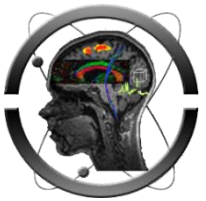
Tehran University of
Medical Sciences



NeuroImaging
and
Analysis Group (NIAG)

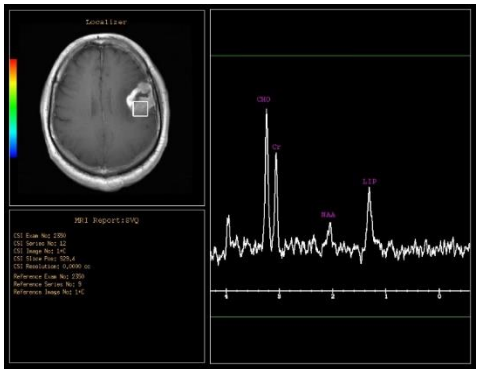
Clinical Application of Advanced Neuro-Imaging techniques

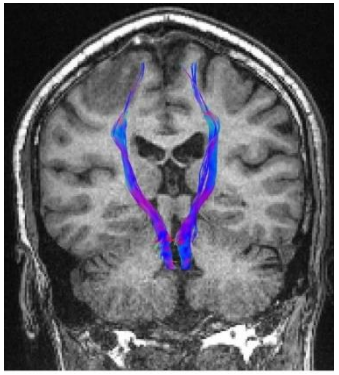
fMRI for pre-surgical planning

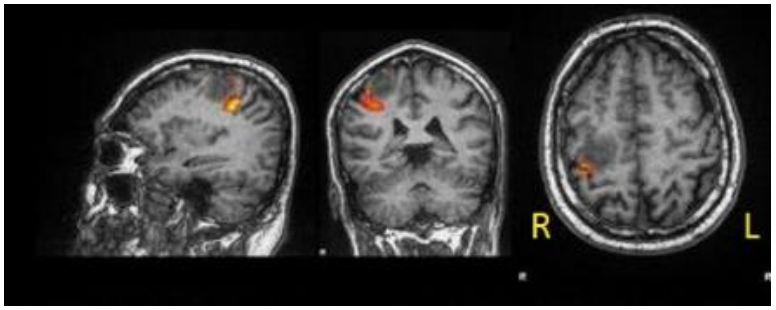
Dr M A Oghabian

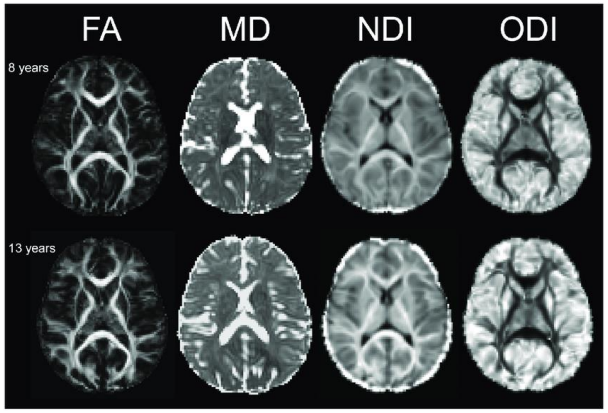
www.oghabian.ir

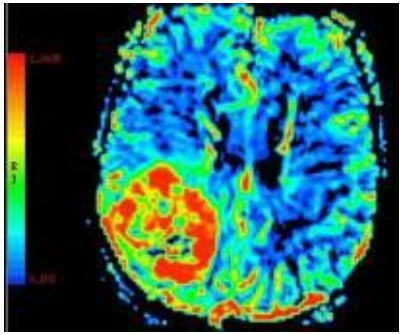
Advanced Neuro-Imaging Methods

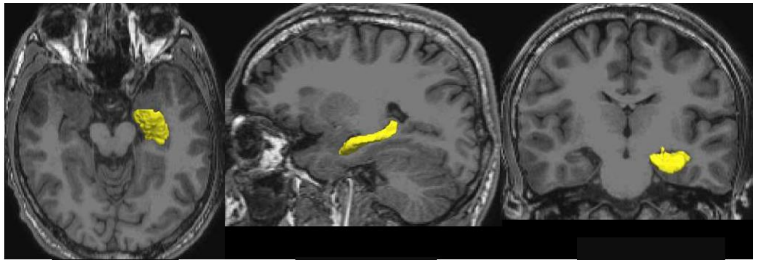






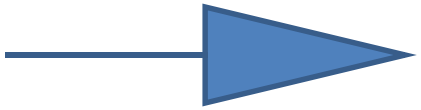






What can be seen in fMRI?

- CBF and CBV using Perfusion MRI
- Glucose in PET
- BOLD
- Not $CMRO_2$ or OEF



fMRI BOLD imaging is based on inherent Contrast Agents

- Contrast agent is a Substance that alter magnetic susceptibility of tissue, leading to changes in MR signal

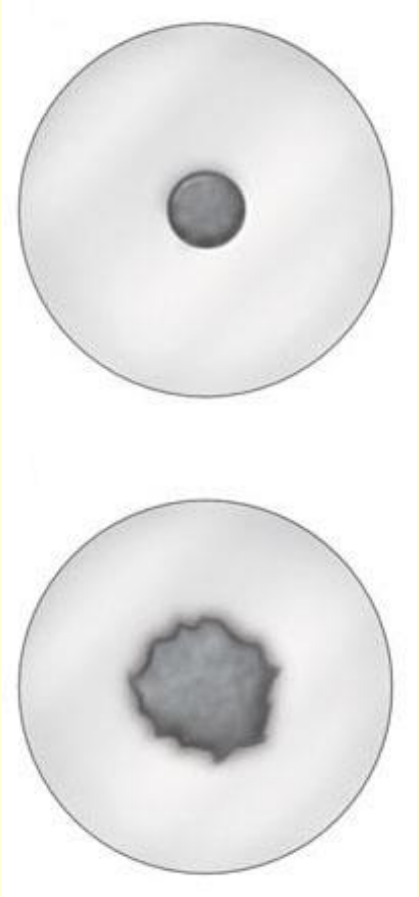
  Affects local magnetic homogeneity: decrease in T1 or T_2*

- Two types

  Exogenous: Externally applied, non-biological compounds (e.g., Gd-DTPA)

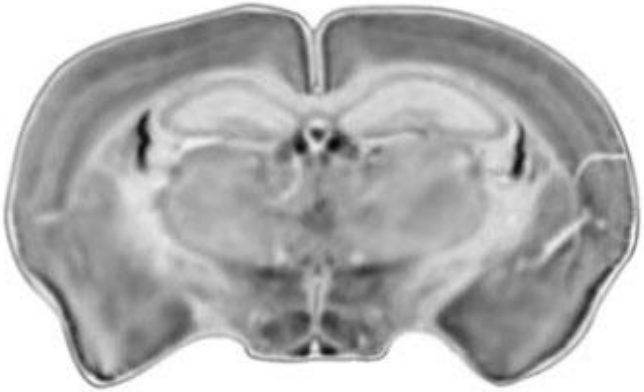
  Endogenous: Internally generated biological compound (e.g., deoxyhemoglobin, dHb)

Deoxygenated Blood ⟹ Signal Loss



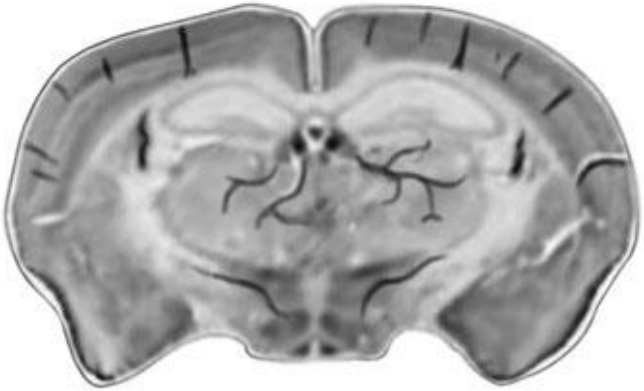
Oxygenated blood?

No signal loss…



Deoxygenated blood?

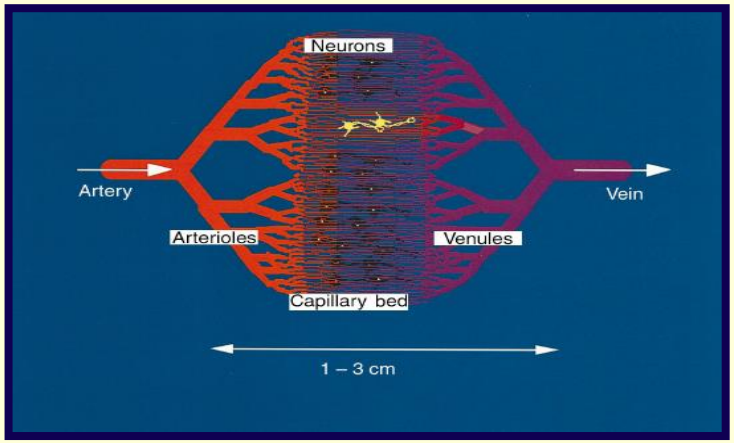
Signal loss!!!



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

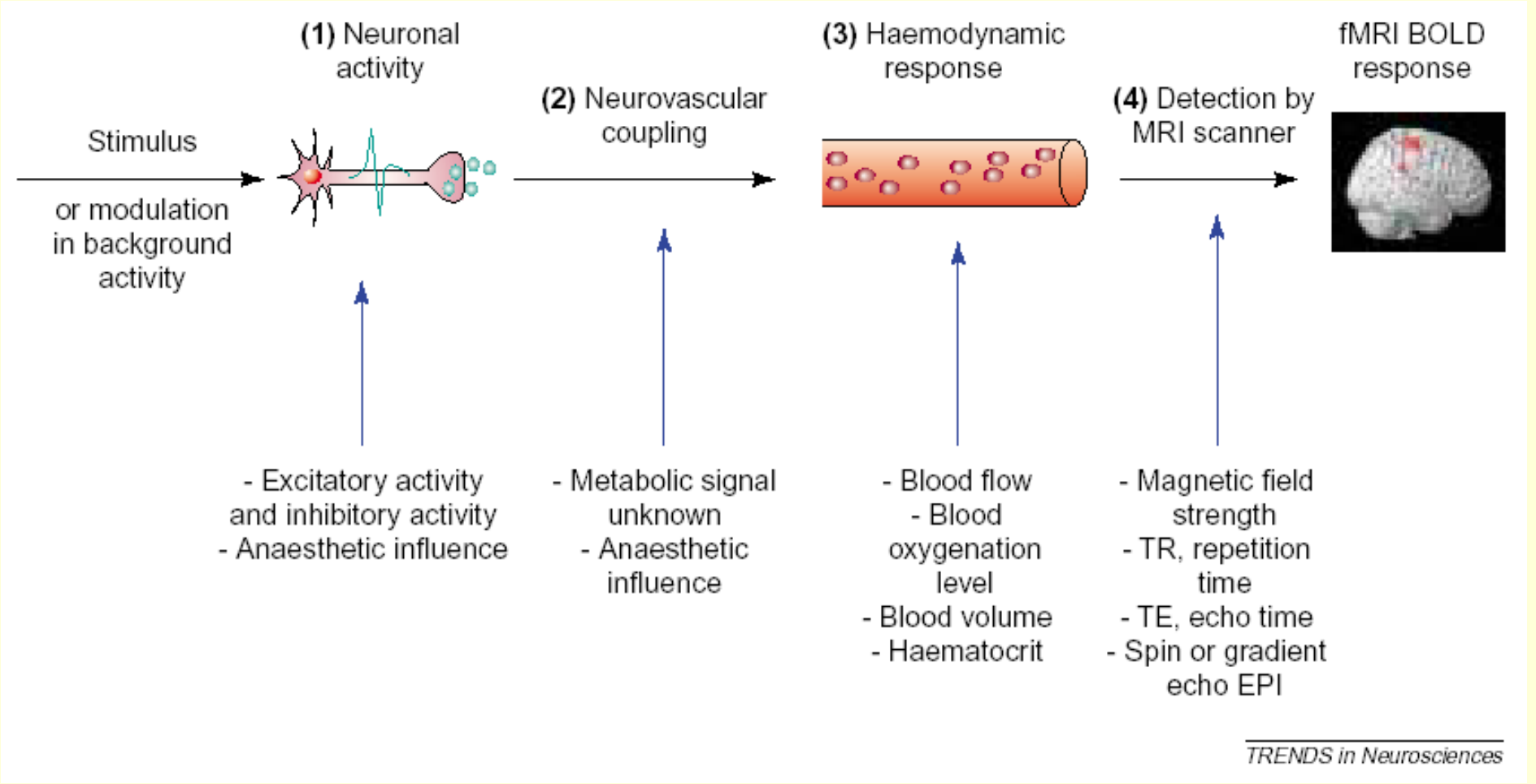
BOLD Endogenous Contrast

- Blood Oxyenation Level Dependent Contrast
  - Deoxyhemoglobin is paramagnetic
  - Magnetic susceptibility of blood increases linearly with increasing Deoxygenation



- Oxygen is increased during passage through capillary bed
  - Brain arteries are fully oxygenated
  - During activation Venous (and capillary) blood has increased proportion of Doxyhemoglobin
  - Then oxygen is compensated in veins
  - Difference between oxy and deoxy states becomes greater for veins → BOLD sensitive to venous changes

Stimulus to BOLD



Source: Arthurs & Boniface, 2002, *Trends in Neurosciences*

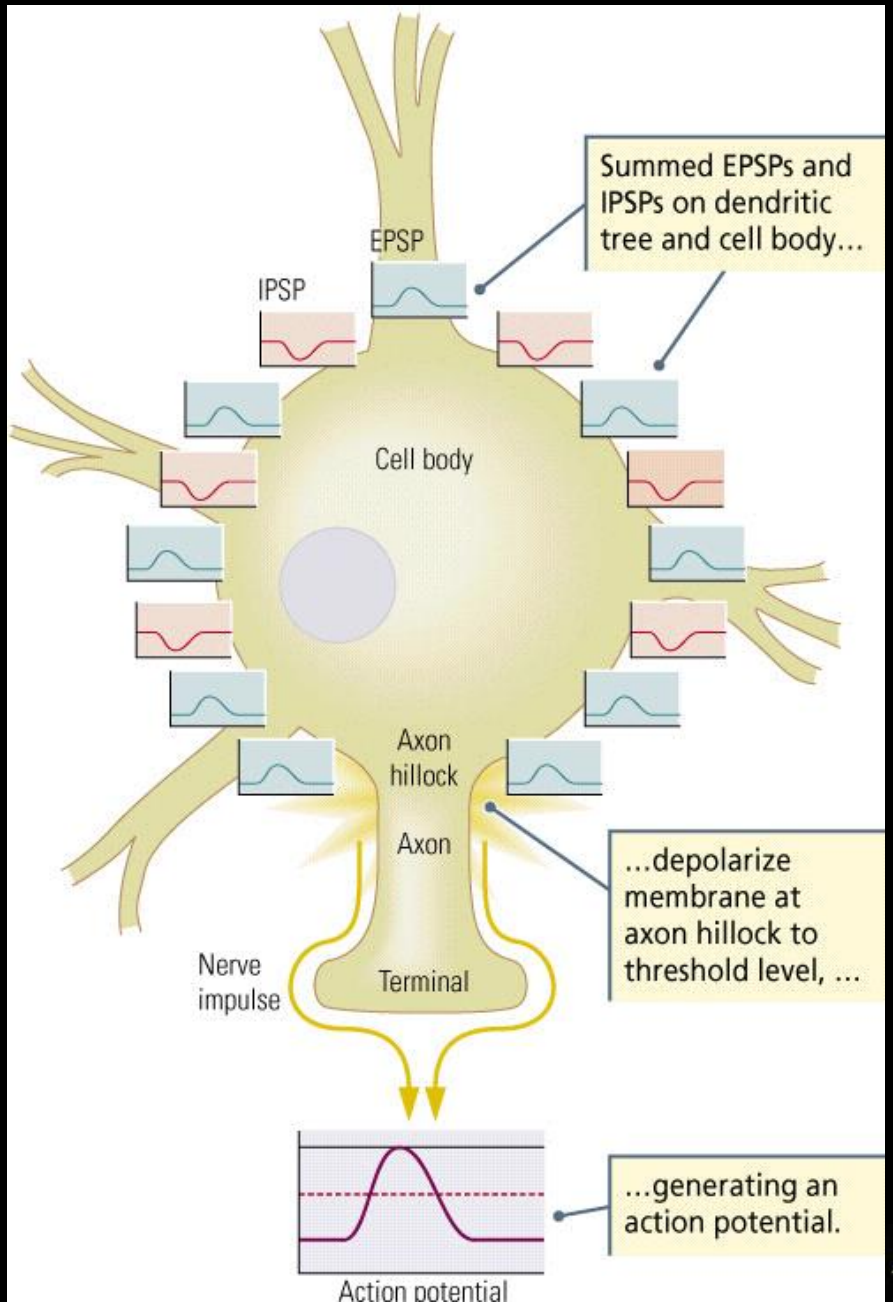
Physiology of BOLD Response

(The Hemodynamic Response)

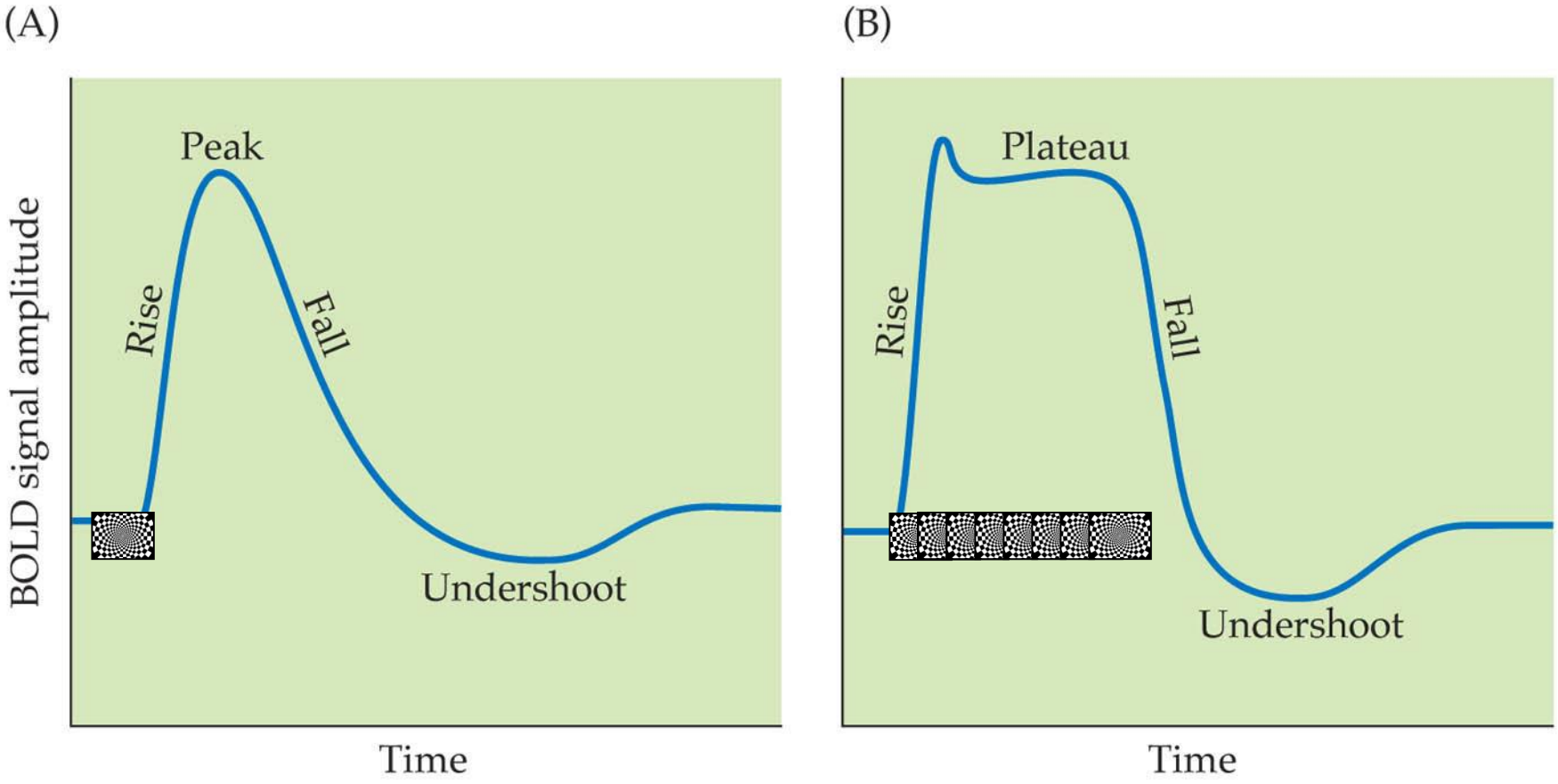
Post-Synaptic Potentials

- The inputs to a neuron (post-synaptic potentials) increase (excitatory PSPs) or decrease (inhibitory PSPs) the membrane voltage

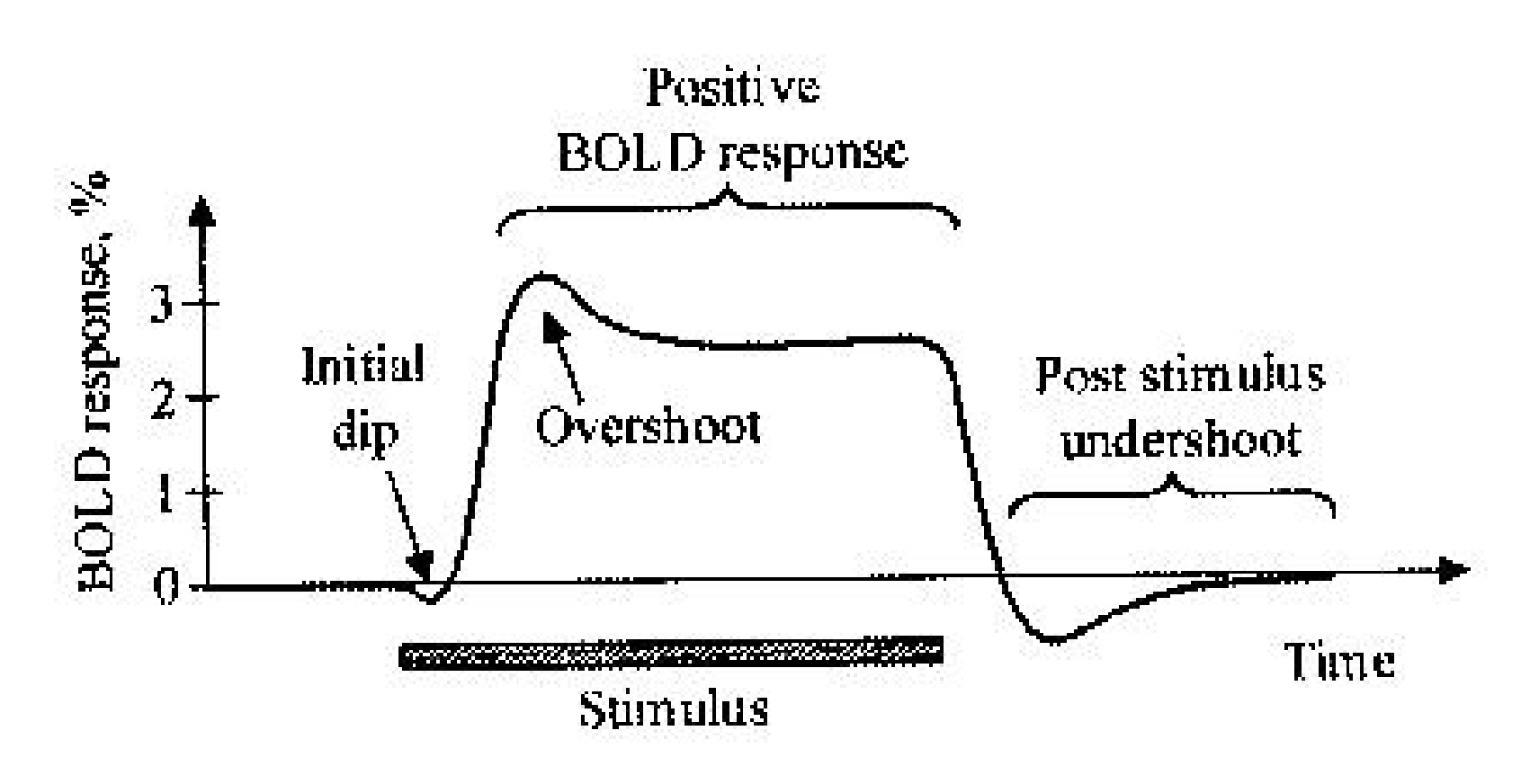
- If the summed PSPs at the axon hillock push the voltage above the threshold, the neuron will fire an action potential

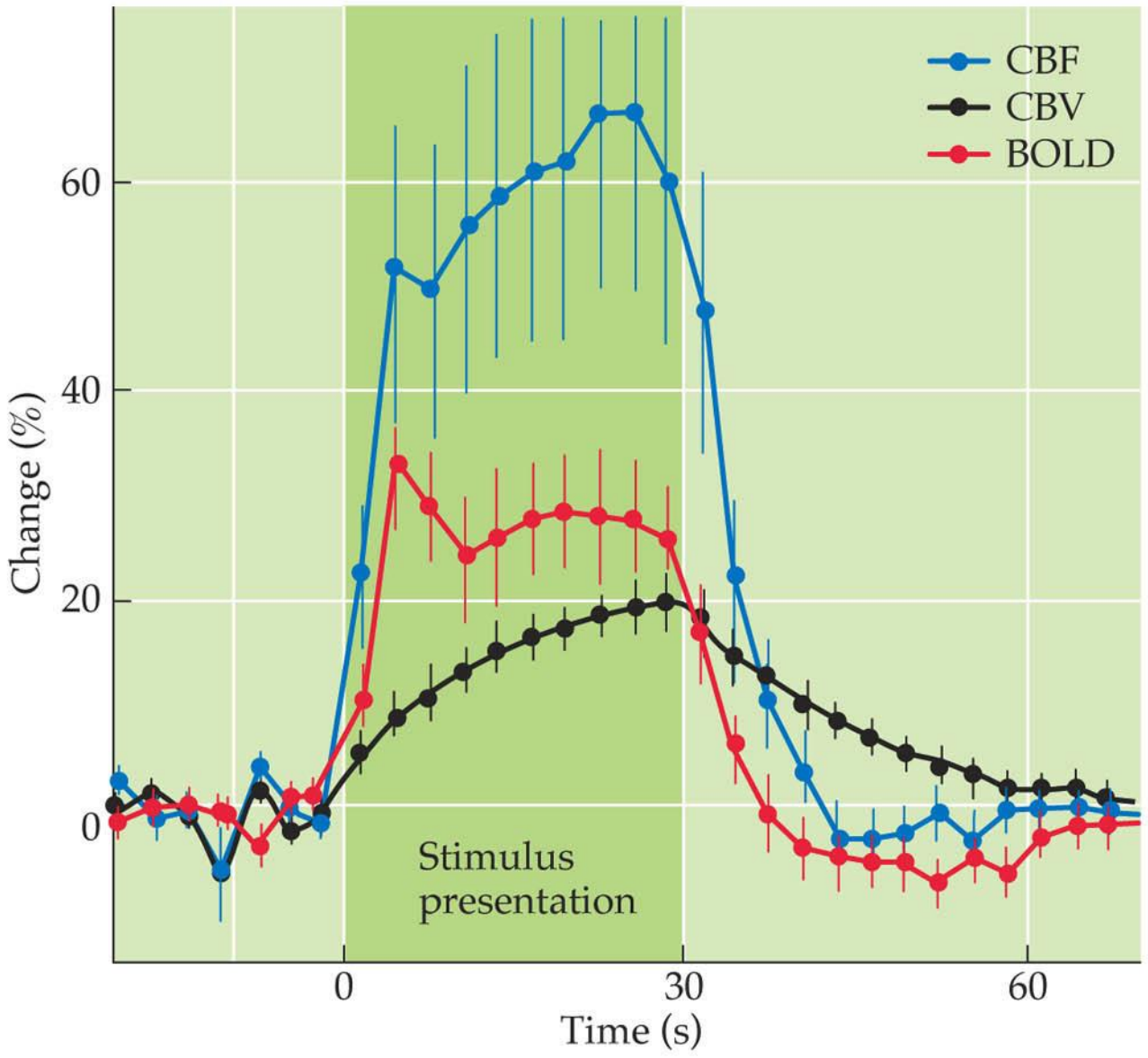


Basic Form of Hemodynamic Response



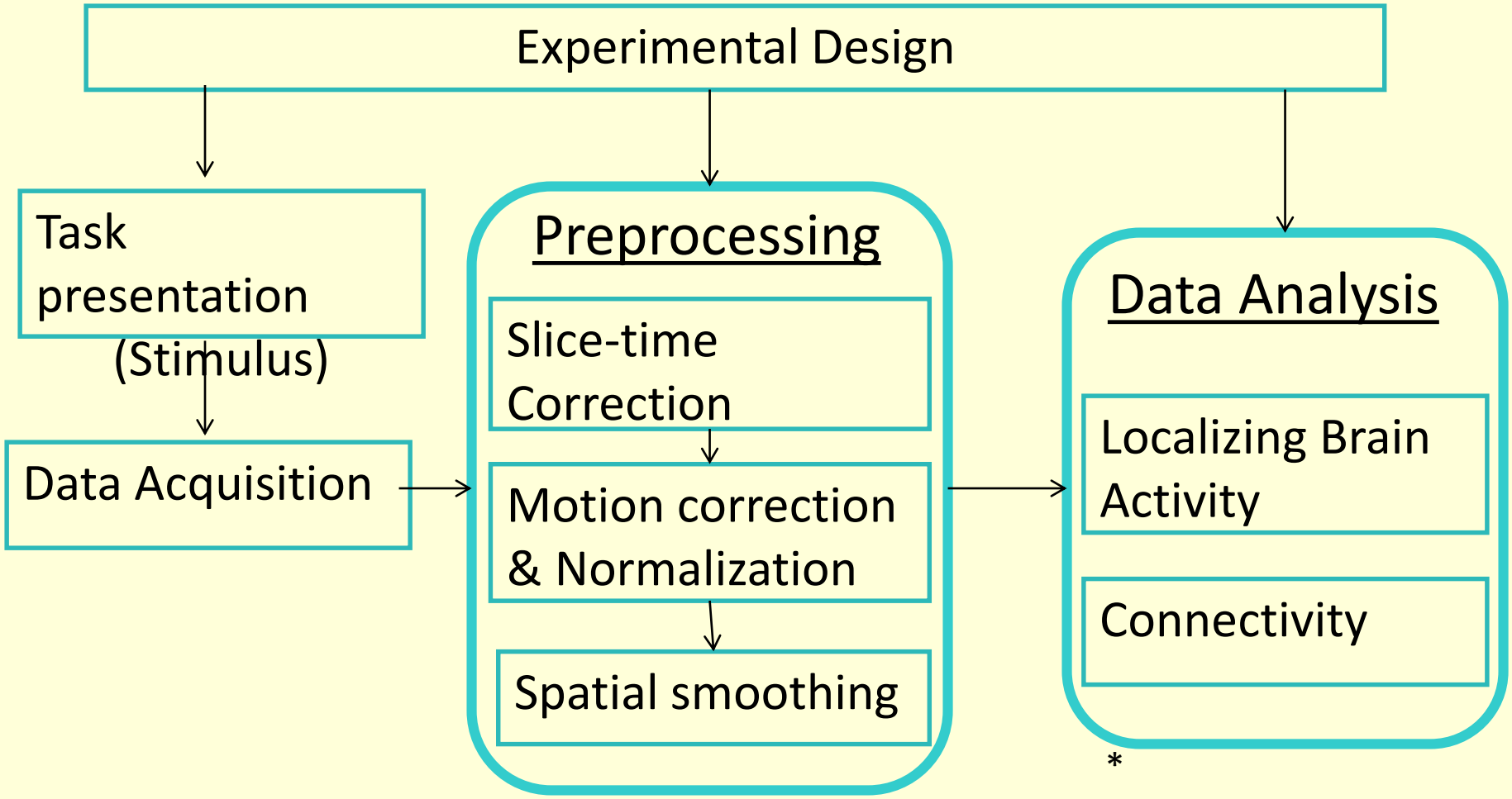
BOLD Time Course





FUNCTIONAL MAGNETIC RESONANCE IMAGING, **Figure 7.16**

How to perform fMRI experiment?

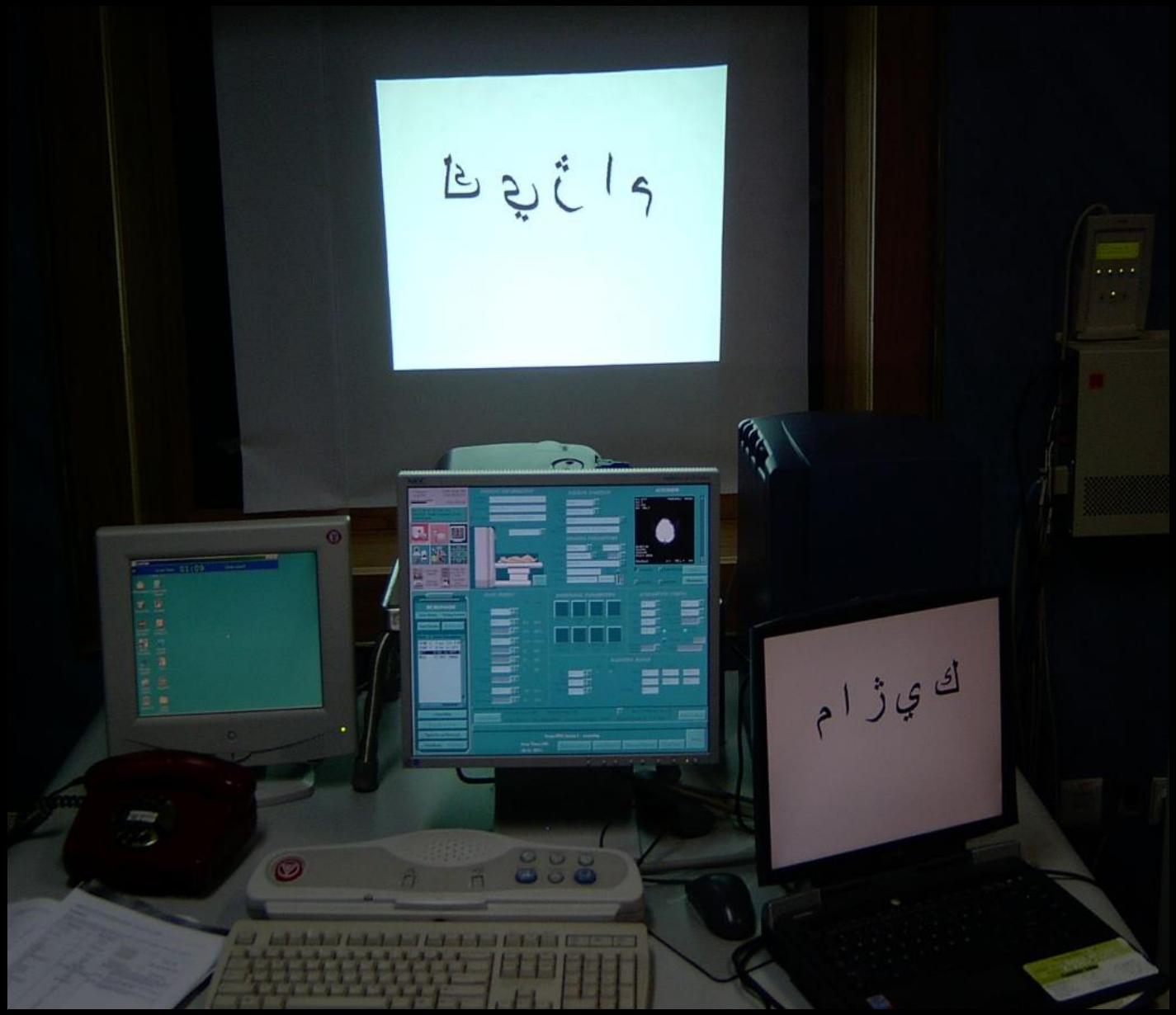


Difference between research and clinical application

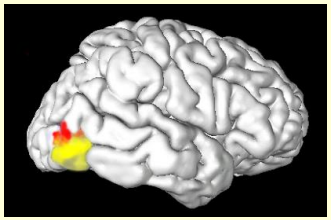
- Validation concern in any subject
- Patient specific experimental design
- Patient specific tasks
- Patient specific paradigm

How to perform fMRI experiment?

How to perform fMRI task?

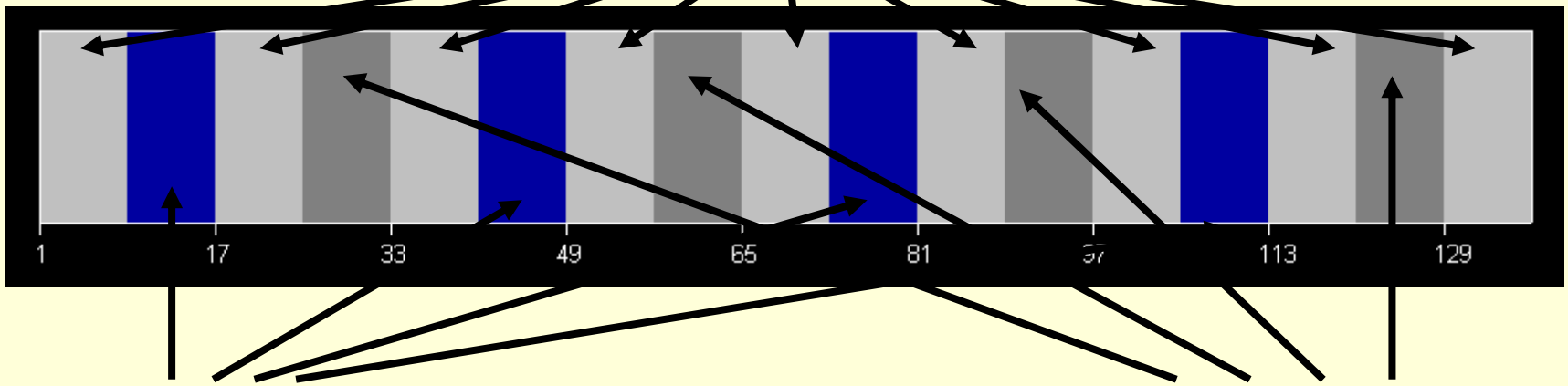


A Simple Experiment

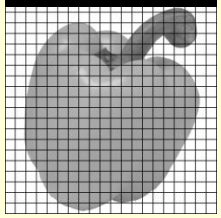


Lateral Occipital Complex
• responds when subject views objects

Blank Screen

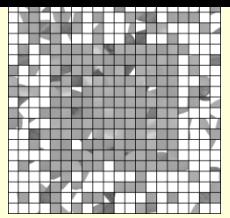


Intact Objects



TIME →

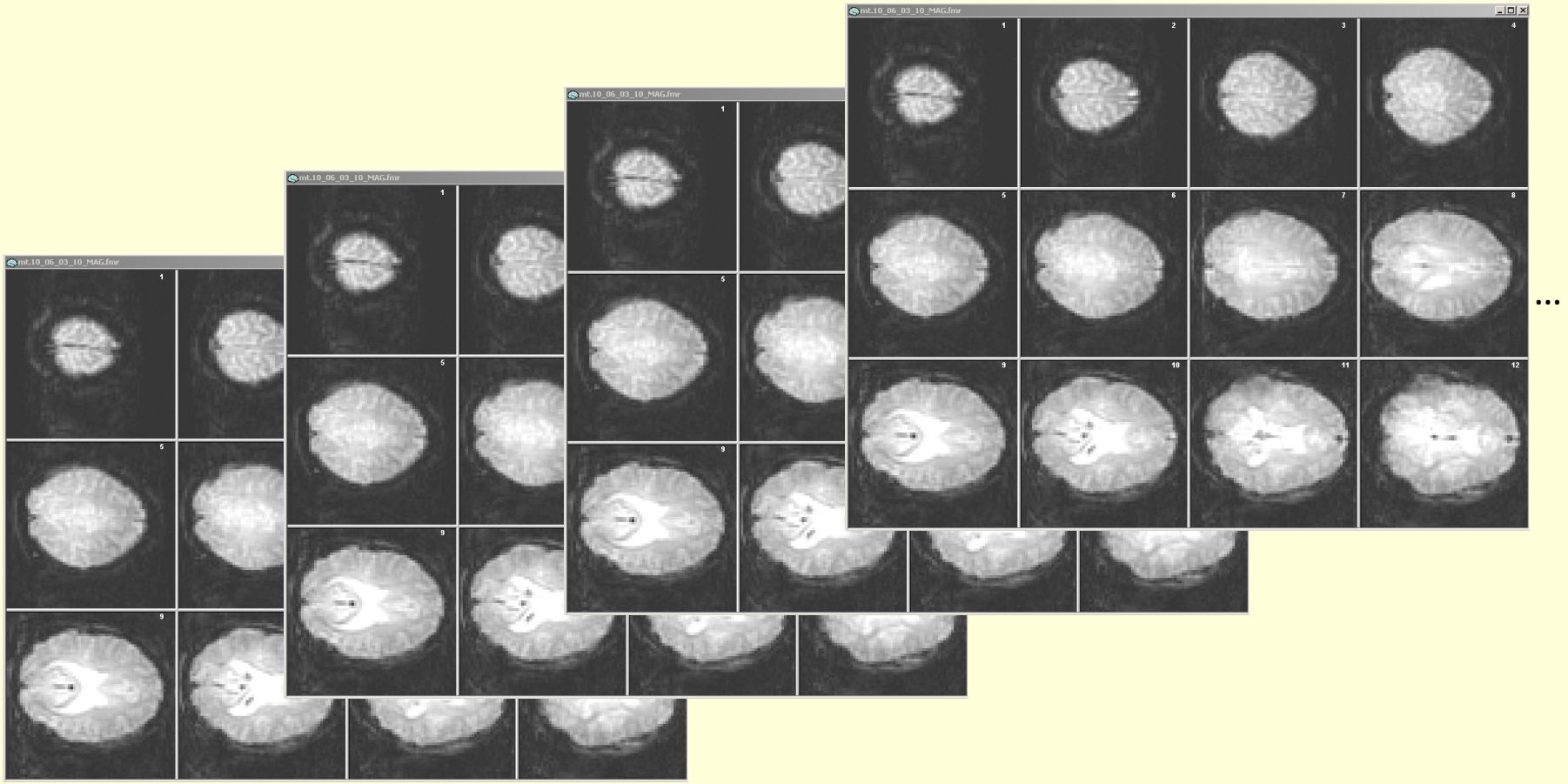
Scrambled Objects



Condition changes every 16 seconds (8 volumes per Block), 17 block
One volume (12 slices) every 2 seconds

for 272 seconds (4 minutes, 32 seconds)

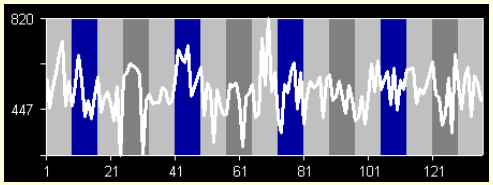
What data do we start with



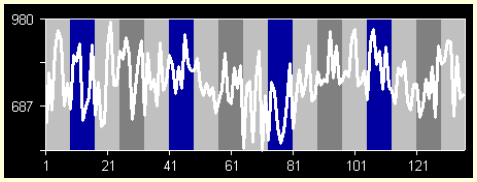
- 12 slices * 64 voxels x 64 voxels = 49,152 voxels
- Each voxel has 136 time points
- Therefore, for each run, we have 6.7 million data points
- We often have several runs for each experiment

Why do we need stats?

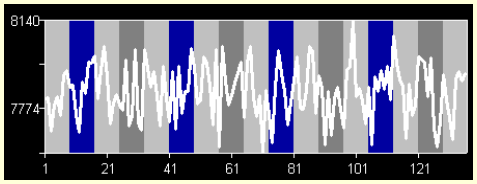
- We could, in principle, analyze data by voxel surfing: move the cursor over different areas and see if any of the time courses look interesting



Slice 9, Voxel 0, 0



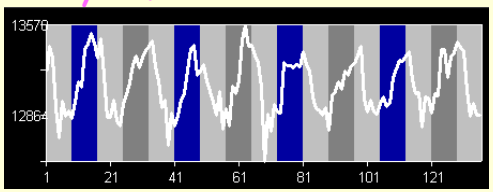
Slice 9, Voxel 1, 0



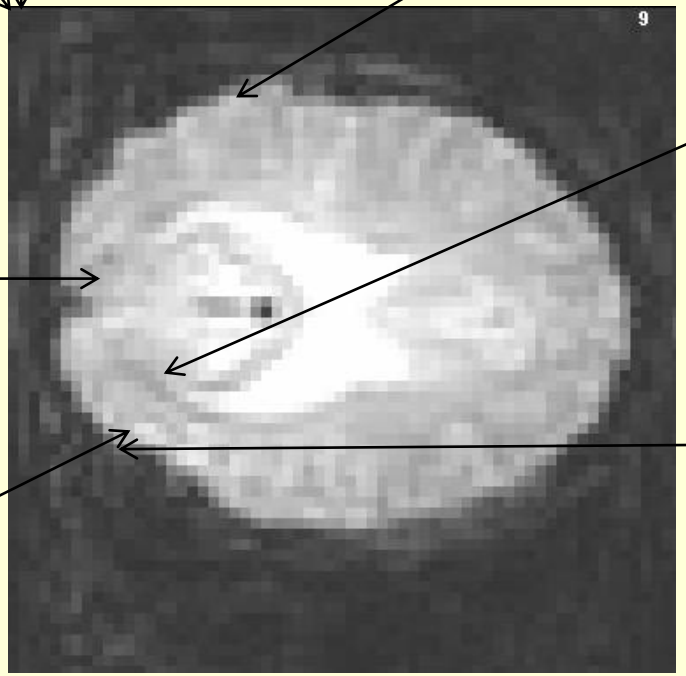
Slice 9, Voxel 22, 7

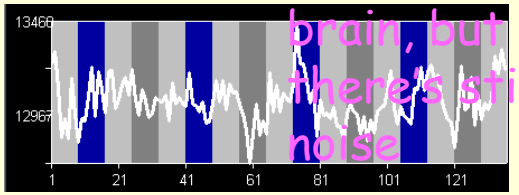
The signal is much higher where there is brain, but there's still noise

Even where there's no brain, there's noise



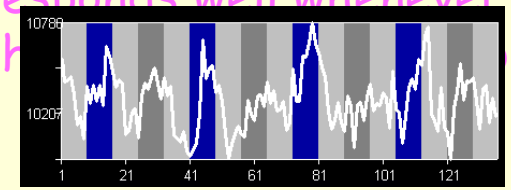
Slice 9, Voxel 9, 27





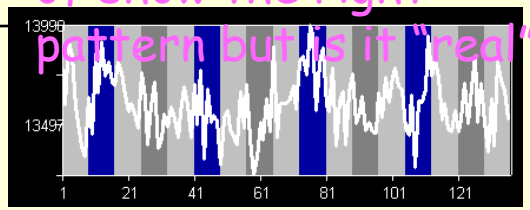
Slice 9, Voxel 18, 36

Here's a voxel that responds well whenever th[illegible]n



Slice 9, Voxel 13, 41

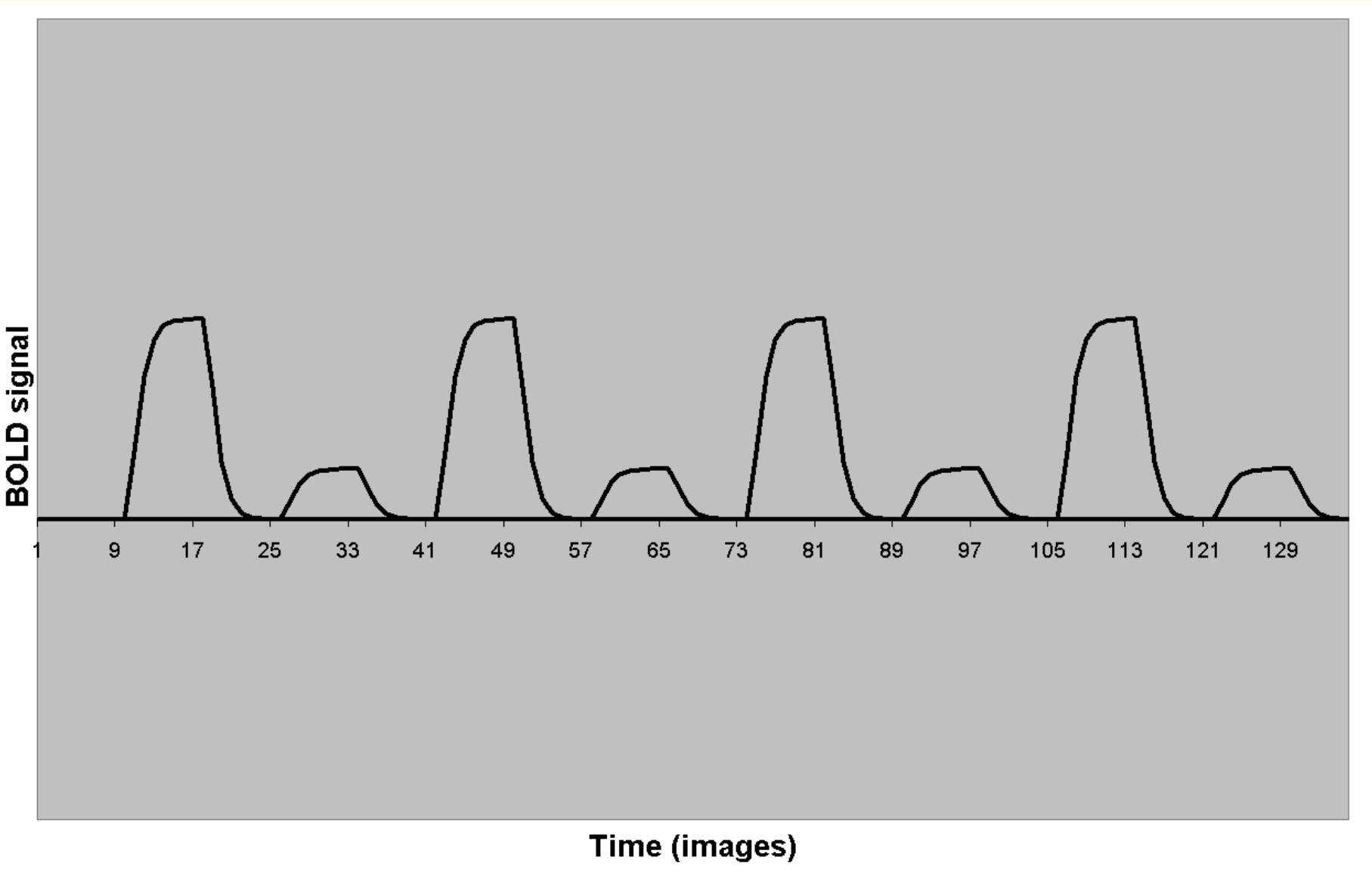
Here's a couple that sort of show the right pattern but is it "real"?



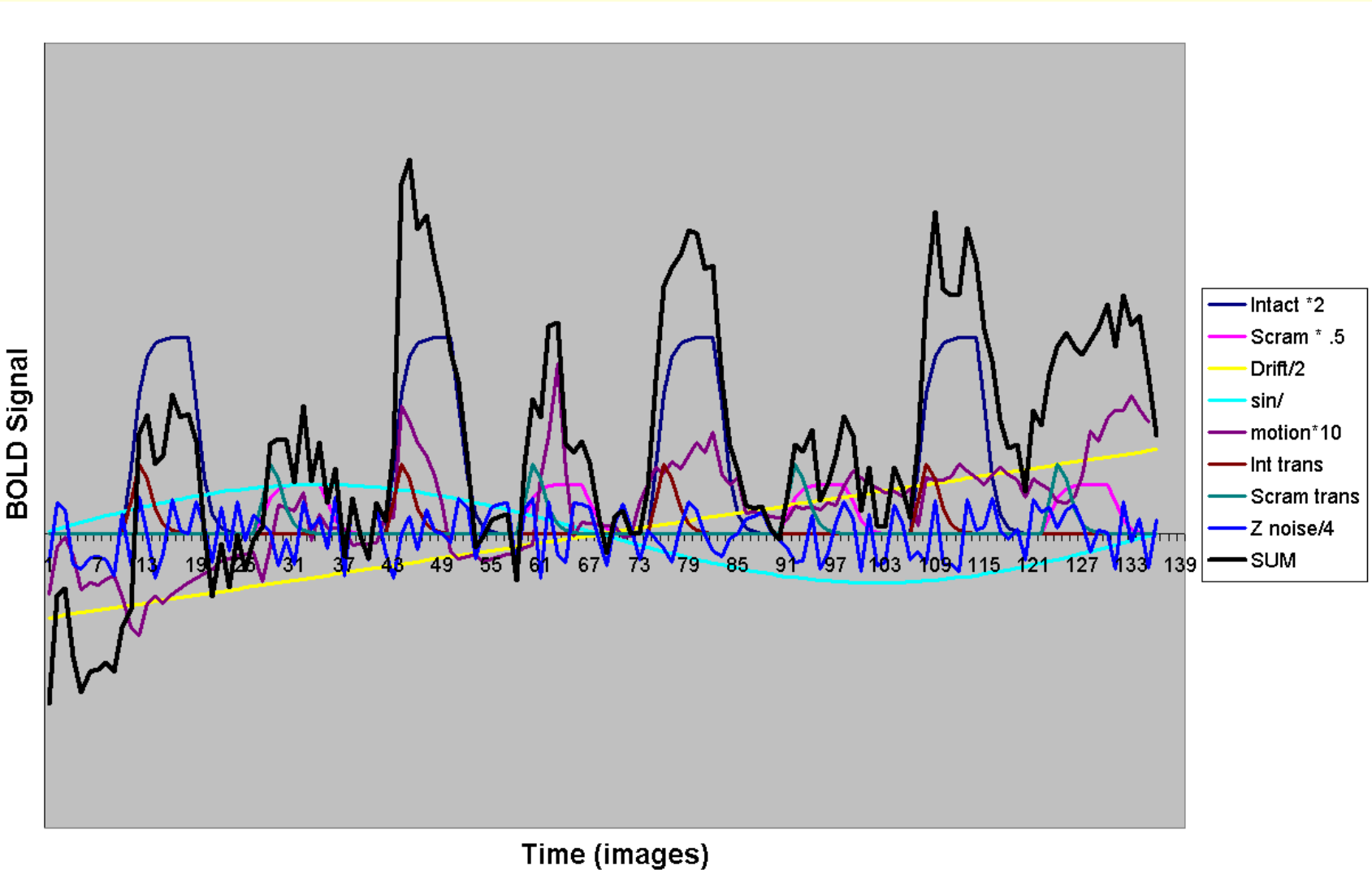
Slice 9, Voxel 14, 42

Here's one that responds well whenever there's intact objects

Response to Intact Objects which is 4X greater than Scrambled Objects



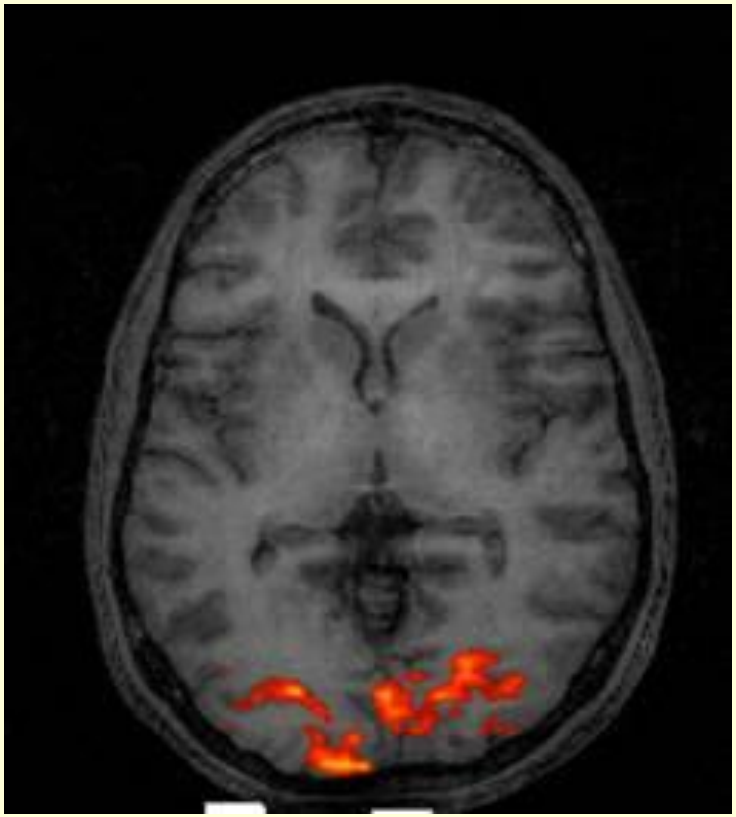
When we add these all together, we get a realistic time course

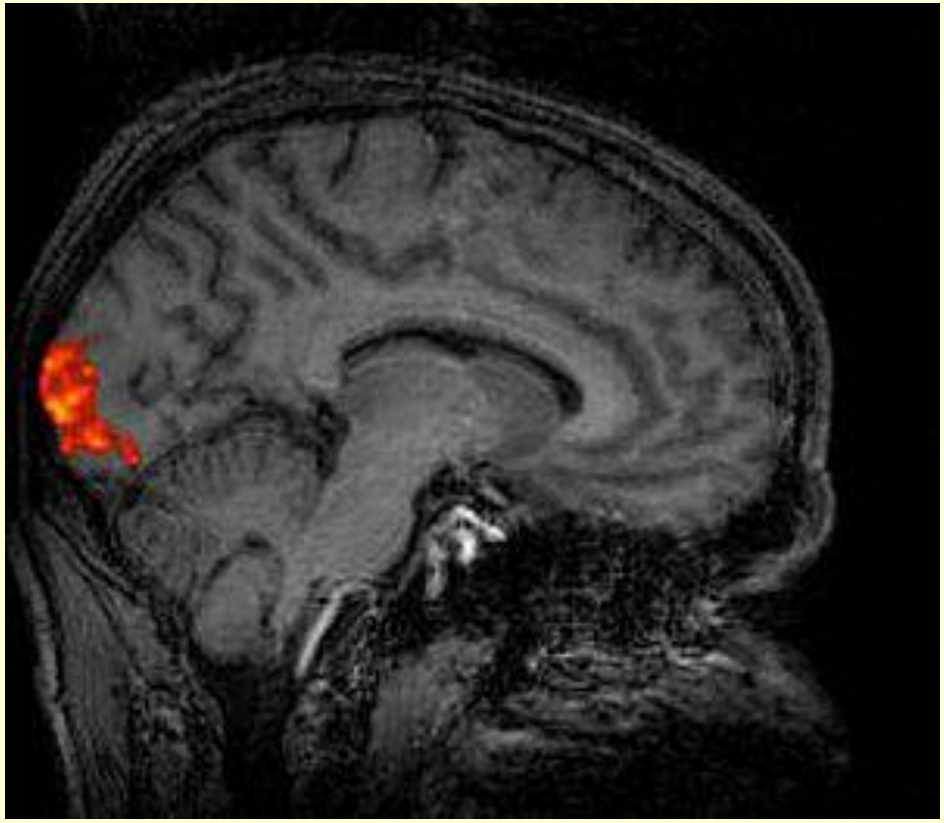


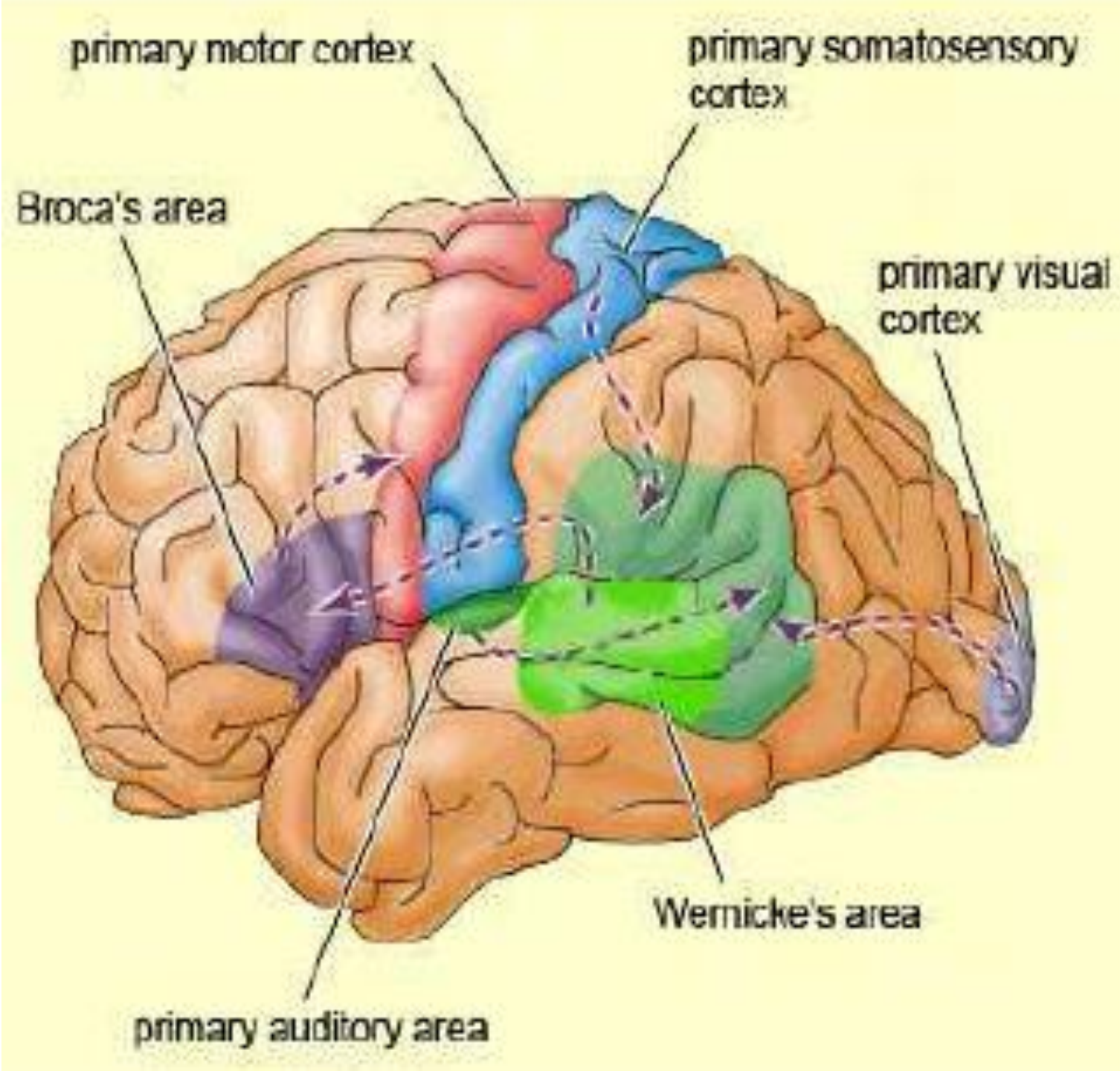
Major components of post-processing and Analysis

1. Quality control (data free from noise and artifacts)
2. Motion correction
3. Slice timing correction
4. Spatial normalization (alignment into common spatial framework)
5. Spatial smoothing
6. Temporal filtering
7. Statistical modeling (GLM & data fitting)
8. Statistical Inference (estimation of statistical significance)
9. Visualization

Visual activation area

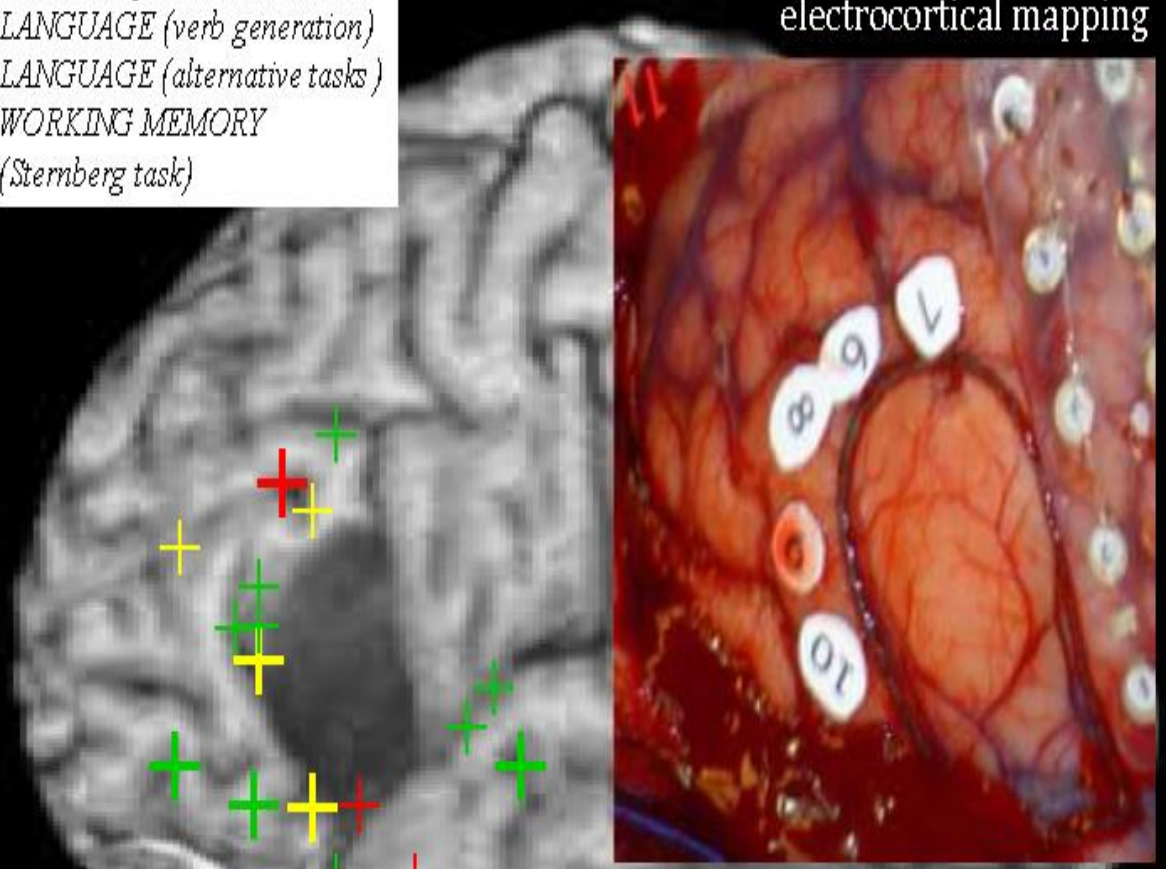





primary motor cortex
primary somatosensory cortex
Broca's area
primary visual cortex
Wernicke's area
primary auditory area

Brain plasticity

IMAGE:	*Functional foci around tumour*
Yellow:	*LANGUAGE (verb generation)*
Green:	*LANGUAGE (alternative tasks)*
Red:	*WORKING MEMORY (Sternberg task)*



Speaking without Broca's area after tumor resection

M Plaza: Neurocase. 2009 Aug;15(4):294-310. doi: 10.1080/13554790902729473. Epub 2009

Main aims of Pre-surgical planning

- fMRI - LANGUAGE DOMINANCE

  DIFFERENT TASK --> DIFFERENT PATTERN OF BRAIN AREAS
  eg: verb-generation, sentence comprehension,WG, ON, RWR

  Lateralization Index = (L – R)/(L + R)

- fMRI – Critical activation area LOCALIZATION
  high sensitivity (crucial not to miss functional areas)

- Evaluating surgery approach (surgery planning)

Most favourable activation areas

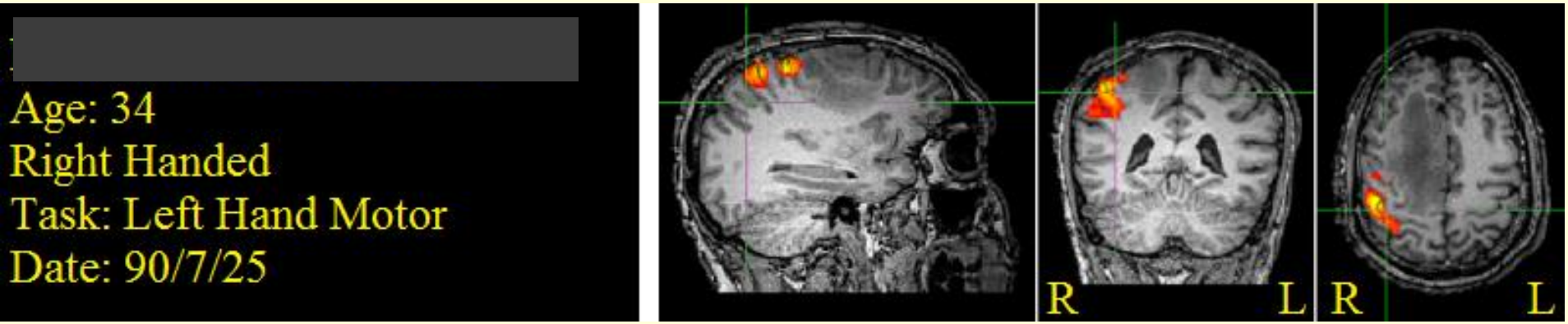
- Motor areas (mostly for tumour resection)
- Language (mostly for Lateralization)
- Memory (mostly for TLE)
- Also

  Vision

  Auditory

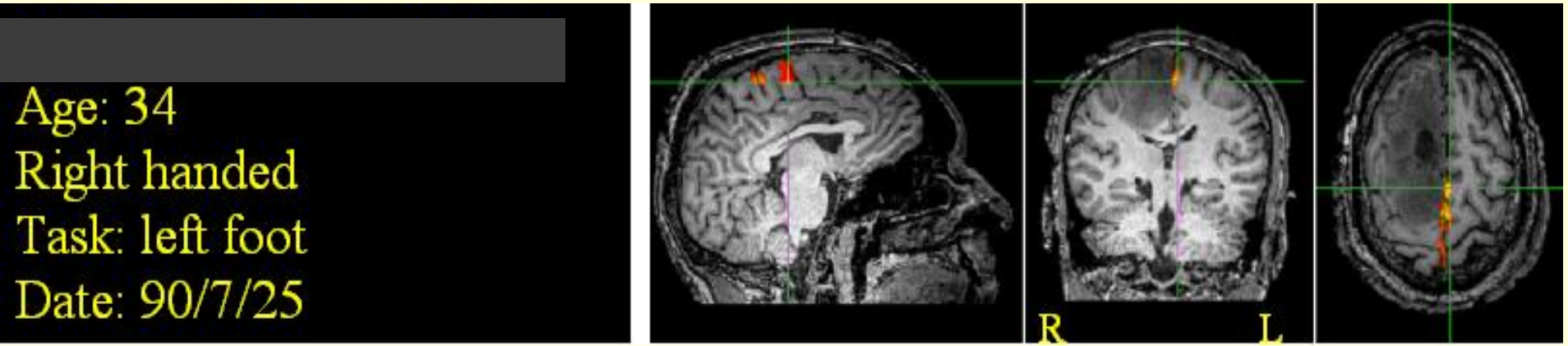
Left Hand activation

close to surrounding edema of astrocytoma tumour



Left Foot activation for the same patient

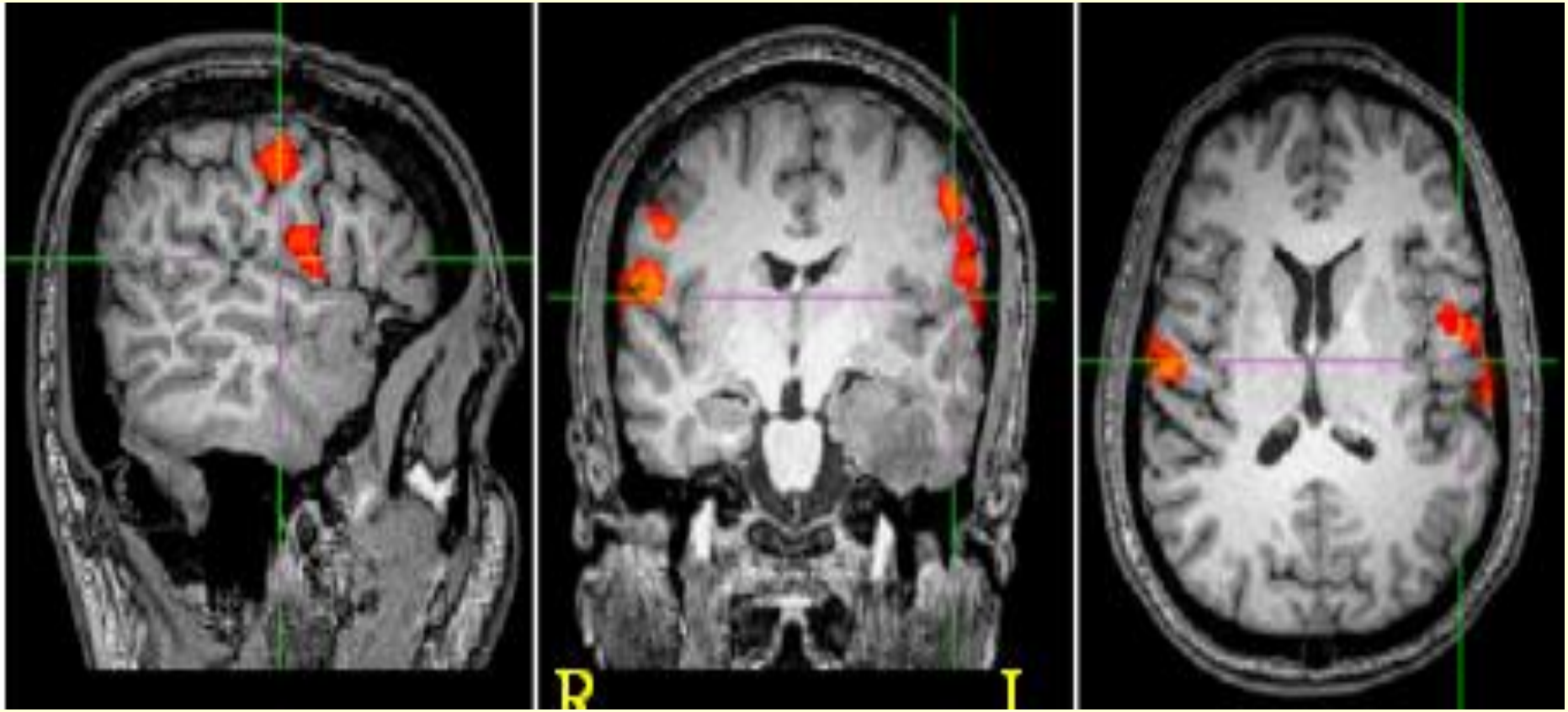
Attached to the edematus area of tumour



Language activation area

Low T1 lesion with surrounding edema in Lt temporal lobe

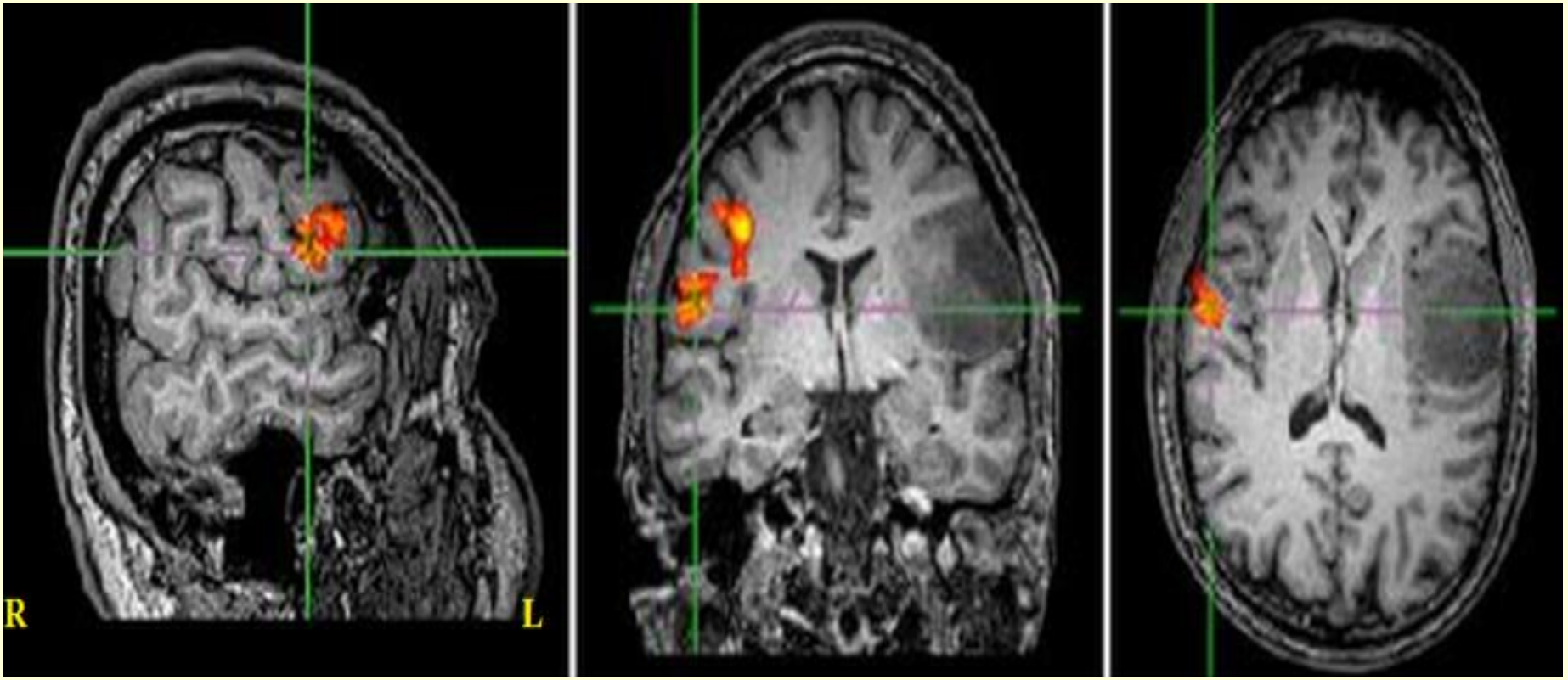
(Right-handed patient)



Language activation using “WG” task

Temporo-parietal mass

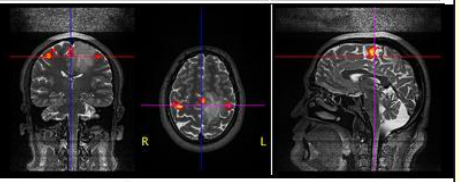
(left-handed patient)

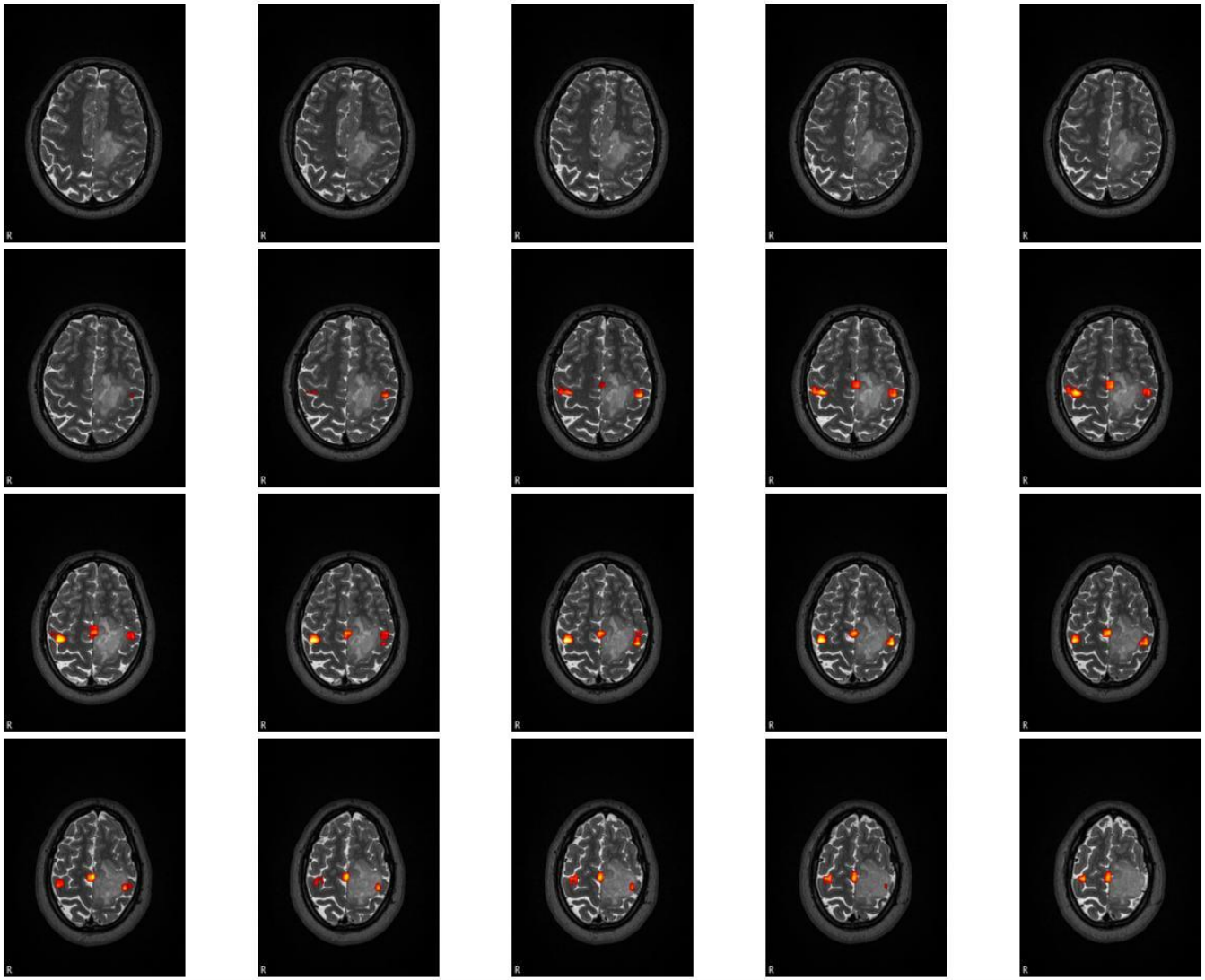


NeuroImaging and Analysis Group
101 Tehran Medical Imaging Center

NIAG

Patient Name:
Age: 34
Right Handed
Task: Hands Motor
Threshold: 2 -7
Date: 97/8/21

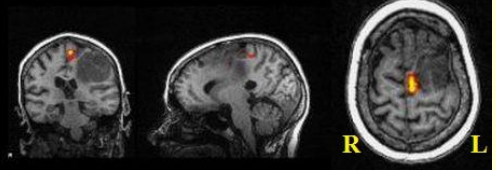


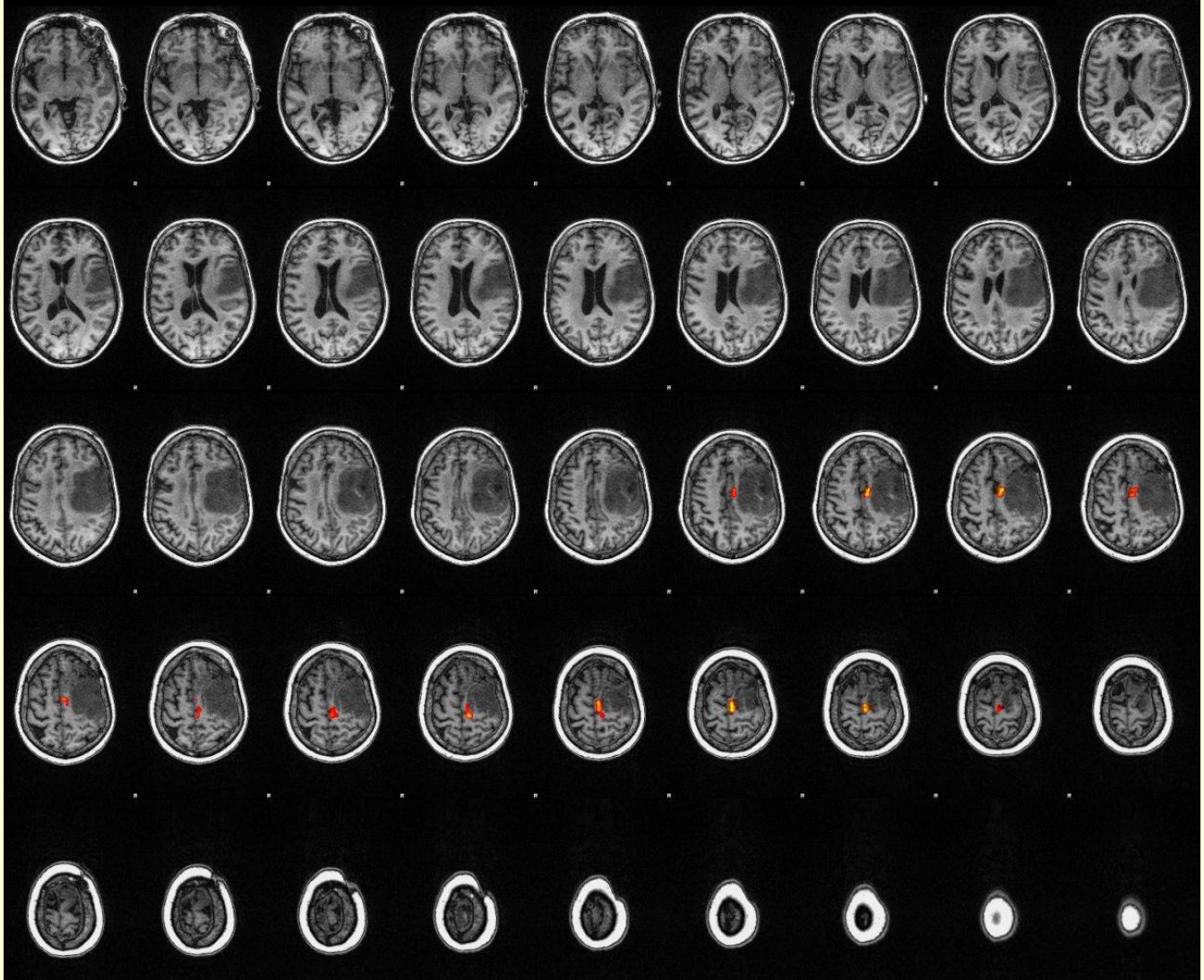


NeuroImaging and Analysis Group
Saadat Abad Medical Imaging Center

NIAG

Patient Name:
Age: 47
Right Handed
Task: Right Foot Passive Motor
Threshold: 2 -5
Date: 97/8/30

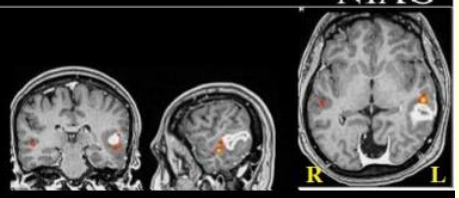


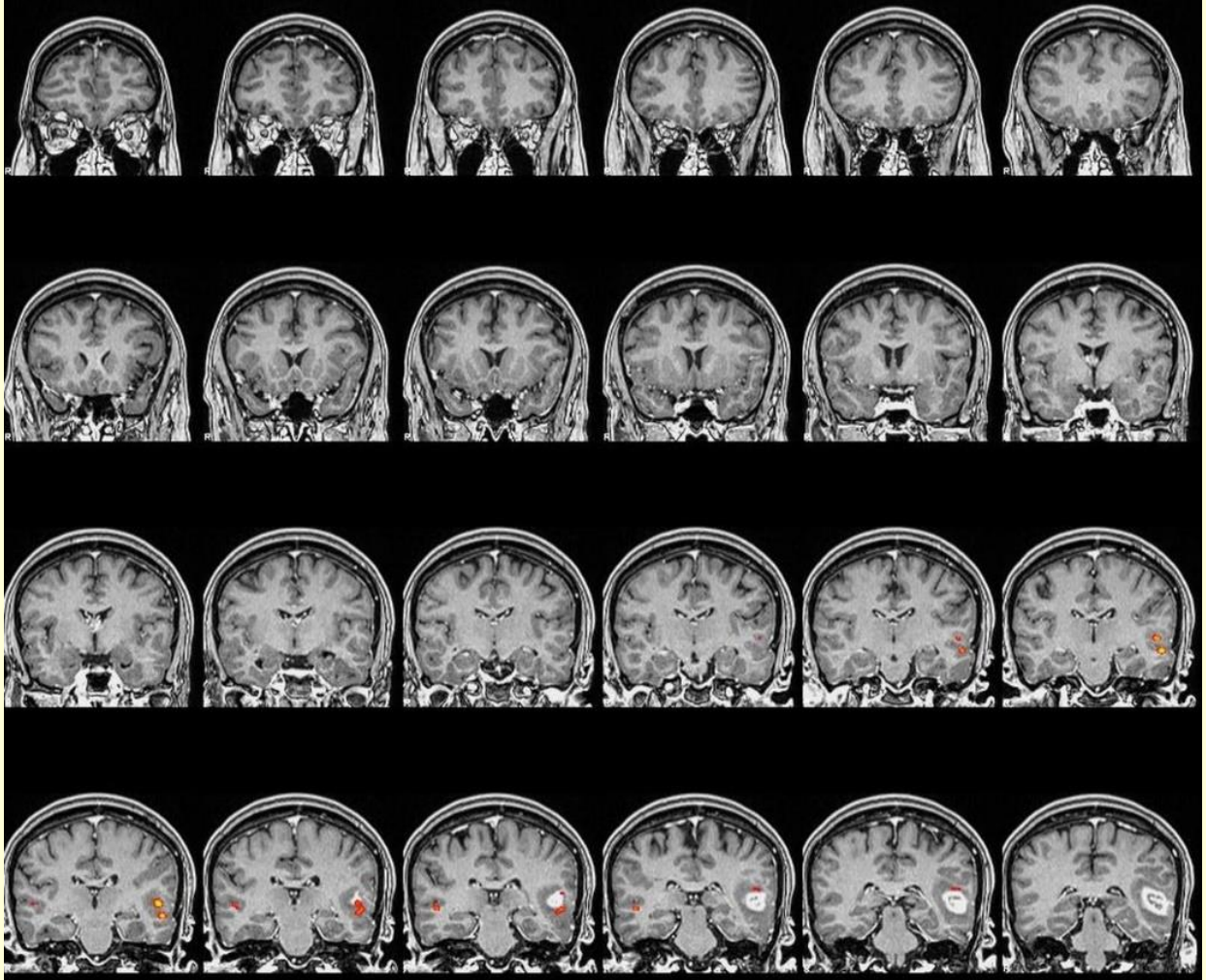


NeuroImaging and Analysis Group
Tehran 101 Medical Imaging Center

NIAG

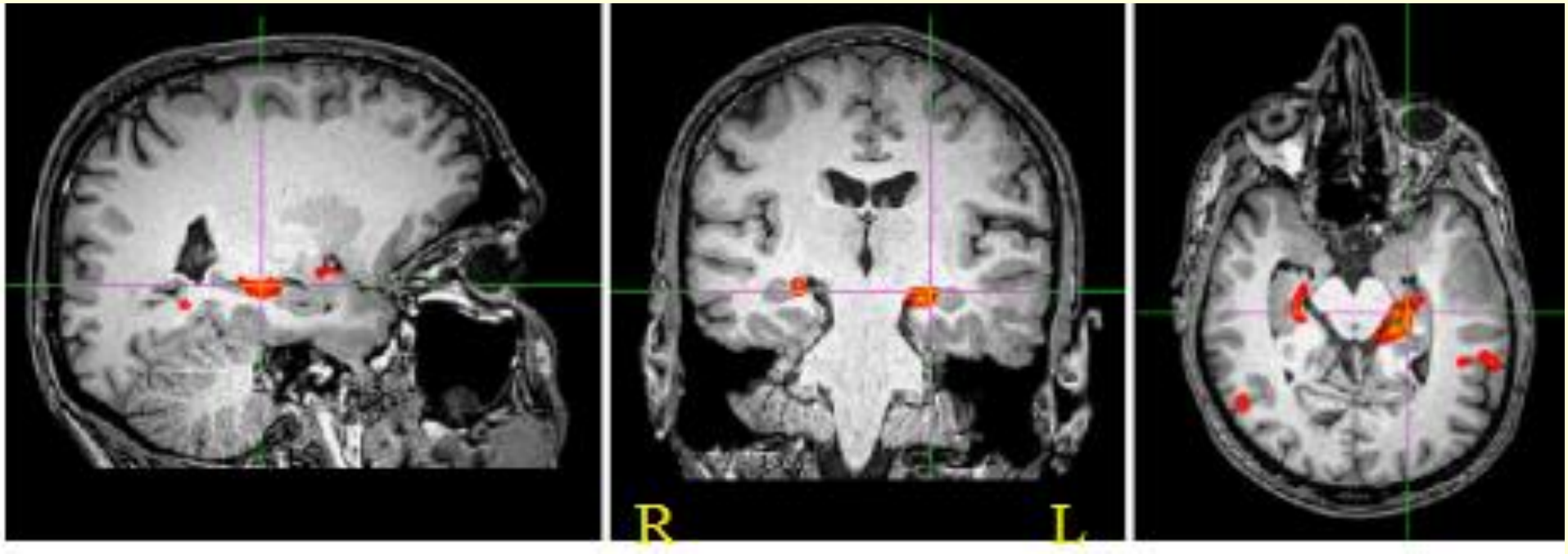
Patient Name:
Age: 41
Right Handed
Task: Language(Rhyming)
Threshold: 2 -6
Date: 97/8/26





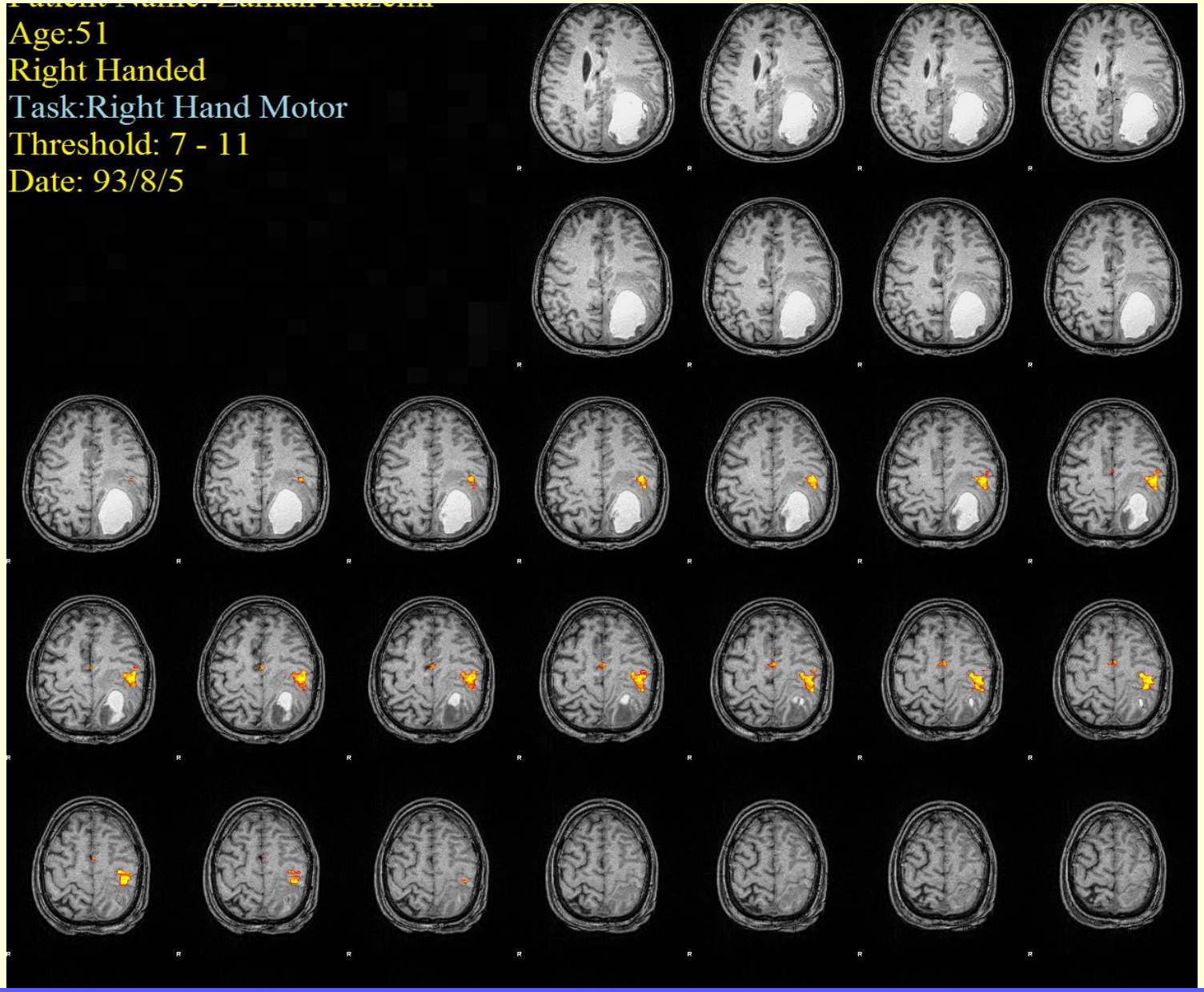
Episodic memory (word encoding task)

On patient with Lt Temporal lobe lesion



Word encoding memory shows more activation in left Hippocampus

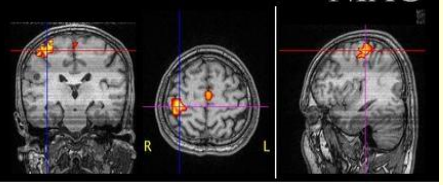
Care for Peripheral edema

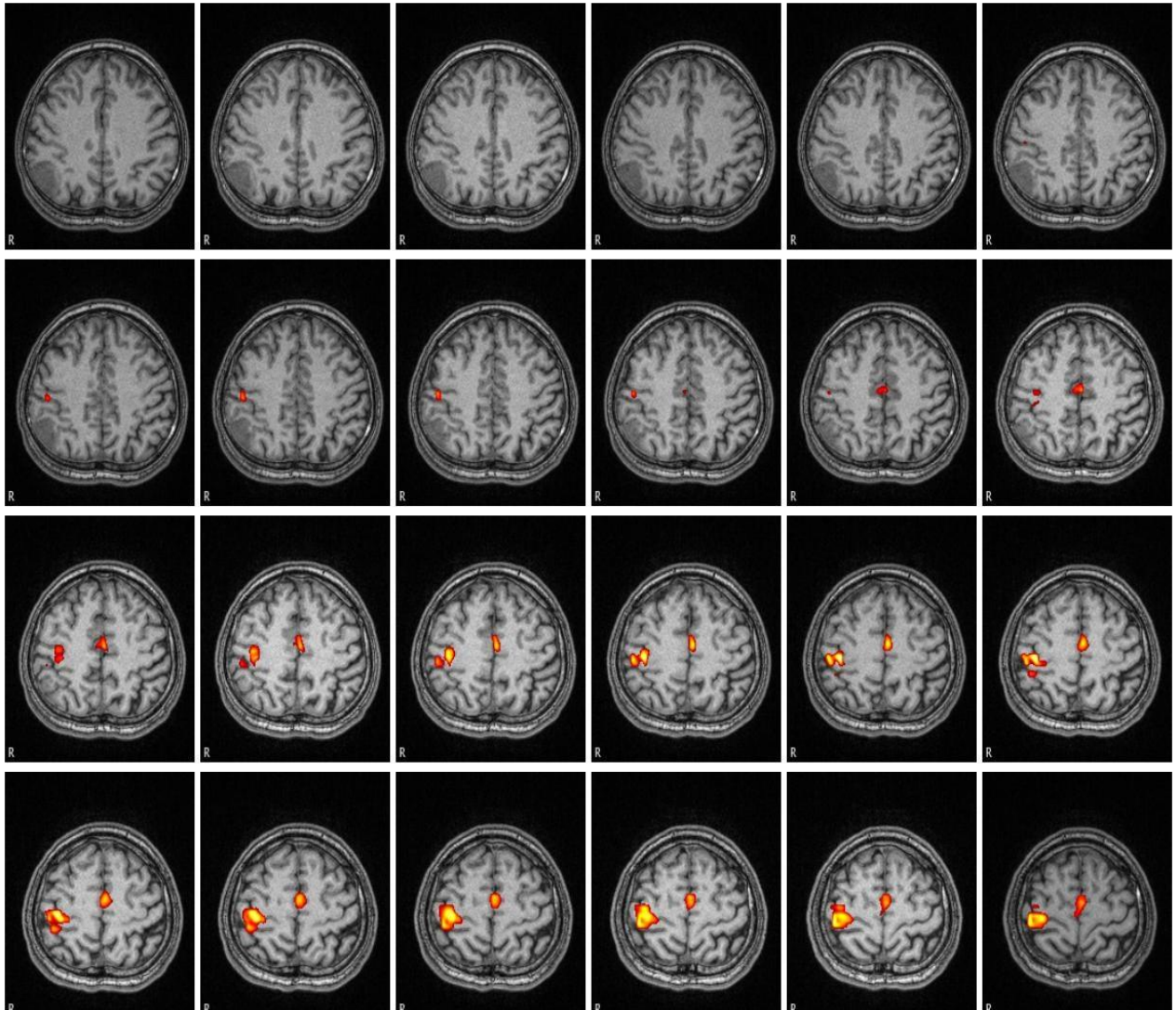


NeuroImaging and Analysis Group
Shahed Medical Imaging Center
Tehran/Iran

NIAG

Patient Name:
Age: 42
Right Handed
Task: Left Hand Motor
Threshold: 2.3 –7
Date: 96/10/26

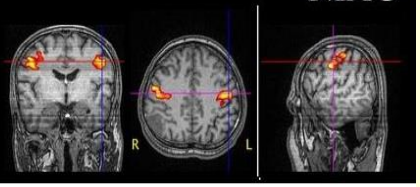


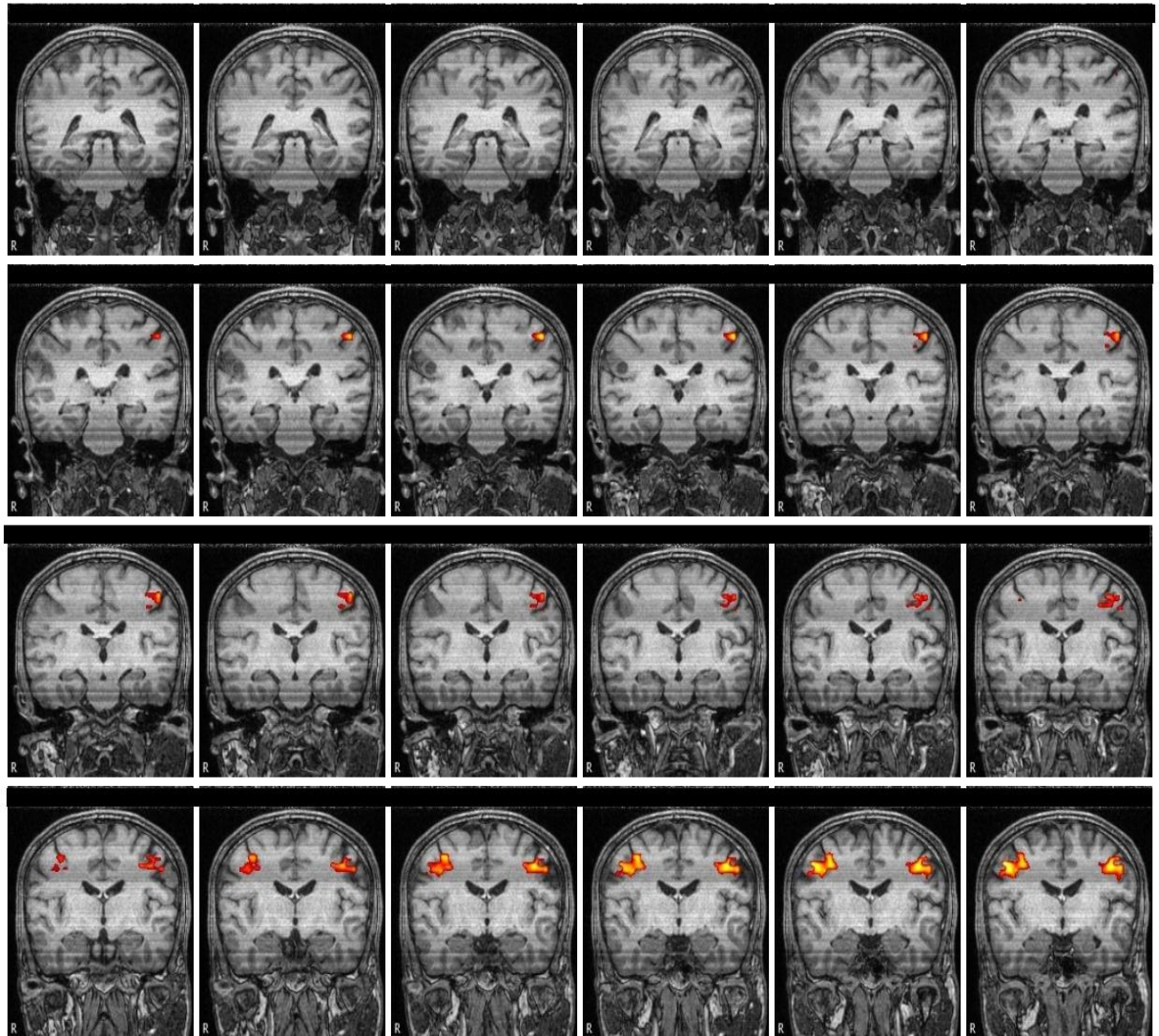


NeuroImaging and Analysis Group
Shahed Medical Imaging Center
Tehran/Iran

NIAG

Patient Name:
Age: 42
Right Handed
Task: Lip Motor
Threshold: 2.3 -6
Date: 96/10/26

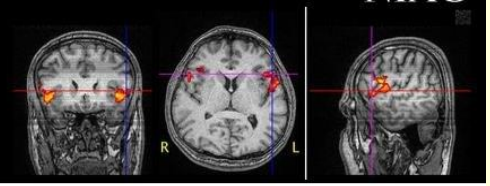


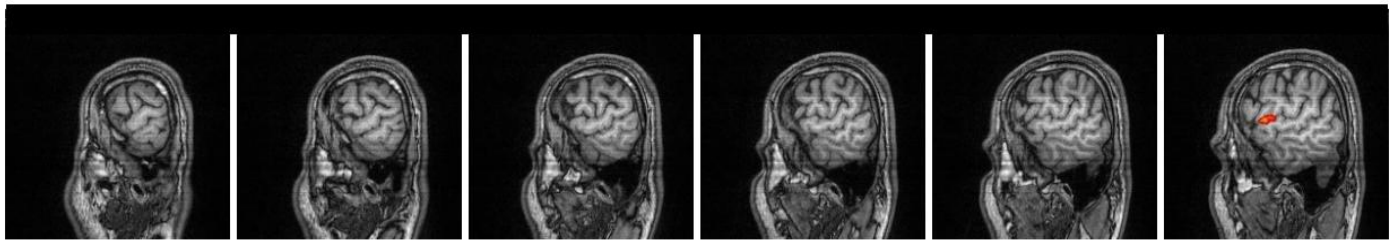


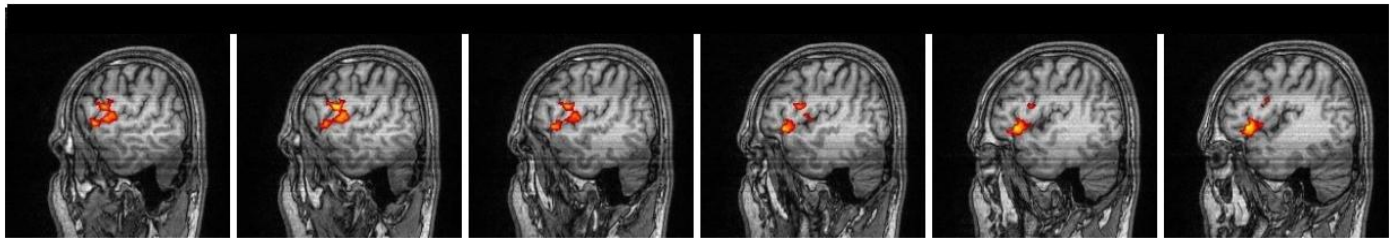
NeuroImaging and Analysis Group
Shahed Medical Imaging Center
Tehran/Iran

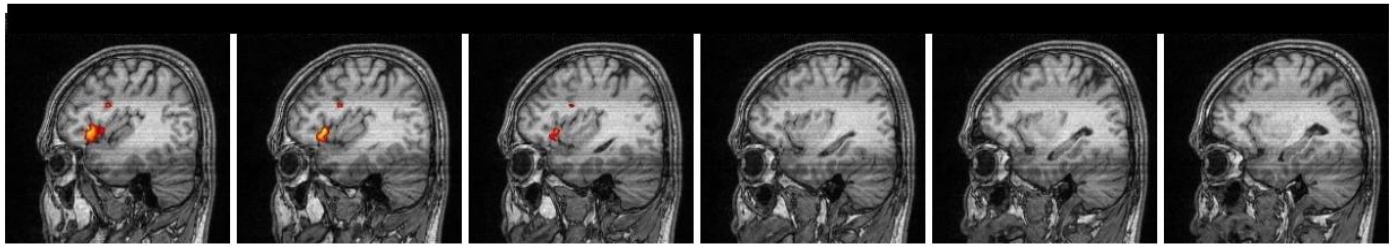
NIAG

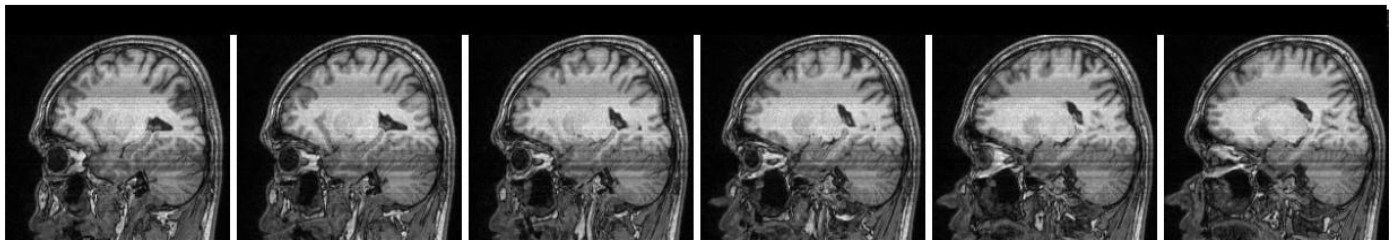
Patient Name:
Age: 42
Right Handed
Task: Language(RWR)
Threshold: 2.3 -6
Date: 96/10/26



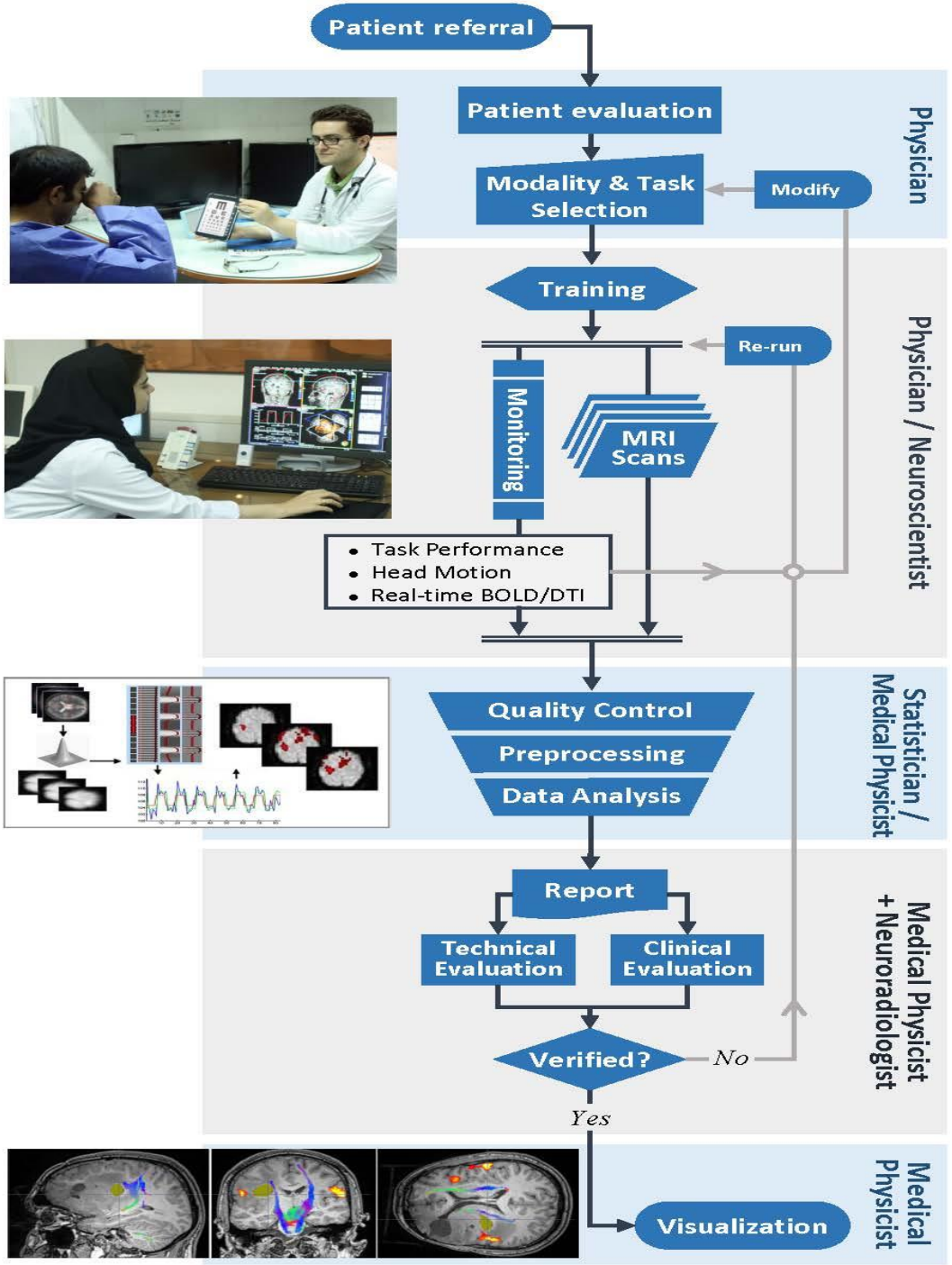






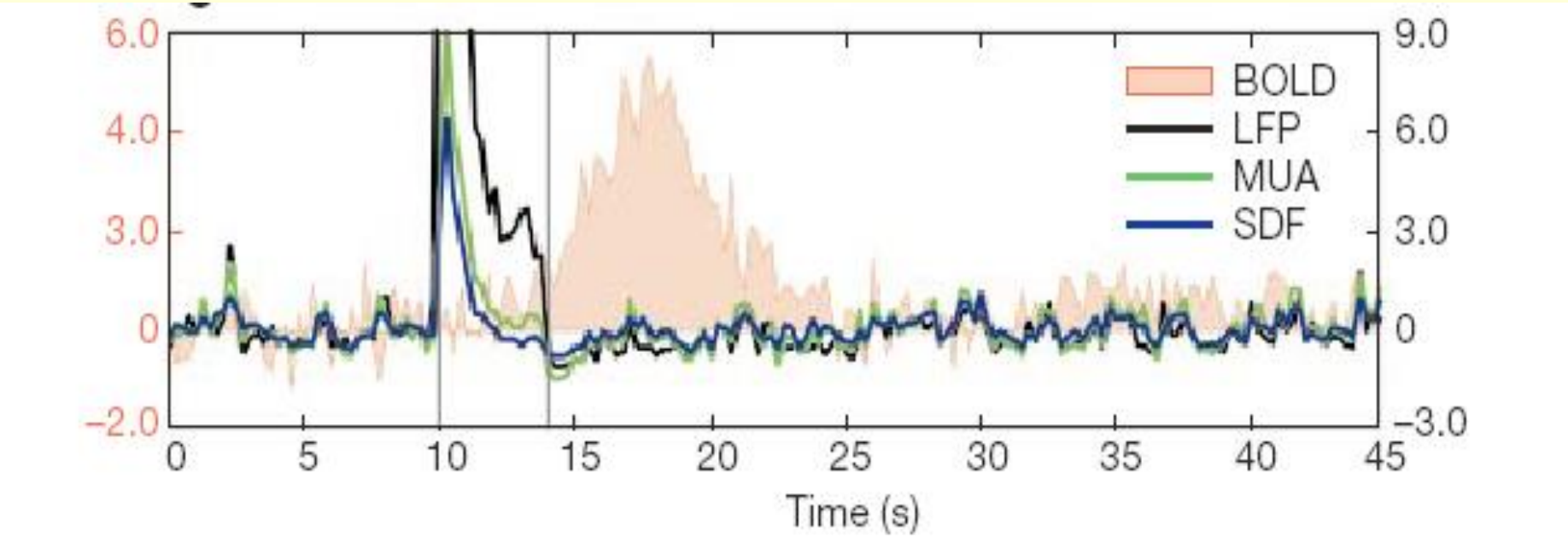


Work flow for pre-surgical Planning


Patient referral
Patient evaluation
Modality & Task Selection
Modify
Physician
Training
Re-run
Monitoring
MRI Scans
Task Performance
Head Motion
Real-time BOLD/DTI
Physician / Neuroscientist
Quality Control
Preprocessing
Data Analysis
Statistician / Medical Physicist
Report
Technical Evaluation
Clinical Evaluation
Verified?
No
Yes
Medical Physicist + Neuroradiologist
Visualization
Medical Physicist

How BOLD is Accurate?

Time Lag in BOLD (Hemodynamic) effect



Post-synaptic potentials can be measured using EEG (ERPs) and MEG measure

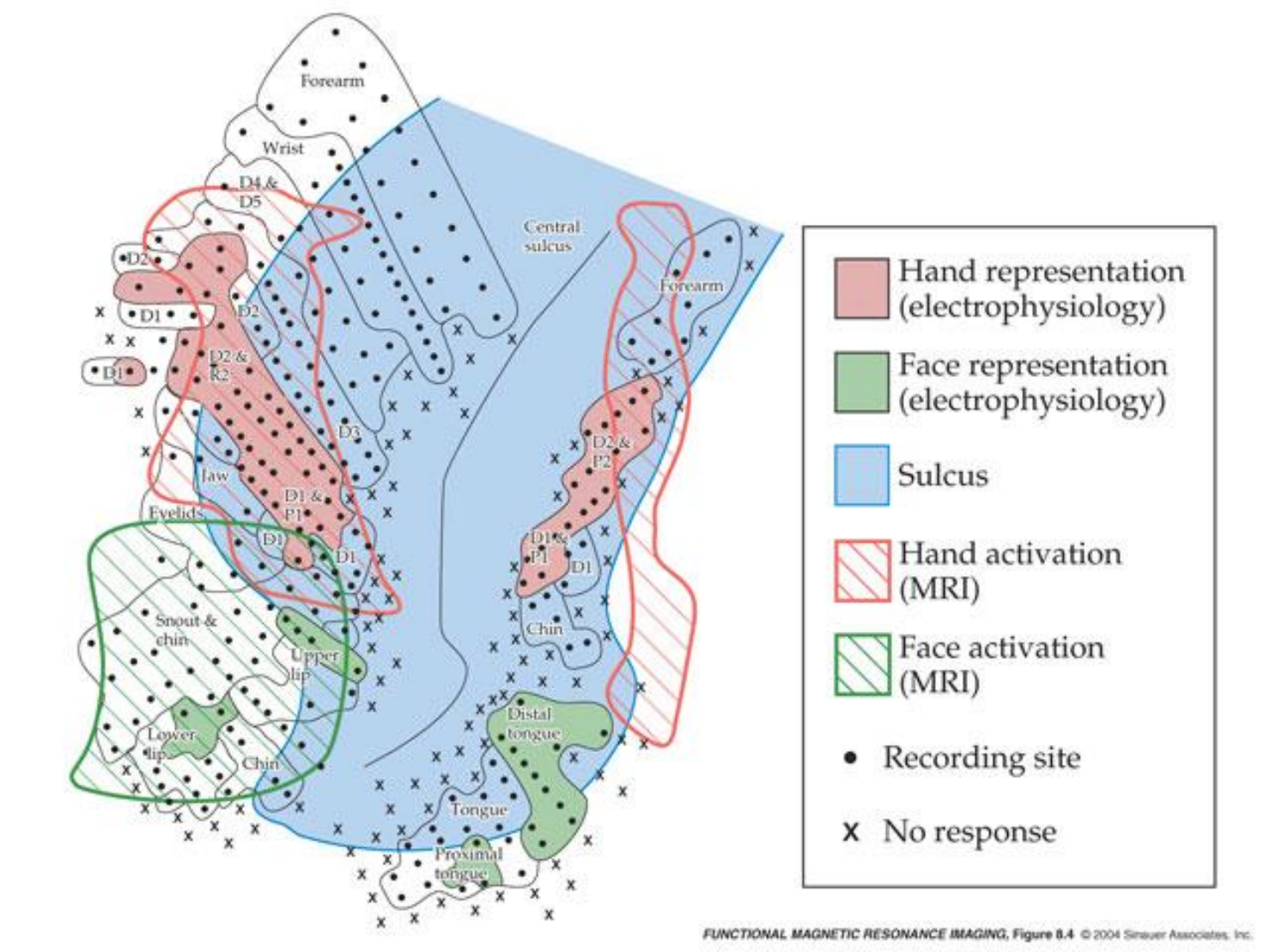
Action potentials can be measured using electrophysiology (Electro-Corticography) methods

BOLD activity is more closely related to EEG than ECG

Hemodynamic activity lags neuronal activity

Source: Logothetis et al., 2001, *Nature*

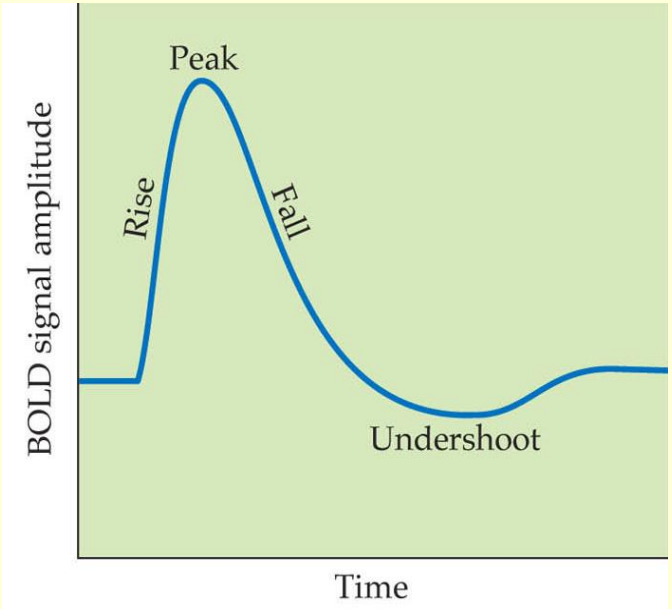
Localization of BOLD



Data Source: Disbrow et al., 2000, *PNAS*
Figure Source, Huettel, Song & McCarthy, *Functional Magnetic Resonance Imaging*

Variability of hemodynamic response

- HDR is:
  - Task dependent
  - Brain Region Dependent
  - Subject Dependent
  - Disease Dependent
- Linearity and time invariancy of the HDR



Major Sources of Artifact/Variation in fMRI

Susceptibility artifacts
  - Image distortion
  - Intravoxel dephasing
  - k-space (sequence) dependence
- Physiological noise
  - Cardiac
  - Respiratory
- Motion
- Contrast
  - T2* (BOLD) or T1
- Random noise and trends

Biological Concerns

Pre-surgical application of fMRI: cares and hopes

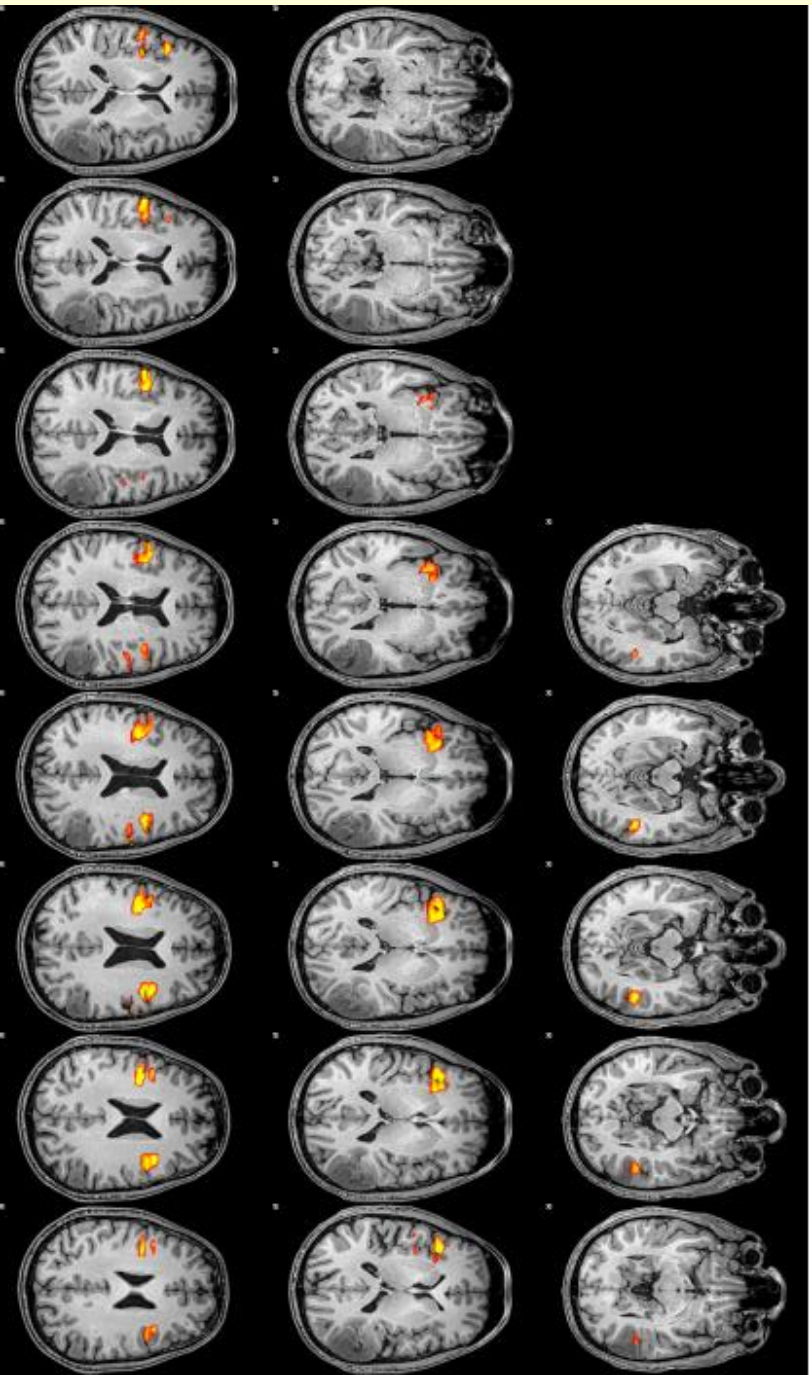
1. fMRI and Brain tumours

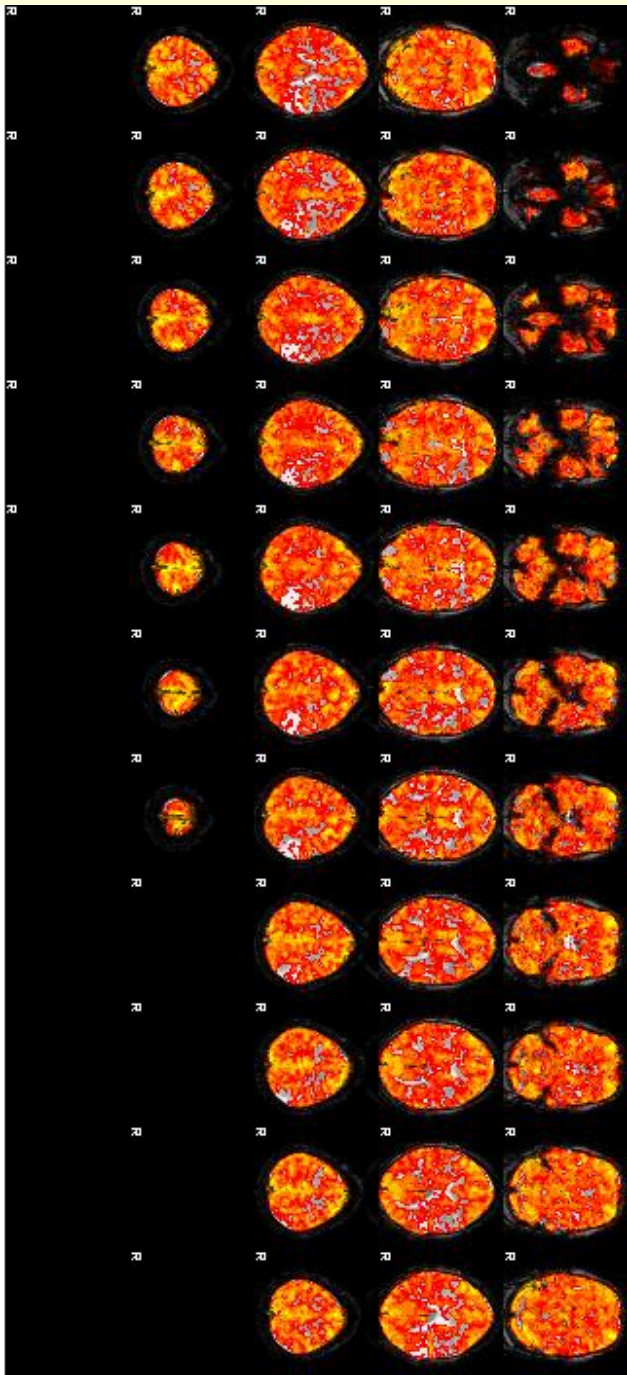
- Low grade tumours preserve function within the lesion
- Non-glial tumours (low infiltrative) does not alter fMRI activation
- Malignant gliomas loses vasculature autoregulation ⟶ loses activation
- Large Tumour masses compress veins ⟶ no bold effect

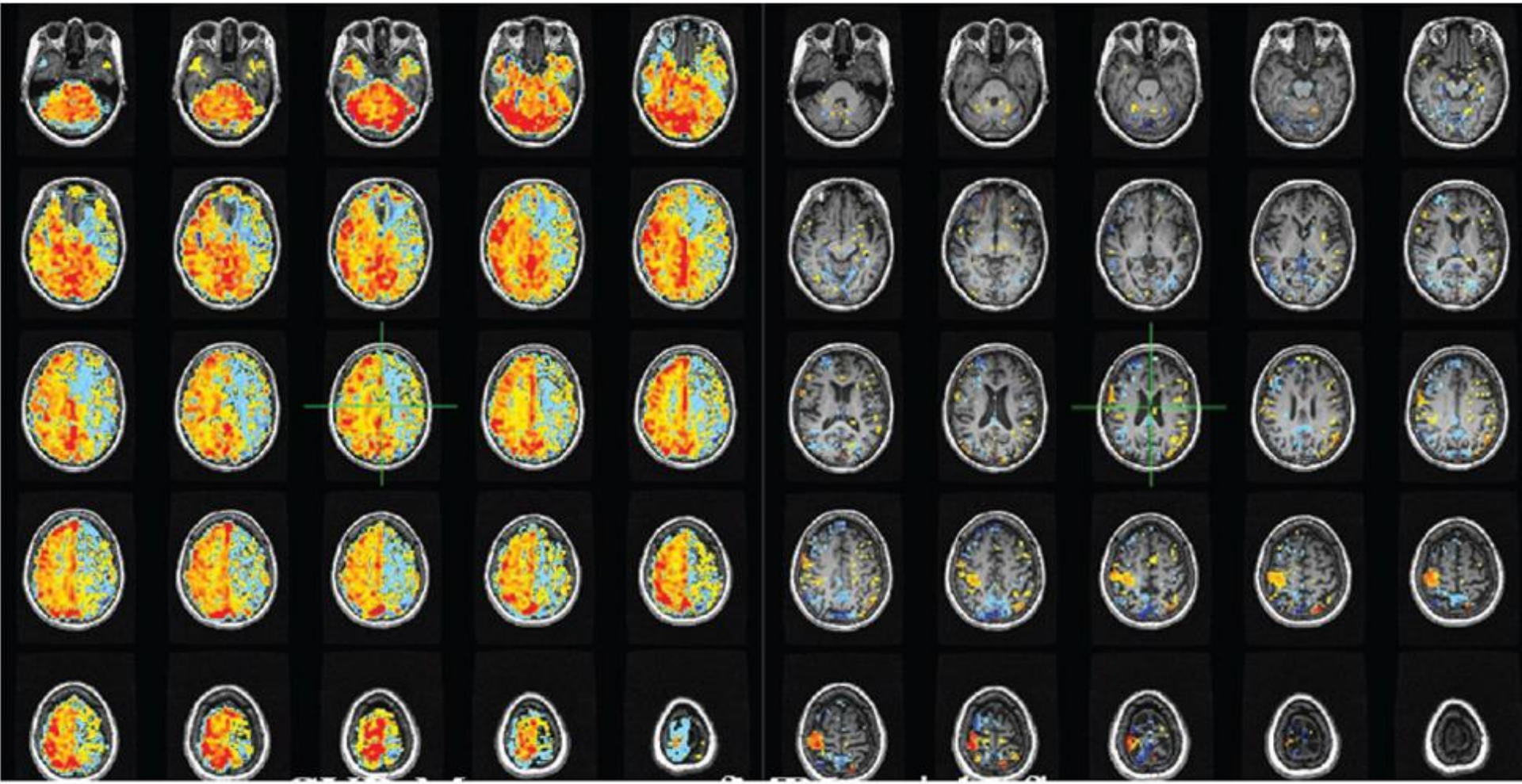
2. fMRI and Epilepsy

- Bilateral (& widespread/atypical) activation in earlier onset of dominant temporal lobe seizure, also in children

CVR (Clebro-Vascular Reactivity) Showing CBV defect around tumor region







CVR Map

fMRI – right finger tap

CVR in patient with stenosis of the left internal carotid artery (MCA territory).

A right-sided finger-tap motor paradigm shows only right-hemispheric activation. This is due to type II error caused by neurovascular uncoupling.

Pre-requisites for fMRI/DTI analysis

- Probability and Statistics
- Computer programming: ATHLAB/python/UNIX shell scripting
- Linear Algebra: GLM/image processing
- MRI: data acquisition/artifacts
- Neurophysiology & biophysics: Neuron activities & blood flow/hemodynamic response
- Signal & Image processing: Fourier analysis based processing

2007 (Res. 3)*

PRACTICE GUIDELINE FOR THE PERFORMANCE OF FUNCTIONAL MAGNETIC RESONANCE IMAGING OF THE BRAIN (fMRI)

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily

Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

This guideline was developed and written collaboratively by the American College of Radiology (ACR) and the American Society of Neuroradiology (ASNR).

fMRI Report for patients

MIC

NeuroImaging and Analysis Group
Research Center for Molecular and Cellular Imaging
Imam Khomeini Imaging Center, Imam Khomeini Hospital, Tehran/Iran

NIAG

Brain fMRI with BOLD effect **Imaging date: ……..**

Patient Name: ---------- **Age**: --------- Right/Left Handed

Infarct/Lesion location (based on MRI report): ----------
Other MRI studies exist for this Patient: □ Post Gd, □ fMRI, □ MRS, □ DWI, □ DCE/Perfusion

MRI Sequence: 2D EPI, 20 Axial slices: 3 mm thick, Resolution: 3×3 mm, ----- Volume,
Co-planar with AC–PC line
***Task and Experimental Design*:** Block design, Task: ----------: Paradigm----------

Pre-processing steps: B0 distortions Slice timing correction | | HP Filtering size LP Spatial filtering size: ---------- Motion correction □, DOF (3/6/9/12)--------
fMRI statistical Analysis: All activation maps were reconstructed by GLM analysis using FSL (FMRIB Software Library), with optimized parameters developed in NIAG lab. BOLD signal above Z- value (activation strength) of ……. were obtained, and superimposed on □T1/□T2/□post-Gd data with accuracy of few millimeters. Clusters small than …….. voxels were deleted in order to increase False Positive (FP) voxels. Anatomical Mask was used to delete FP voxels □, Type of Masks used: ……

fMRI Report for patients

Results specification:

Activation area with red color (less z-stat) shows the lowest activation level accepted as significant activation with p-value of p<……. The maximum activation strength produced for this patient is also indicated on each image in (yellow color).

Finding:

Please check and describe location of lesion as compared to regional anatomy (sulcus and gyrus), lesion dimension, mass effect, etc.

Motor fMRI:

Check for localization of motor cortex, supplementary motor area, and describe proximity between the lesion and any given functional areas (eg; PMC, SMA, sensory representation of the upper/lower limb or face) (close or far). Check if tumor/lesion invaded the activation area and WM fibers (eg. cortico-spinal track).

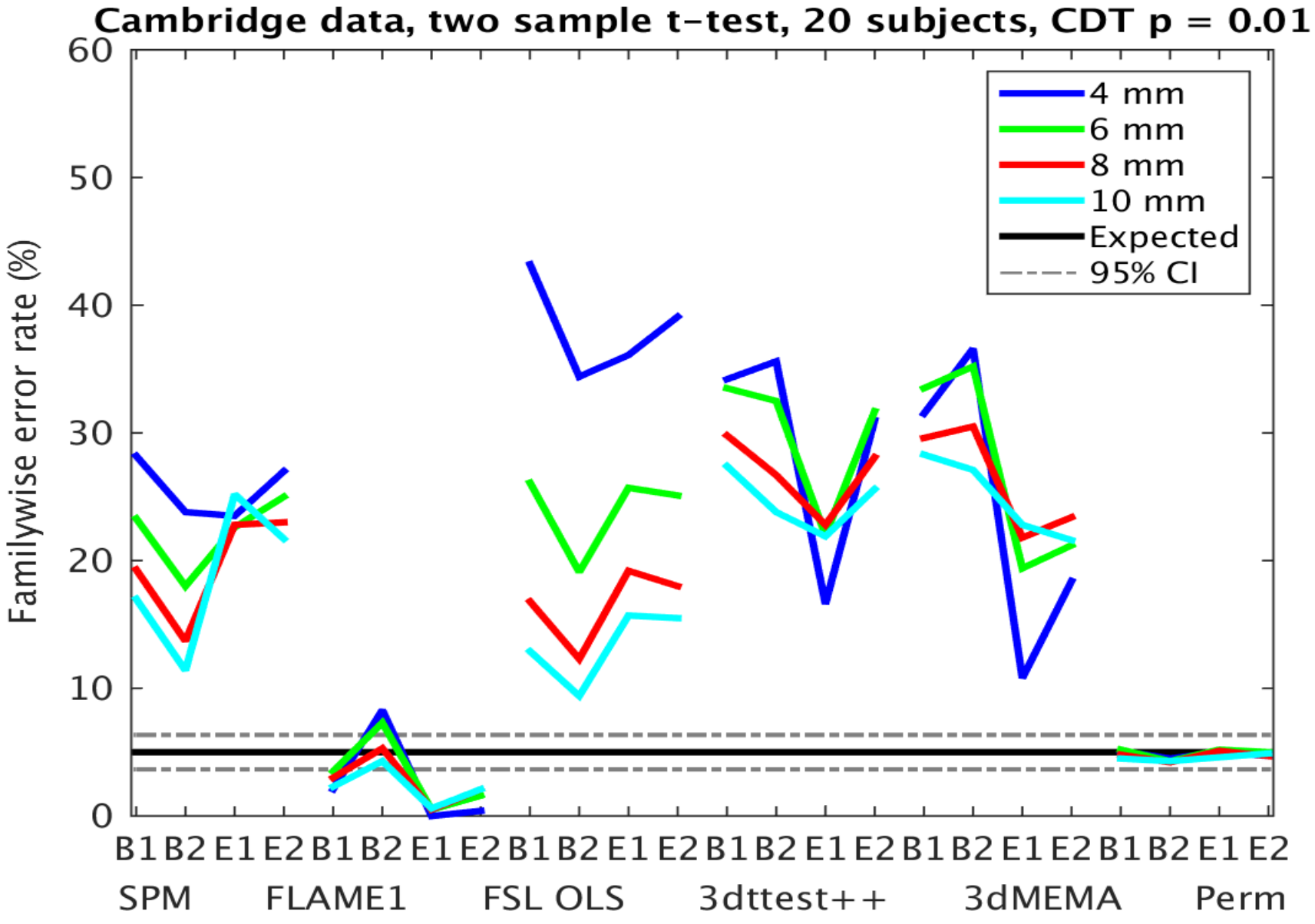
Language fMRI:

Check for hemispheric dominance for language in frontal and temporal lobes (right/left/bilateral with left or right dominance symmetrical). Describe location of activation as compared with lesion and proximity (close or far).

You may also be interested to check for any possible relocation of known functional areas due to lesion.

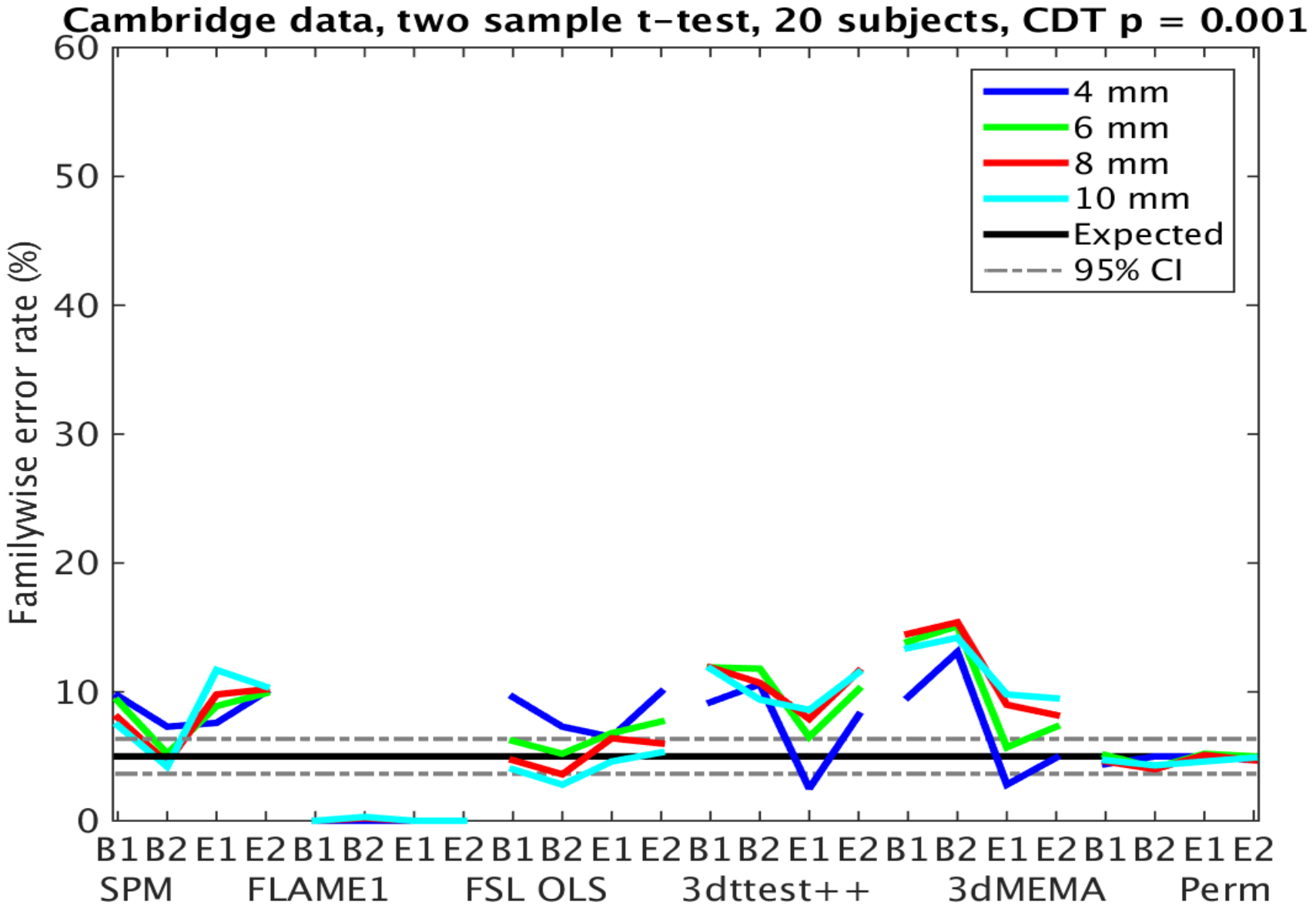
Medical Physicist: **Radiologist:**

Can any software be Trusted for fMRI or DTI studies?

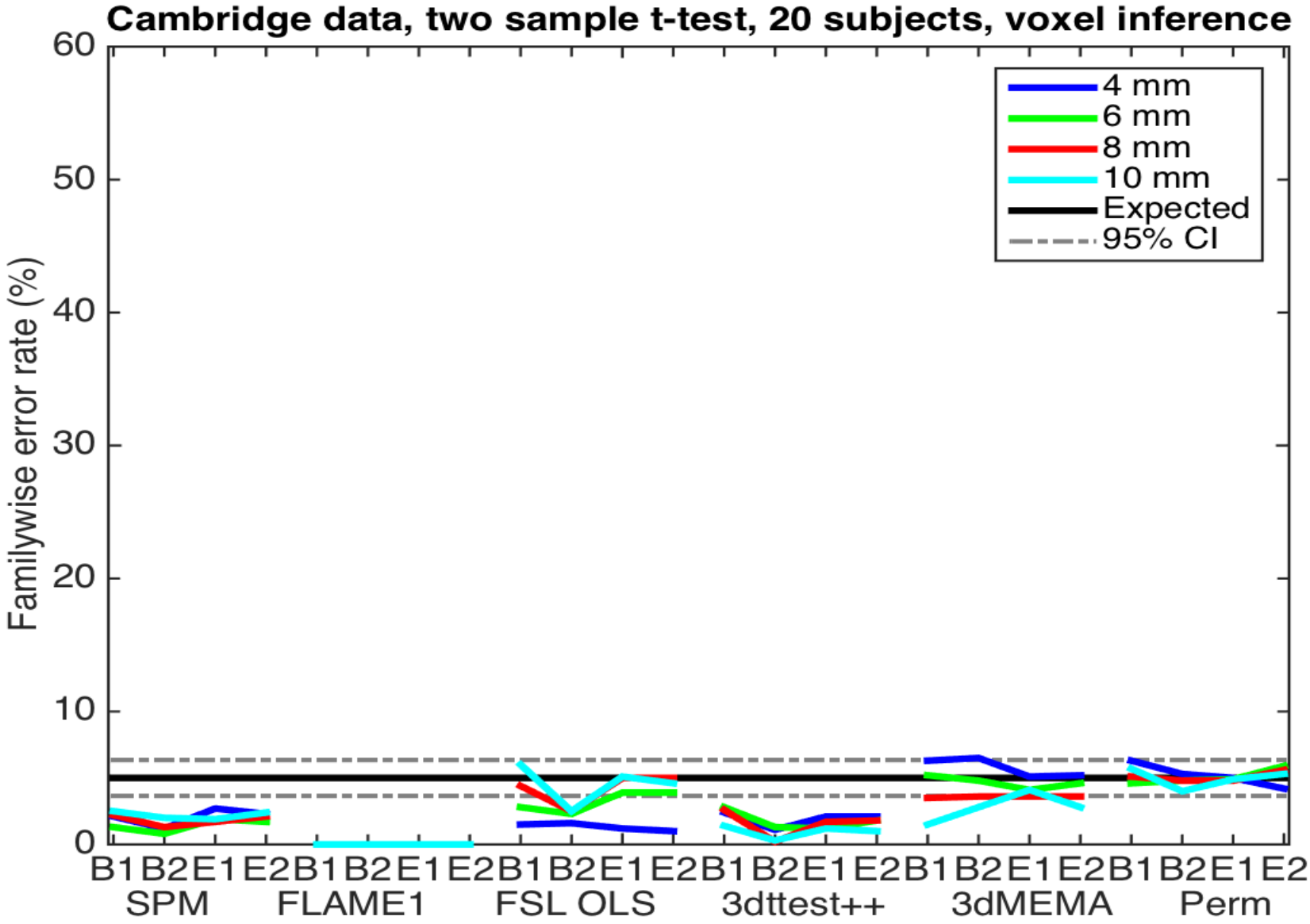


Results for cluster-wise inference, showing estimated familywise error rates for 4-10 mm of smoothing for SPM, FSL, AFNI and a permutation test. These results are for a group size of 10 (giving a total of 20 subjects)

CAN PARAMETRIC STATISTICAL METHODS BE TRUSTED FOR FMRI BASED GROUP STUDIES?
Anders Eklund , Thomas Nichols , Hans Knutsson



Same test for p=0.001



Same test using voxel-wise inference

Conclusive Remarks

- Technician-operated and automated vendor procedures, using streamlined software and turnkey hardware are not sufficient for accurate pre-surgical fMRI/DTI mapping.

- Interdisciplinary teamwork is necessary for standard presurgical brain mapping.

- We believe the role of neuroimaging research laboratories in promoting and validating presurgical planning services is not avoidable.
  - Such institutes possess the essential infrastructure and skills and can provide patients with standard presurgical planning services, given that they develop collaborations with clinical departments.

Tehran University of Medical Sciences

Research Center for Molecular and Cellular Imaging

NeuroImaging and Analysis Group

Medical Imaging Center, Imam Khomeini Hospital Complex

Thanks

Oghabian@tums.ac.ir

www.NIAG.ir

NIAG
NeuroImaging and Analysis Group

You may visit our Lab here or in the Emam-Khomeini Hospital