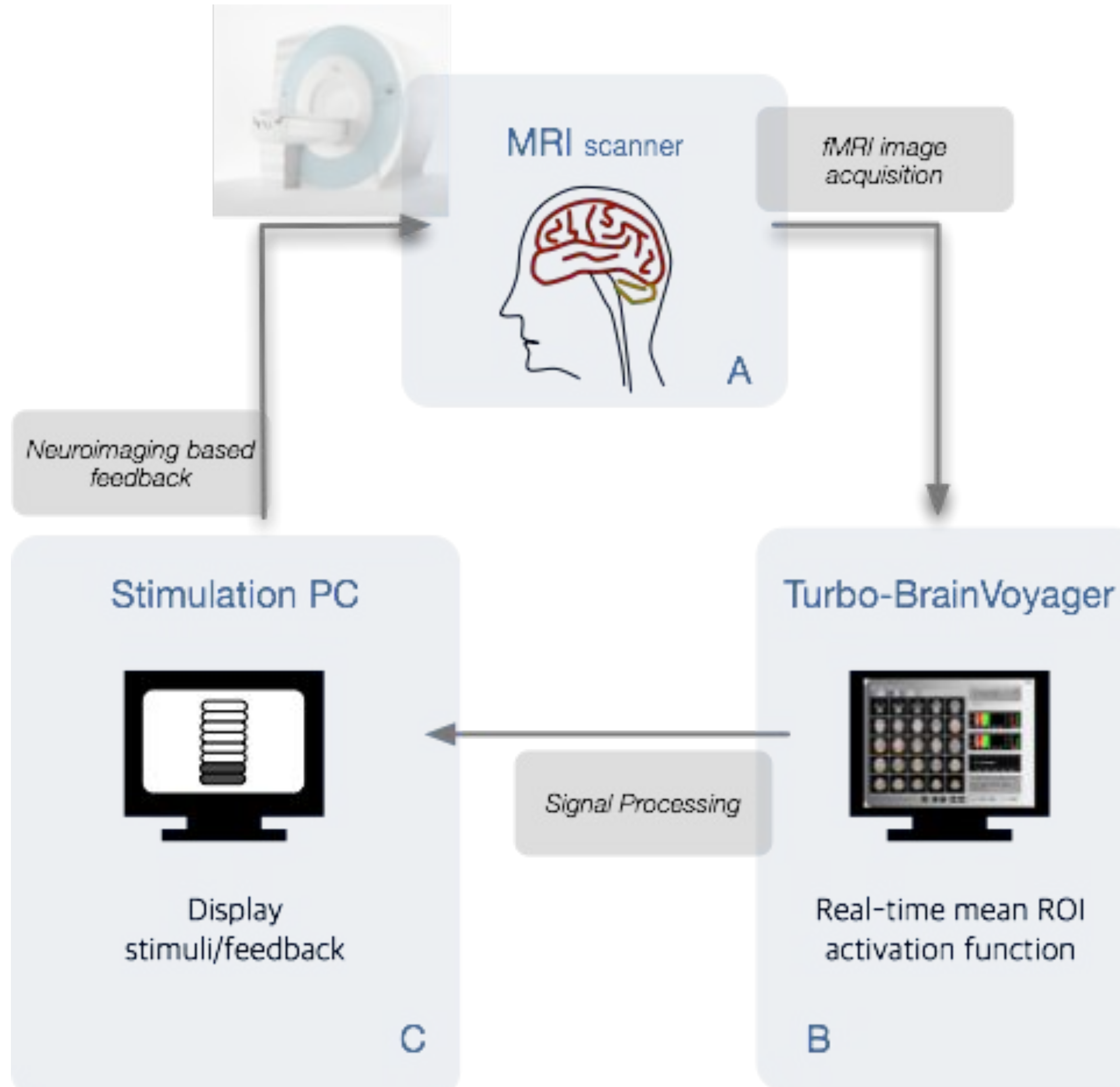


Training and self-regulation of brain activity

- Modulation of the activity of specific brain regions and/or neural networks
  - Restore function
    - Improve clinical symptoms
  - Induce changes on impaired underlying mechanisms
  - Optimisation / functional reorganisation
    - *Neuroplasticity*

Technical implementation

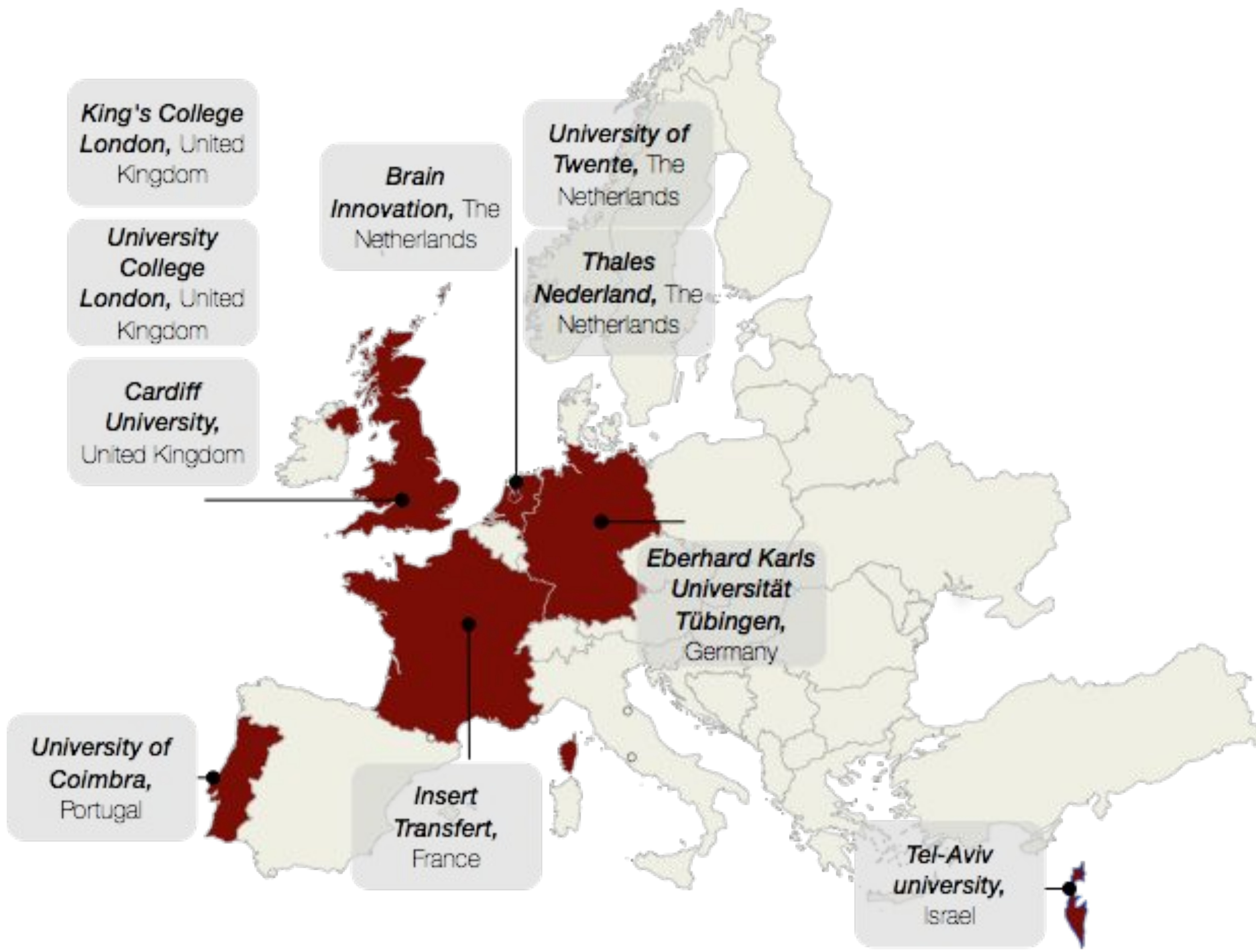
- Acquisition equipment (A)
  - MRI scanner (3T Siemens Magnetom TimTrio) t
  - Collecting and saving data in a network shared folder
- Accessed by Turbo Brain-Voyager 3.2 software (B)
  - Data preprocessing (3D motion correction) and real-time statistical analysis (online GLM - General Linear Model)
- Subsystem (C) is responsible for the computation of neuroimaging-based feedback



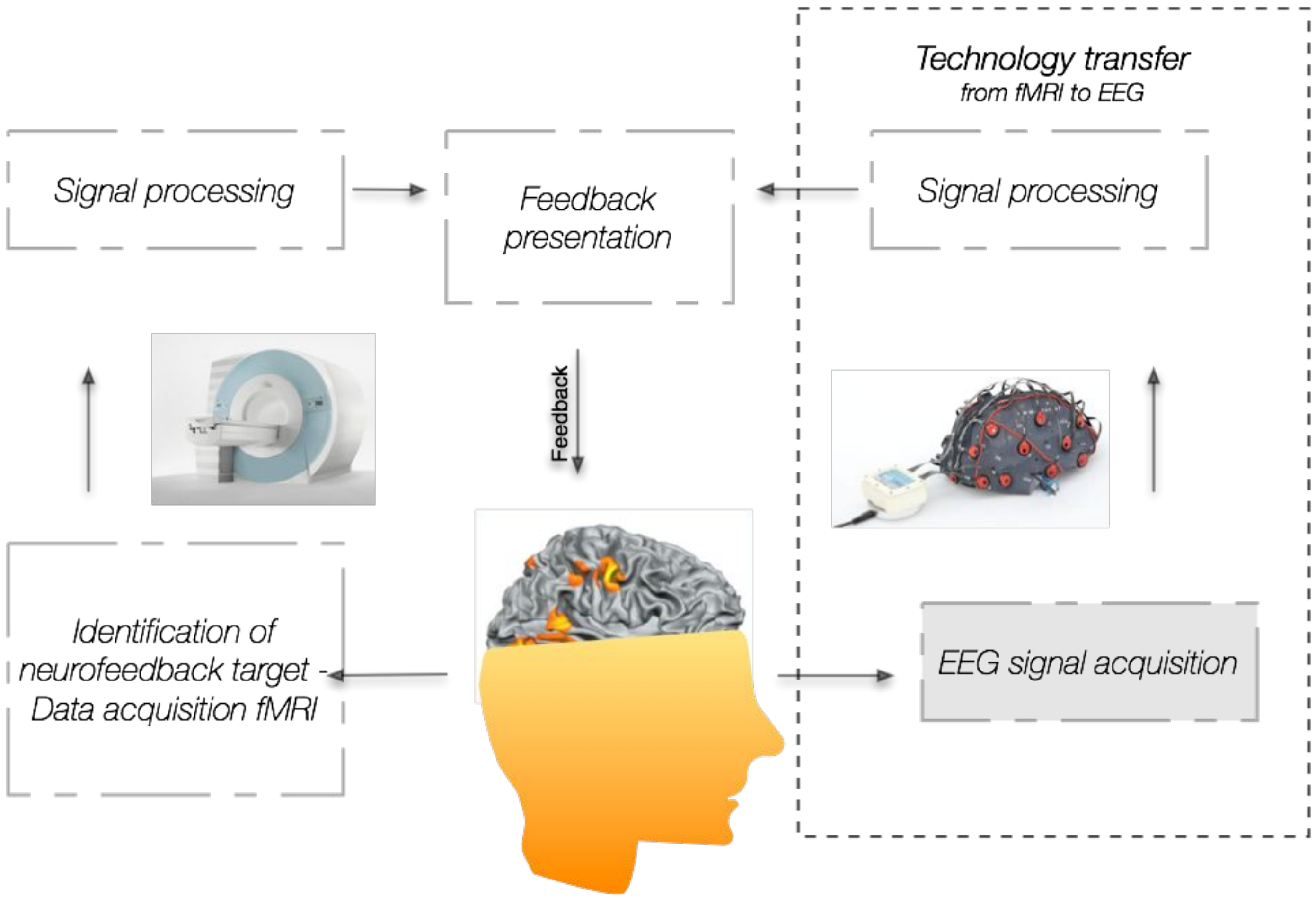
BrainTrain example

- Let us take a look at the setup using an example…

BrainTrain *Taking imaging into the therapeutic domain: Self-regulation of brain systems for mental disorders*



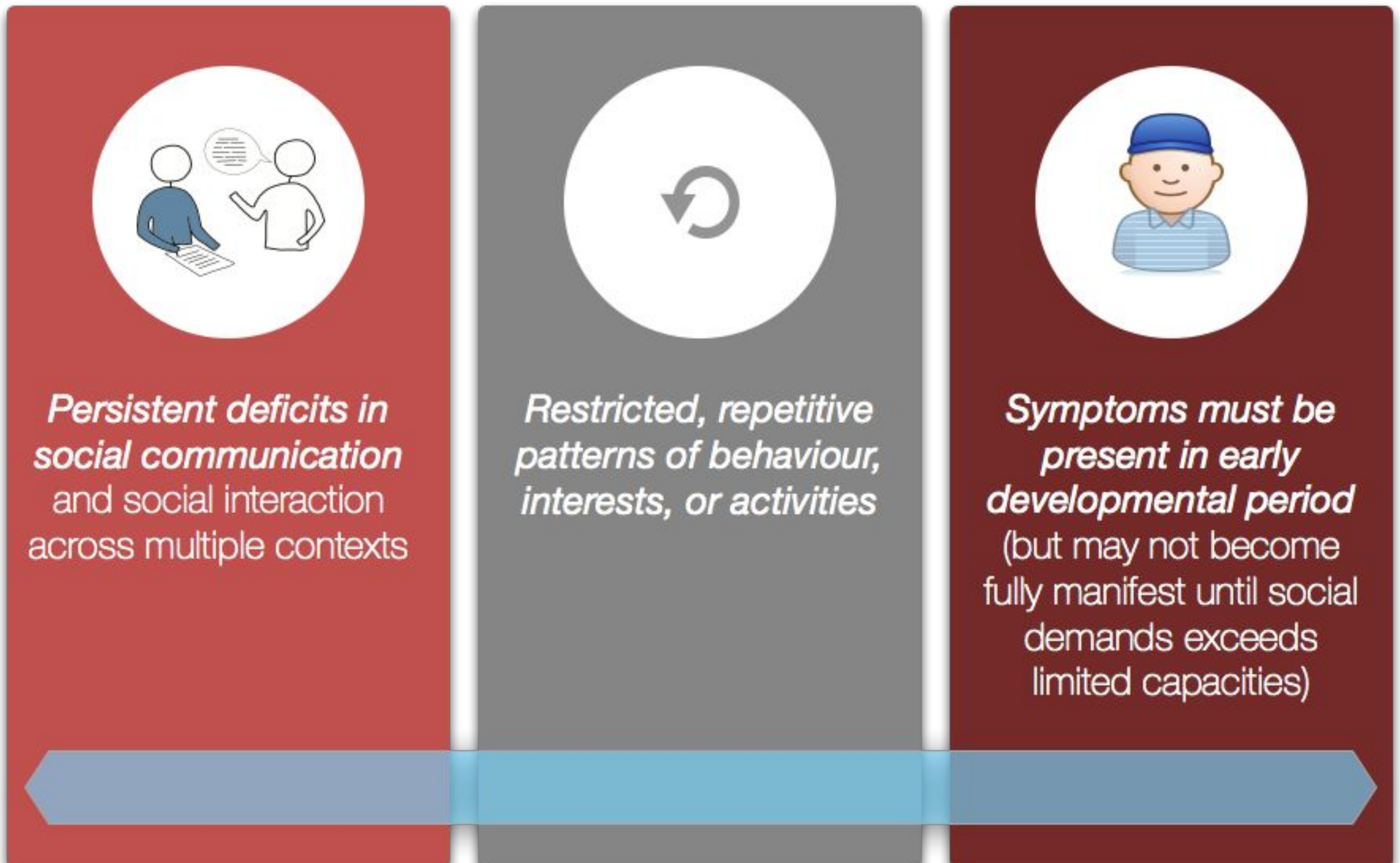
Research Objectives



From Basic Science to Applied Science

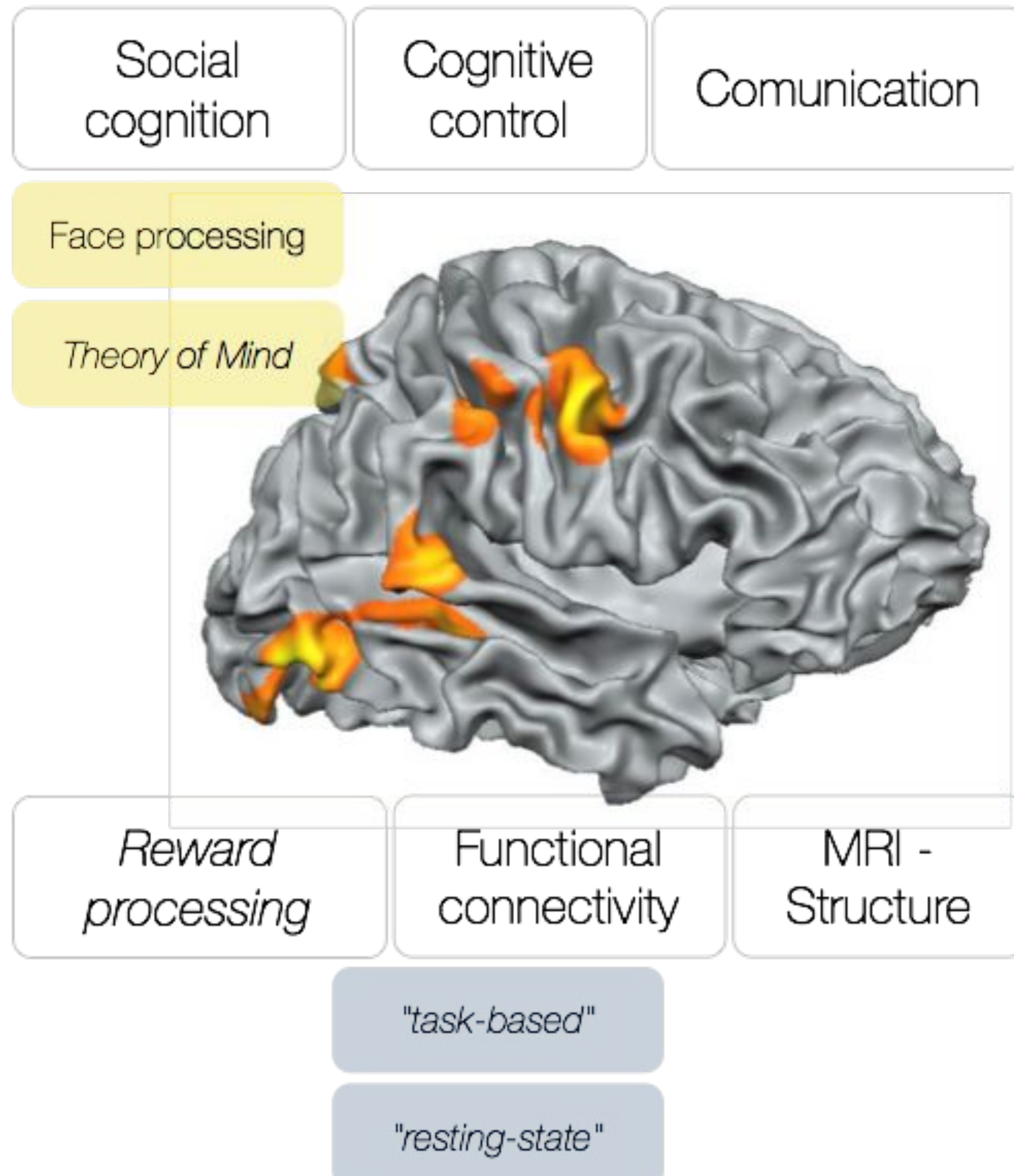
Development of new therapeutic/interventional techniques for the improvement of ASD clinical symptoms

Autism Spectrum Disorder (ASD)



Autism Spectrum Disorder (ASD)

- Neuroimage and ASD
  - *What have we found thus far?*

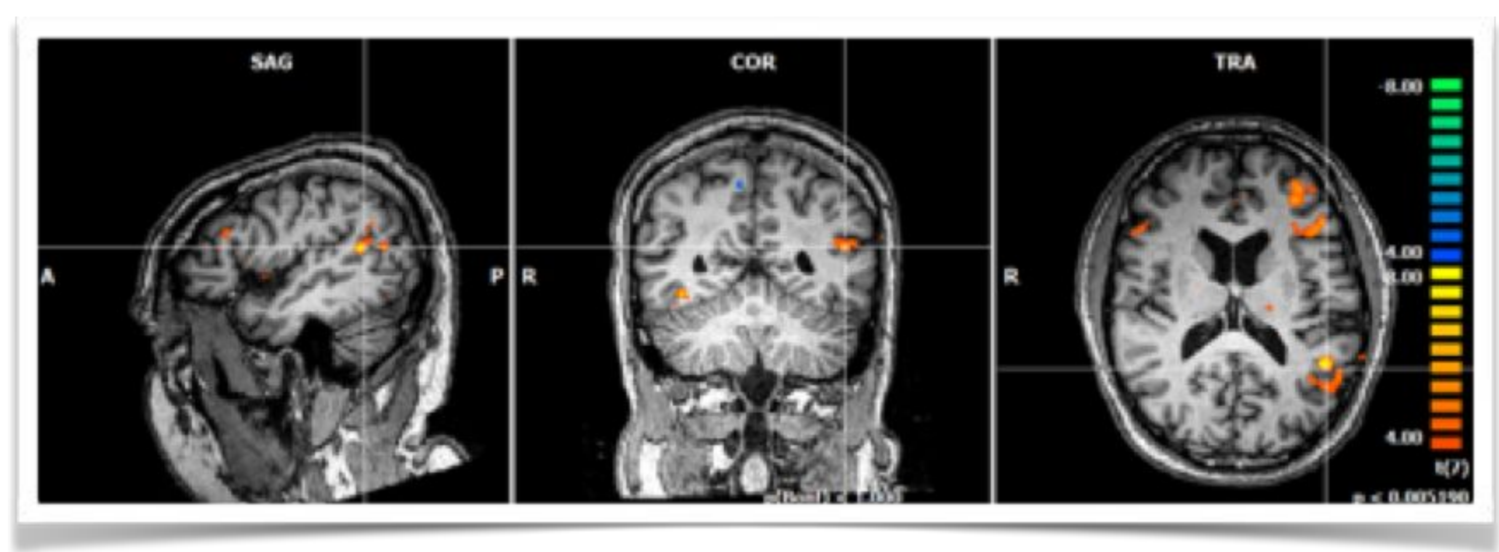


NF-ASD

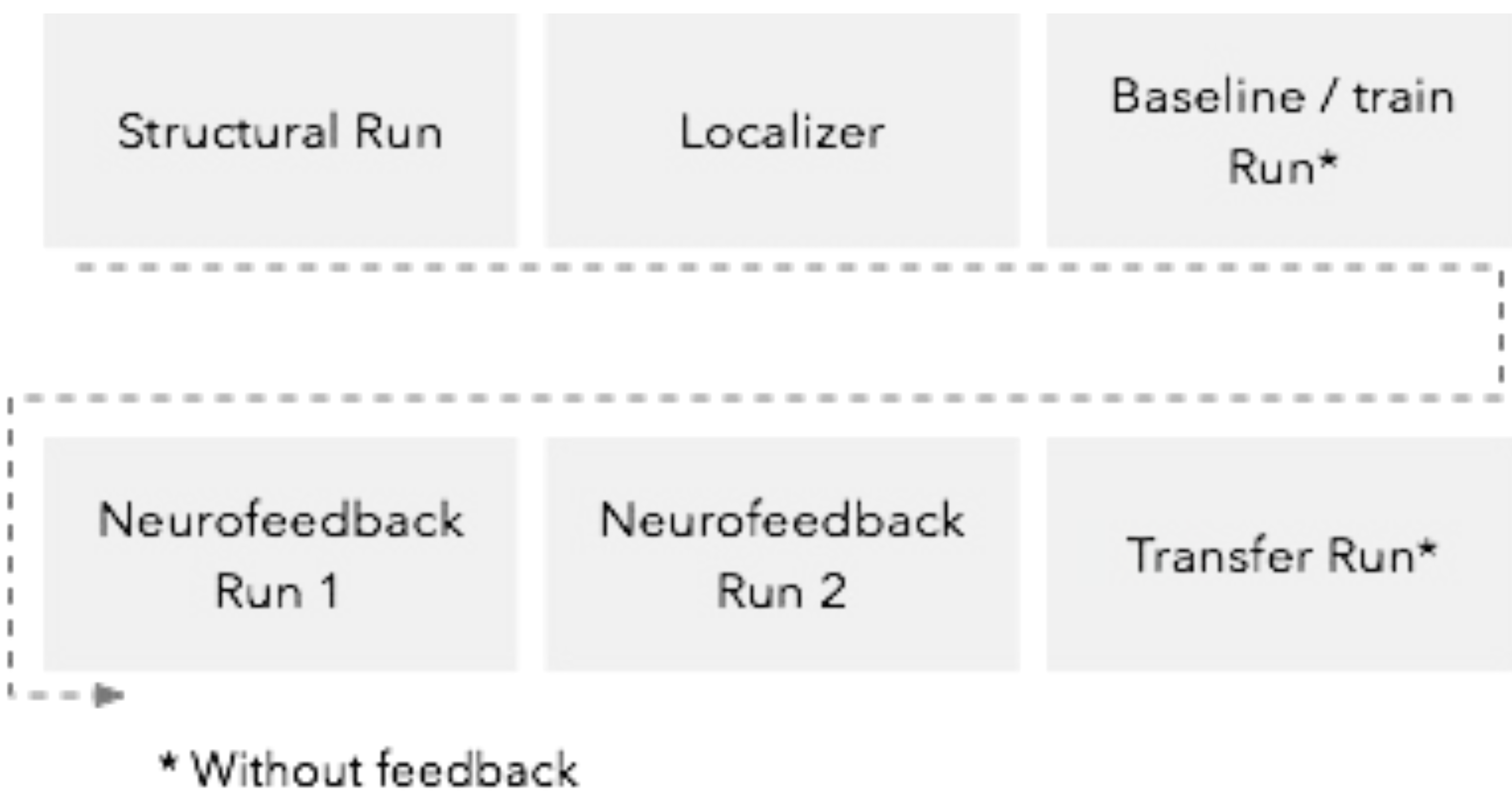
A *neurofeedback* strategy for the improvement of facial expression recognition/perception in ASD

NF-ASD A *neurofeedback* strategy for the improvement of facial expression recognition/perception in ASD

- *Identification, perception* and *mental imagery* of facial expressions
    - Brain activity in areas related to social cognition and facial expression interpretation
    - posterior portion of the superior temporal sulcus (pSTS)



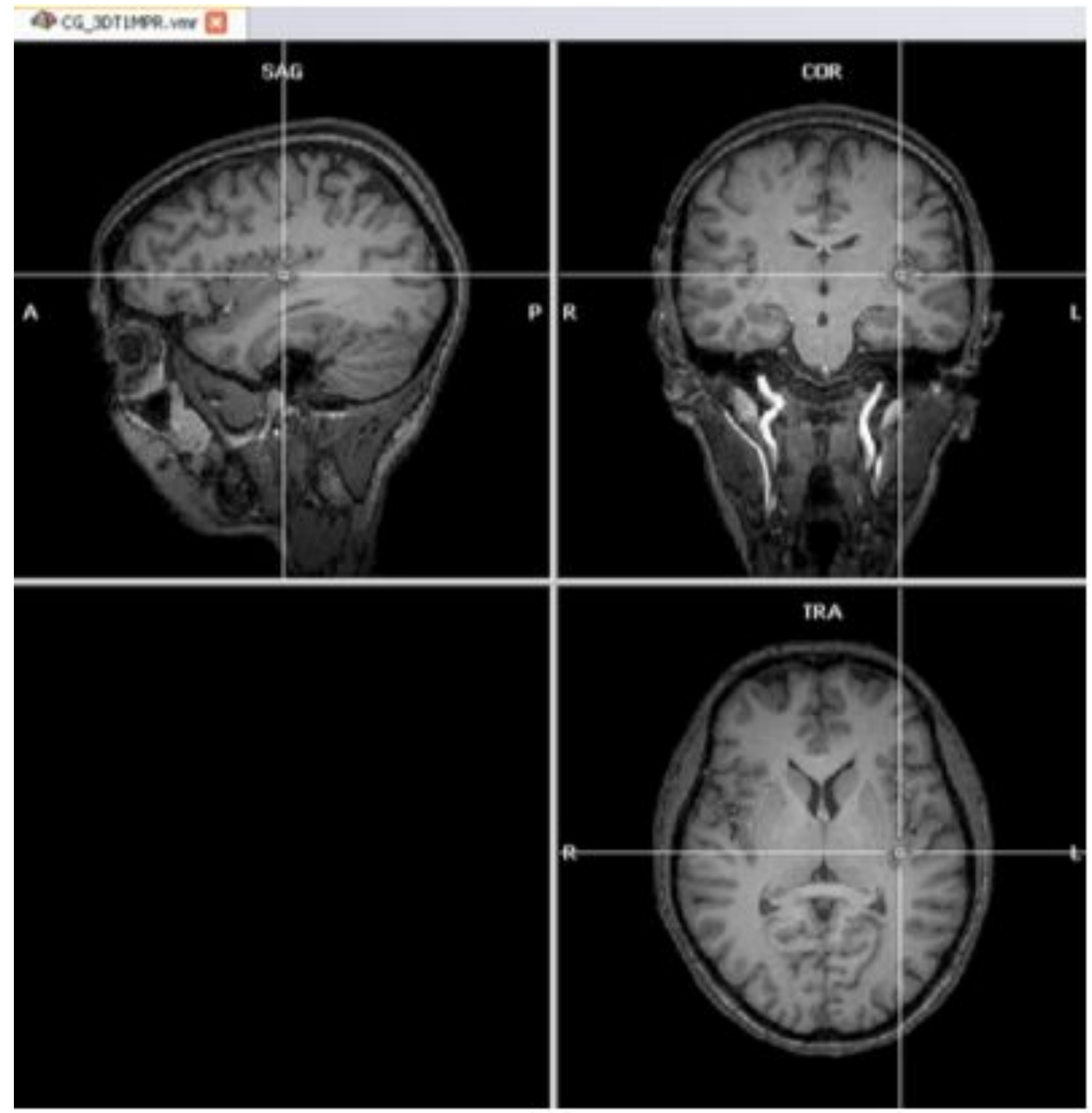
Task, clinical trial organisation and main objectives



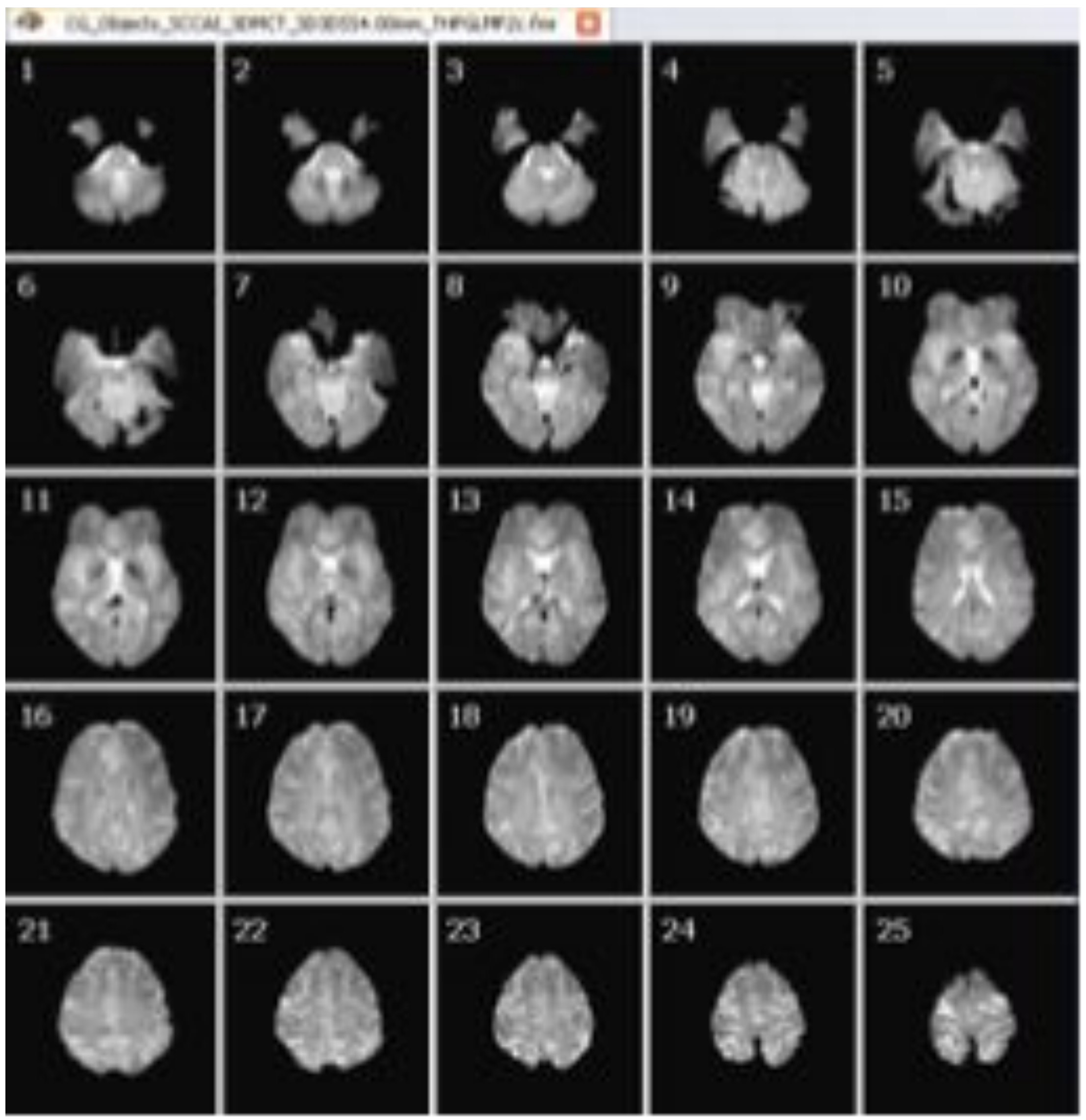
- Duration of the protocol is around 1 hour

Structural run

- *rapid acquisition gradient echo* (MPRAGE) sequence for co-registration of functional data
  - 176 slices
  - TE: 3.42 ms
  - TR: 2530 ms
  - voxel size 1.0×1.0×1.0 mm^3
- 3 axes representation

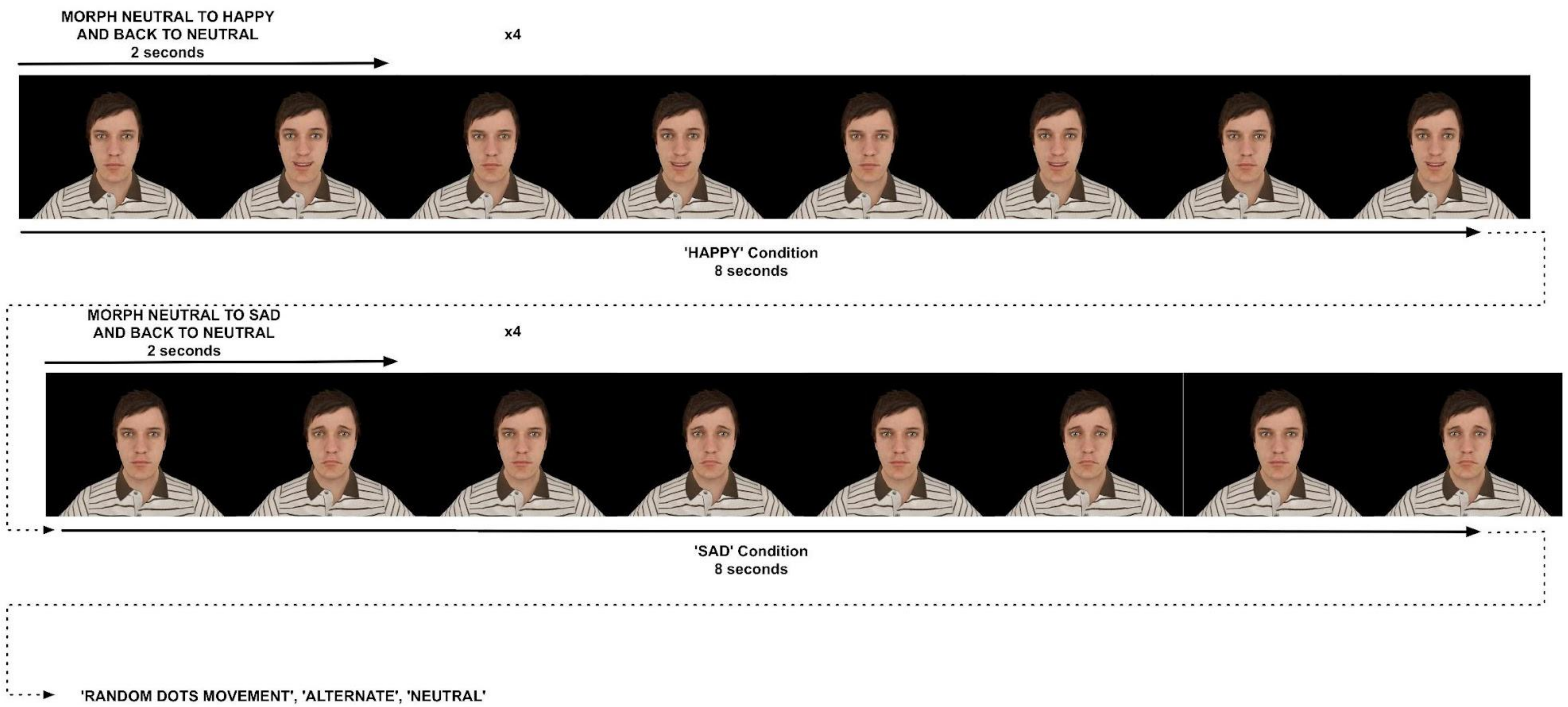


Functional runs



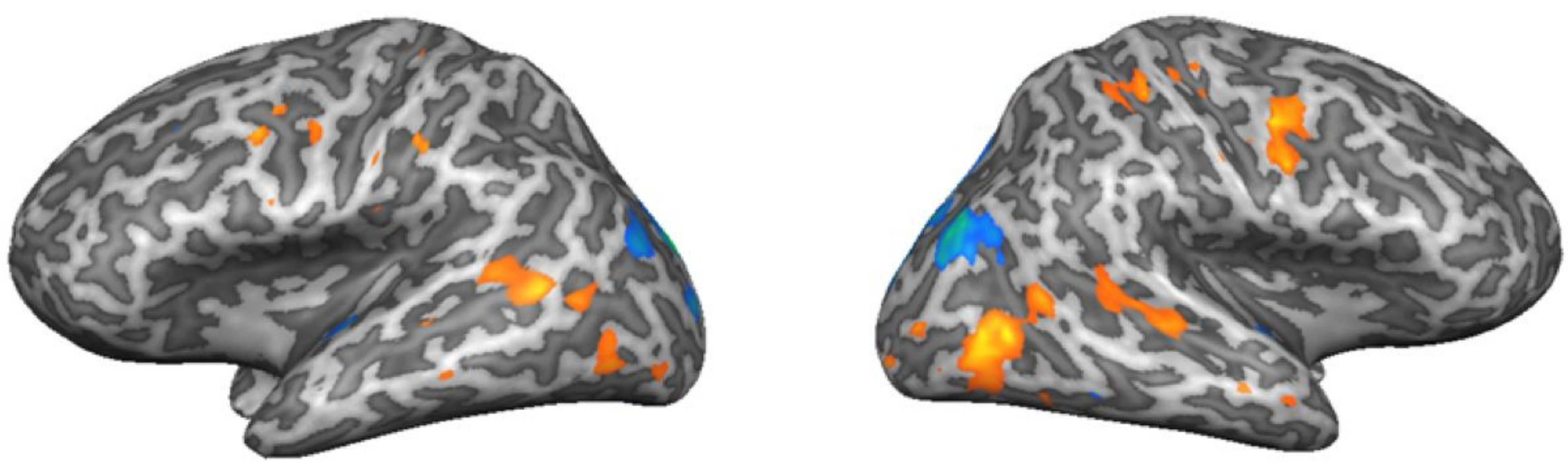
- Functional images of the localizer, neurofeedback and control runs
    - 33 slices,
    - in-plane resolution: 4×4 mm2,
    - field of view (FOV): 384×384 mm,
    - slice thickness: 3 mm,
    - flip angle (FA): 90°) covered occipital and posterior temporal lobe.
    - Repetition time (TR) was 2000 ms (Echo Time (TE): 30 ms).

Localizer run

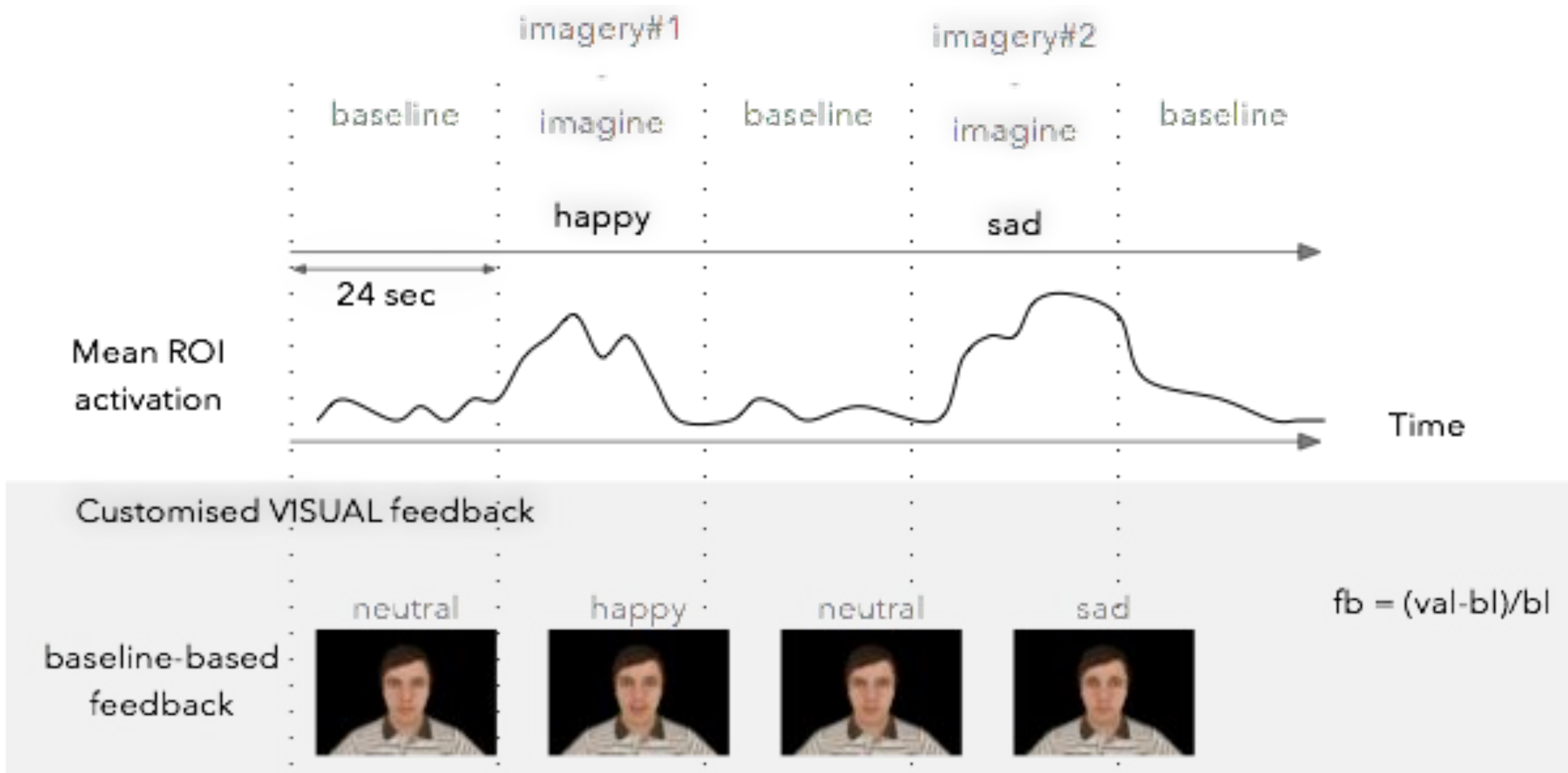


Localizer run

- *Preliminary results*
  - *Ability to correctly identify the correct region of interest or neurofeedback target*

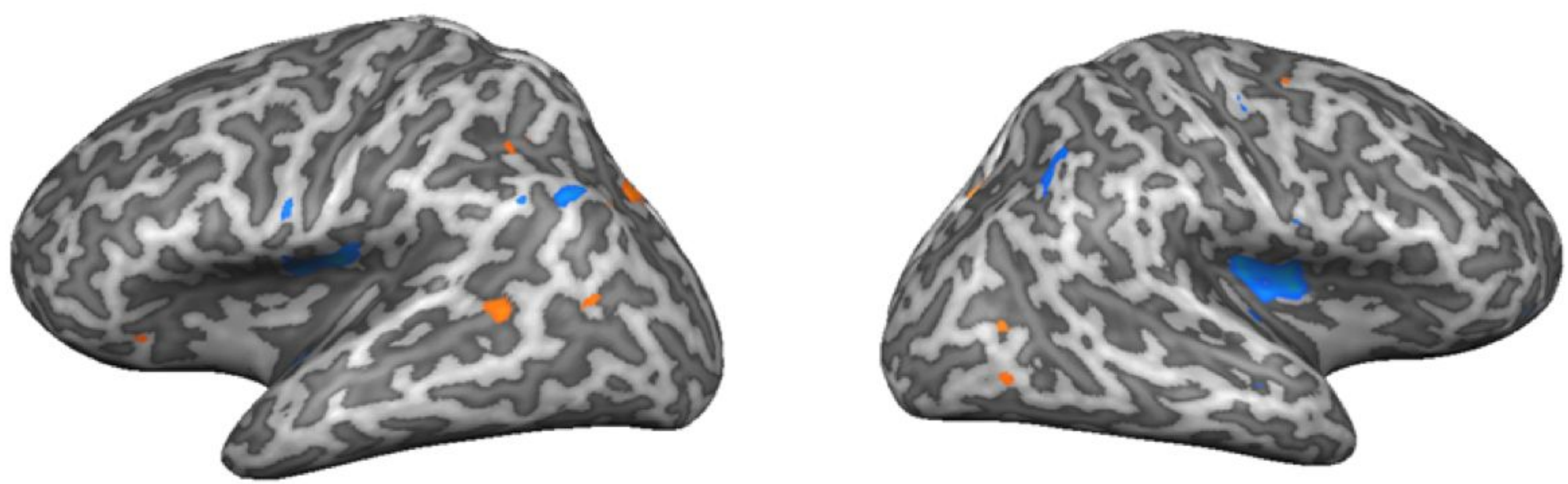


Neurofeedback runs



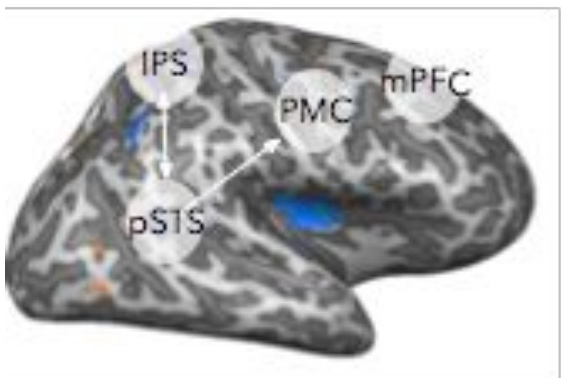
Neurofeedback runs

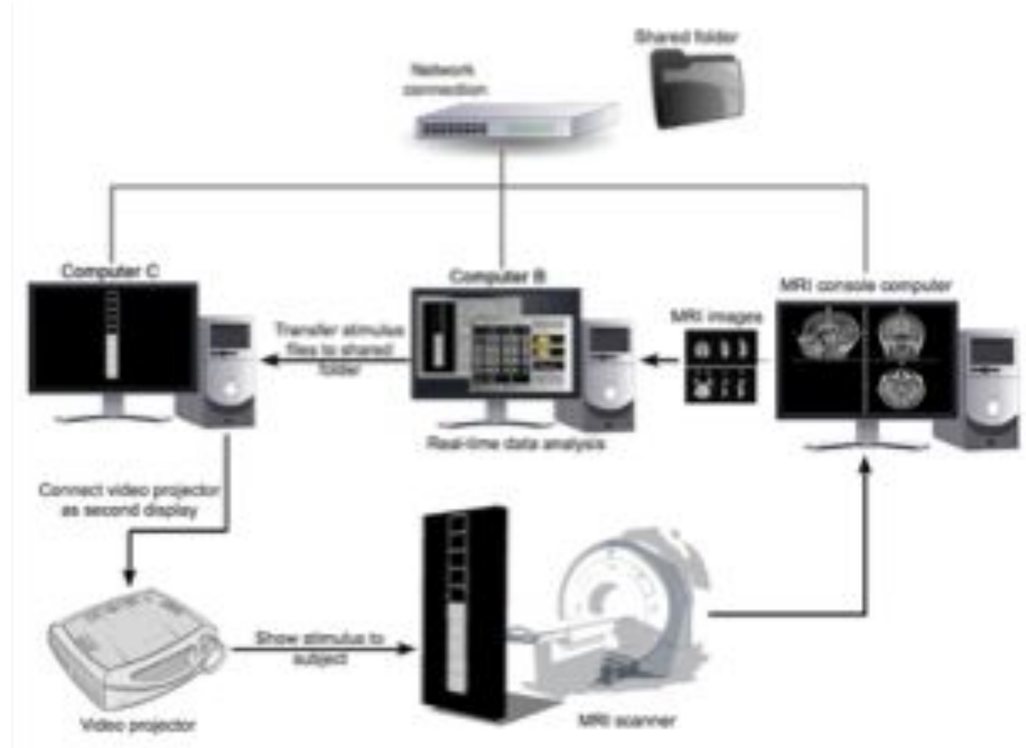
- *Preliminary results*
  - *Ability to correctly identify the correct region of interest or neurofeedback target*

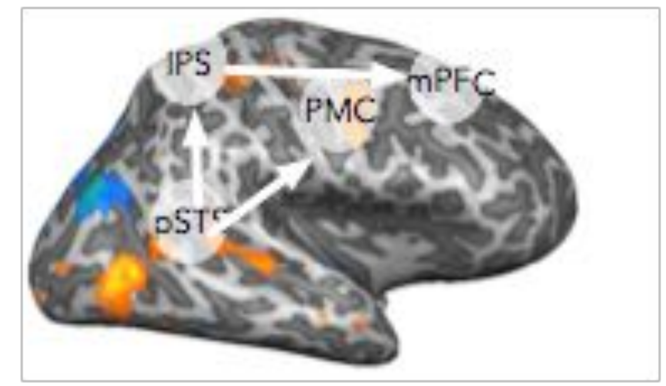


Challenges

- Physiological
  - Hemodynamic delay (pseudo real-time)
  - Rest conditions
- Turbo BrainVoyager Software
  - Region of interest (ROI) selection and movement compensation
  - Real-time GLM performance
- Network communication
- Feedback calculation
  - Direct BOLD? BOLD Signal Variation? Based on what baseline values?
- Feedback presentation
  - Facial expressions realism







pre-intervention evaluation

neurofeedback intervention

post-intervention evaluation

The network and connectivity analysis

work in progress.

Effective connectivity as measured by Granger causality

- Granger Causality (Granger, 1969)

- Vector Auto-regression model to calculate causality based on Time Series data

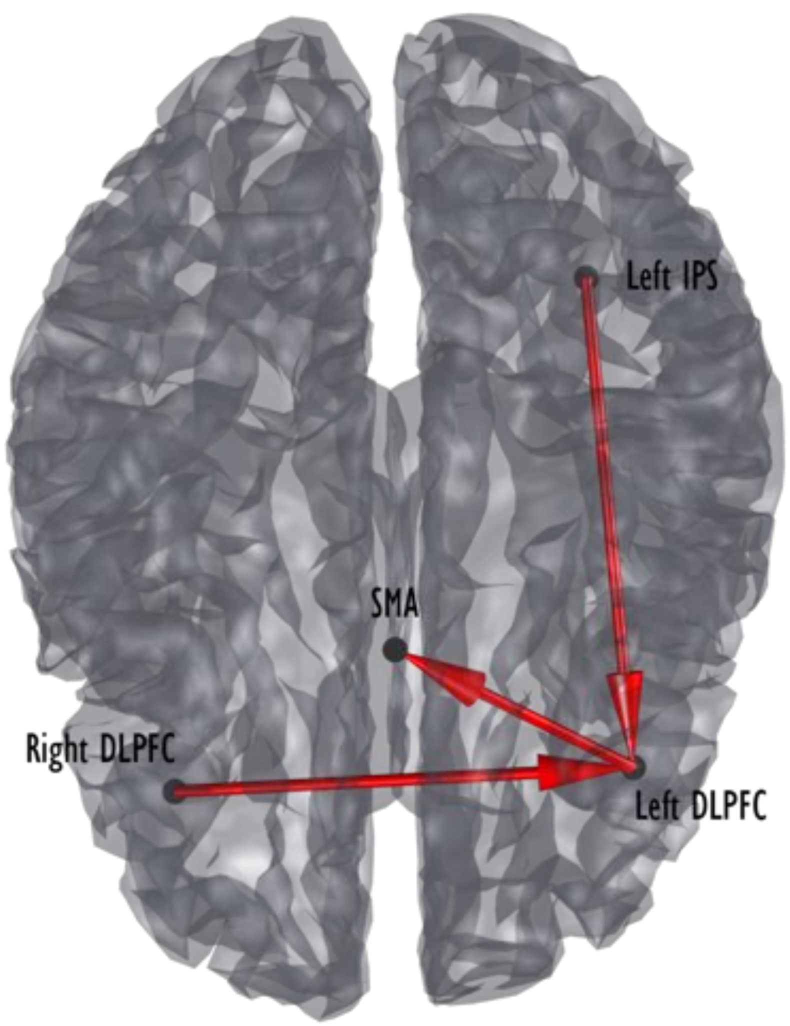
  - *BOLD activity derived from different ROIs*

    - $$X_1(t) = \sum_{i=1}^{p} A_{11i} X_1(t-i) + \sum_{j=1}^{p} A_{12j} X_2(t-j) + \epsilon_1(t)$$
    - $$X_2(t) = \sum_{j=1}^{p} A_{21j} X_1(t-j) + \sum_{i=1}^{p} A_{22i} X_2(t-i) + \epsilon_2(t)$$
      - "If past values of X1 and X2 can predict future value of X2 better than past values of X2 alone, then X1 granger cause X2"

Effective connectivity - as measured by MVGC

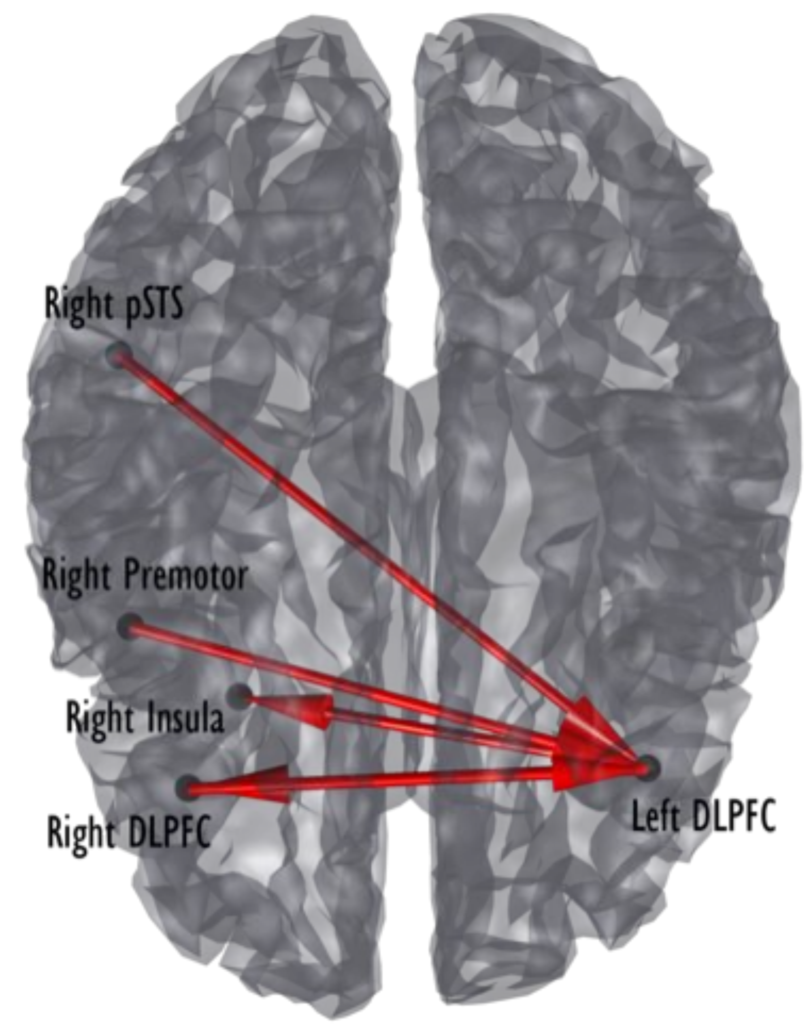
Localizer

1-back + 2.back > basel.



NF runs

imagination > basel.



New approaches to rt—fMRI connectivity feedback

MSc student João Pereira

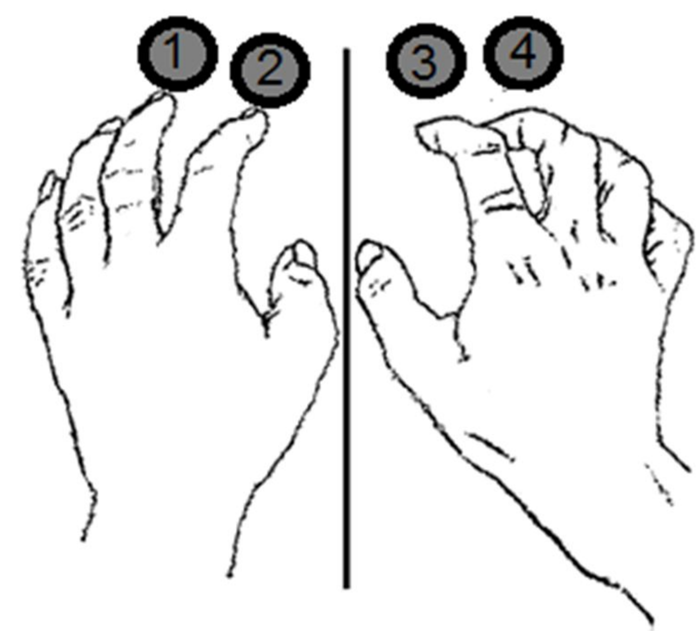
“Real-time fMRI neurofeedback based on Interhemispheric functional connectivity: a motor imagery paradigm”

Aula IIM, 16 de Dezembro

Motor imagery

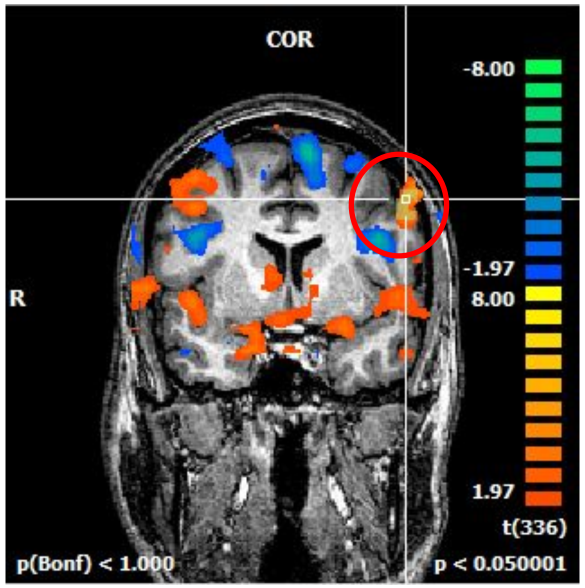
"Dynamic state in which the subject simulates a particular action in a mental way so that he can feel himself performing the action for him imagined" (Decety, 1996)

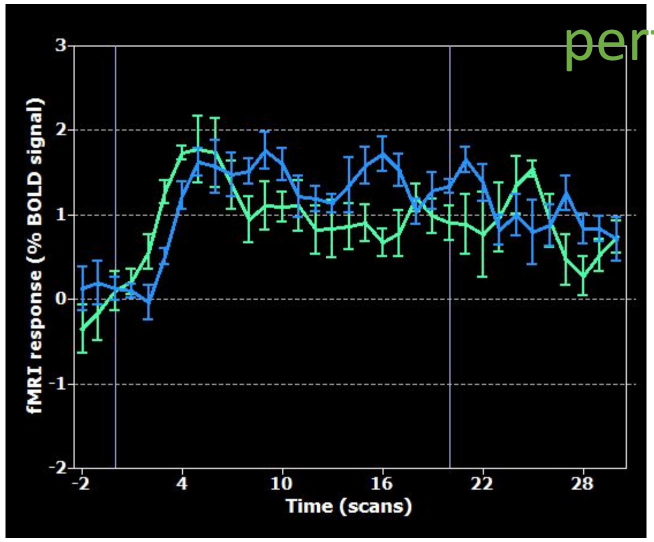
Sequence : 4-1-2-1-3-4-3



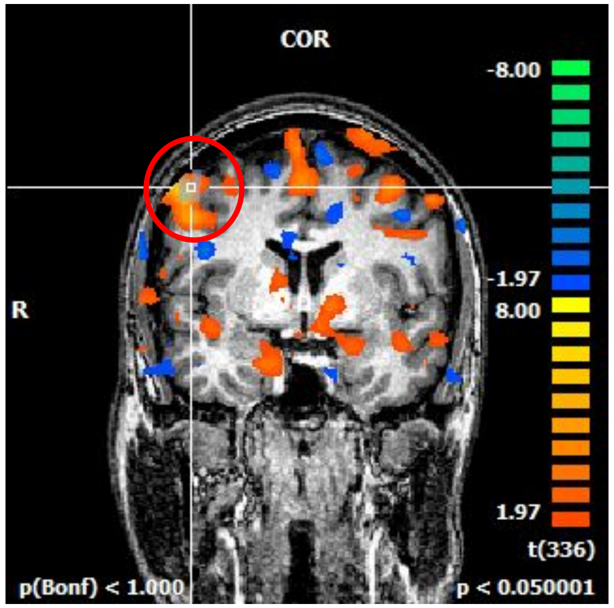
ROI Selection : Localizer

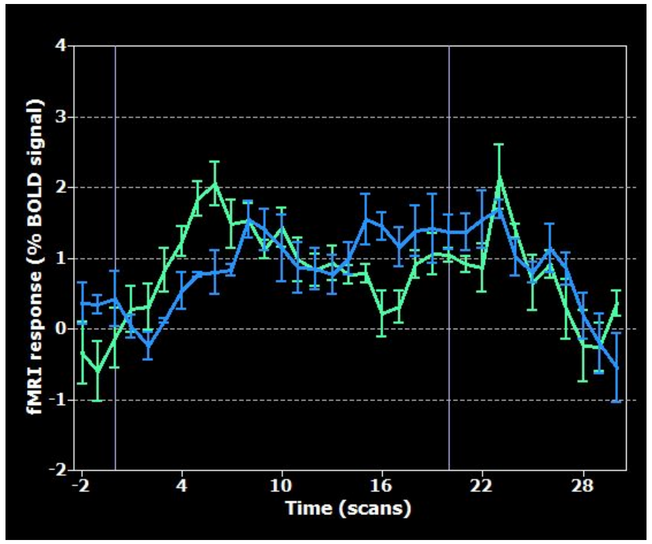
Motor imagery
Motor performance





.lpmc





.rpmc

Neurofeedback calculation

$$\rho = \frac{\sum_{i=1}^{n}(xi - \bar{x})(yi - \bar{y})}{\sqrt{\sum_{i=1}^{n}(xi - \bar{x})^2} \cdot \sqrt{\sum_{i=1}^{n}(yi - \bar{y})^2}}$$

$$= \frac{cov(X,Y)}{\sqrt{var(X).var(Y)}}$$

The feedback value ranges in values from -1 to 1 and it is transformed and presented to the subject in the form of a thermometer that is divided in 20 levels (+10 to -10)

Training, NF and Transfer Runs

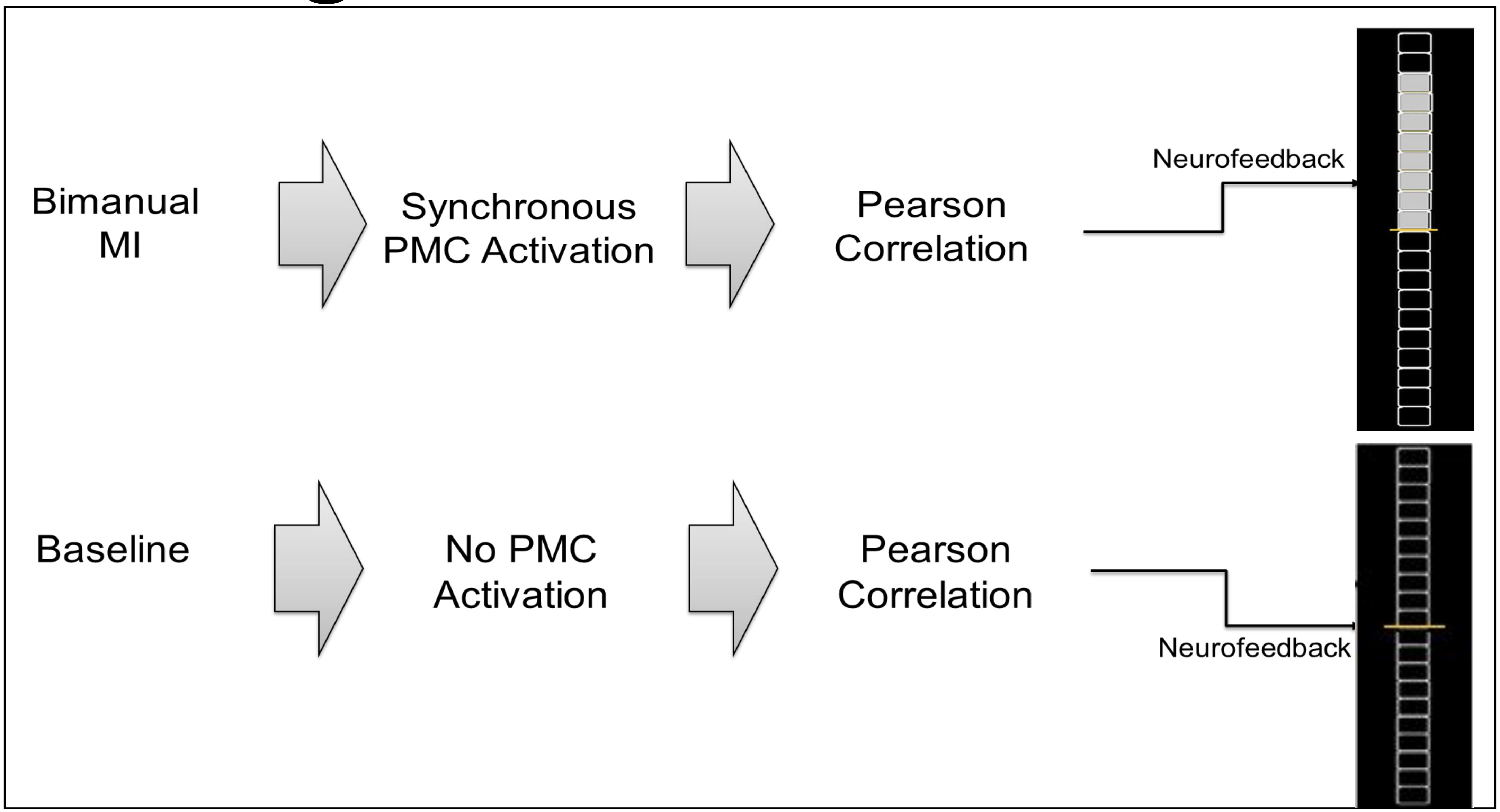
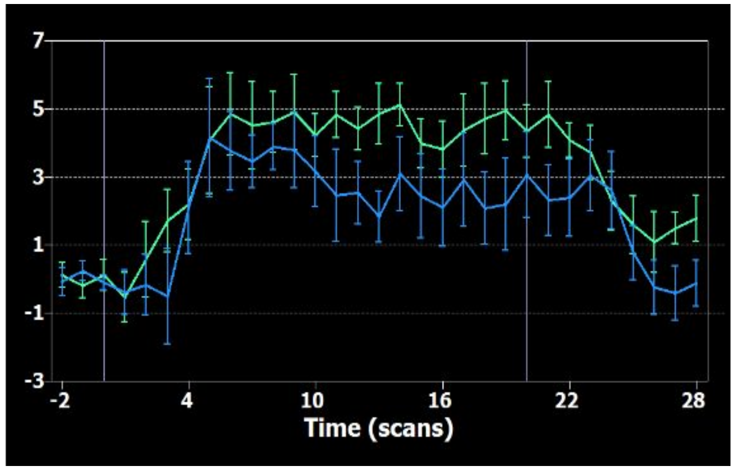
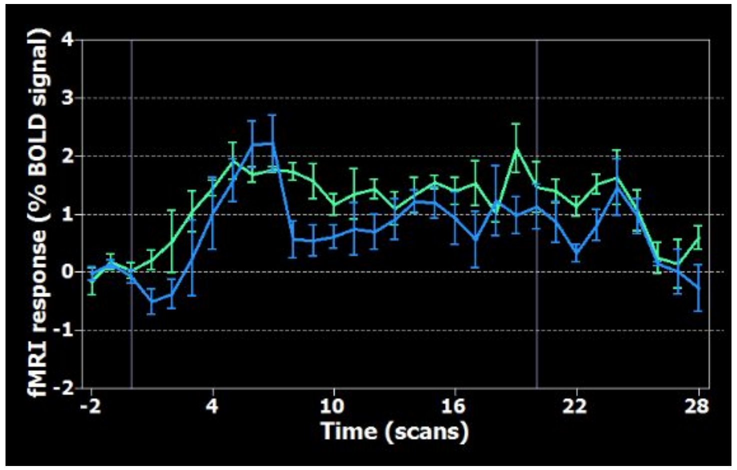


Fig. Motor Imagery (MI) tasks proposed for the training, neurofeedback and transfer runs

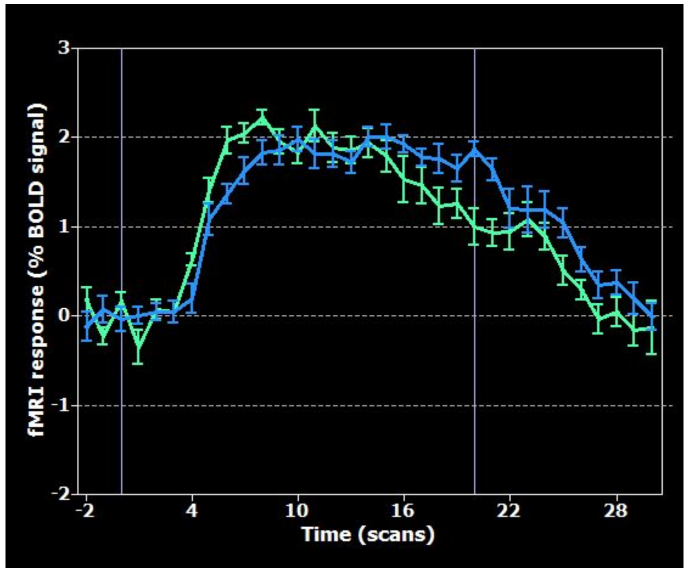
NeuroFeedback Runs : Then and Now



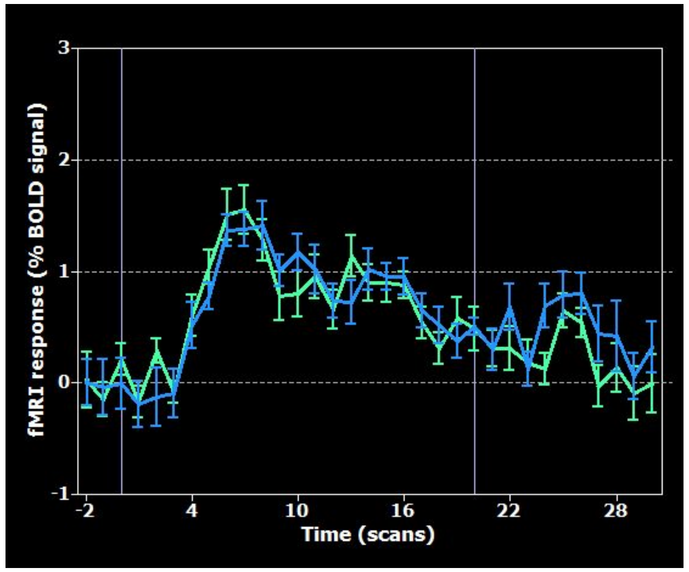
.lpmc



.rpmc



.lpmc

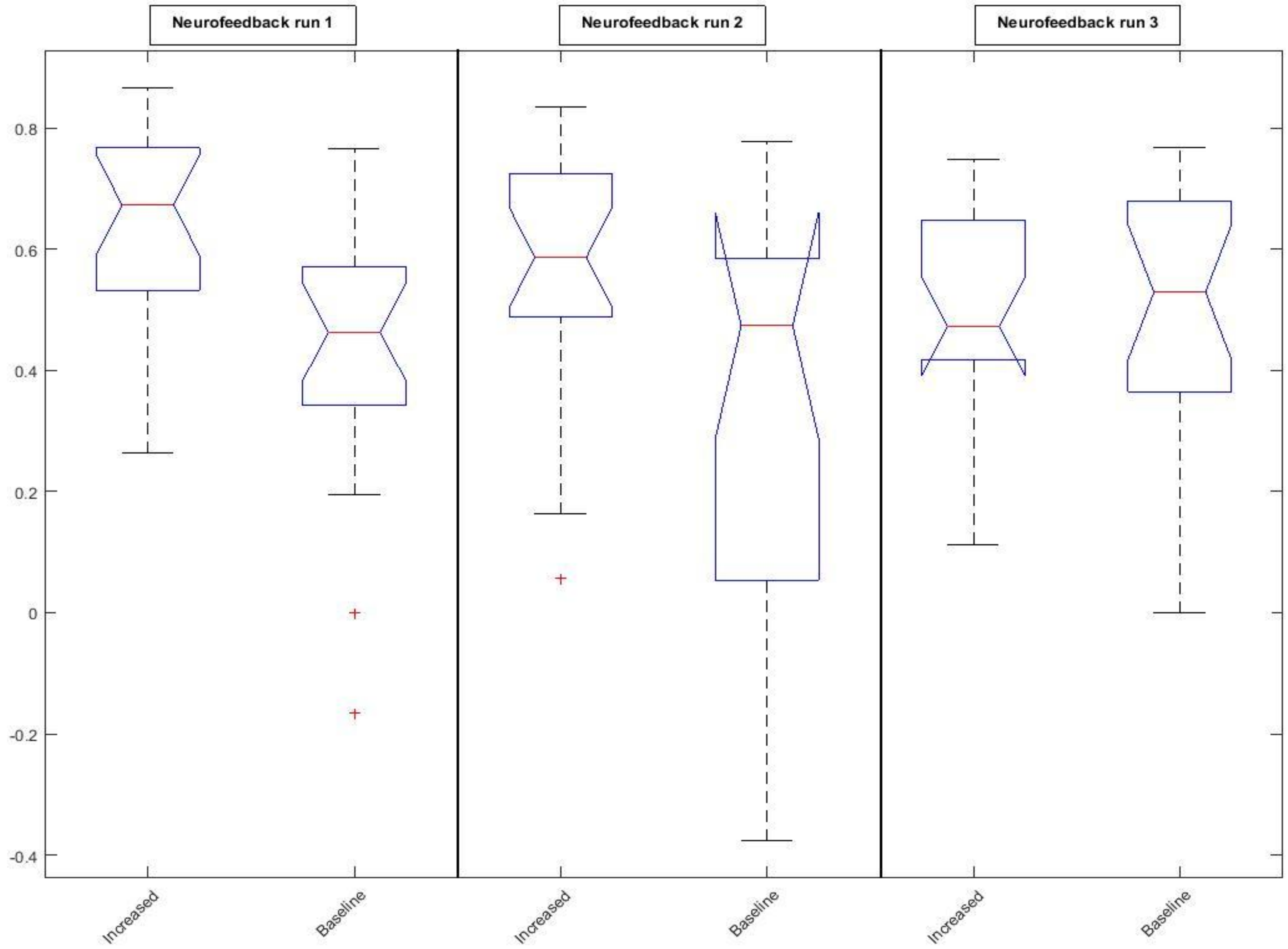


.rpmc

Unimanual imagined movements

Bimanual imagined movements

NeuroFeedback Runs



Correlation distributions were statistically different in two neurofeedback runs.

Expectations

- Assess PMC as a suitable neurofeedback target for MI rt-fMRI-NF.
- Study real time Pearson Correlation between two regions as a neurofeedback approach.
- Study interhemispheric PMC effective connectivity offline using Granger Causality in order to evaluate networks involved and how NF could affect them.
- Relevance of the project: possible usage of these strategies in diseases that are related with interhemispheric connectivity impairment (Alzheimer's, Parkinson, ALS and in particular in stroke patients).