fMRI: Theoretical Principles and Clinical Applications

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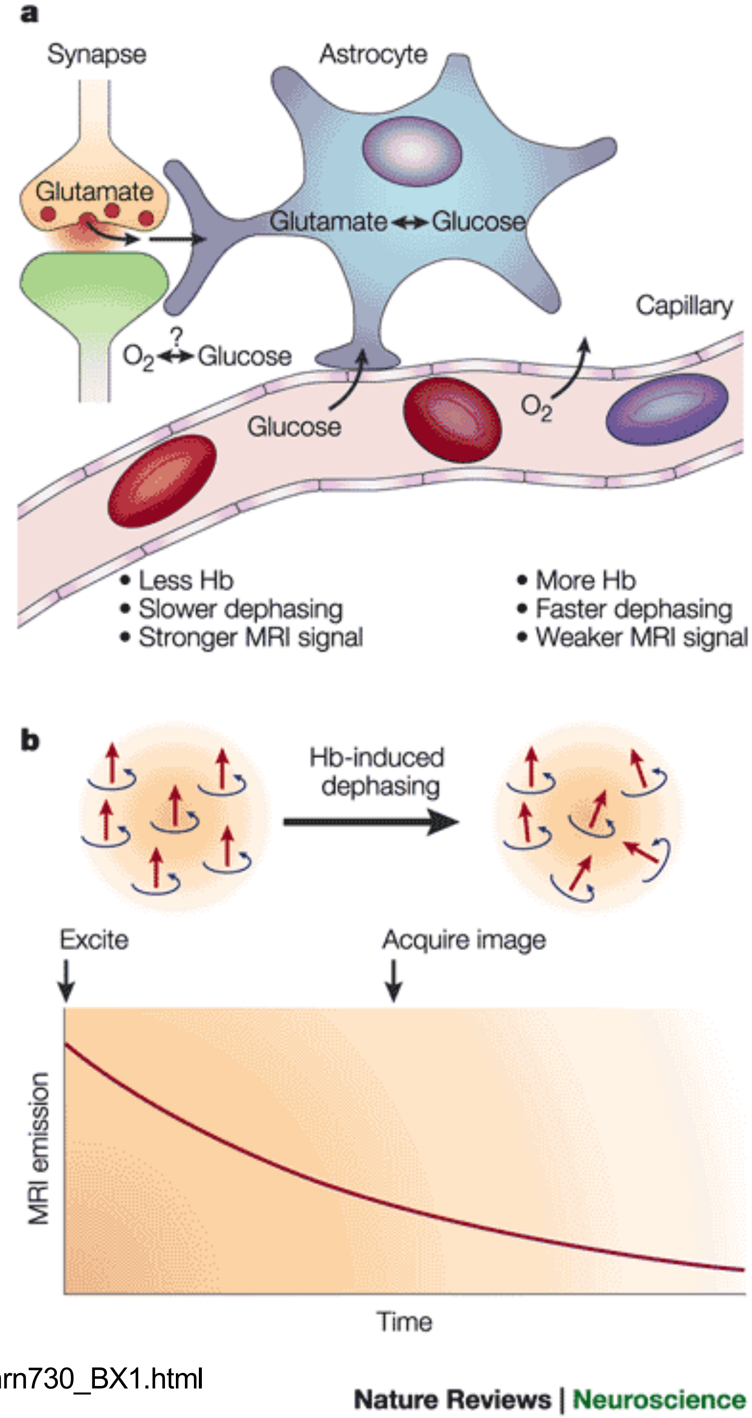
Overview

1. Where does the fMRI signal come from
2. How is fMRI acquired
3. Block design
4. Event-related design
5. Experimental design
6. Caveats
7. The use of clinical fMRI

Where does the fMRI signal come from

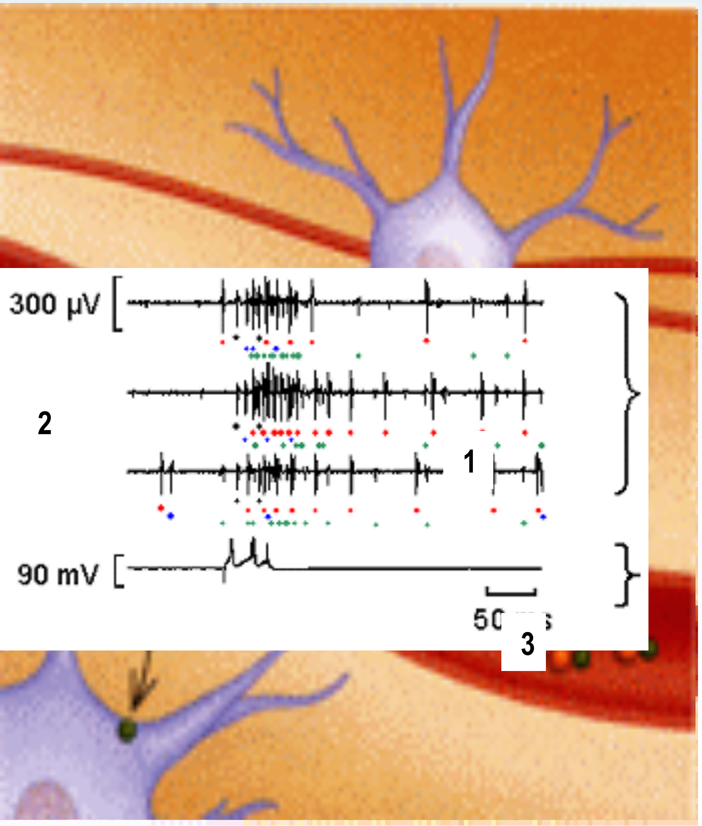
Functional MRI

- Evaluating physiological alterations in brain tissue during normal activity
- Blood oxygen level dependent (BOLD) effect
  - Oxyhaemoglobin (diamagnetic)
  - Deoxyhaemoglobin (paramagnetic)



http://www.nature.com/nrn/journal/v3/n2/box/nrn730_BX1.html

Visualising the brain at work



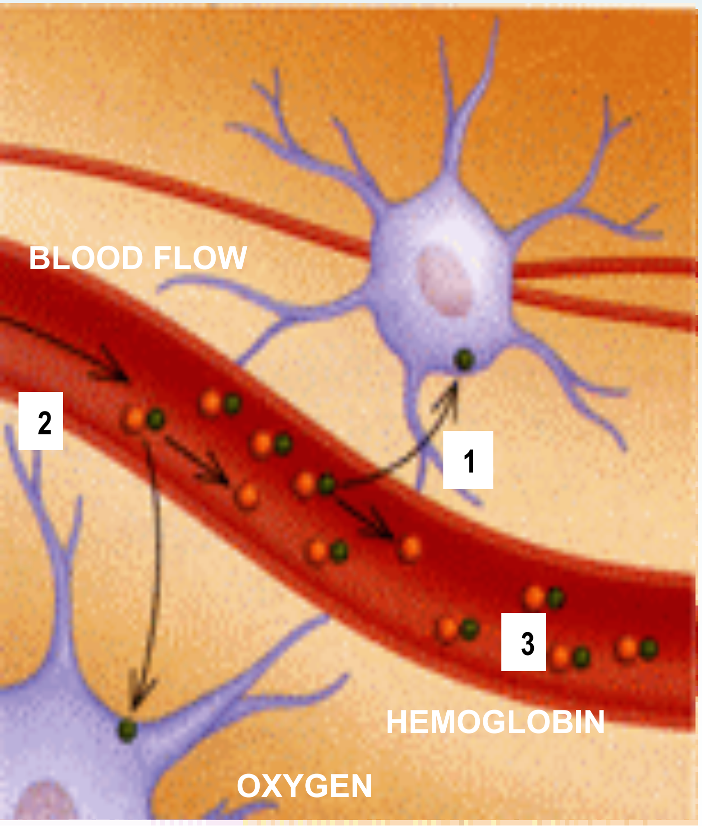
Increase in
neuronal activation

slight increase in O_2 extraction (1)
+
large increase in perfusion (2)

increase oxyHb / deoxyHb (3)

increase in T2* MR signal

Visualising the brain at work



Increase in
neuronal activation

↓

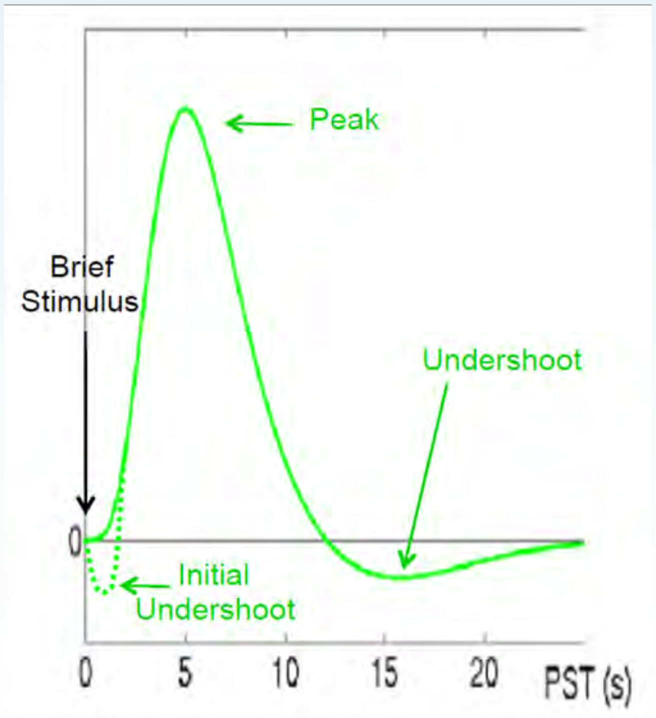
slight increase in O_2
extraction (1)
+
large increase in perfusion (2)

↓

increase oxyHb / deoxyHb (3)

↓

increase in T2* MR signal



BOLD fMRI

- Indirect measure of neuronal activation
- Small contribution of veins to signal change
- Influence of pathology/drugs on BOLD contrast
  - Compression of microvasculature by tumor & edema
  - Metabolism changes induced by pathology, .e.g pH changes
  - Metabolism/CBF/CBV changes induced by drugs

=> fMRI activation reduced or absent

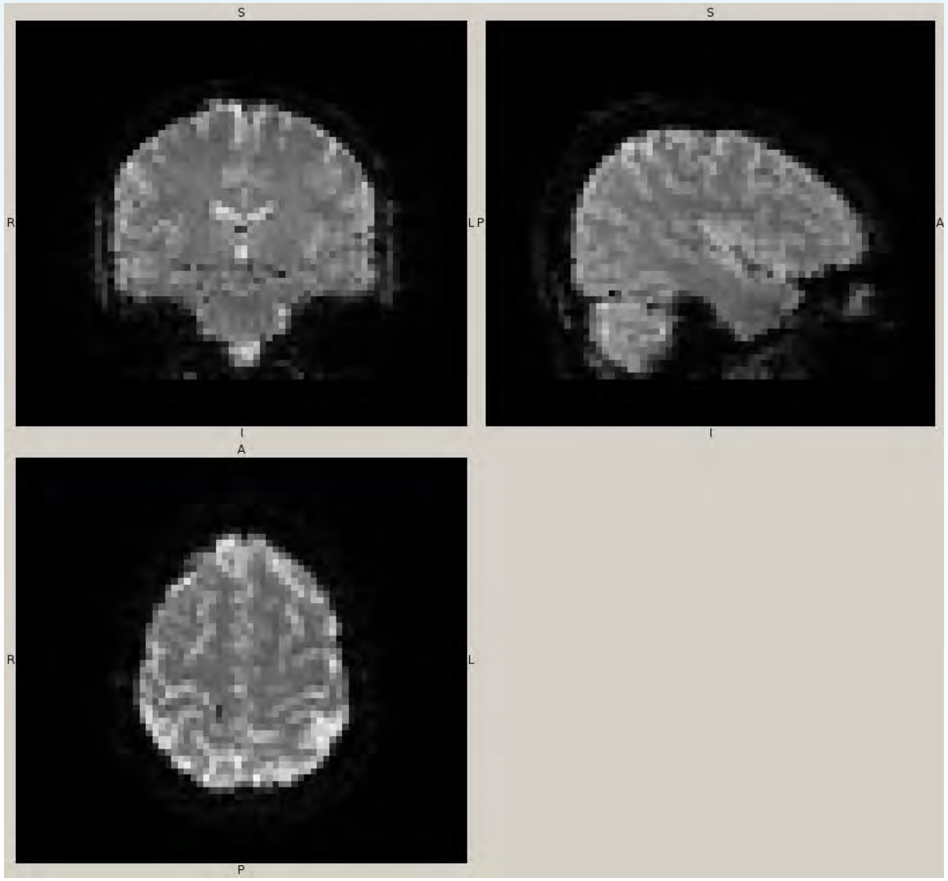
How is fMRI acquired

Paradigm presentation

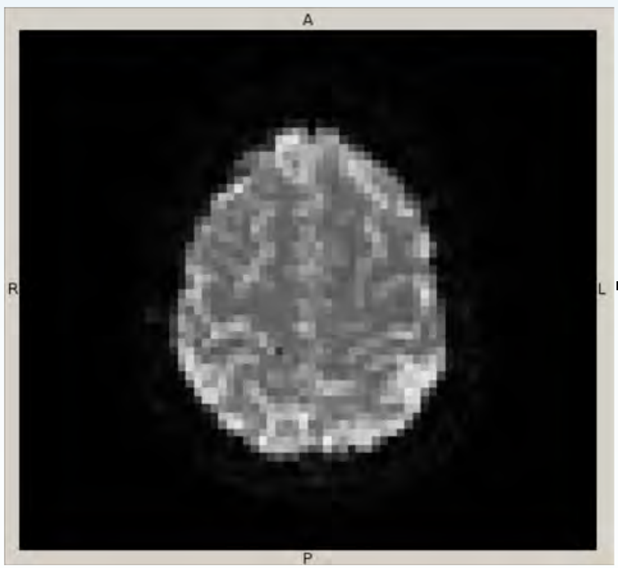
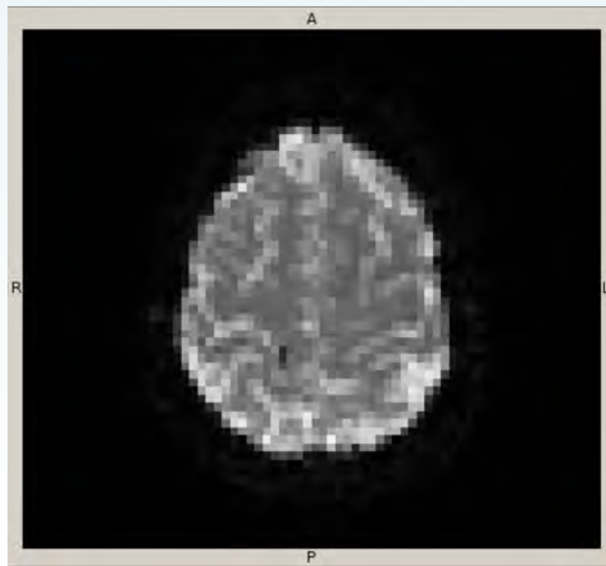
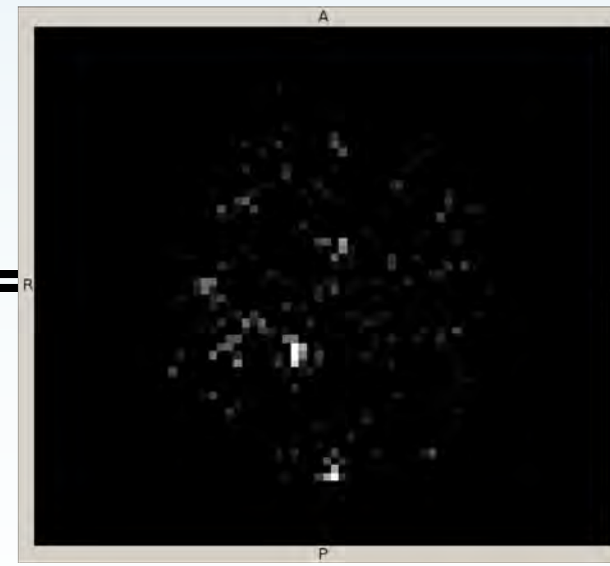
- Monitor or Screen + projector or goggles
- Computer with vendor or in-house software
- Connection Scanner Trigger to Computer
- Response device

MRI Basis: T_2*- contrast

– Gradient Echo
– Fast Imaging WHOLE HEAD
– EchoPlanarImaging:
  • 64x64 matrix
  • TE ~ 30/50 ms (3T/1.5T)
  • up to 49 slices
  • TR ~ 2 to 3 s
– SMALL voxels
  • about 3 x 3 x 3 mm^3
– Large bandwidth
– Parallel imaging / Multiband



MRI Basis: Subtraction

Finger movement		Rest		Activation
	-		=	

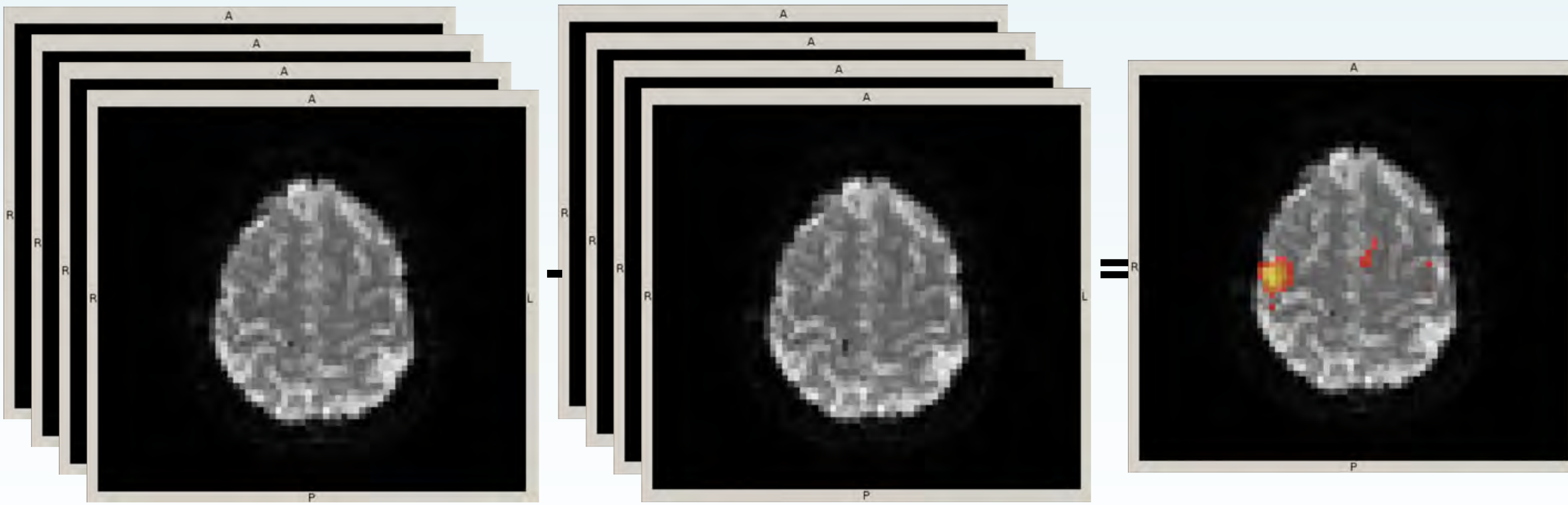
Changes < few %

MRI Basis: Subtraction

Task

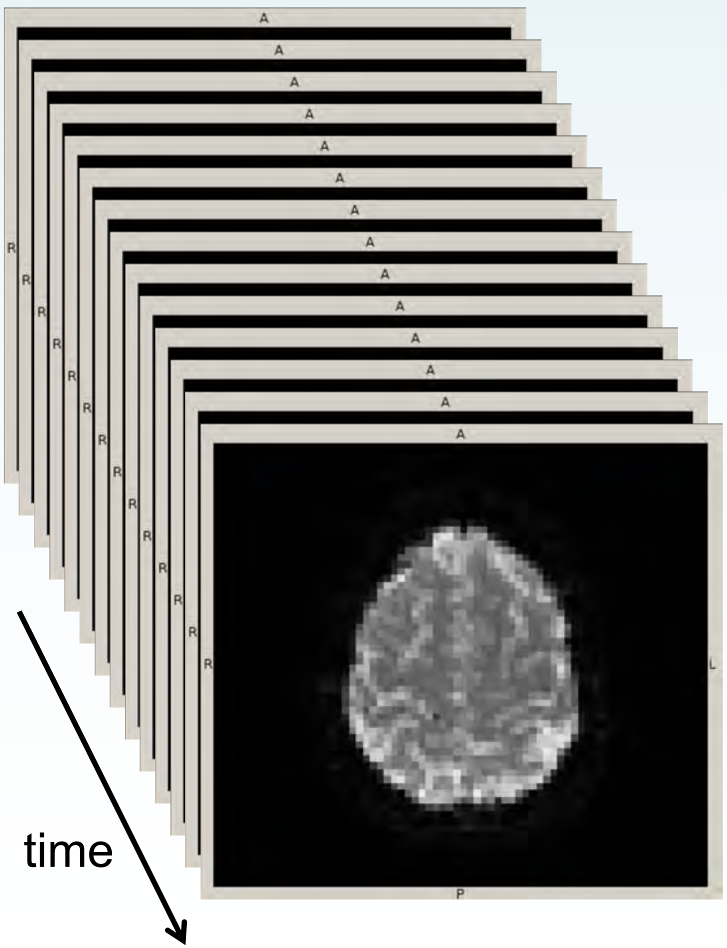
Rest

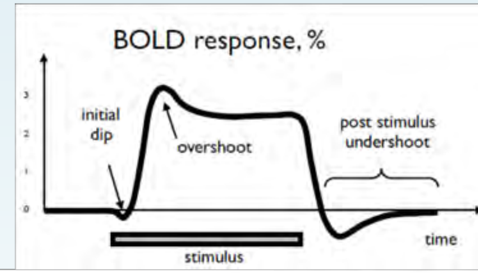
Activation

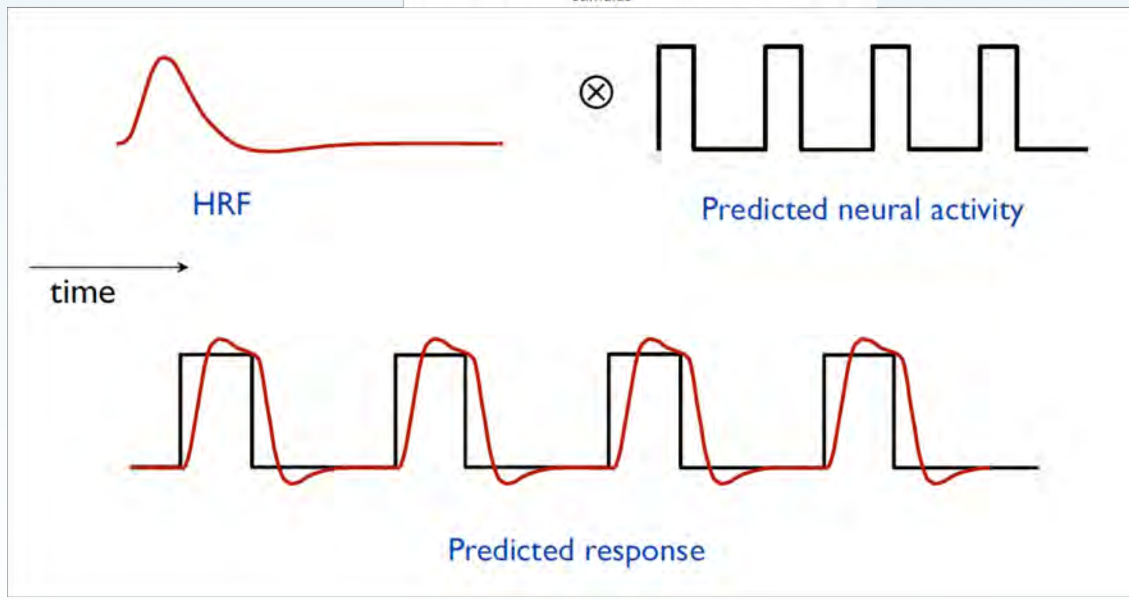


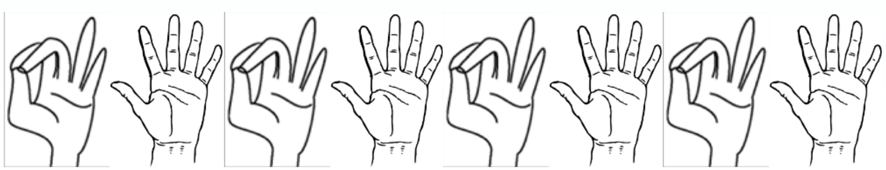
Block design

Block design





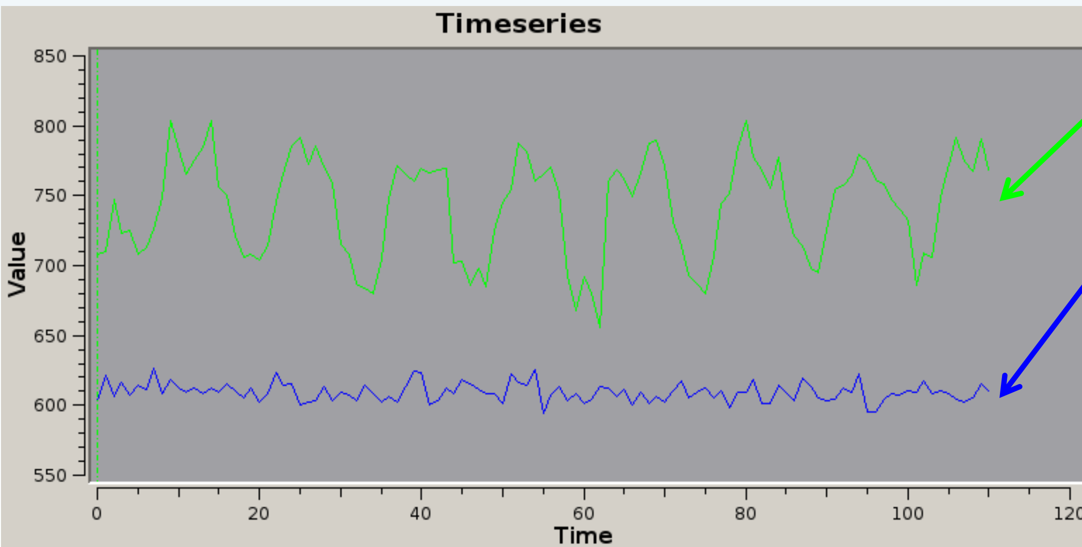


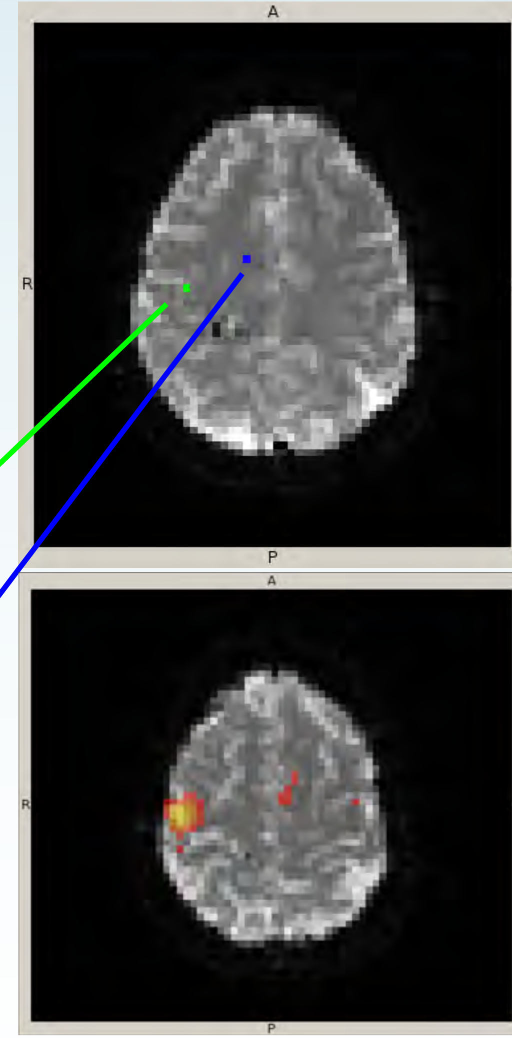


Block design

Fitting predicted response

to timeseries data





The coloured (statistical) map represents the degree of confidence that a voxel signal has changed according to the paradigm

Postprocessing – first steps

- Reconstruction
  - create image and remove gross artefacts
- Motion Correction
  - Get consistent anatomical coordinates (always do this)
- Slice Timing
  - Get consistent acquisition timing (use temporal derivatives instead)
- Spatial Smoothing
  - Improves SNR & validate GLM

Postprocessing – statistical inference

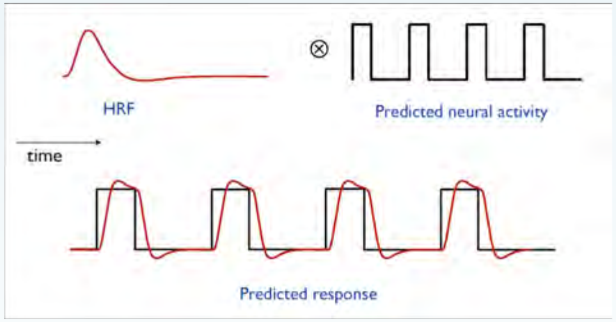
- Multiple-comparison corrections
  - Bonferroni
  - Family Wise Error (FWE)

    on average, 5% of all experiments have one or more false positive voxels

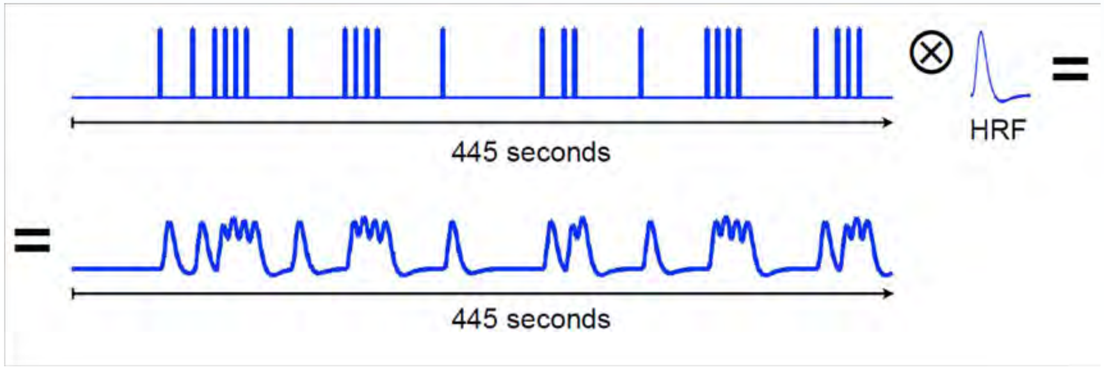
Event-related design

Block vs Event-related design

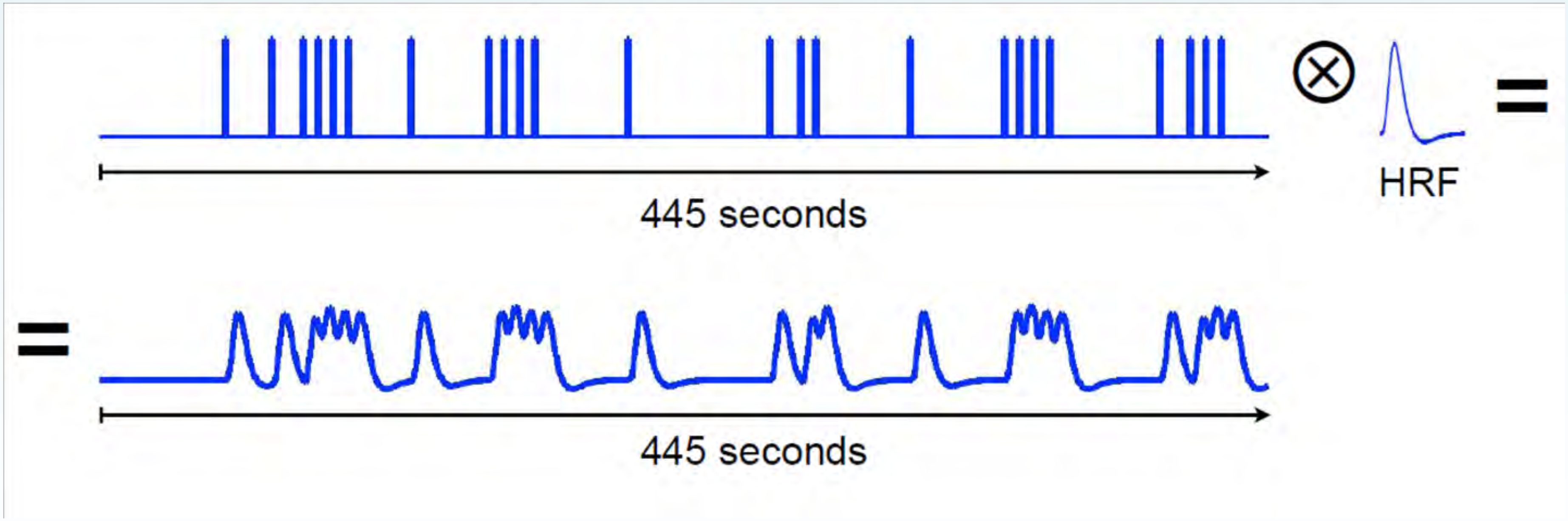
- Block/epoch designs examine responses to series of similar stimuli



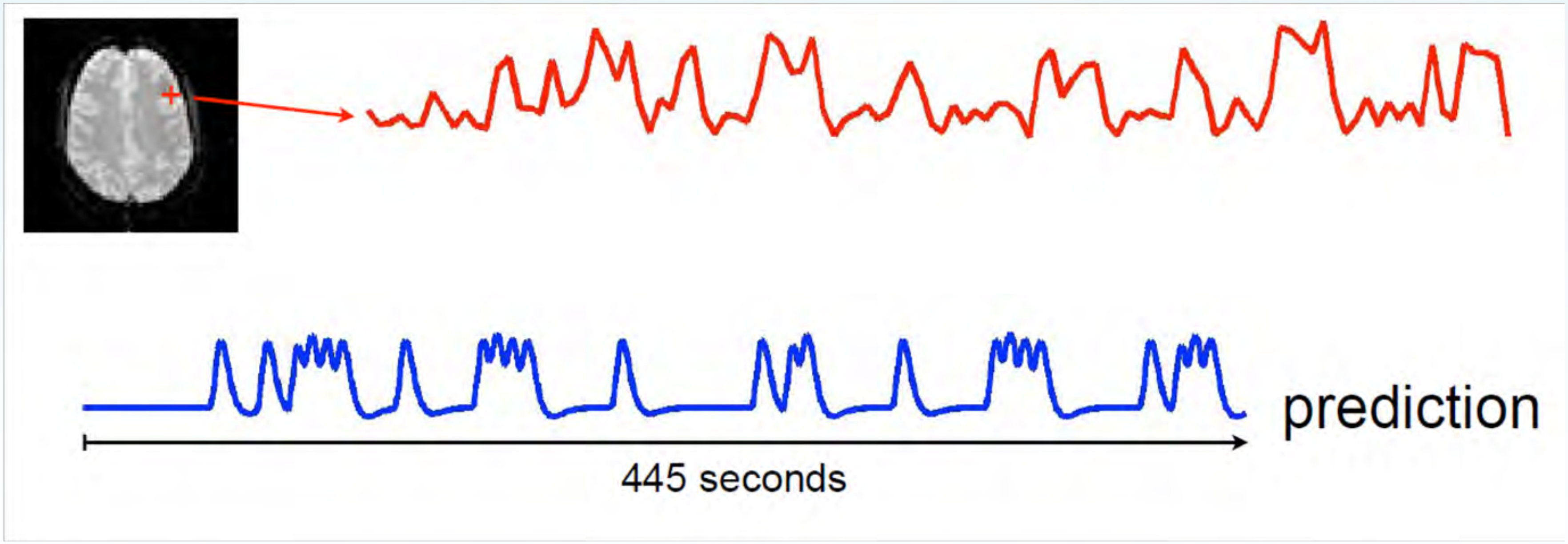
- Event-related designs account for response to each single stimulus



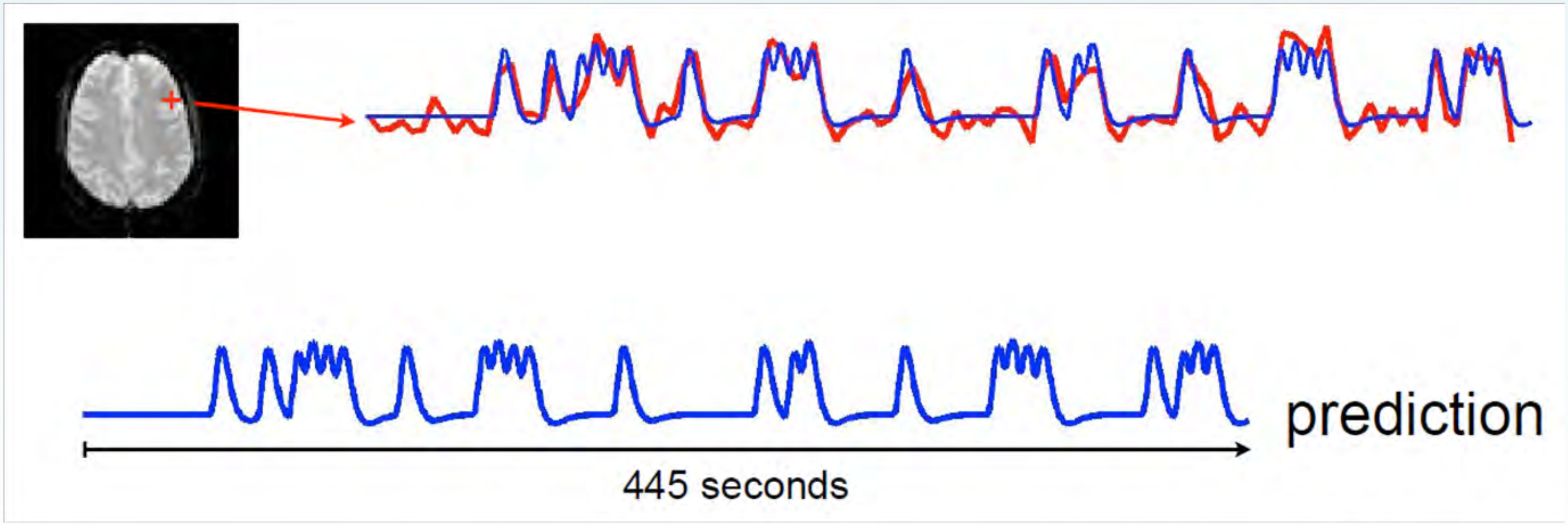
Event related design



Event related design



Event related design



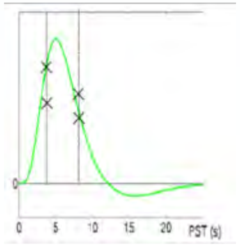
Advantages of event-related fMRI

- Randomised trial order
- Post-hoc subjective classification of trials
- Some events can only be indicated by participants
- Some events cannot be blocked due to stimulus context

Disadvantages of intermixed designs

- Less efficient for detecting effects than blocked designs
- Some psychological processes have to / may be better blocked (e.g. If difficult to switch between states, or to reduce surprise effects)

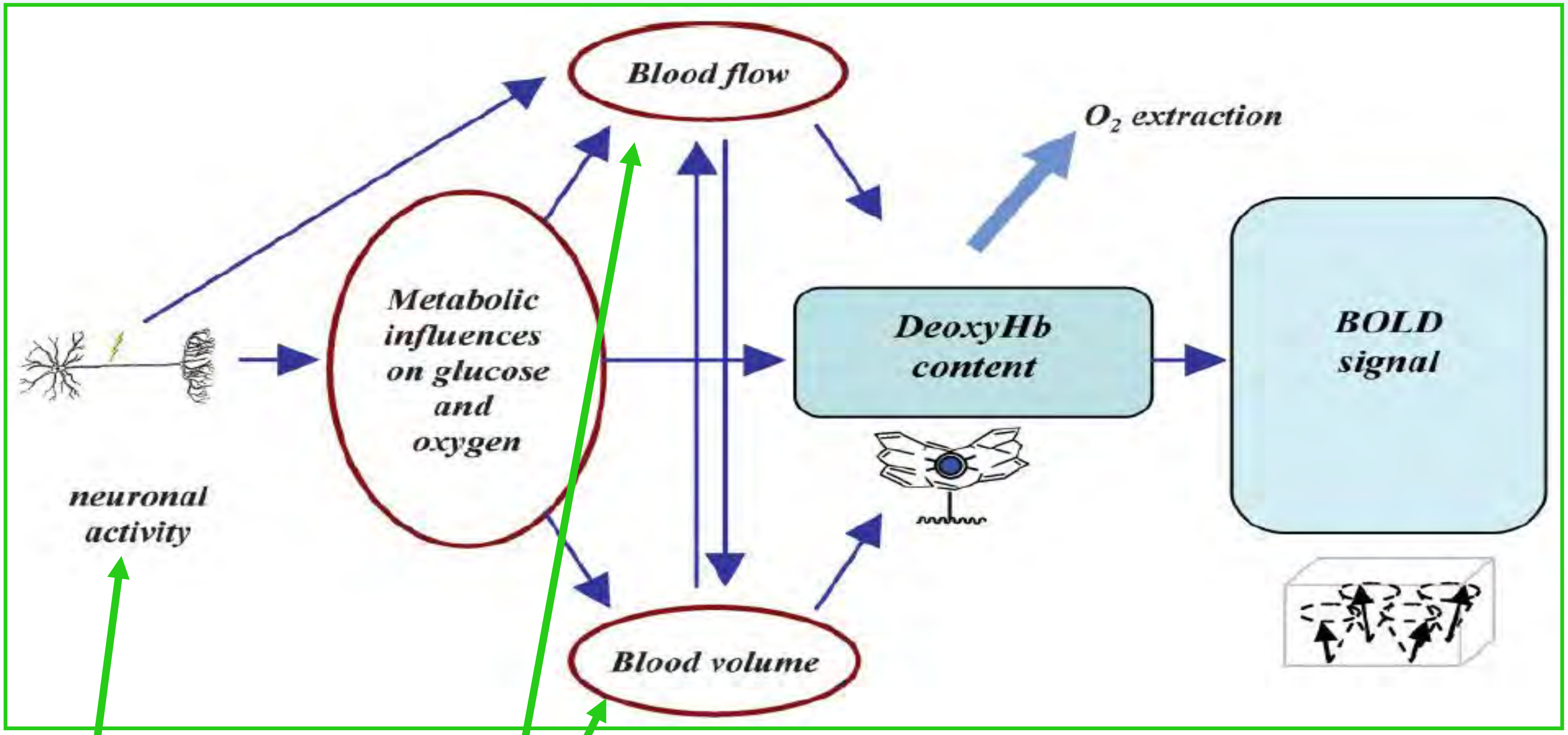
- Timing issue (sampling) particularly important for event-related design (“wrong“ post-stimulus timing might miss peak signal)



Caveats

BOLD fMRI

↑neural activity ➔ ↑ blood flow ➔ ↑ oxyhemoglobin ➔ ↑ T2* ➔ ↑ MR signal



pathology

pathophysiology

Source: P Jezzard et al., JMRI 2006;23:787-793

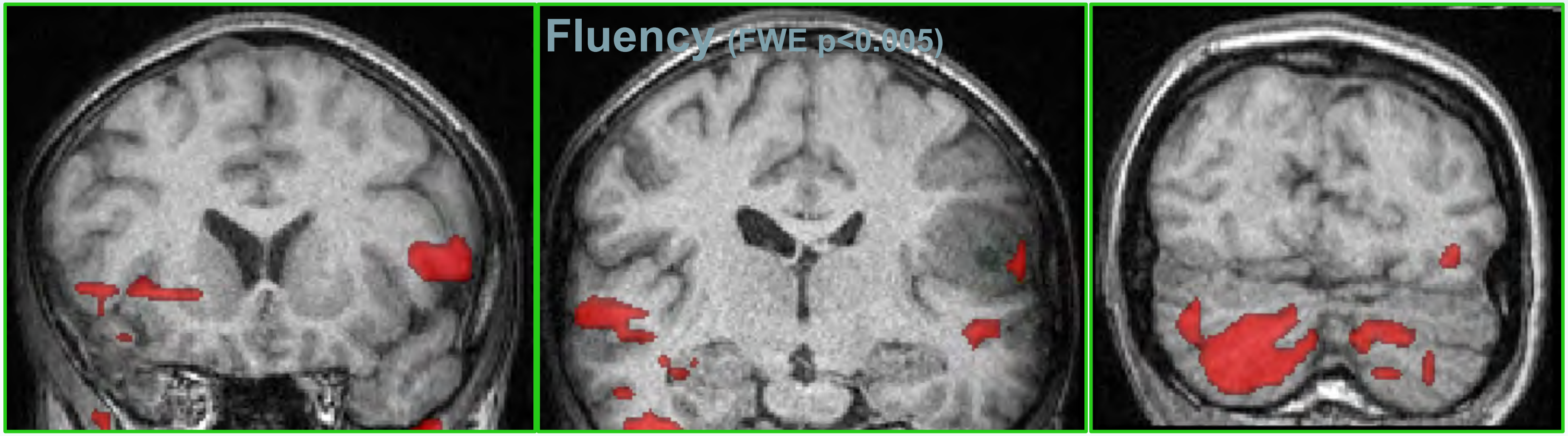
BOLD fMRI

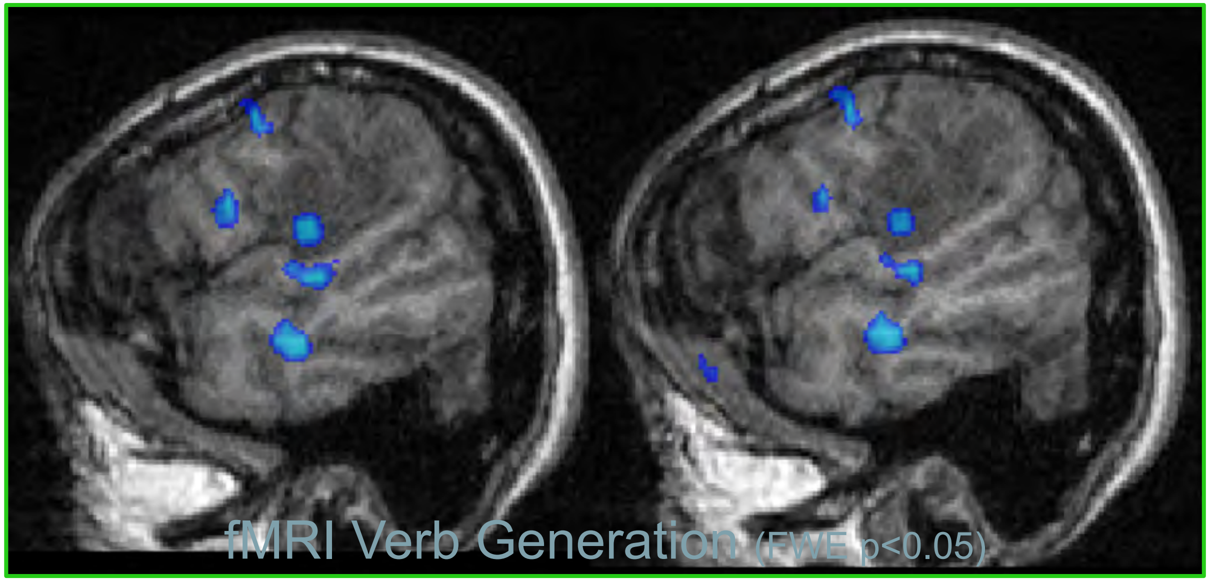
- Statistical maps
  - ⇒ Controls false positives, not false negatives
- No distinction of essential vs expendable brain regions

Pitfalls / Caveats ...

- Absence of activation $\neq$ no eloquent function
- Presence of activation $\neq$ eloquent area
  caution with activation in lesions!

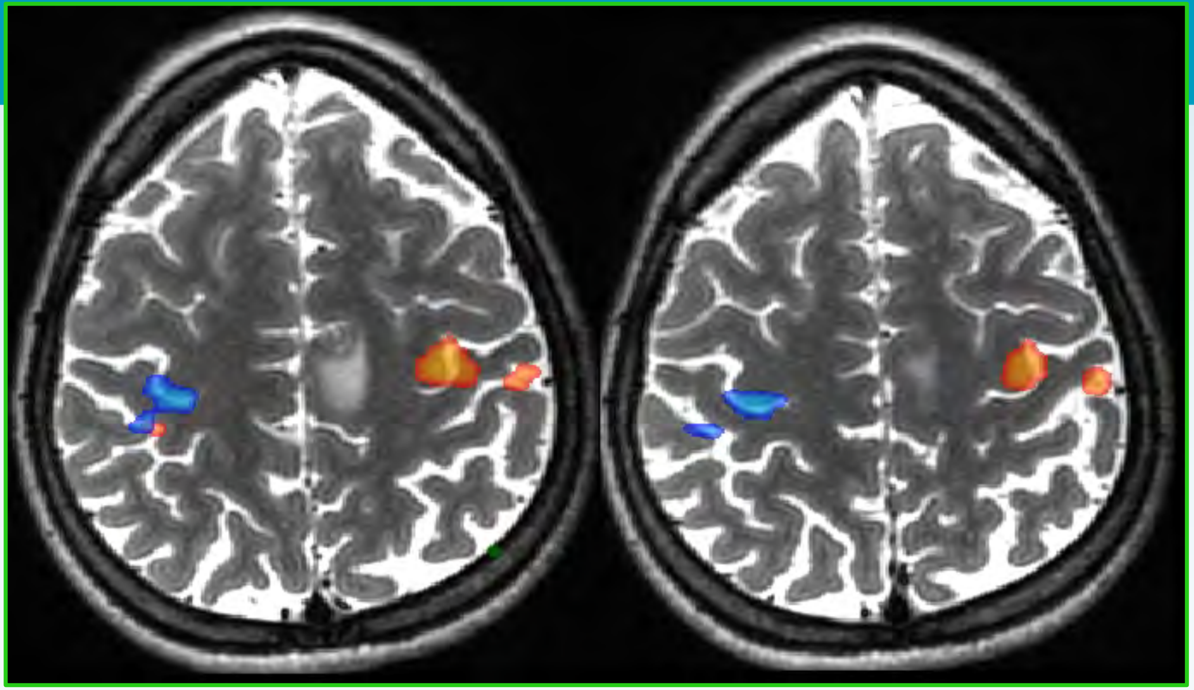
‘Activation’ within lesion



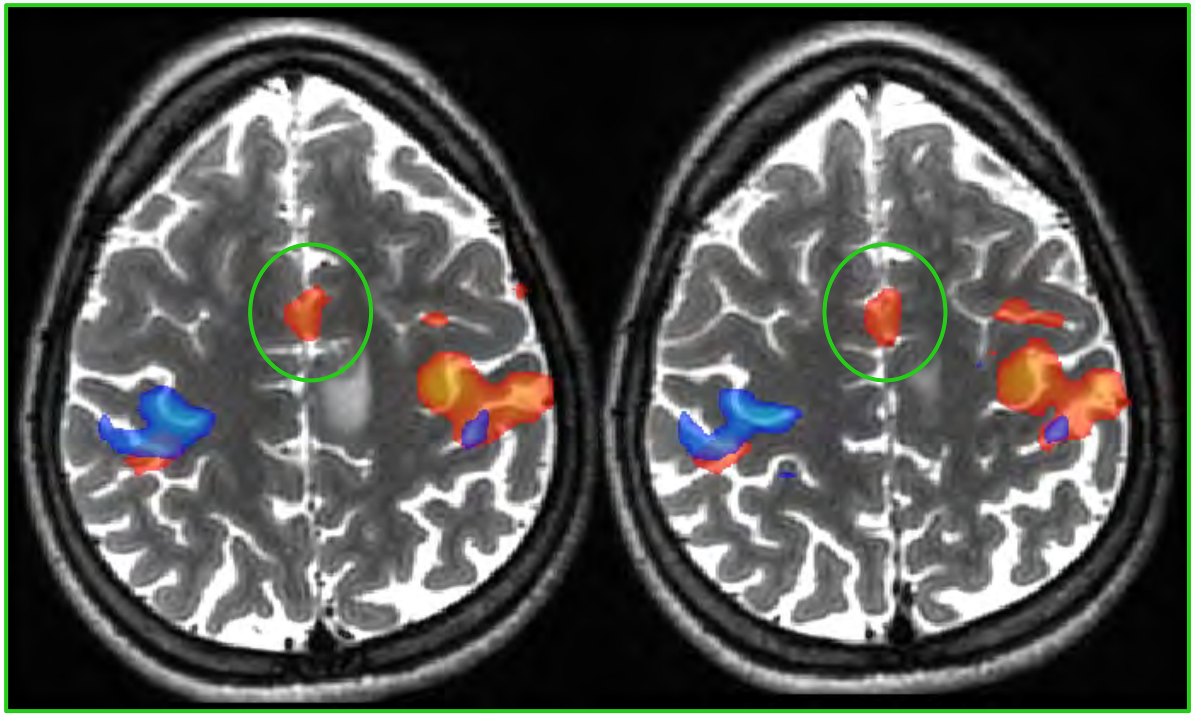


… Pitfalls / Caveats

- Distance between lesion and area of activity varies with varying tresholds



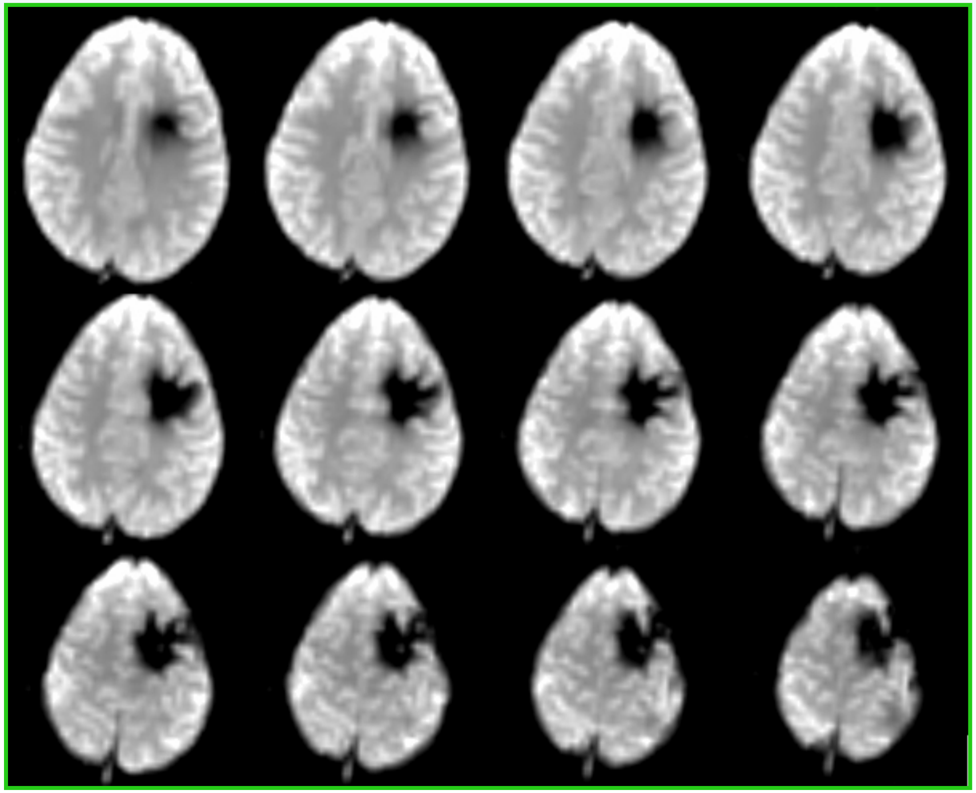
red = R hand FWE p<0.05
blue = L hand FWE p<0.05

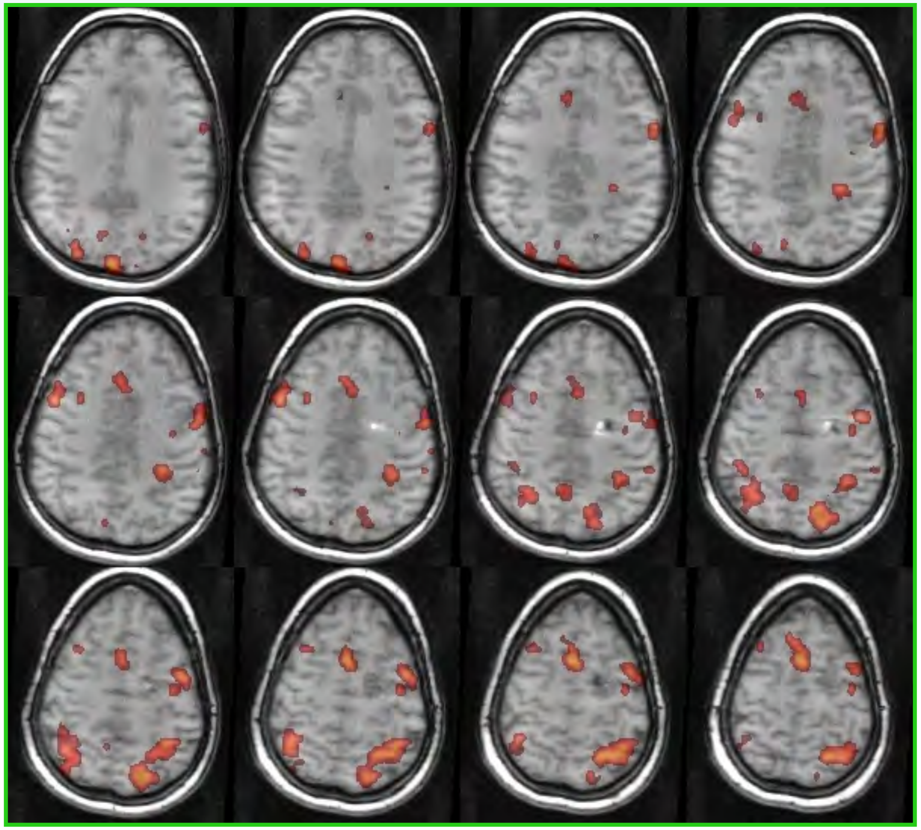


red = R hand FWE p<0.2
blue = L hand FWE p<0.2

… Pitfalls / Caveats

- Artefacts: movement, ghosting, instability, distortions, signal drop: air/tissue interface, haemosiderin deposits





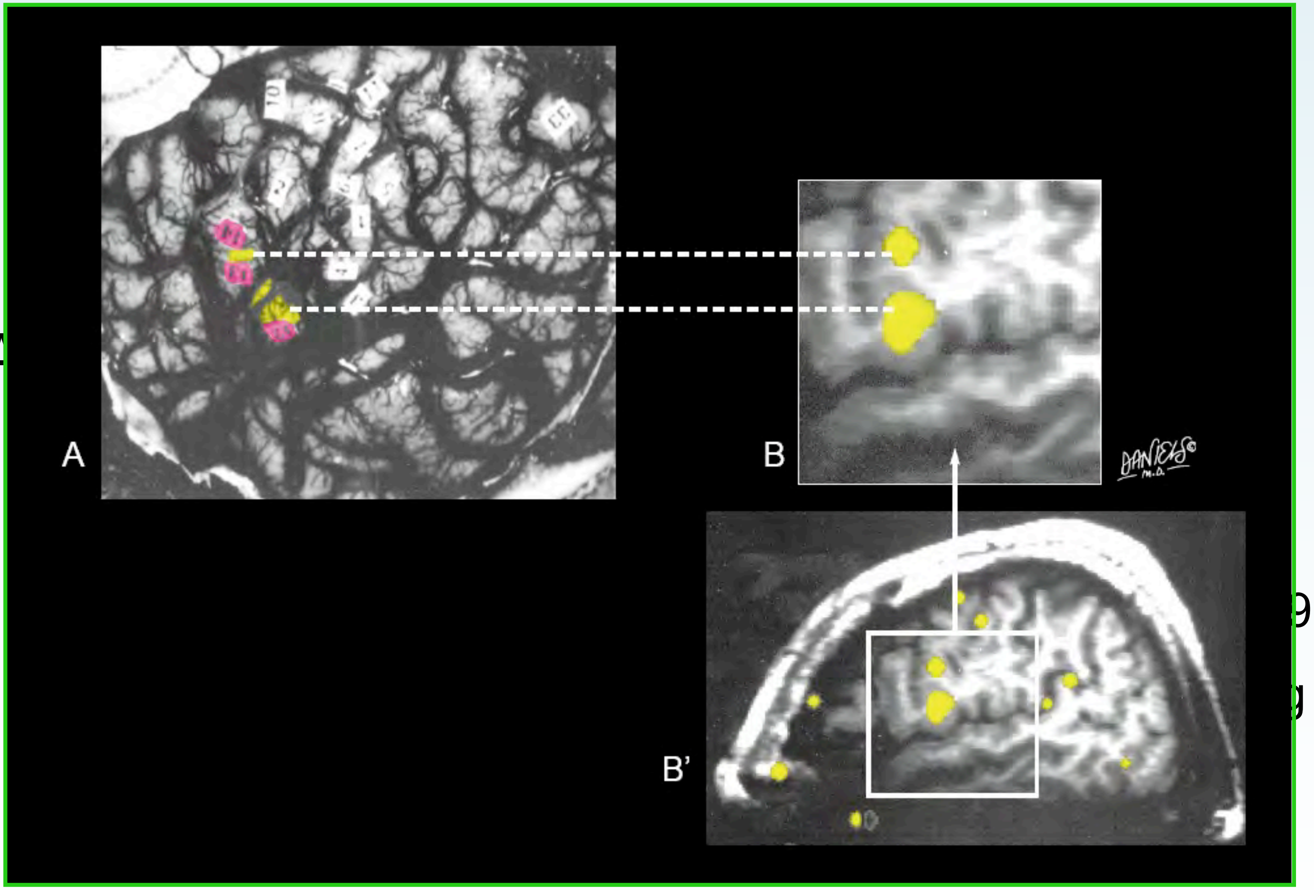
The use of clinical fMRI

Main clinical use today

- Preoperative evaluation
  - Surgical challenge:
    - maximize resection
    - minimize neurological deficit

- Role of fMRI
  - Assessing risk of neurological deficit following procedure
  - Selecting pts for invasive intraoperative mapping
  - Planning surgical approach

PARA



- Hand 95)

g 1996)

- Language/motor 28 < 20 mm (Yetkin AJNR 1997)

… more recently

- **Presurgical planning for tumor resectioning**
  Sunaert S, JMRI 2006

- **Localizing and Lateralizing Language in Patients with Brain Tumors: Feasibility of Routine Preoperative Functional MR Imaging in 81 Consecutive Patients**
  Stippich C, Radiology 2007

- **Presurgical Functional MR Imaging of Language and Motor Functions: Validation with Intraoperative Electrocortical Mapping**
  Bizzi A, Radiology 2008

Rule of thumb

Δ = Distance between lesion and peak activation

- $\Delta < 1$cm => deficit highly probable
- 1cm $< \Delta < 2$cm => deficit possible
- 2cm $< \Delta$ => deficit unlikely

Advantages of BOLD fMRI

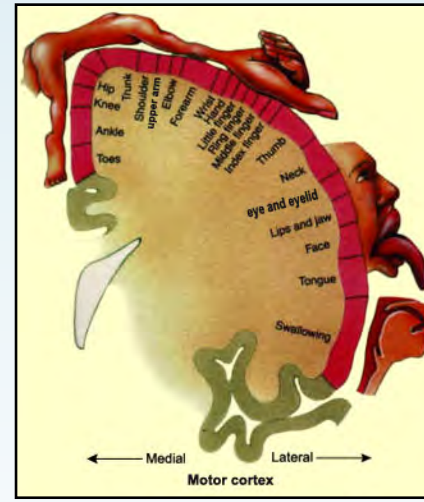
- High spatial and temporal resolution
- Short examination time
- Repetitive and longitudinal studies
- Non-invasive
- Cost effective
- Availability

…clinical applications

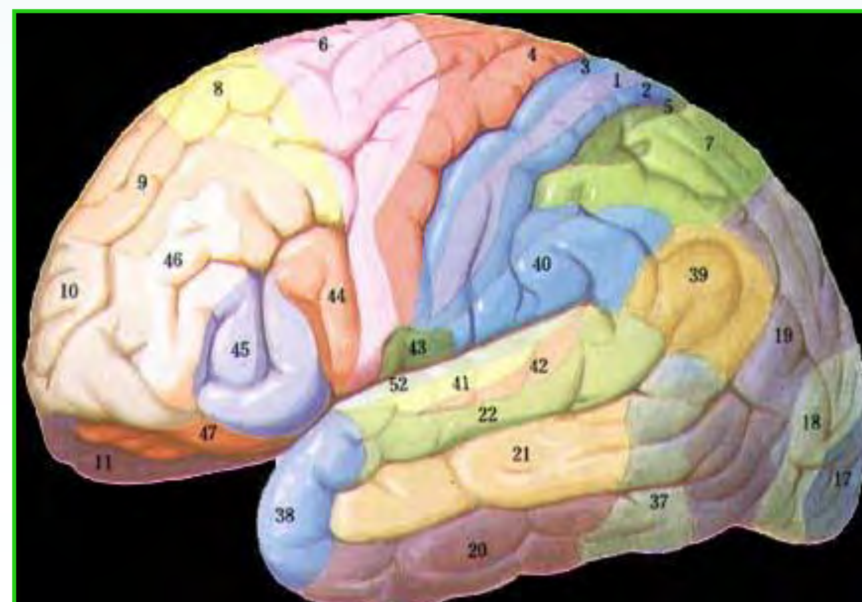
- Mass lesions - Tumours, Vascular malformations
  - Avoid eloquent areas in the surgical approach
  - Distortion / effacement of anatomical landmarks
  - Plasticity / re-organization of functional activity
  - Hemispheric dominance

- Epilepsy
  - Language lateralisation (replaced WADA test)
  - Combined with DTI to avoid optic pathways (Meyer‘s loop)

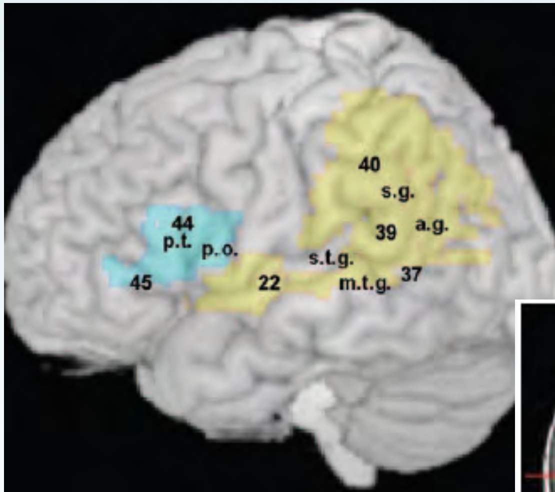
Clinical Paradigms

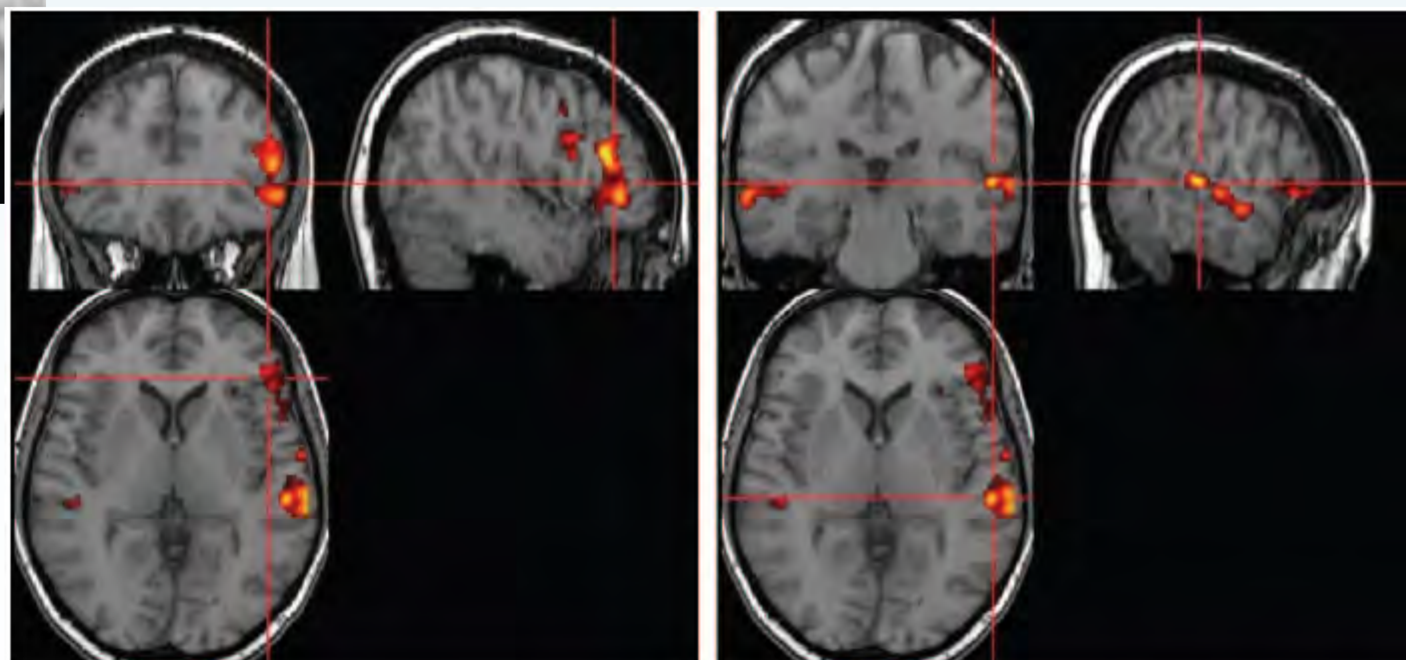


- Sensori-Motor
  - hands, feet, lips, tongue, eyes
- Language
  - verb generation, verbal fluency, naming, sentence comprehension, reading
- Vision
- Often Combined with DTI



Language



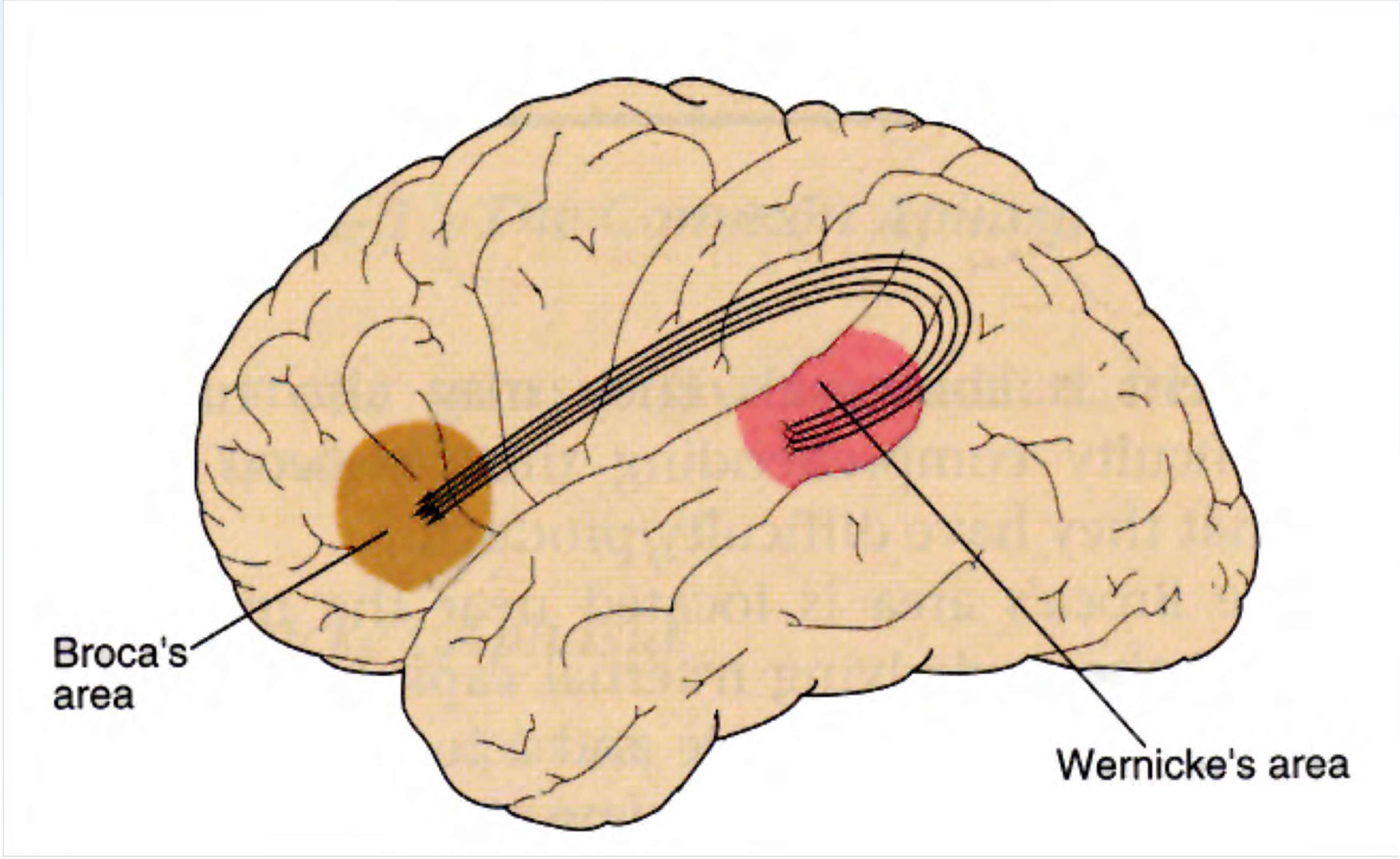


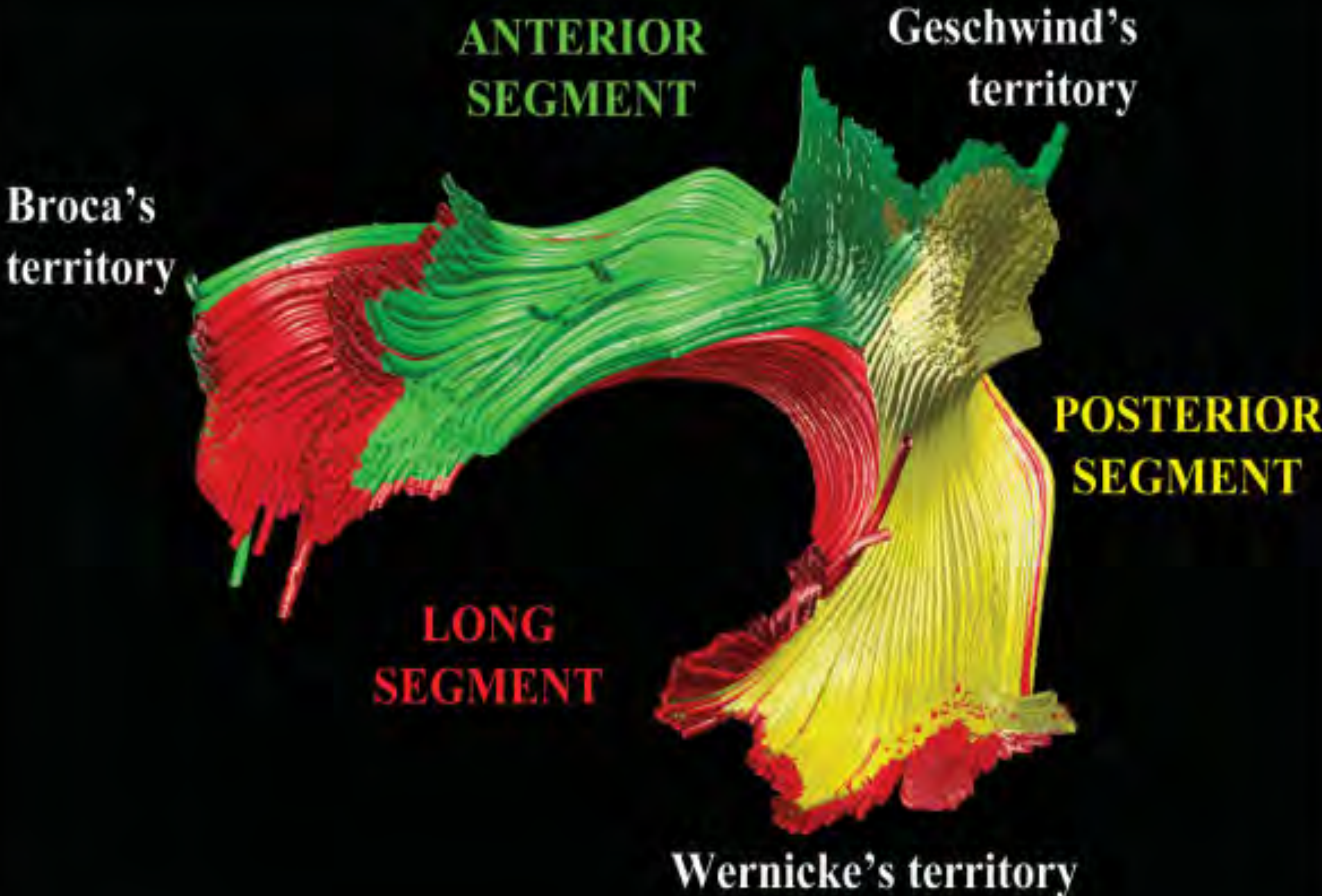
a. b.

Figure 8. Areas of activation for the phonologic paradigm as determined with a fixed-effects group analysis of six right-handed volunteers ($T > 5$, cluster > 10 voxels). High-resolution T1-weighted MR images show superimposed activation in the frontal **(a)** and posterior parietotemporal **(b)** language areas, predominantly in the left hemisphere.

M Smits et al. RadioGraphics 2006; 26:S145-S158

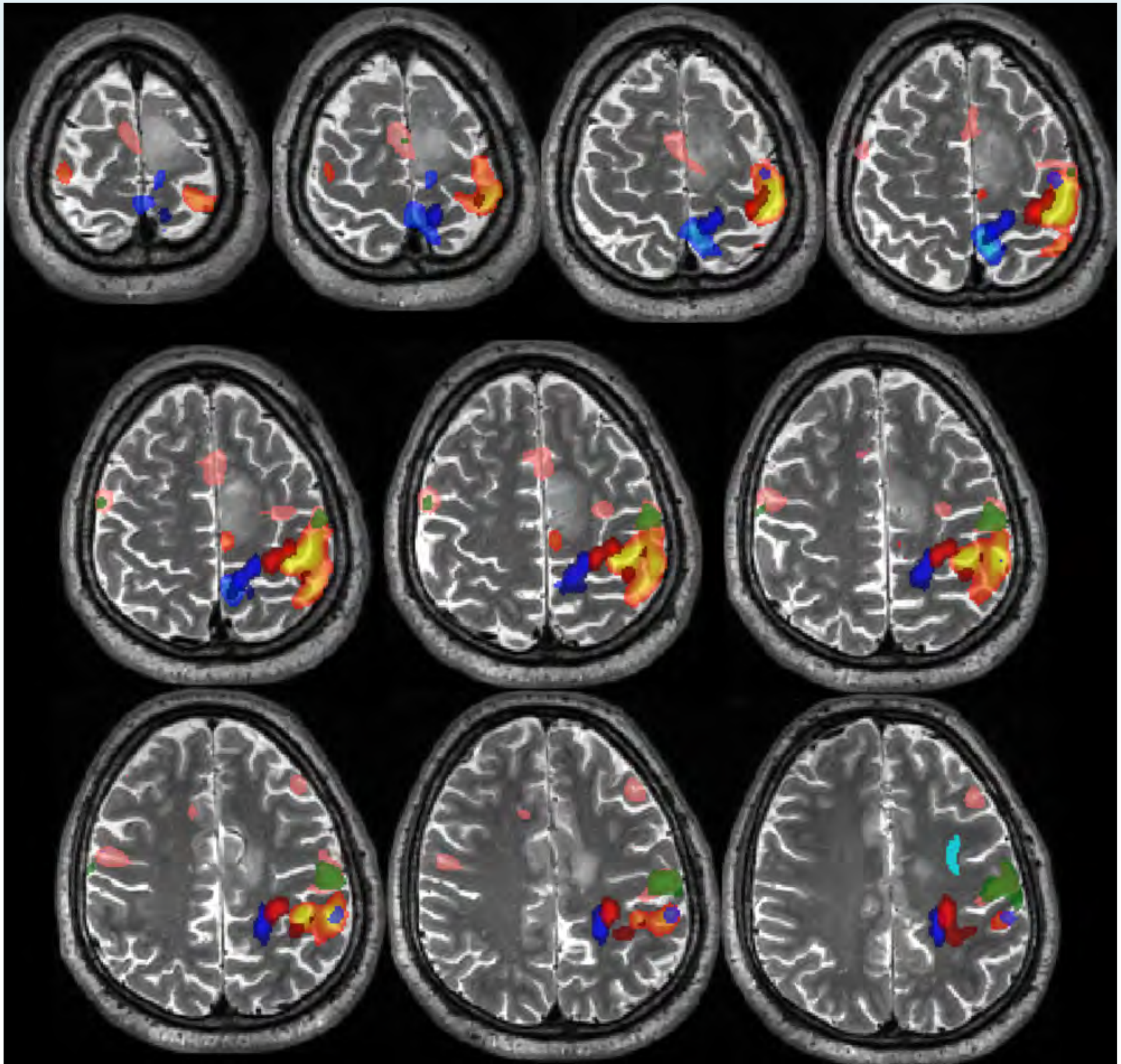
Language network





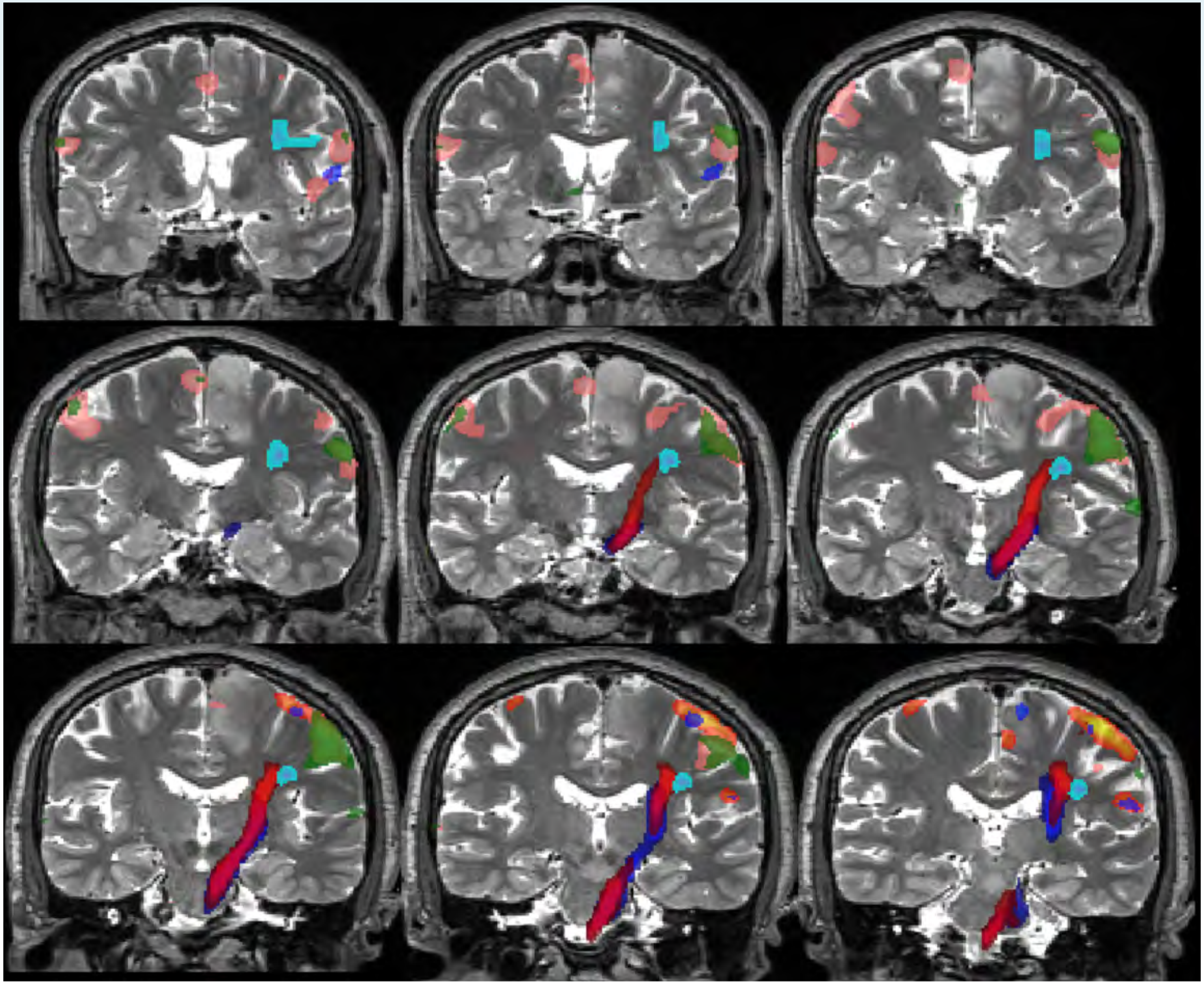
Catani Ann Neurol 2005

R foot, R hand, Verbal Fluency1, Verbal Fluency2
Arcuate Fasciculus, CST: R foot, R hand

R  L

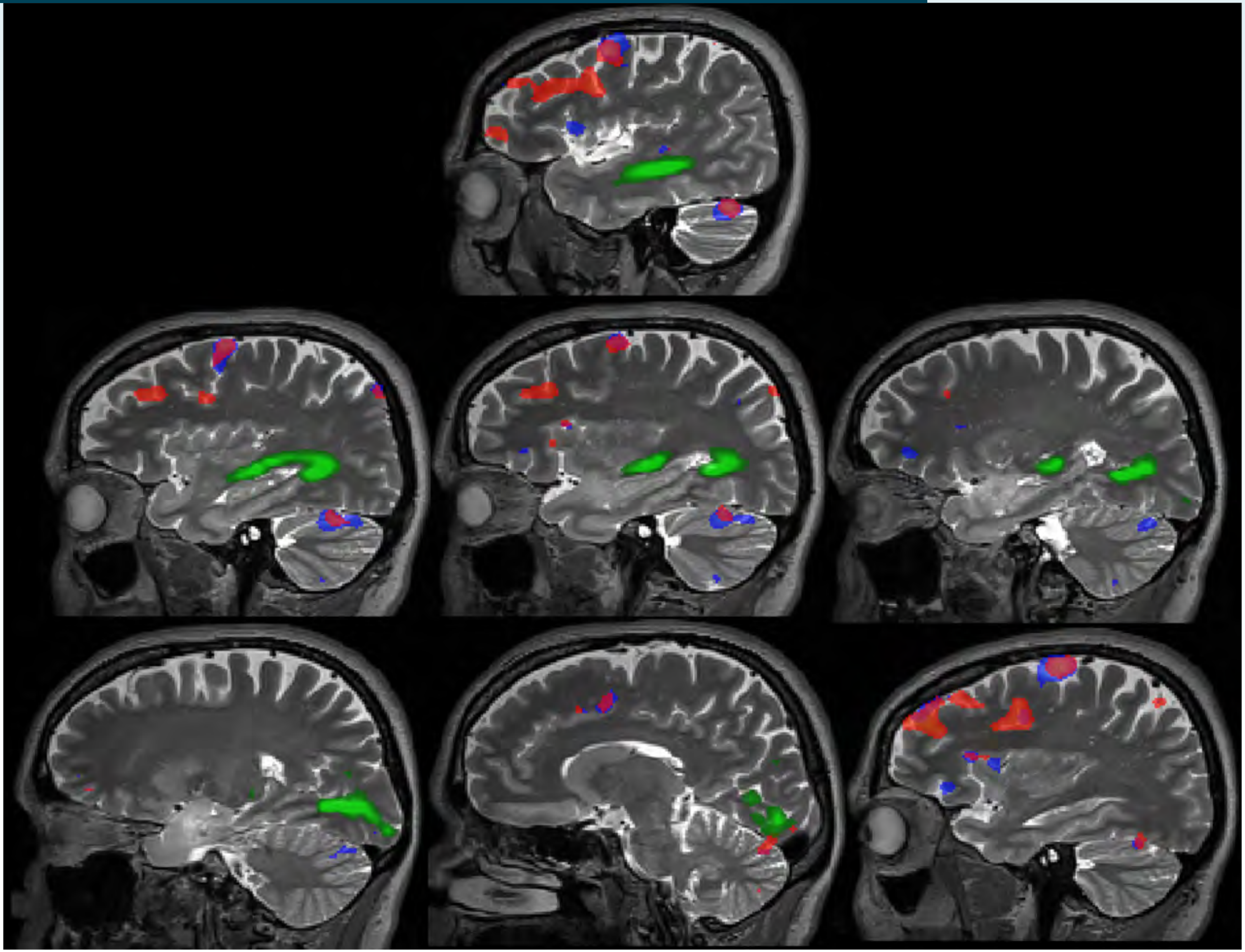
R foot, R hand, Verbal Fluency1, Verbal Fluency2
Arcuate Fasciculus, CST: R foot, R hand

R



L

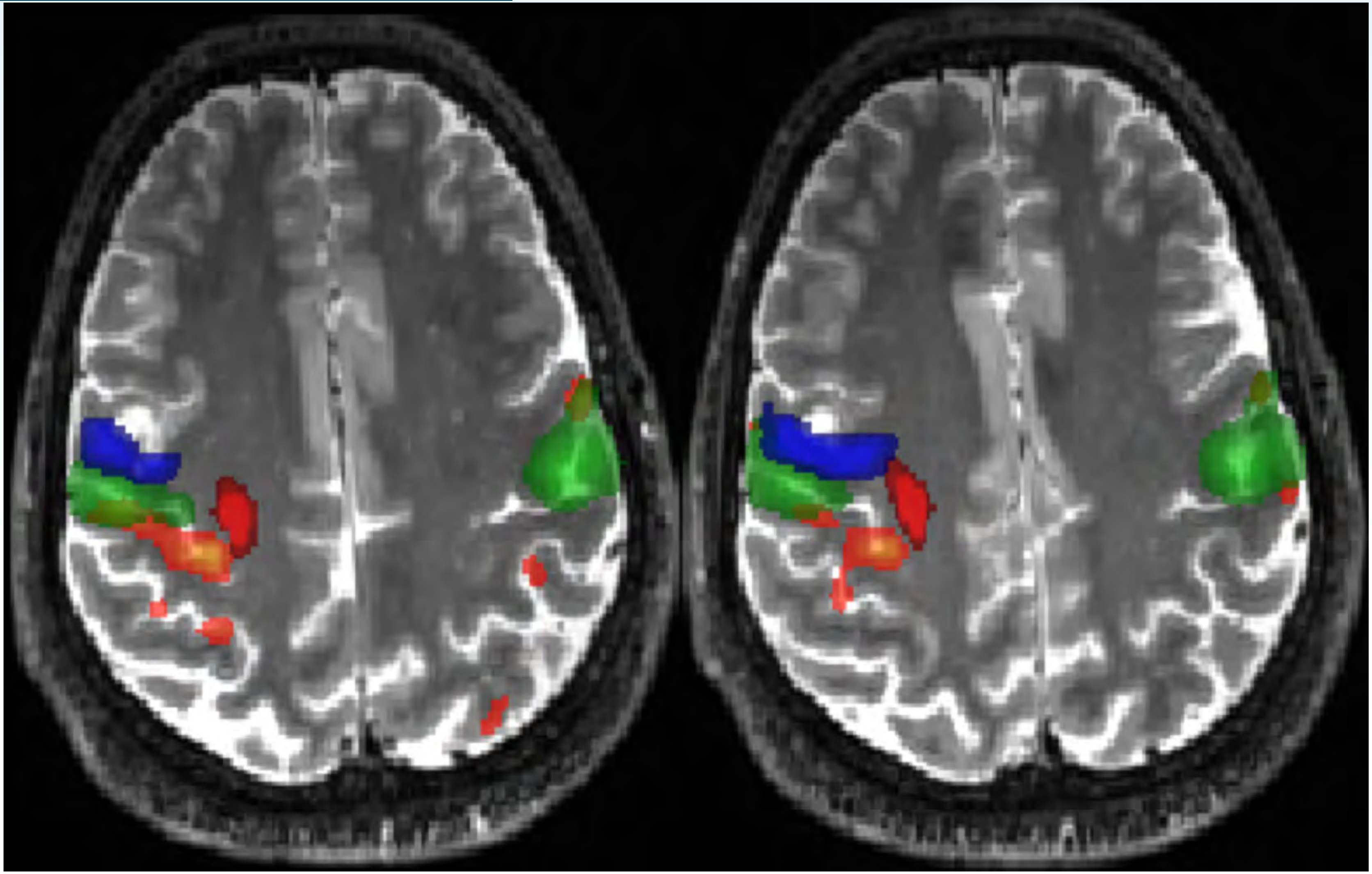
Verbal Fluency, Verb Generation, Optic radiation



UCL

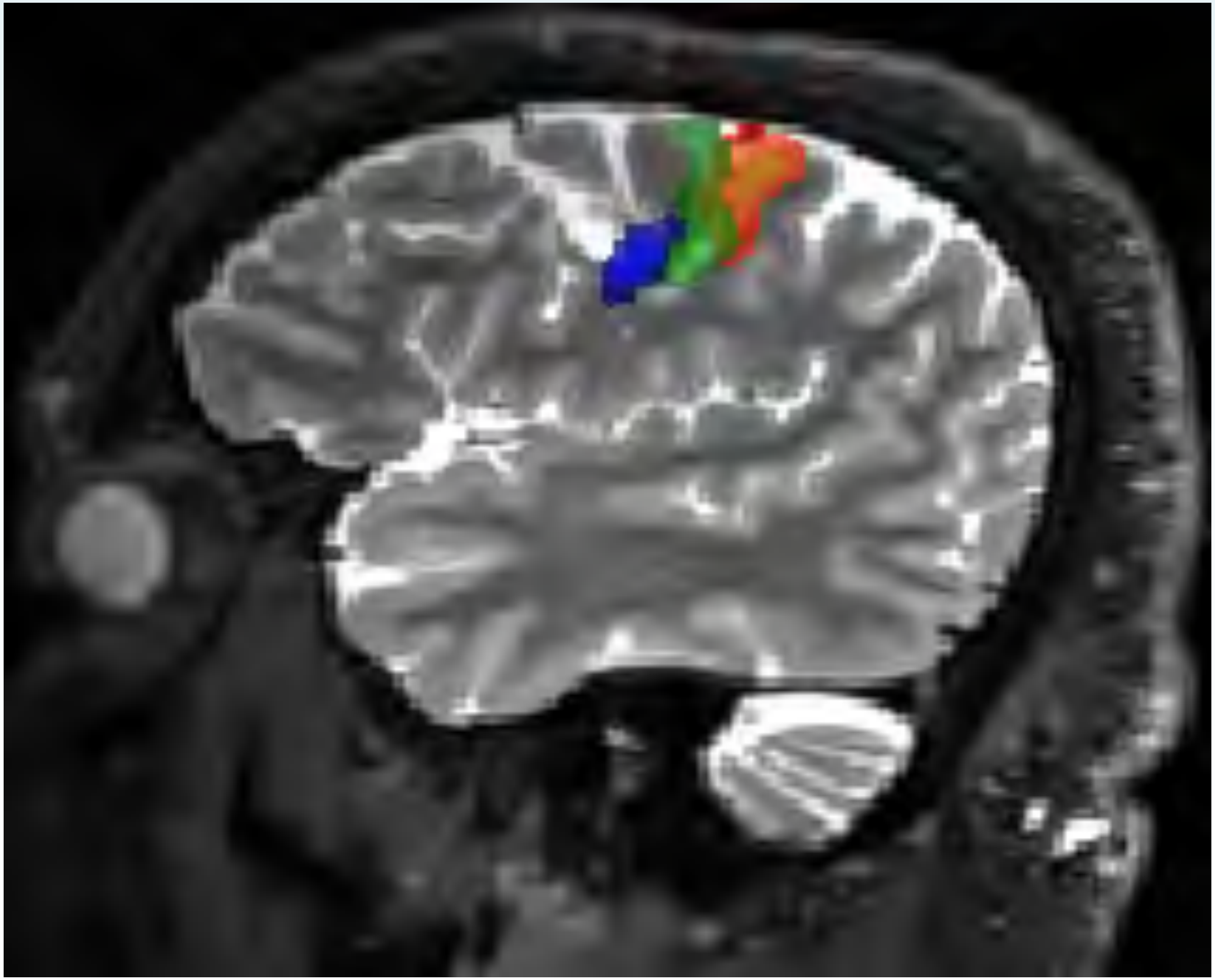
L hand, Lips

CST: L hand, Lips



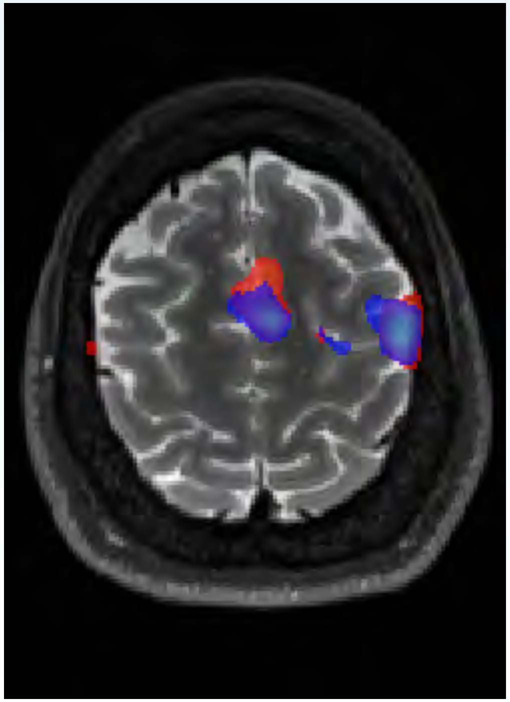
L hand, Lips

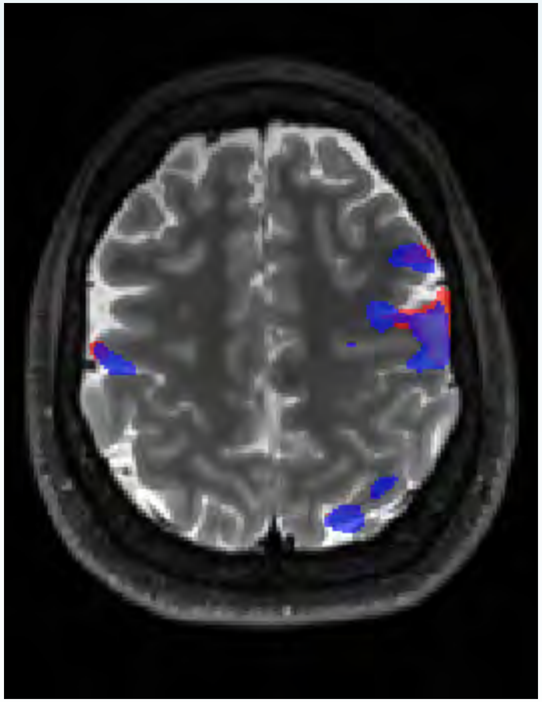
CST: L hand, Lips

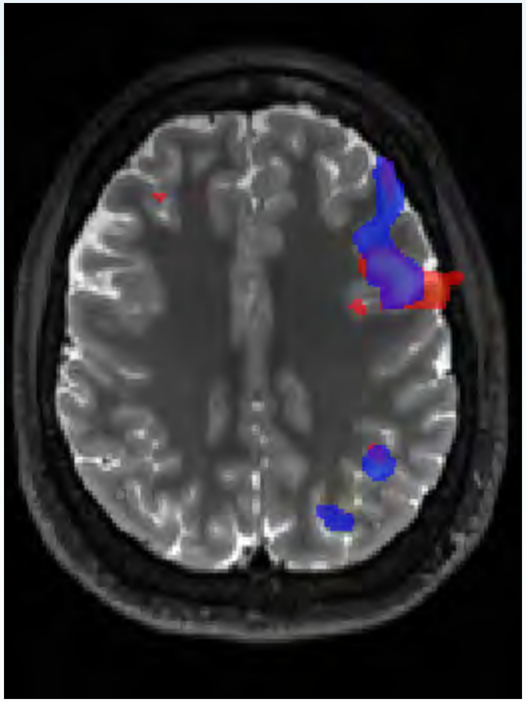


Fluency, Verb Generation

R



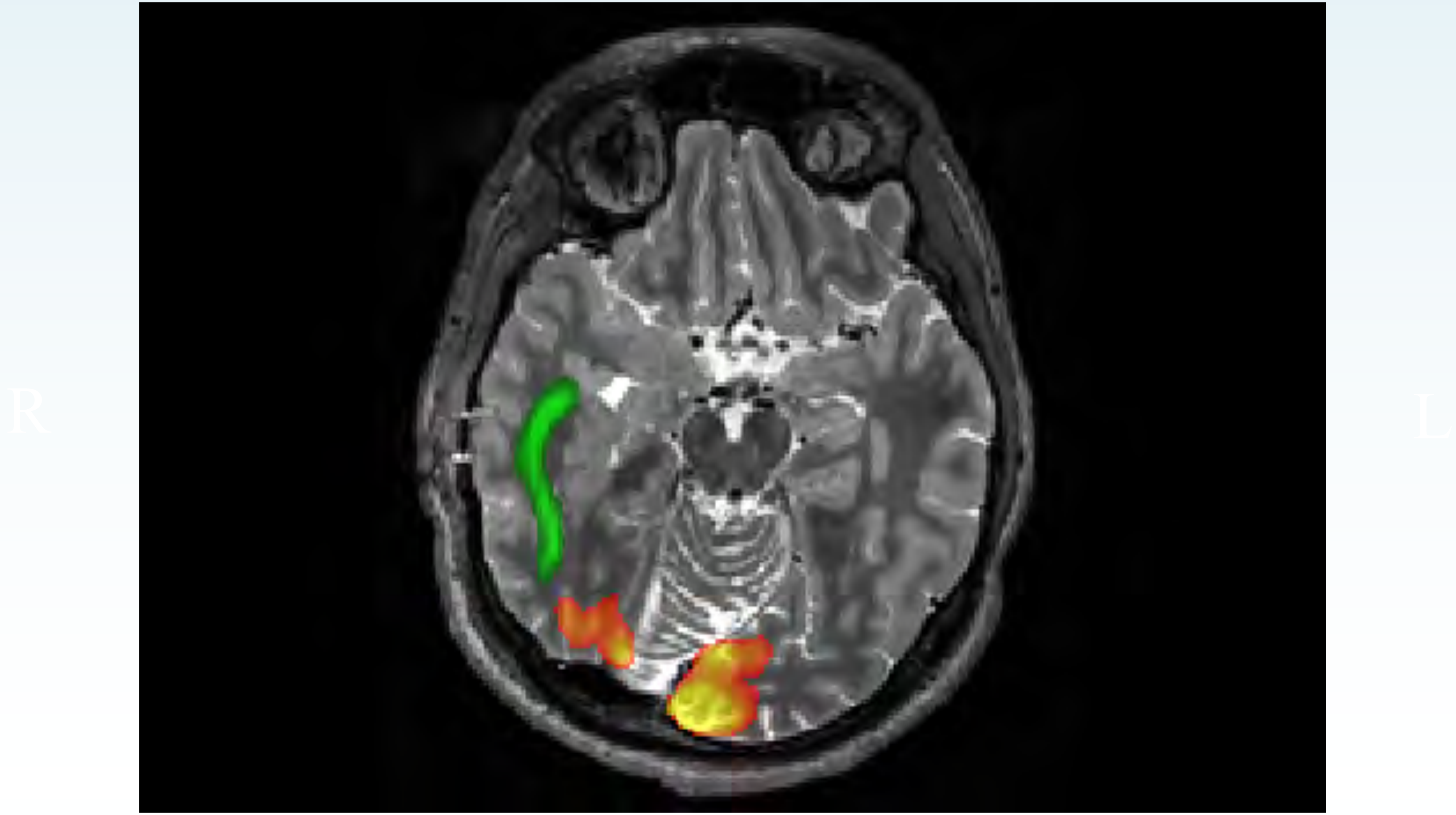




L

Visual fMRI FWE p<1e(-10)

Optic Radiation



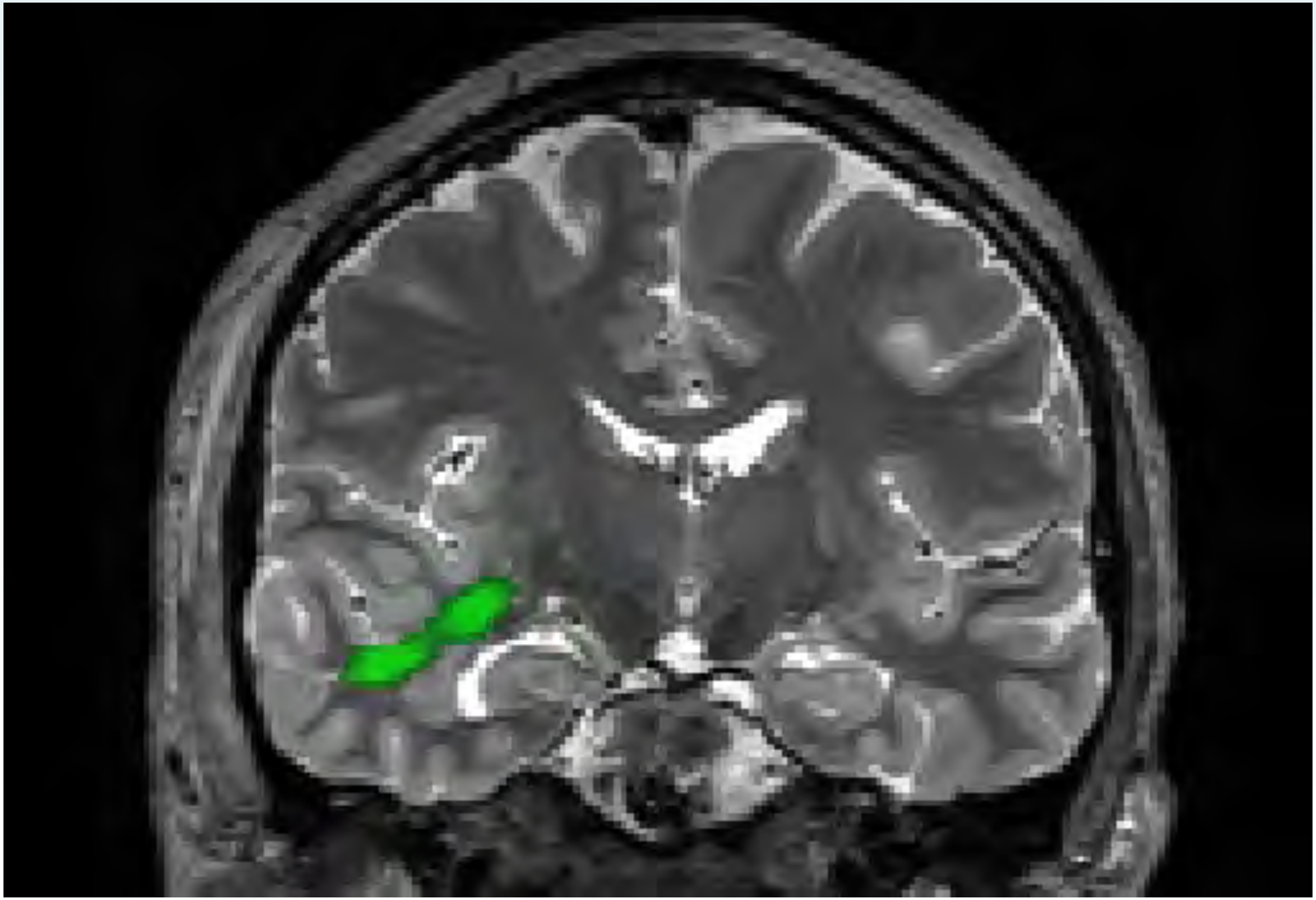
Visual fMRI FWE p<1e(-10)

Optic Radiation

Visual fMRI FWE p<1e(-10)

Optic Radiation

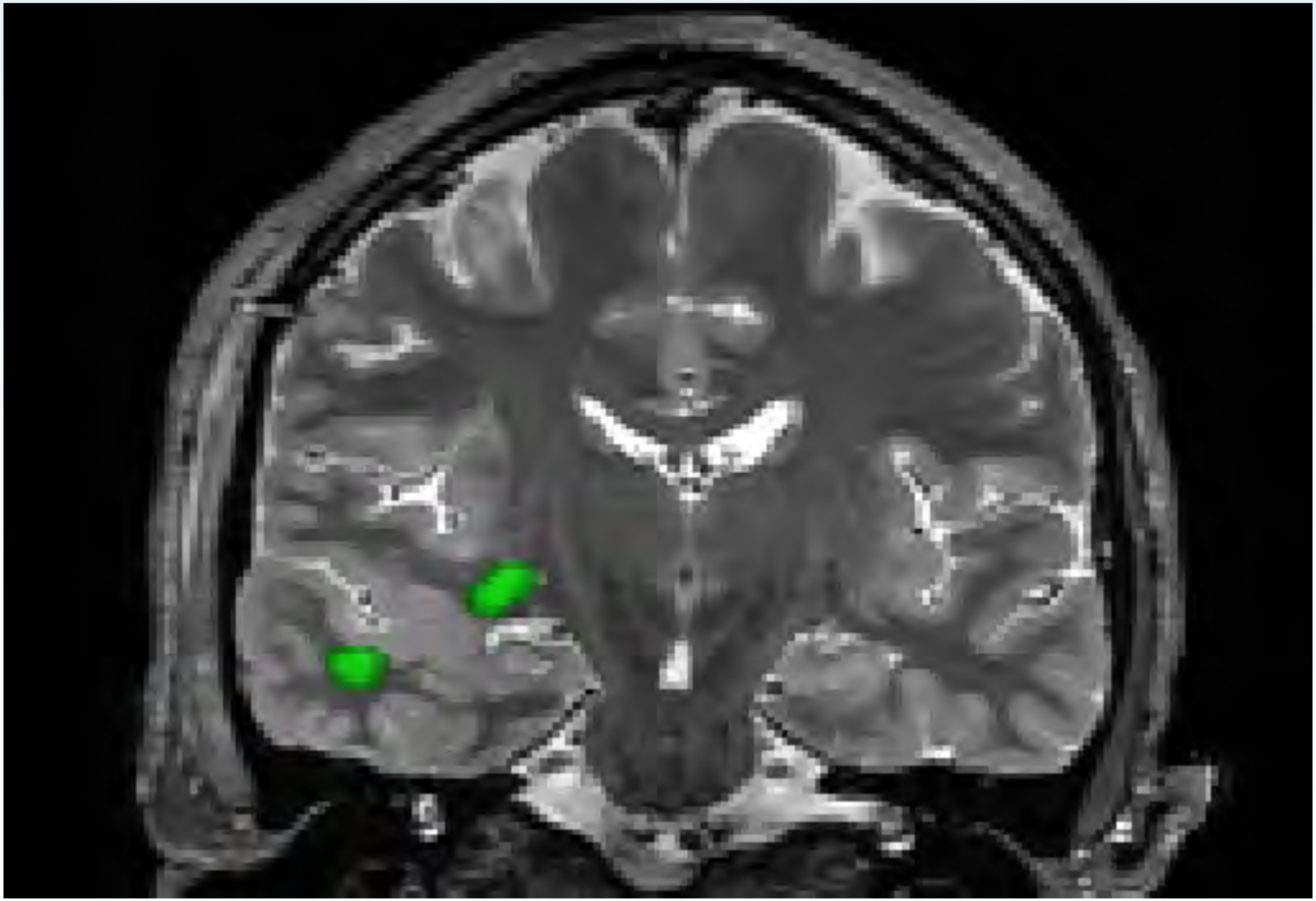
R



L

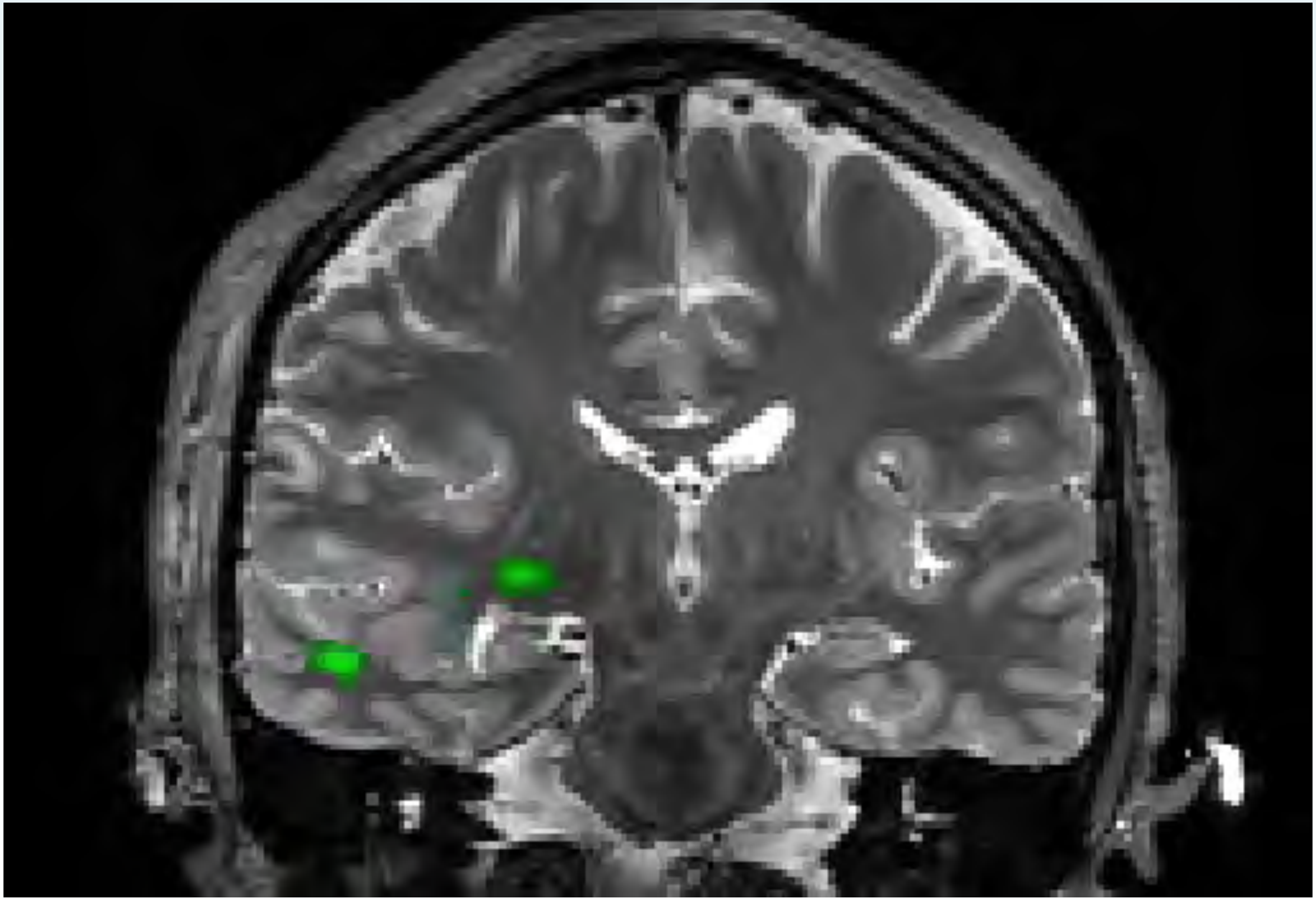
Visual fMRI FWE p<1e(-10)

Optic Radiation

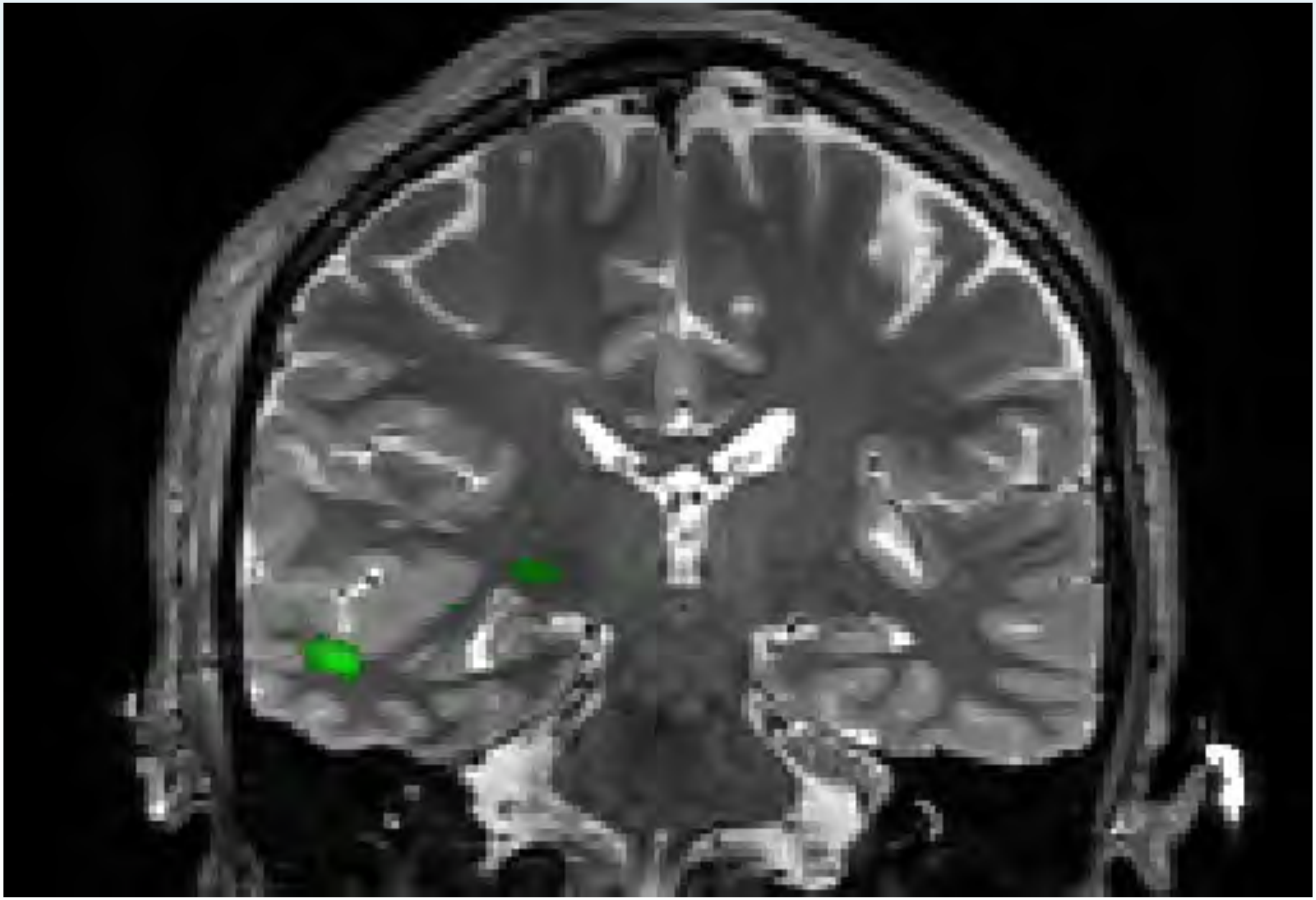


Visual fMRI FWE p<1e(-10)

Optic Radiation



Visual fMRI FWE p<1e(-10)
Optic Radiation



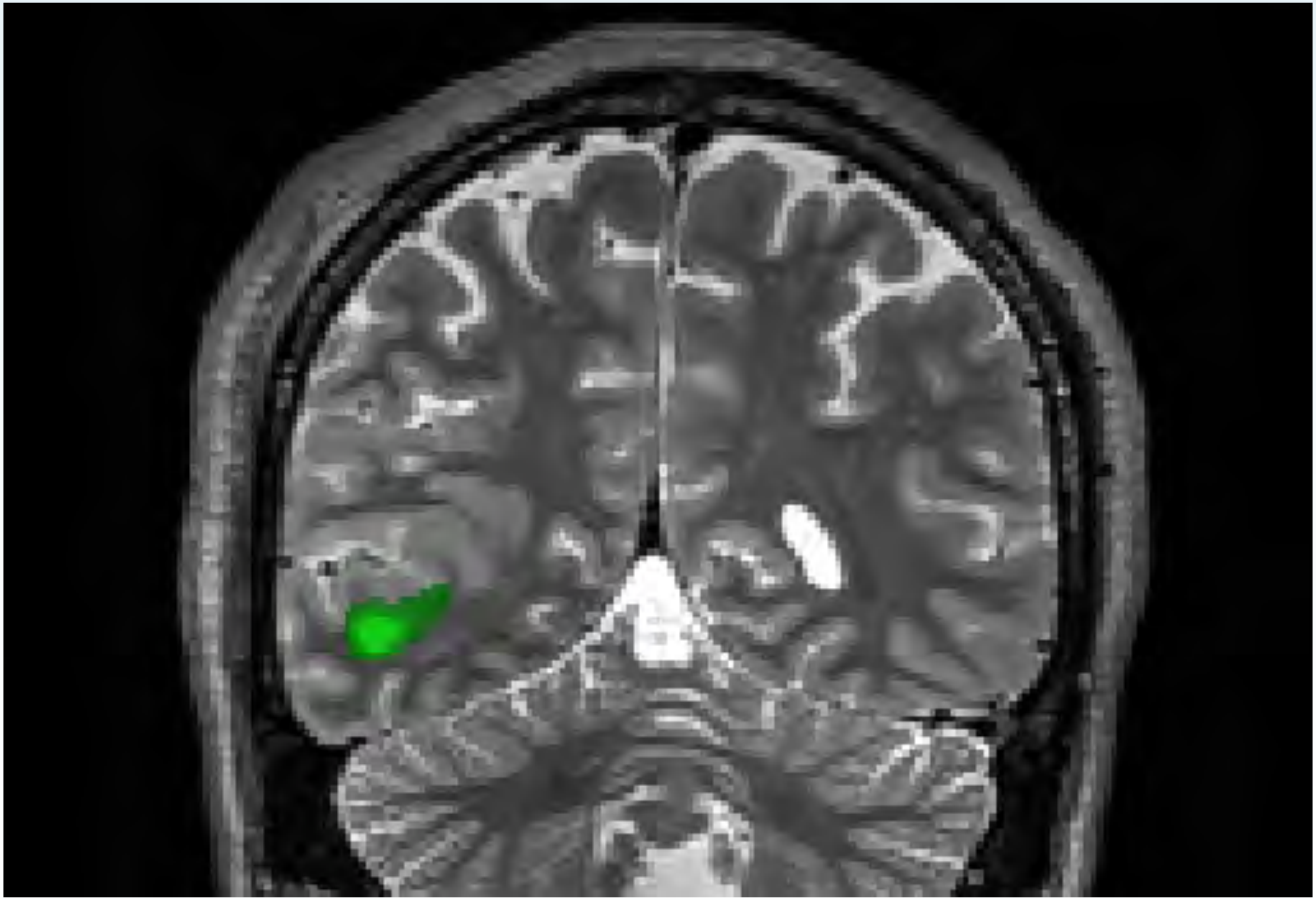
R

L

Visual fMRI FWE p<1e(-10)

Optic Radiation

R



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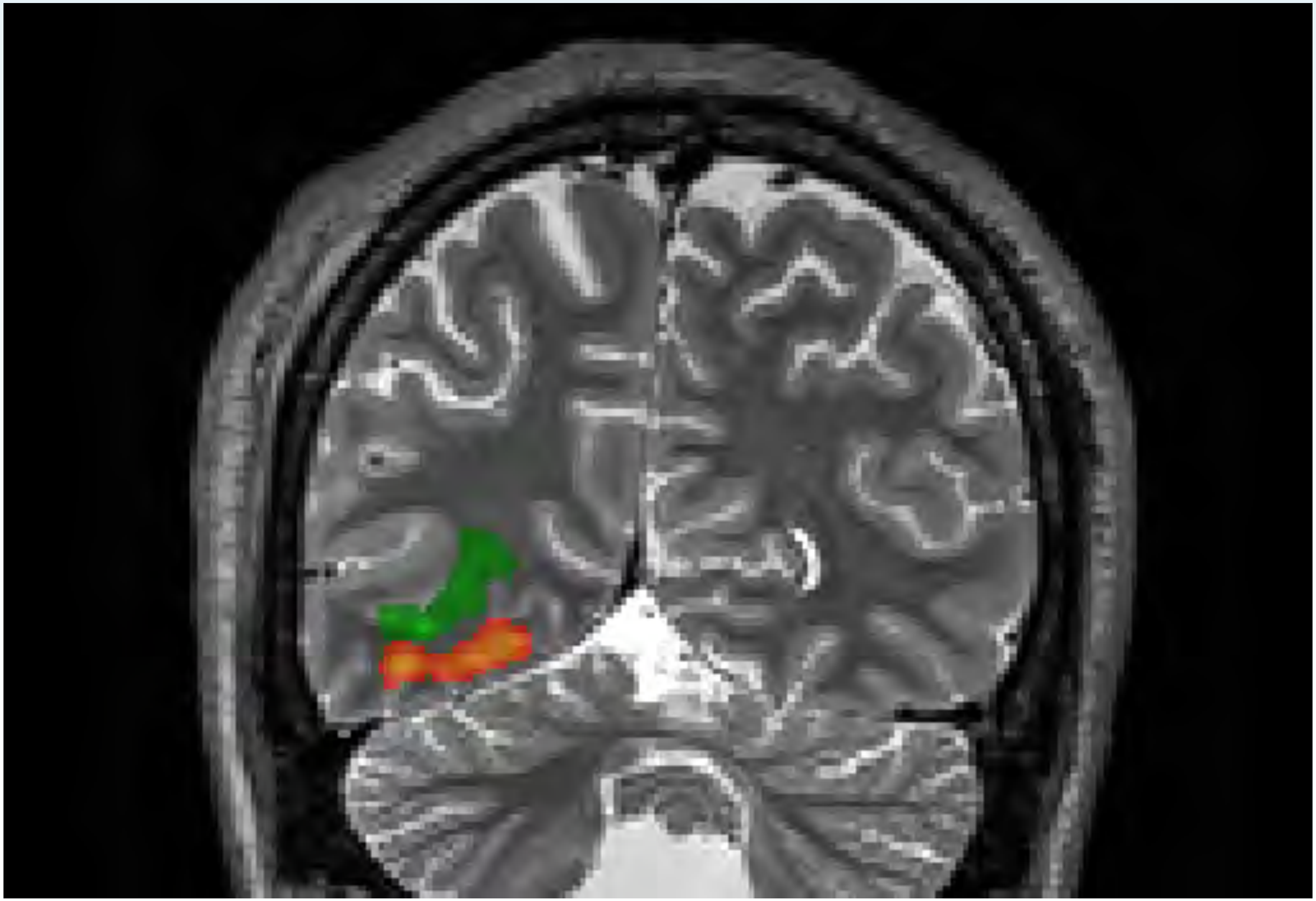
Visual fMRI FWE p<1e(-10)

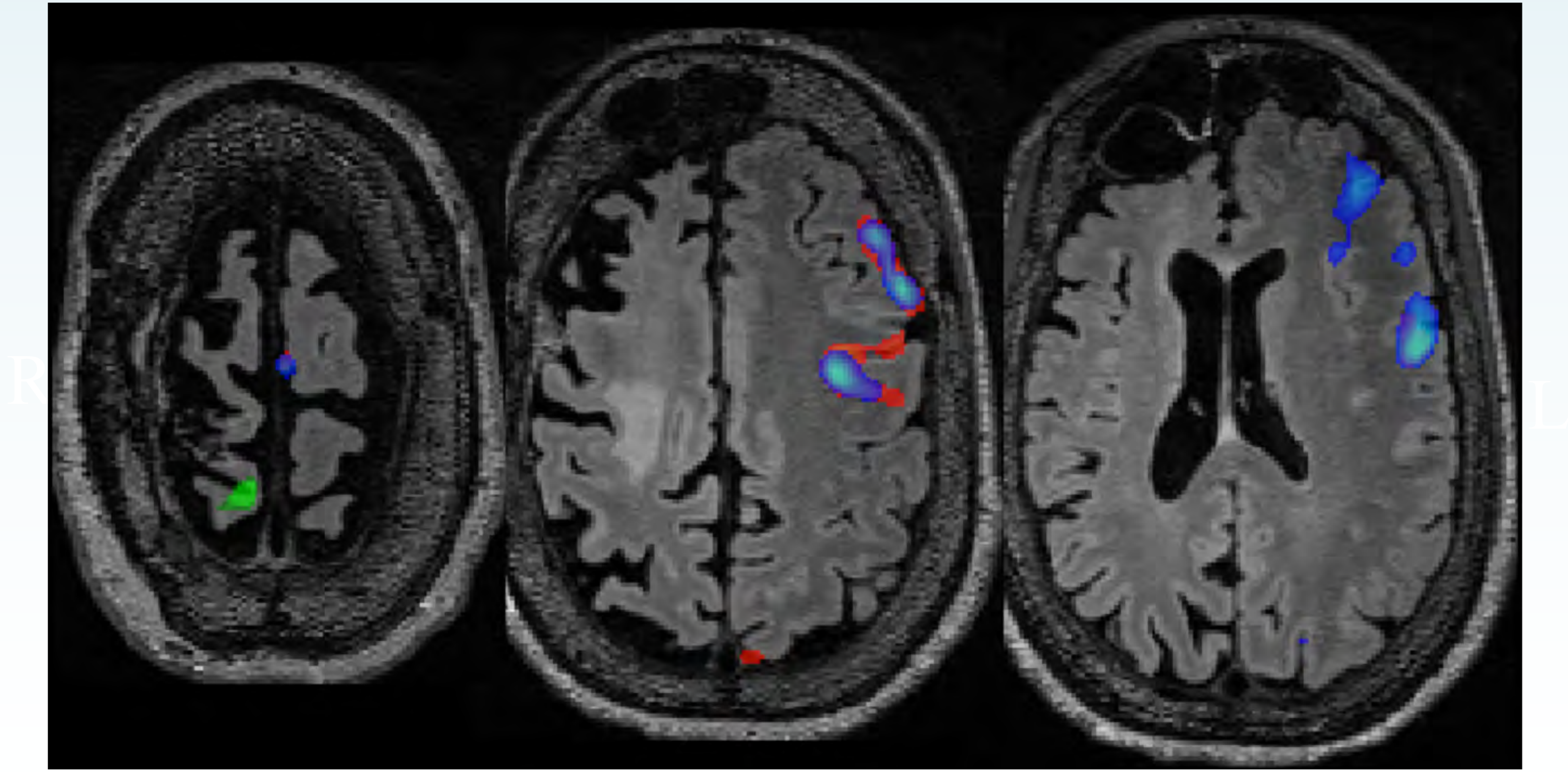
Optic Radiation

R



L

Verbal Fluency1, Verbal Fluency 2, R foot



Team Effort

- Radiographers
  - Helping with set-up and imaging
- Physicists
  - paradigm implementation/optimisation, data acquisition, data check, analysis
- Neuropsychologists
  - Identification of function to be tested/optimisation of paradigm
- Neurologists and Neurosurgeons
  - Identification of function to be tested/optimisation of paradigm
- Neuroradiologists
  - Identification of function to be tested, interpretation of results