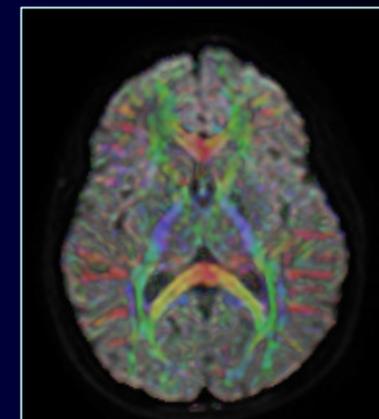
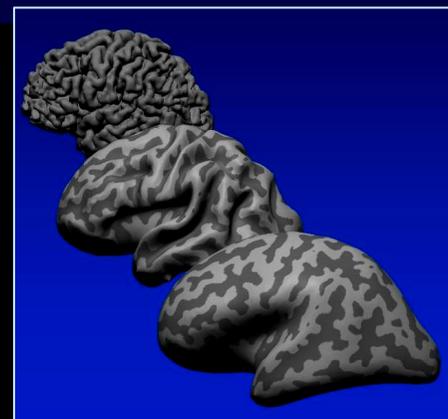
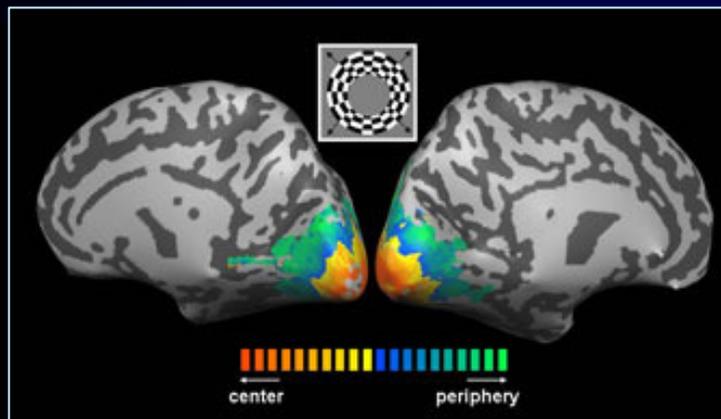


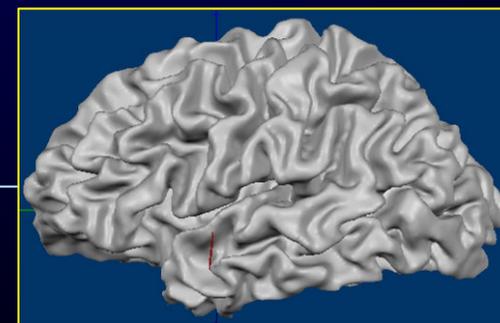
# Risonanza Magnetica funzionale

## $f$ MRI Limiti e obiettivi



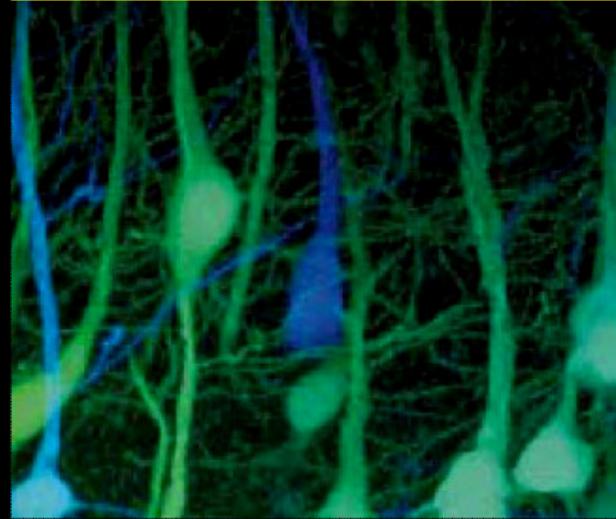
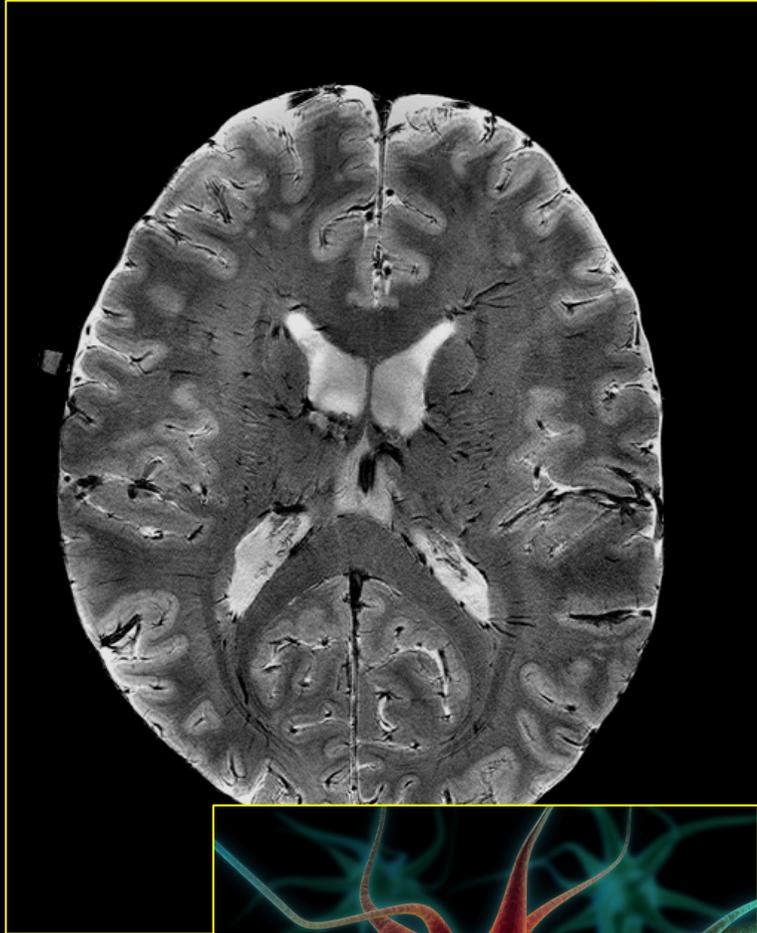
Franco Alessandrini

Servizio di Neuroradiologia  
Ospedale Civile maggiore Bgo. Trento  
Verona



# 78 Mapping the Evolved Functional Organization of Mind and Brain

JOHN TOORBY AND LEDA COSMIDES



intricacy of chem-  
nong roughly one  
ny straightforward



# Cervello

---

Chimica

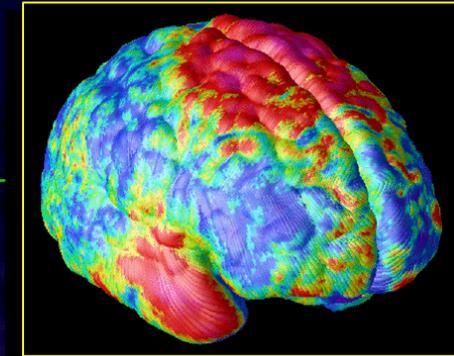
Fisiologia

Elettricità

Magnetismo

---

Analisi



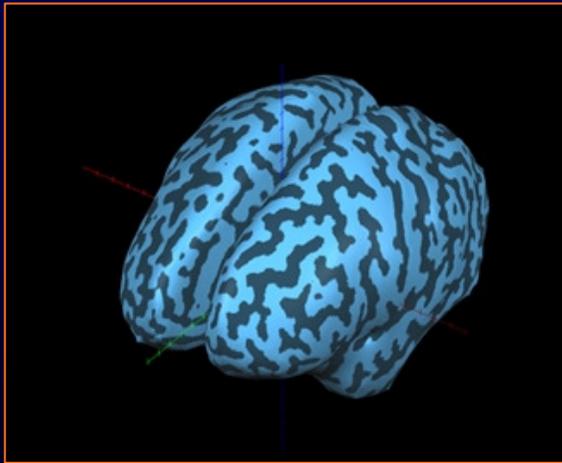
# Funzione

Progressi

PET, SPECT

EEG, MEG

RMN @ alto campo



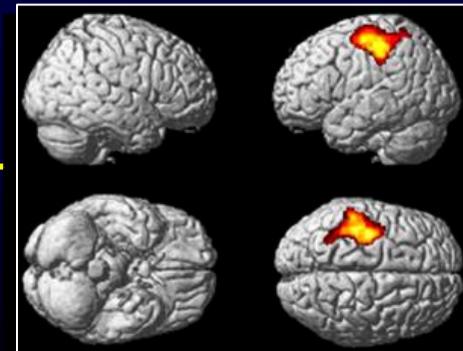
- Spettroscopia
- Diffusione
- Perfusion
- *f*MRI

# Risonanza Magnetica funzionale

## *f*MRI

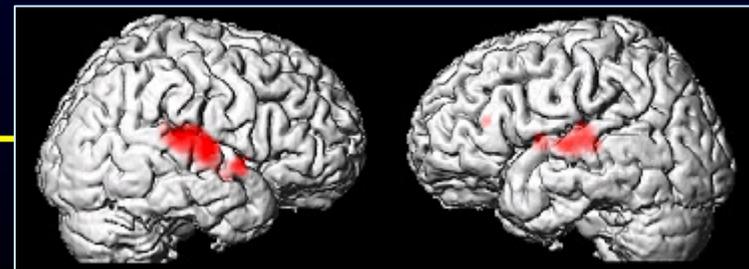
---

Visualizzazione *non invasiva*,  
*in vivo*,  
della *funzione cerebrale*



# Overview

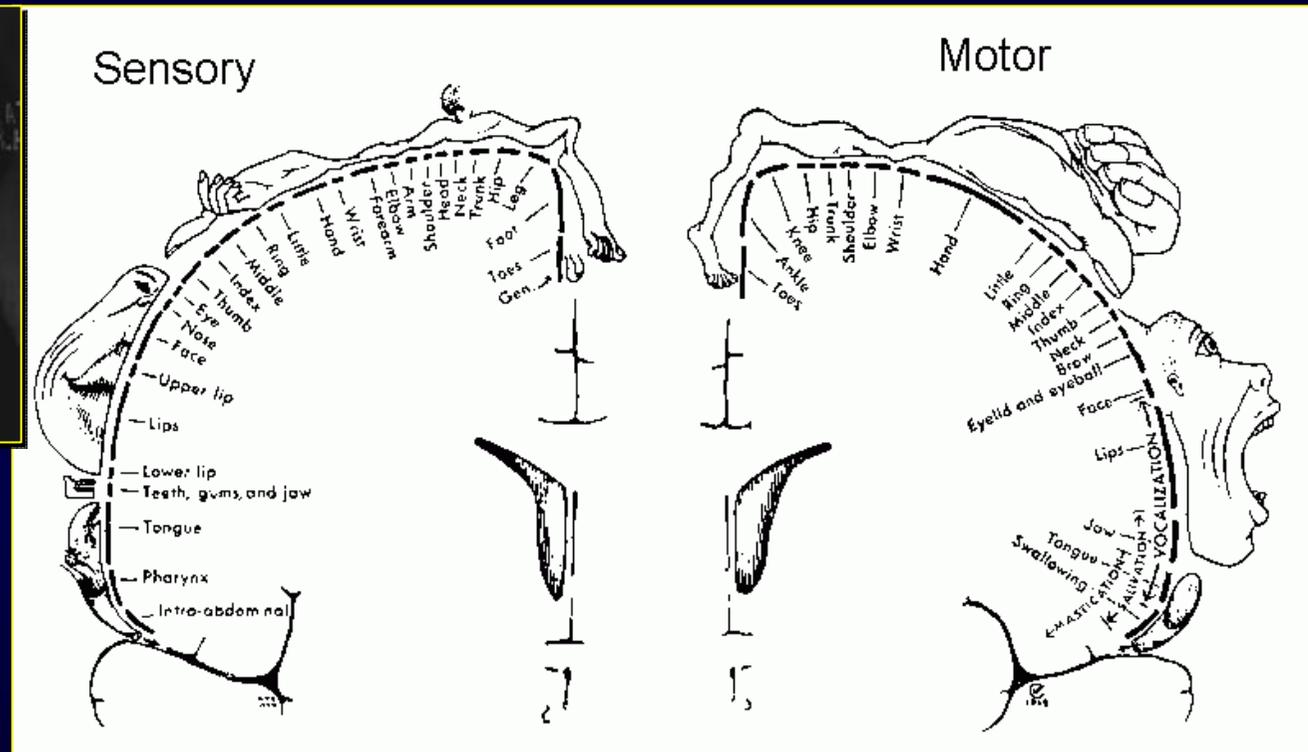
- Principi tecnici
- Applicazioni cliniche
- Livello di standardizzazione
- Pro & contro



# Mappaggio corticale



W. Penfield

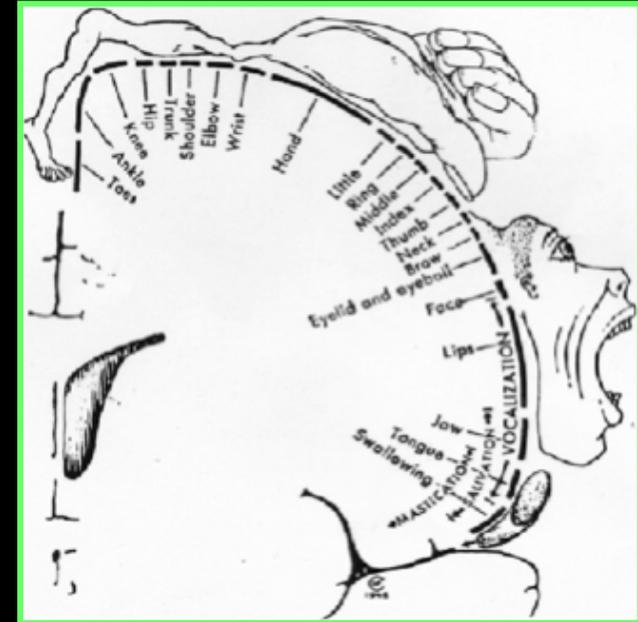


*Cenni storici*

# Mappaggio corticale

- Stimolazione diretta durante interventi
- Rapp. topografica funzioni nelle aree corticali

## Invasività

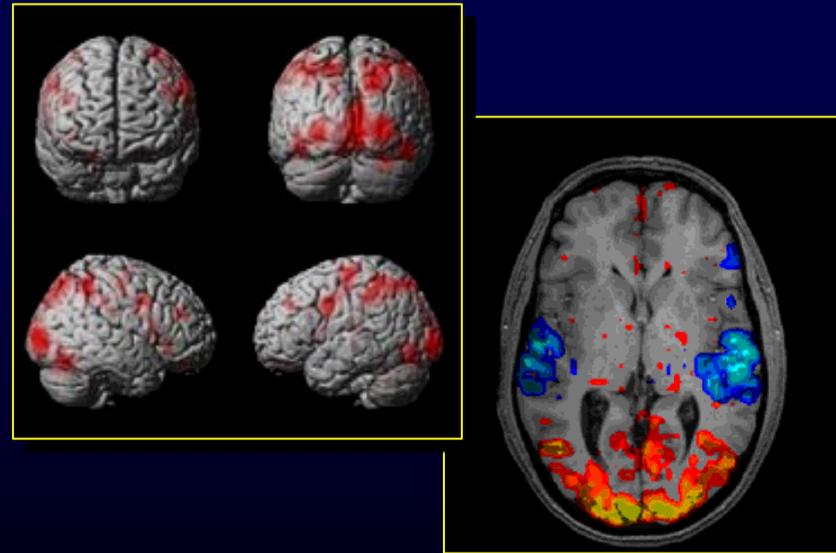


*“homunculus”*

# Funzioni *mappabili*

- Sensitiva
- Motoria
- Uditiva
- Visiva
- Linguaggio

Sistema cognitivo



# Premesse

---

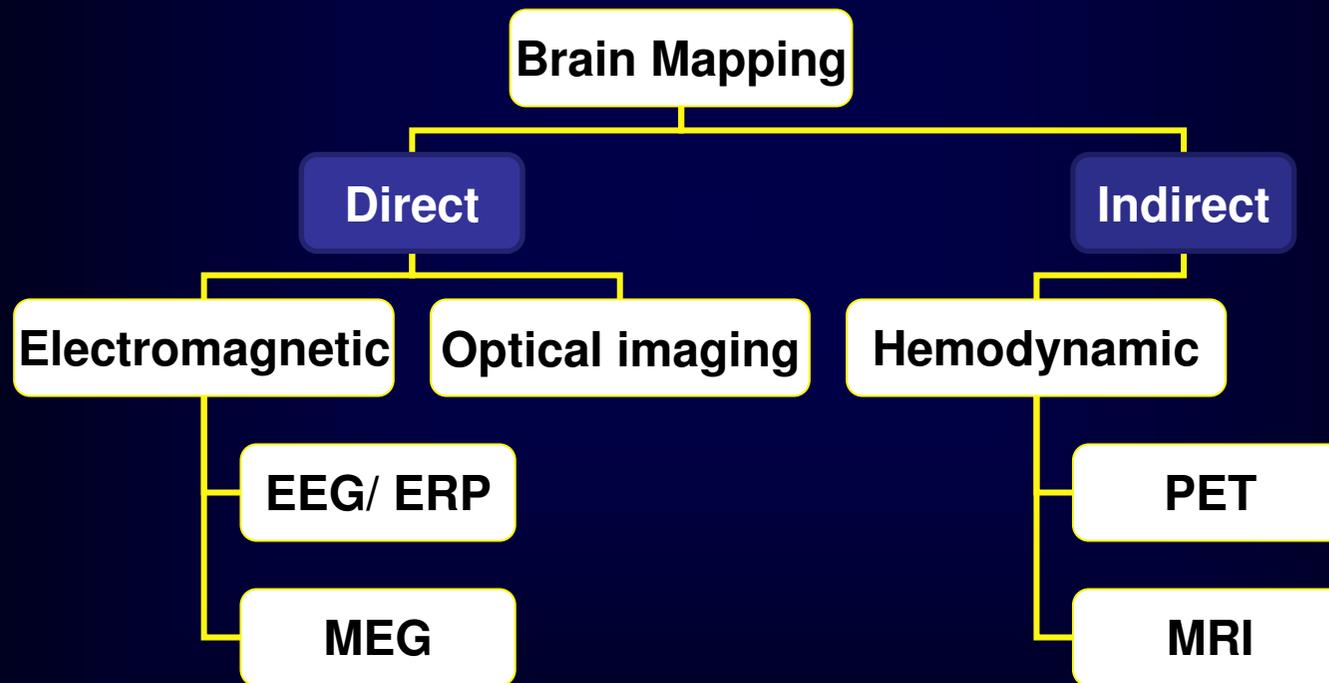
- “Brain mapping”
- PET *vs* *f*MRI
- Segnale *f*MRI

---

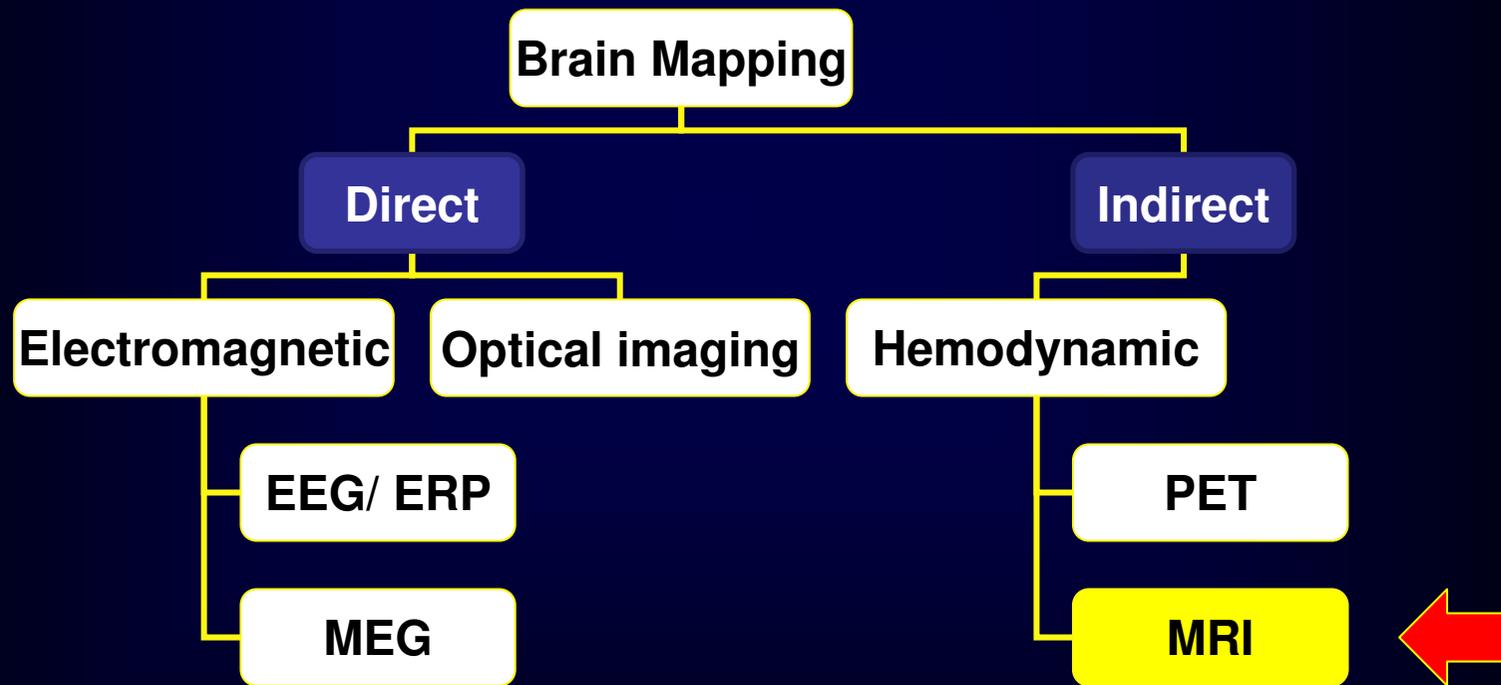
# Definizioni

- Risoluzione *spaziale*  
Spessore di sezione (dettaglio immagine)
- Risoluzione *temporale*  
Tempo di acquisizione dell'immagine

# Tecniche di Brain mapping



# Tecniche di Brain mapping



# Registrazione Elettromagnetica

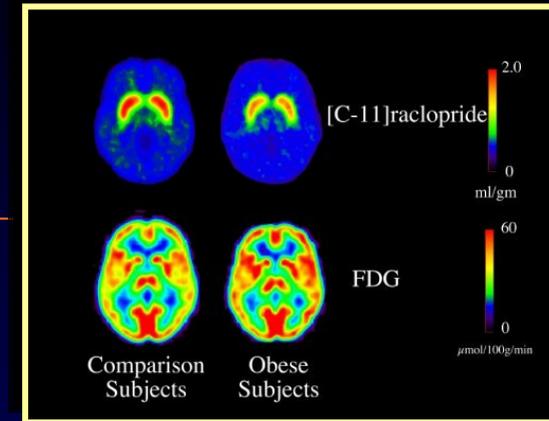
- EEG , MEG
- Registrazione diretta
- Non invasività
- Limitata risoluzione spaziale
- Buona risoluzione temporale

# Registrazione Emodinamica

- PET, *f* MRI
- Registrazione indiretta
- Non invasività
- Ottima risoluzione spaziale

# PET

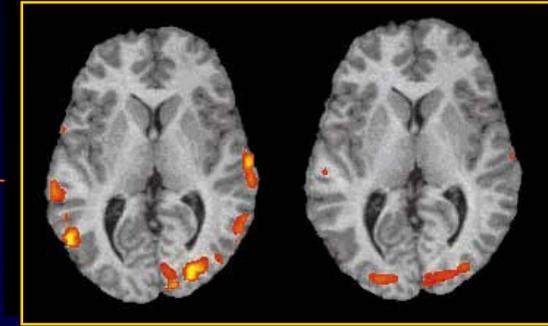
---



- Radiazioni ionizzanti
  - Risoluzione *spaziale* ridotta
  - Sensibilità elevata
- 



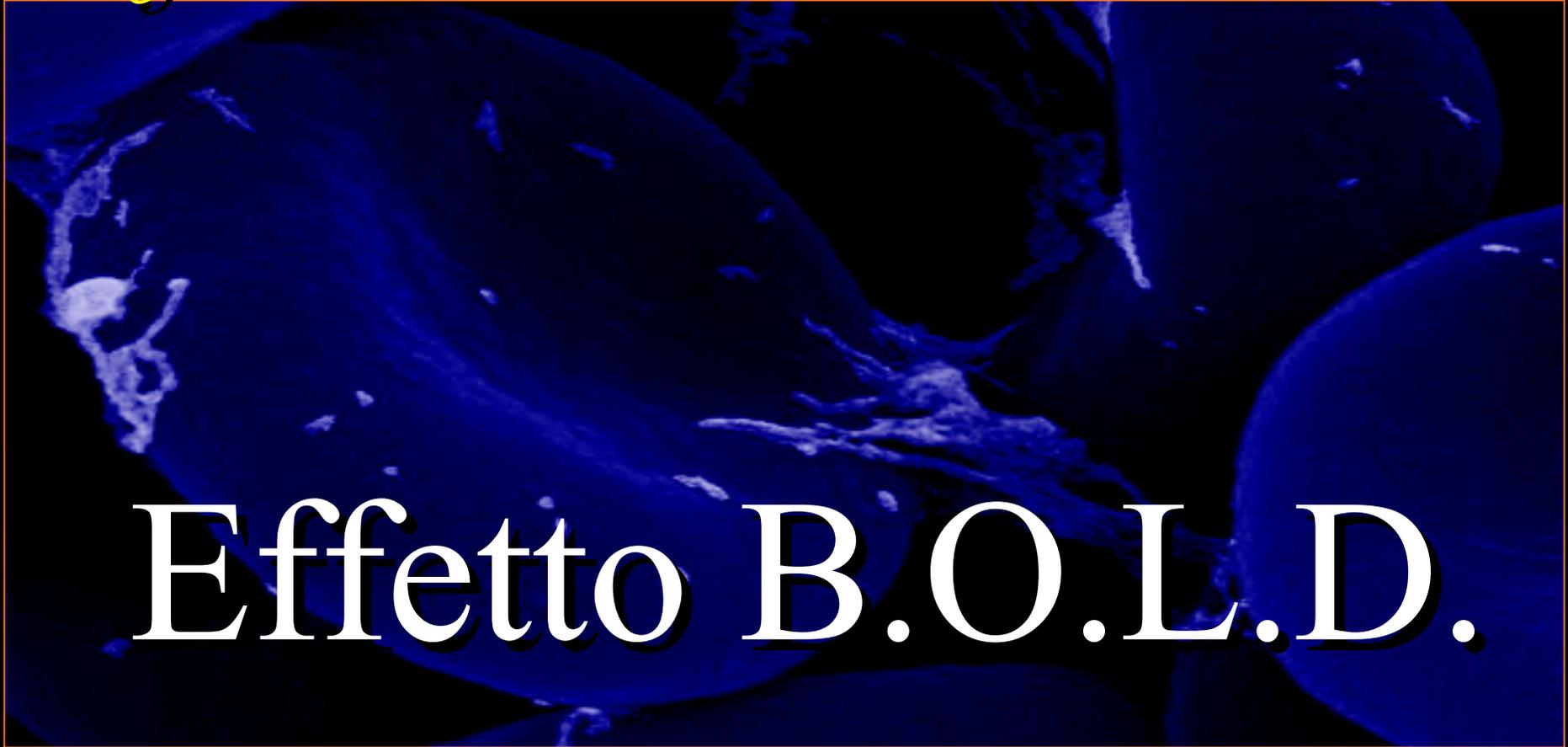
# fMRI



- Campo magnetico + RF
- Ris. *spaziale – temporale* elevata
- Sensibilità elevata



*f*MRI



Effetto B.O.L.D.

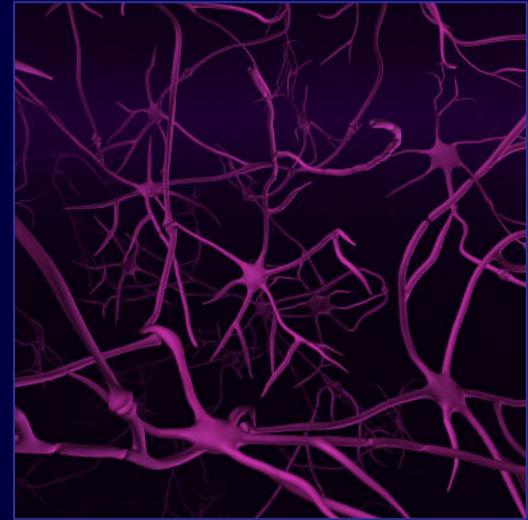
Blood Oxygen Level Dependent

# Effetto B.O.L.D.

---

- Alla base della *f*MRI
- Più evidente a c. magnetico elevato (>1.5T)
- Indotto da scarica neuronale sec. a stimolo
- Sfrutta lo stato di ossigenazione dei g. rossi
- Sede: letto capillare
- No mdc e.v. !!

# Fisiologia



## *Scarica neuronale*

⇒ modificazioni del flusso capillare

⇒ modif. stato di ossigenazione dei g. rossi

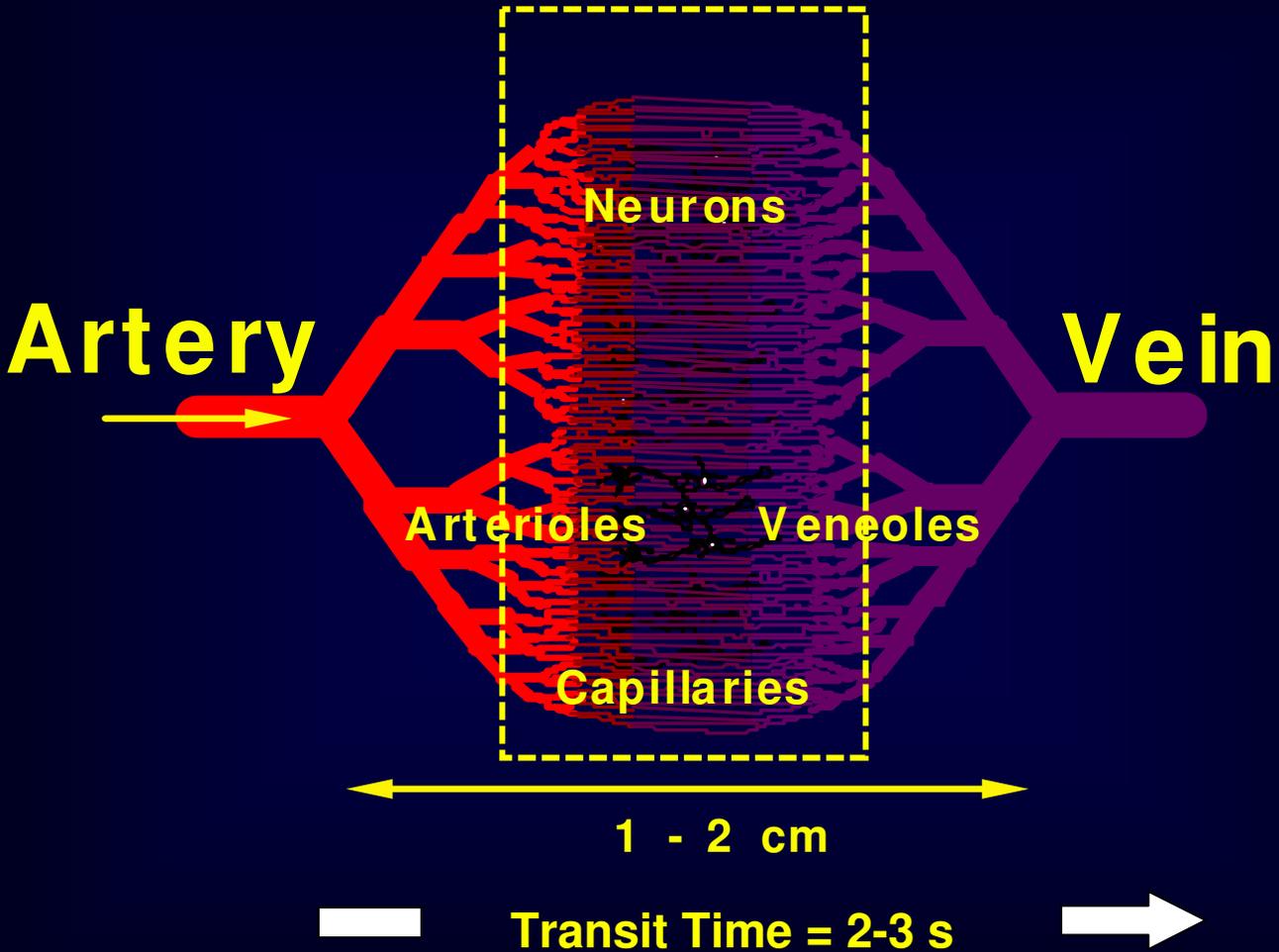
*Ossi-emoglobina  $HbO_2$  → desossi-emoglobina dHb*



Variazioni di segnale locale rilevate da RM

# Effetto BOLD

*sede*



- A riposo* (HbO<sub>2</sub>) = (dHB) sui due versanti
- HbO<sub>2</sub> ha effetto “positivo” sul segnale (lo aumenta)
  - dHb ha effetto “negativo” sul segnale (lo annulla)



**Nessuna variazione di segnale**

# Stimolo

*risposte fisiologiche*

---

Aumento di:

- CBV = Volume ematico cerebrale
  - CBF = Flusso ematico cerebrale
  - CMRO<sub>2</sub> = “Rate” metabolico O<sub>2</sub> (*tasso estrazione O<sub>2</sub>*)
-

*Durante attivazione* , per i fenomeni di flusso descritti,  
si accumula più ossiHb di quanta si trasformi in dHb  
 $(\text{HbO}_2) > (\text{dHB})$



**Incremento del segnale**

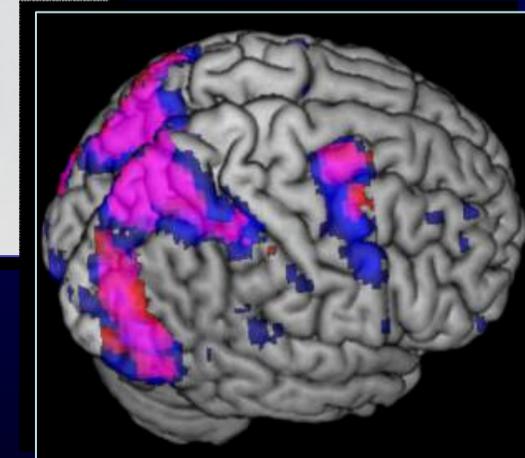
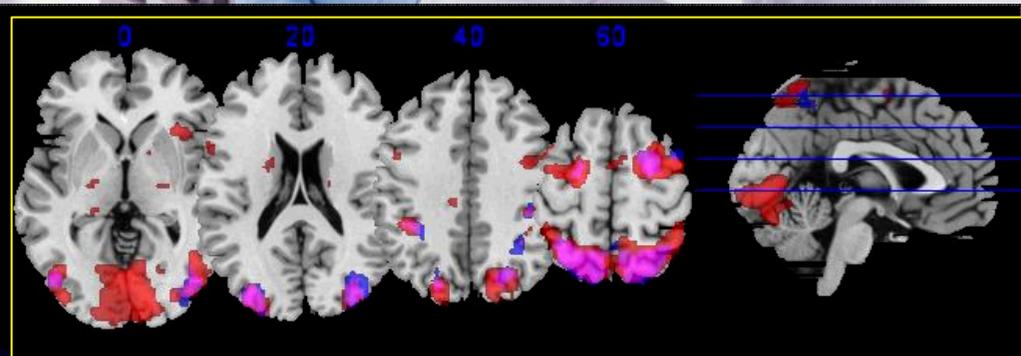
# Effetto B.O.L.D.

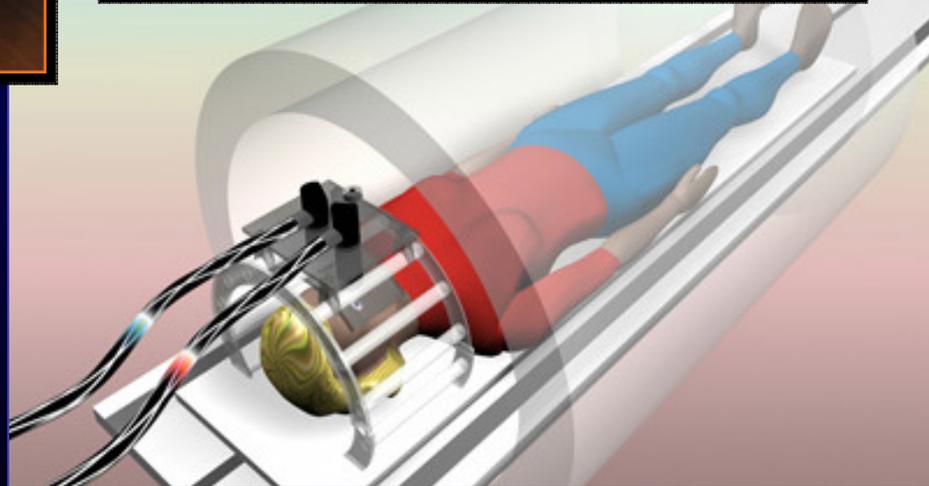
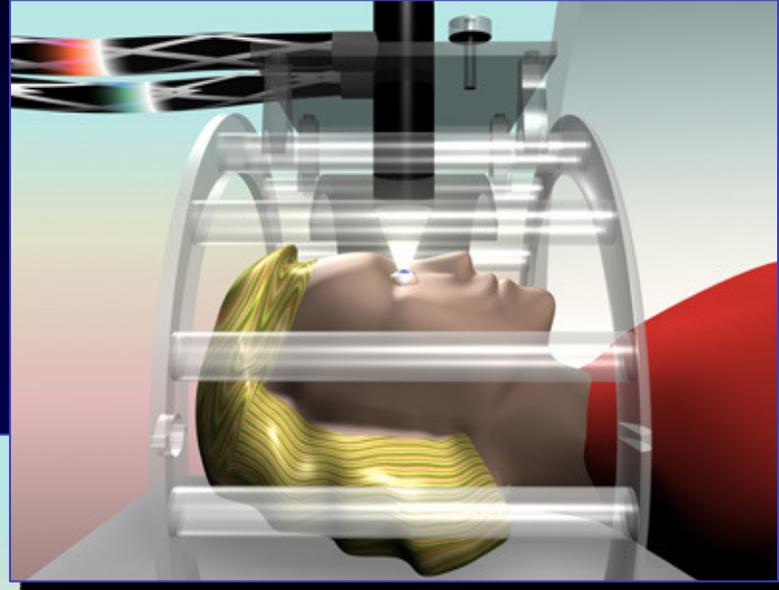
1. Variazioni flusso e volume ematico
2. Concentrazione  $\text{HbO}_2 > \text{HbO}$  nei capillari
3. Eccesso  $\text{HbO}_2$  sul versante venoso
4. Aumento del segnale locale

# Effetto B.O.L.D.

- BOLD : fenomeno durante il quale l'incremento di flusso ematico a livello capillare non viene compensato da proporzionale estrazione di  $O_2$ .
- La riduzione dell'Hb viene utilizzata come sorgente di segnale in fMRI
- In fMRI NON si usa mdc !!

# Applicazioni cliniche





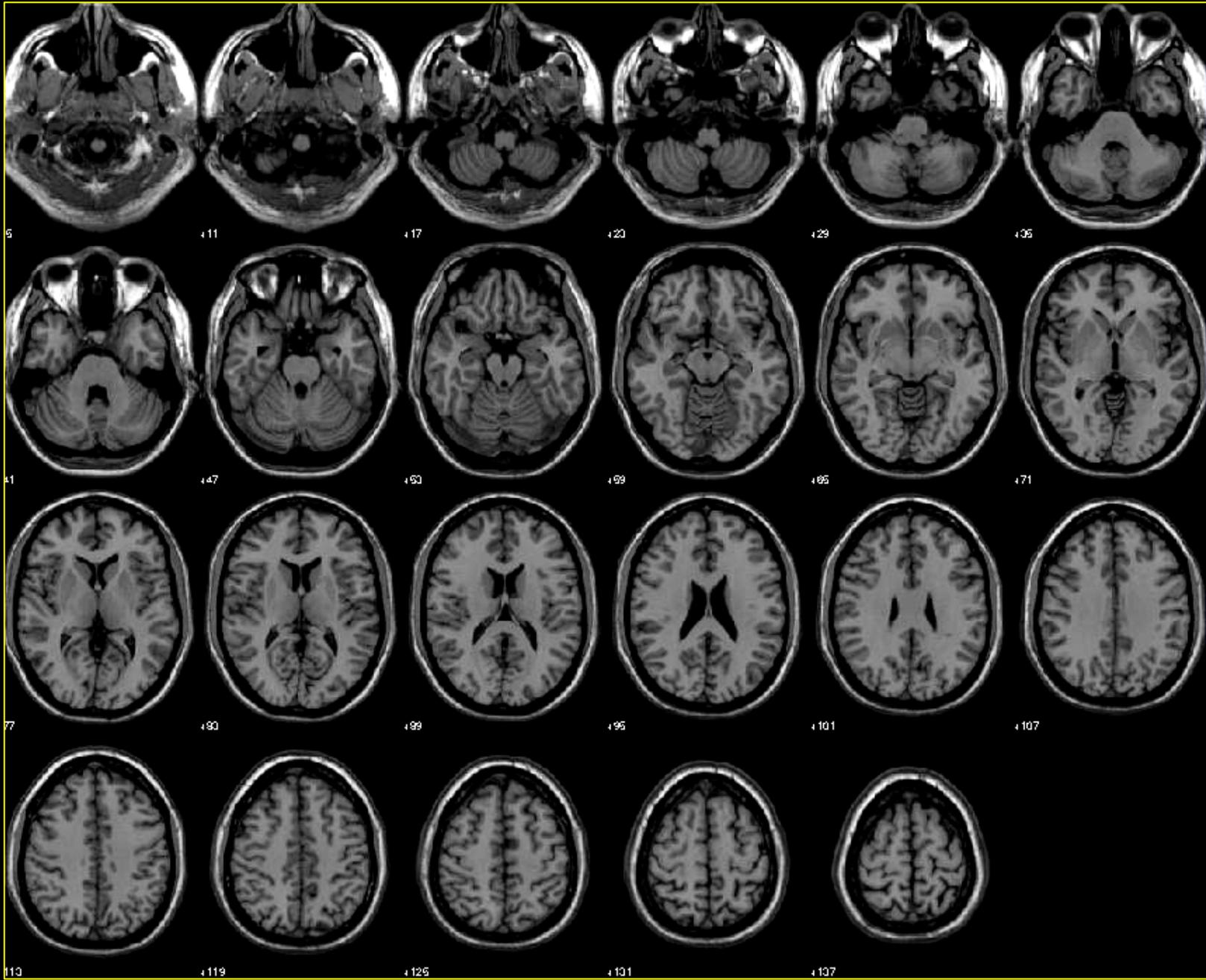
# Esame *f*MRI

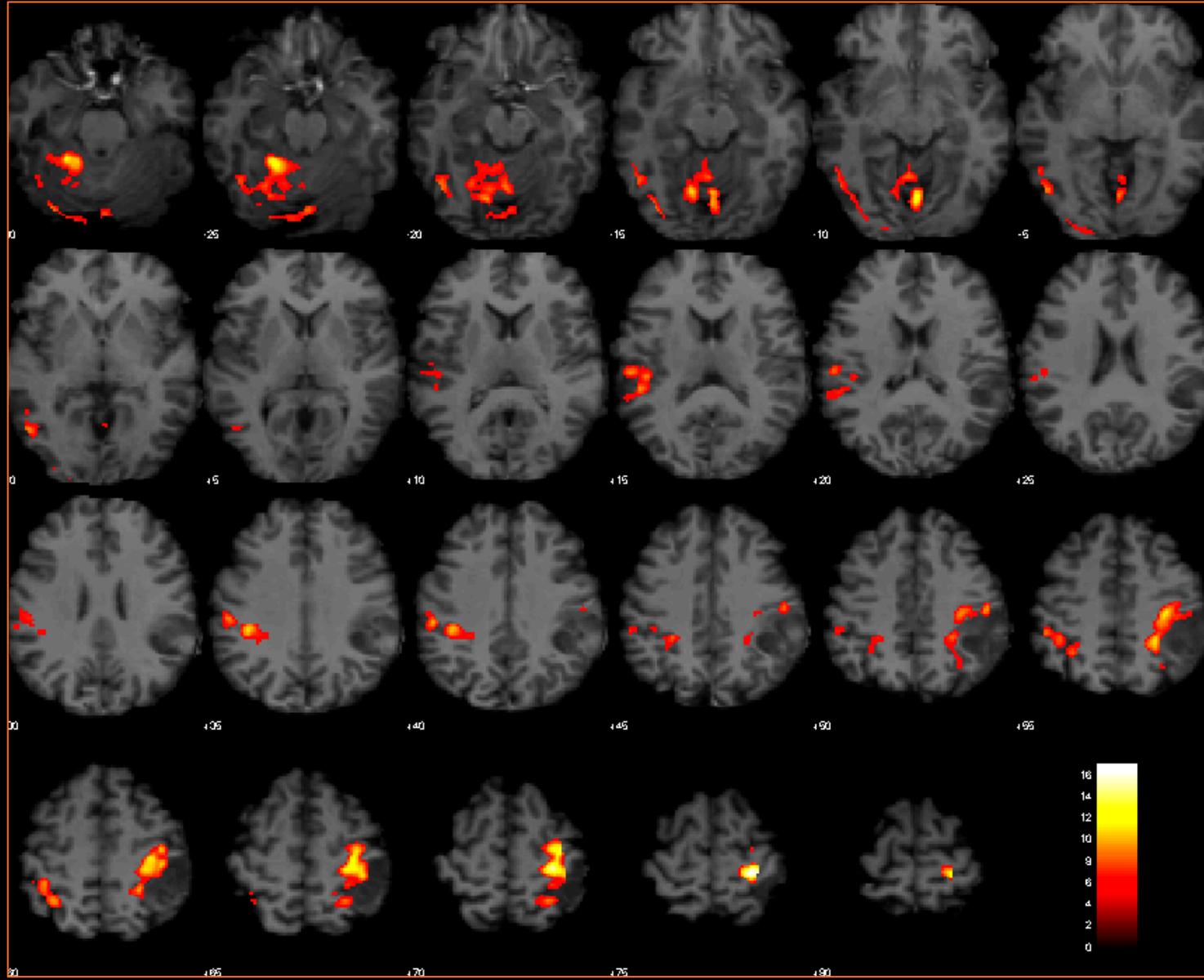
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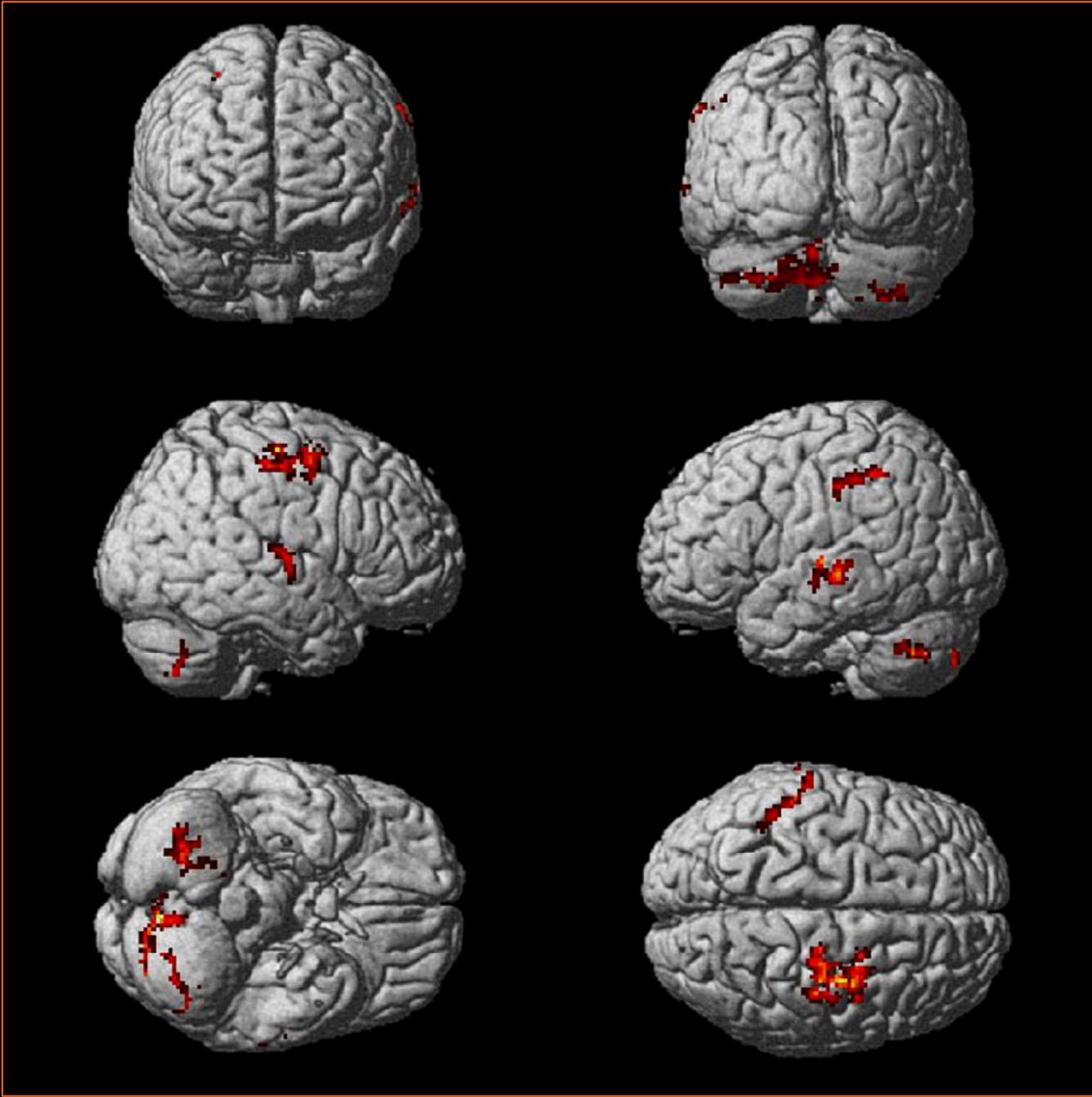
1. Preparazione
2. Acquisizione immagini
3. Post – processing
  - *elaborazione statistica*
  - *verifica*

60 – 120 minuti

---

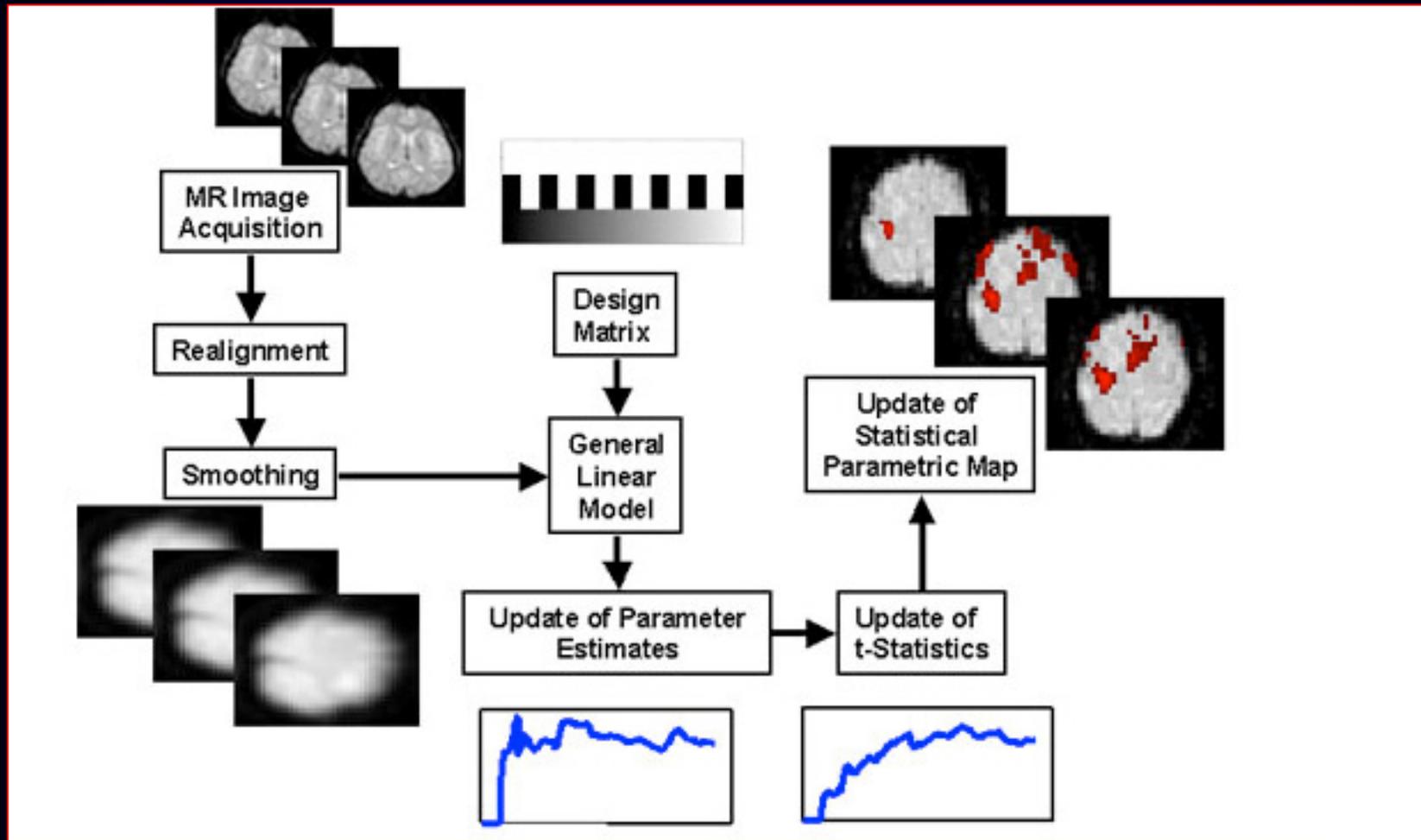




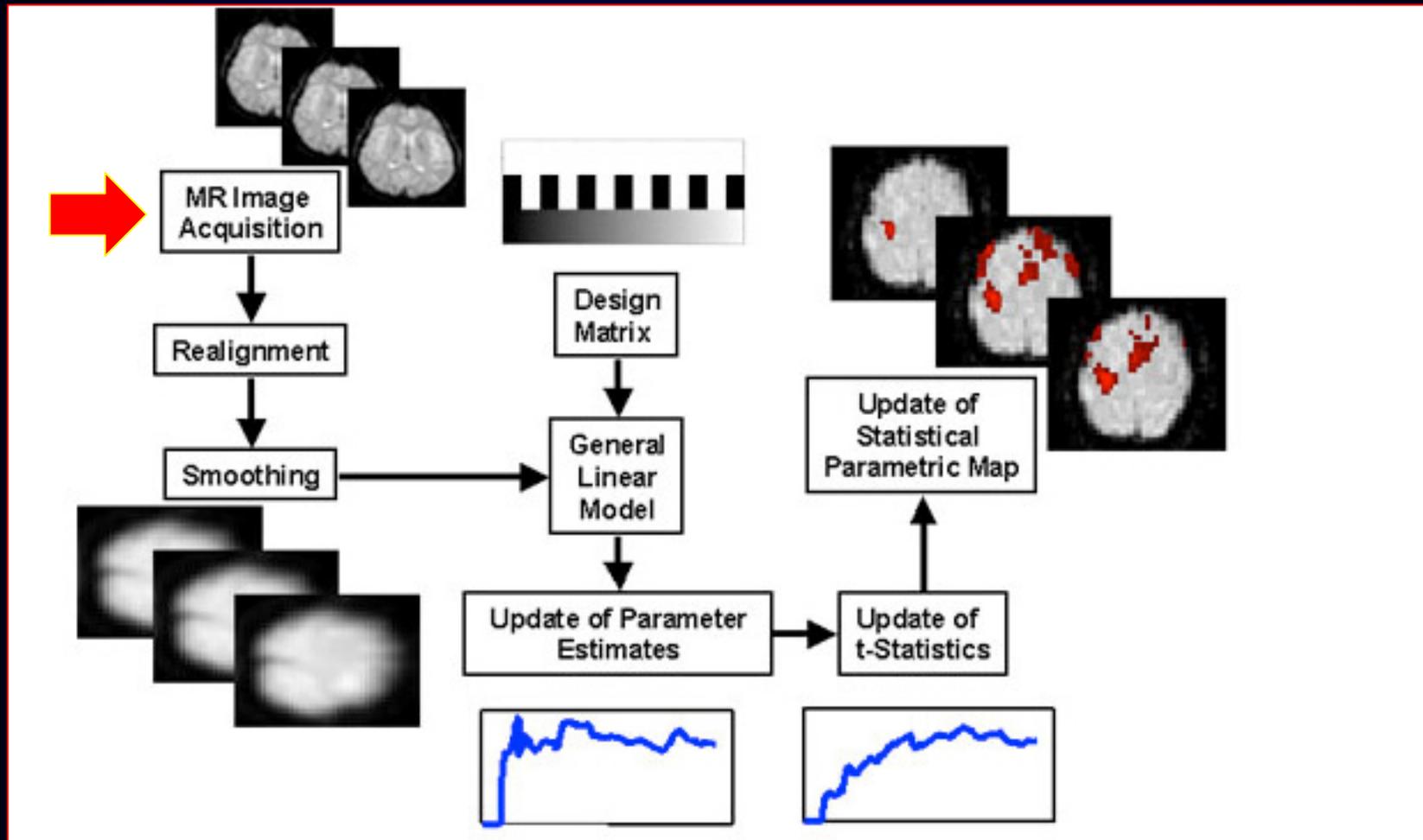


3D

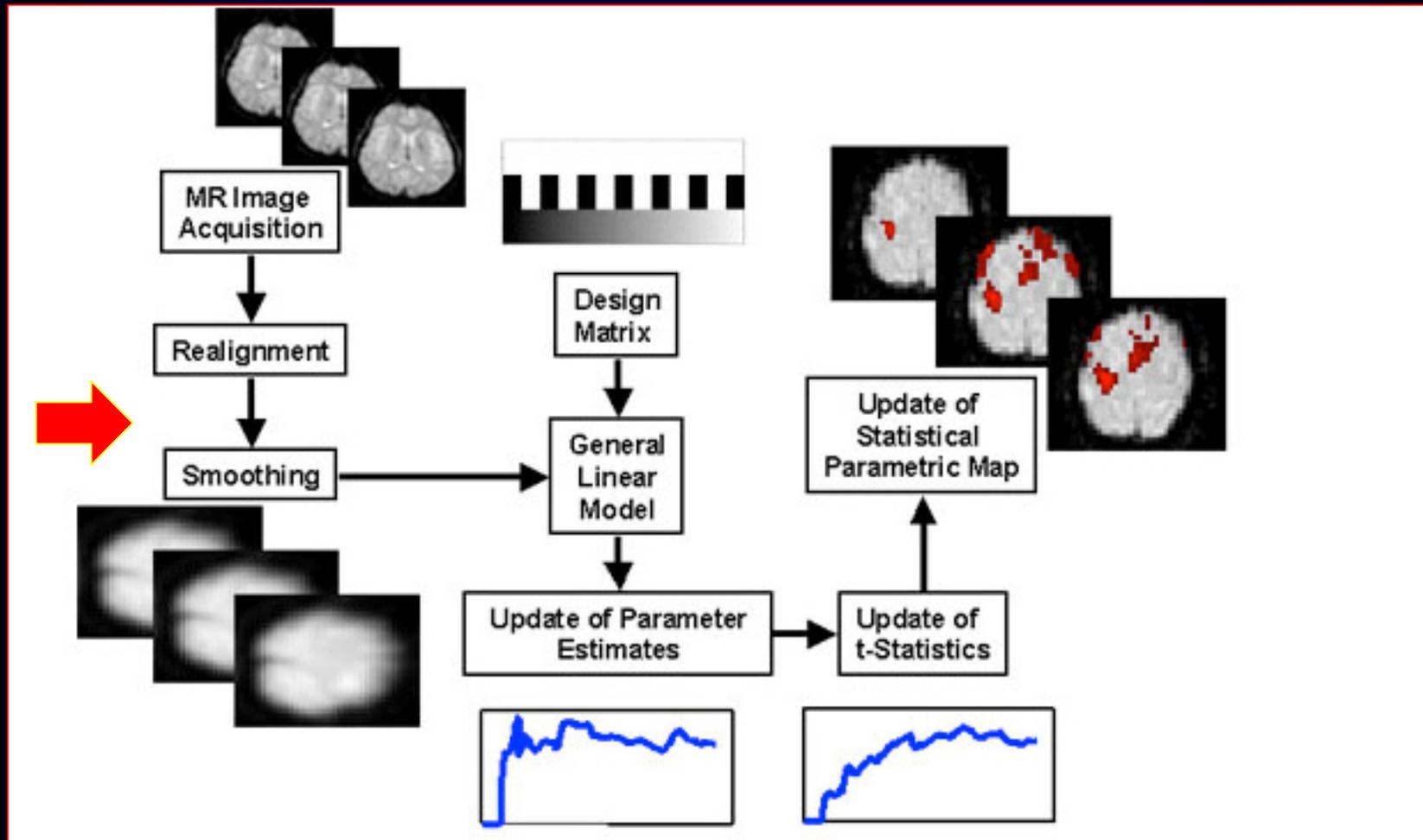
# Post-processing



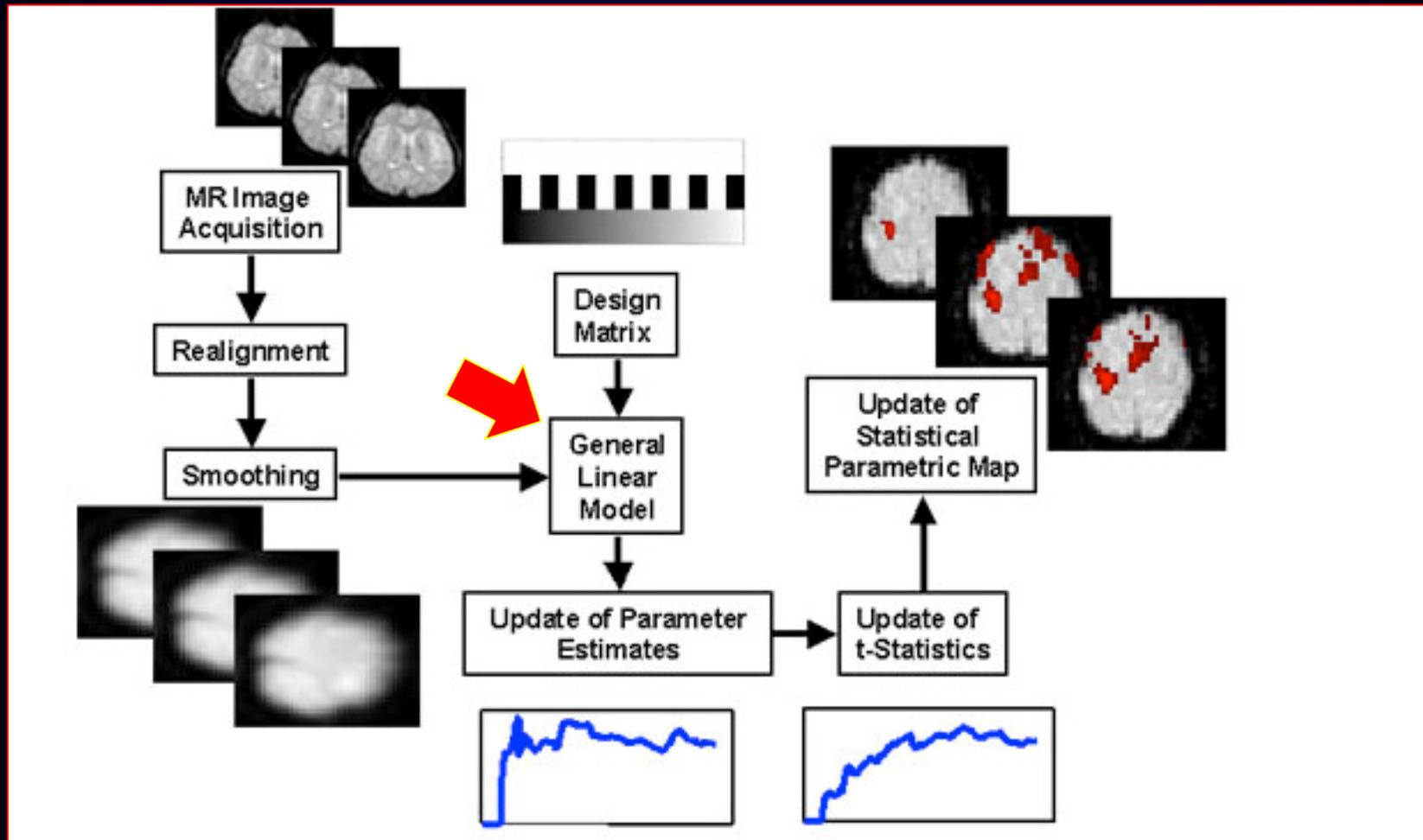
# Post-processing



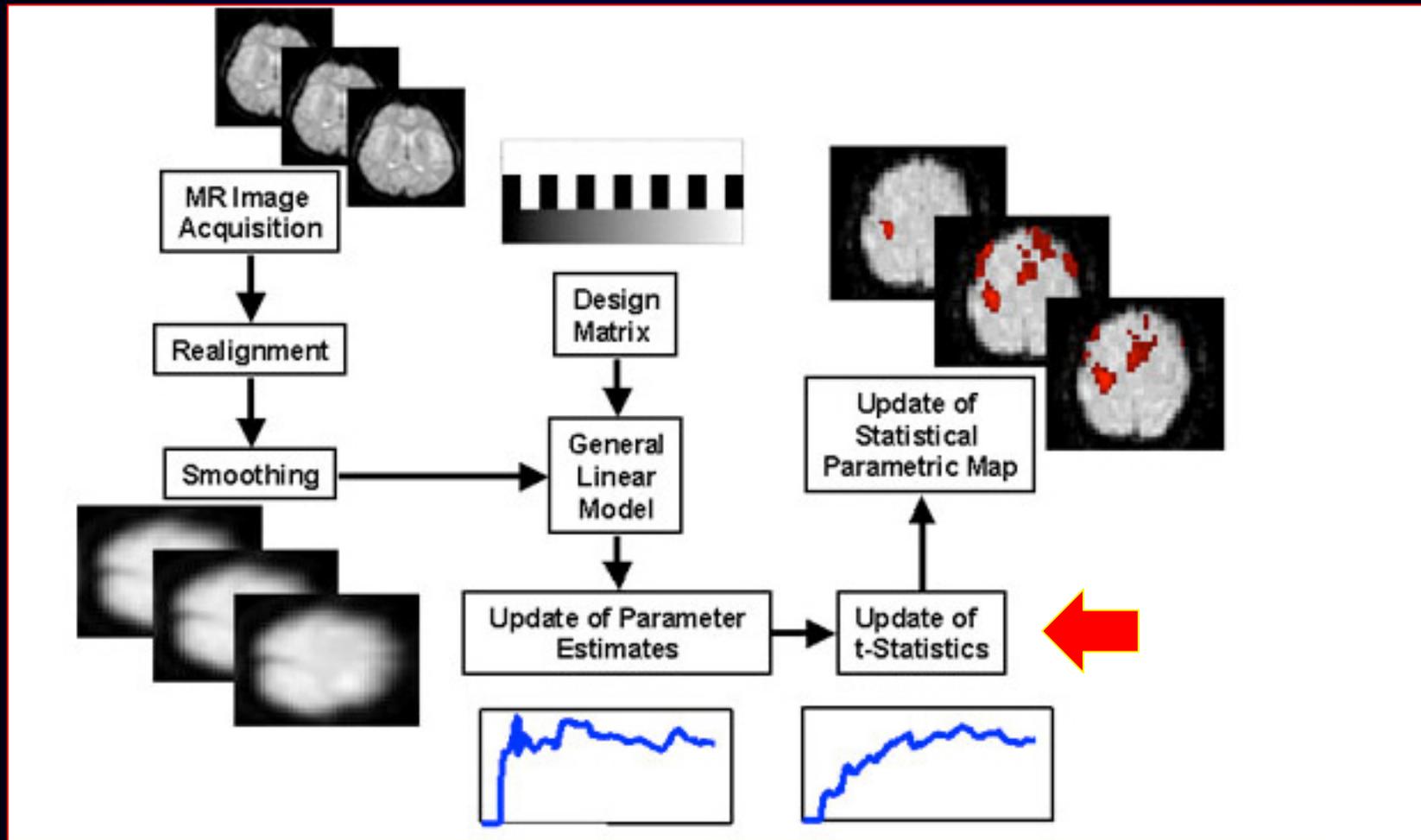
# Post-processing



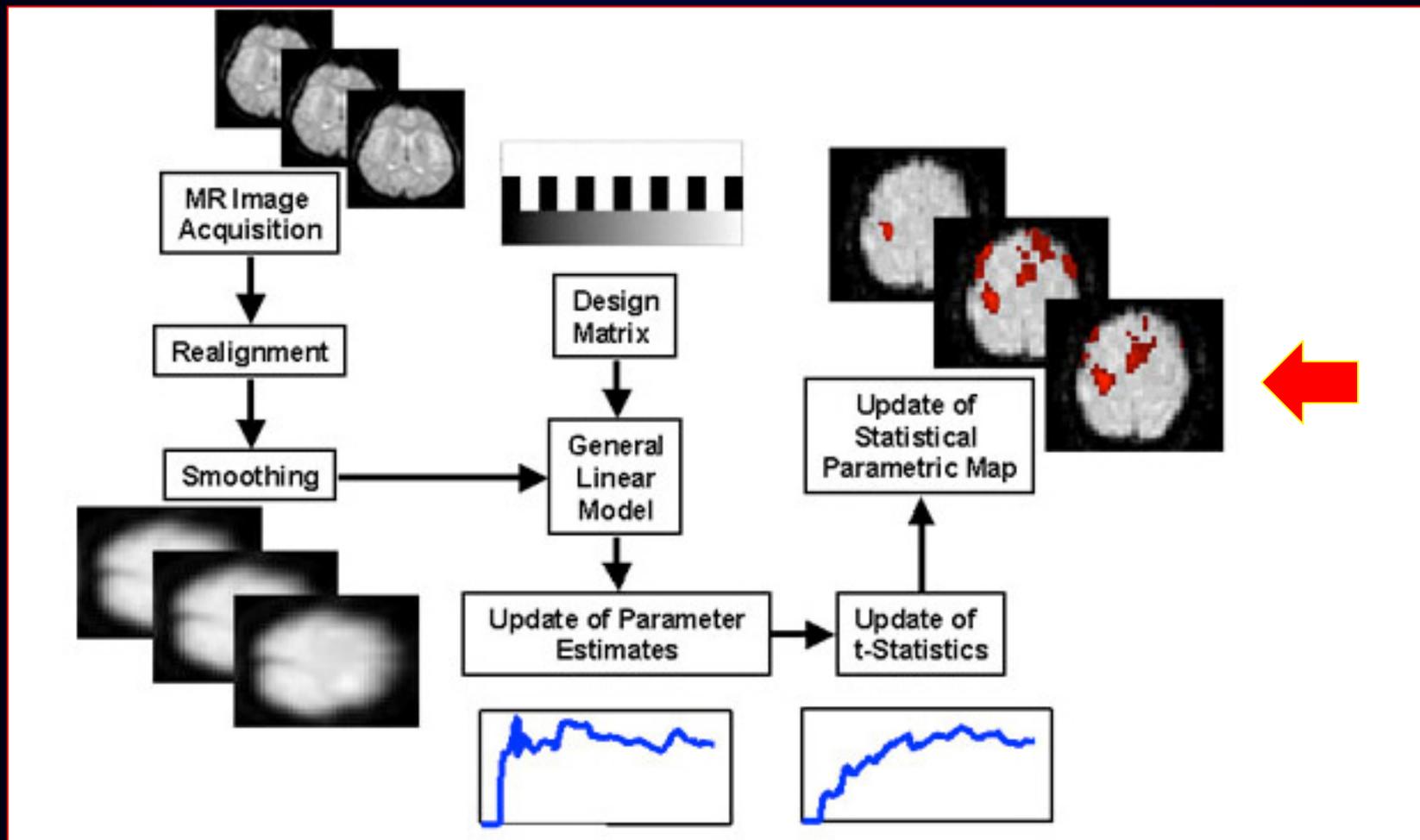
# Post-processing



# Post-processing

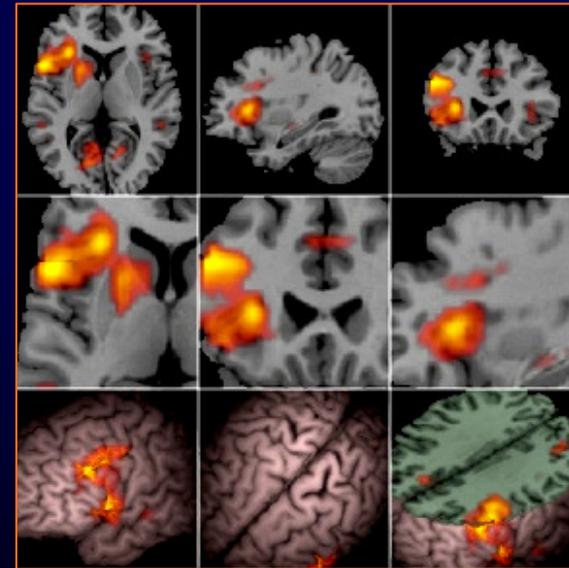
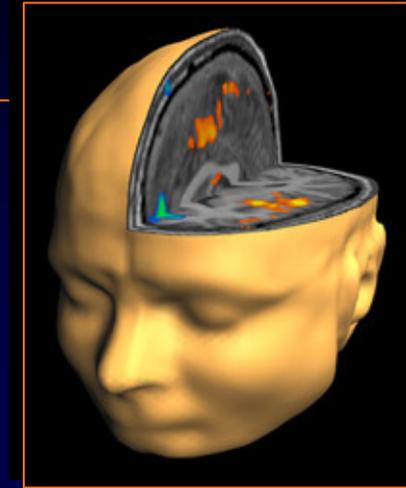


# Post-processing



# Terminologia

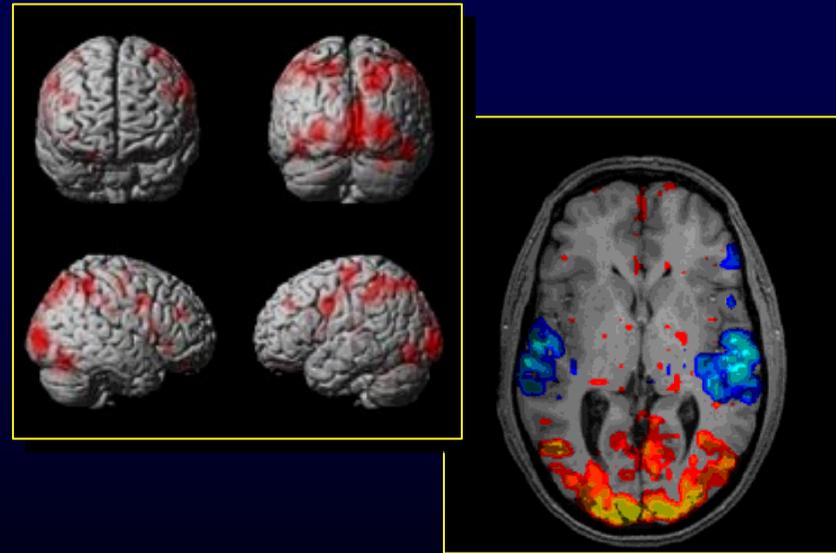
- Paradigma (Task)
- Stimolo
  - sensitivo
  - motorio
  - visivo
  - verbale
  - cognitivo
- Aree funzionali



# Funzioni *mappabili*

- Sensitiva
- Motoria
- Uditiva
- Visiva
- Linguaggio

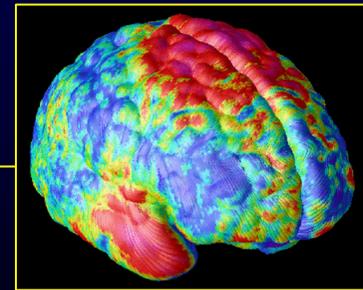
Sistema cognitivo



# Applicazioni

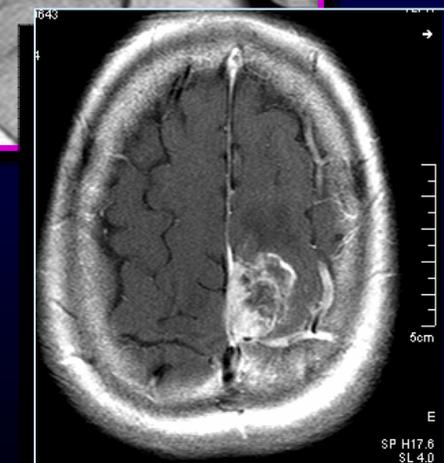
---

- Neurochirurgia
- Neurologia
- Neuroscienze



# RM @ alto campo *caratteristiche*

- Elevata risoluzione spaziale
- Elevata risoluzione temporale
- Elevato contrasto
- Elevata sensibilità
- Non invasiva
- **Versatilità**



# *f*MRI @ alto campo

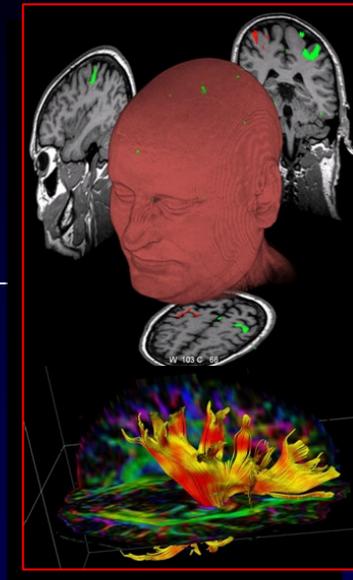
---

Elevata risoluzione *spaziale*

- *migliore informazione funzionale*
- *migliore localizzazione anatomica*

---

*caratteristiche*



# *f*MRI @ alto campo

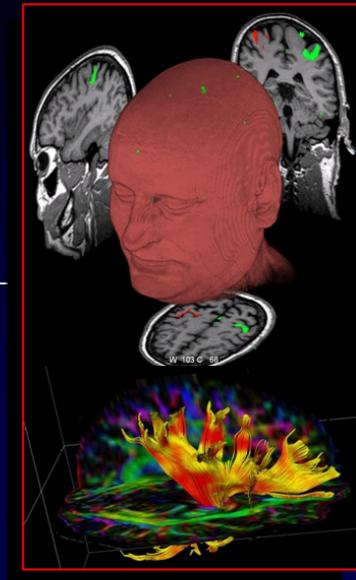
---

Elevata risoluzione *temporale*

- *maggiore conoscenza delle dinamiche neurali*
- *maggiore conoscenza delle strutture neurali*

---

*caratteristiche*



# *f*MRI @ alto campo



Complessità  
paradigmi

Risoluzione  
temporale

Risoluzione  
spaziale



# Neurochirurgia



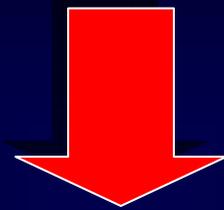
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Tumori cerebrali infiltrativi

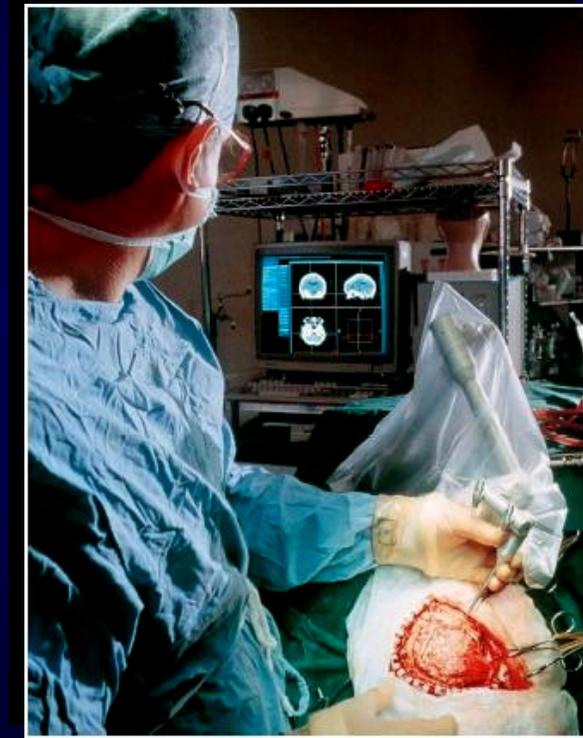
---

Trattamento

Resezione totale



Resezione  
&  
Preservazione funzionale



---

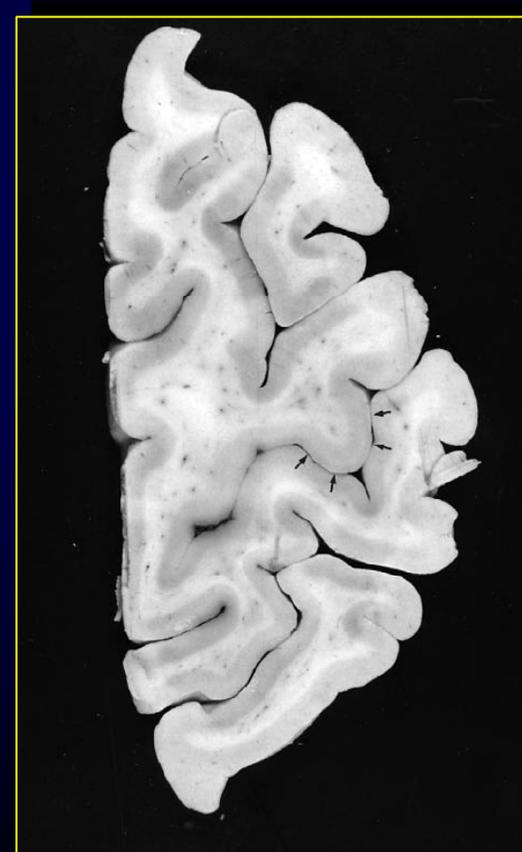
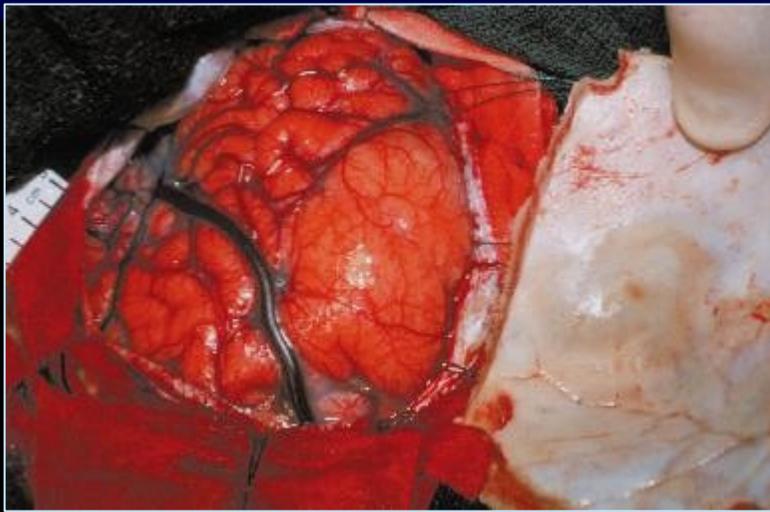
Tumori cerebrali infiltrativi

---

**Trattamento**

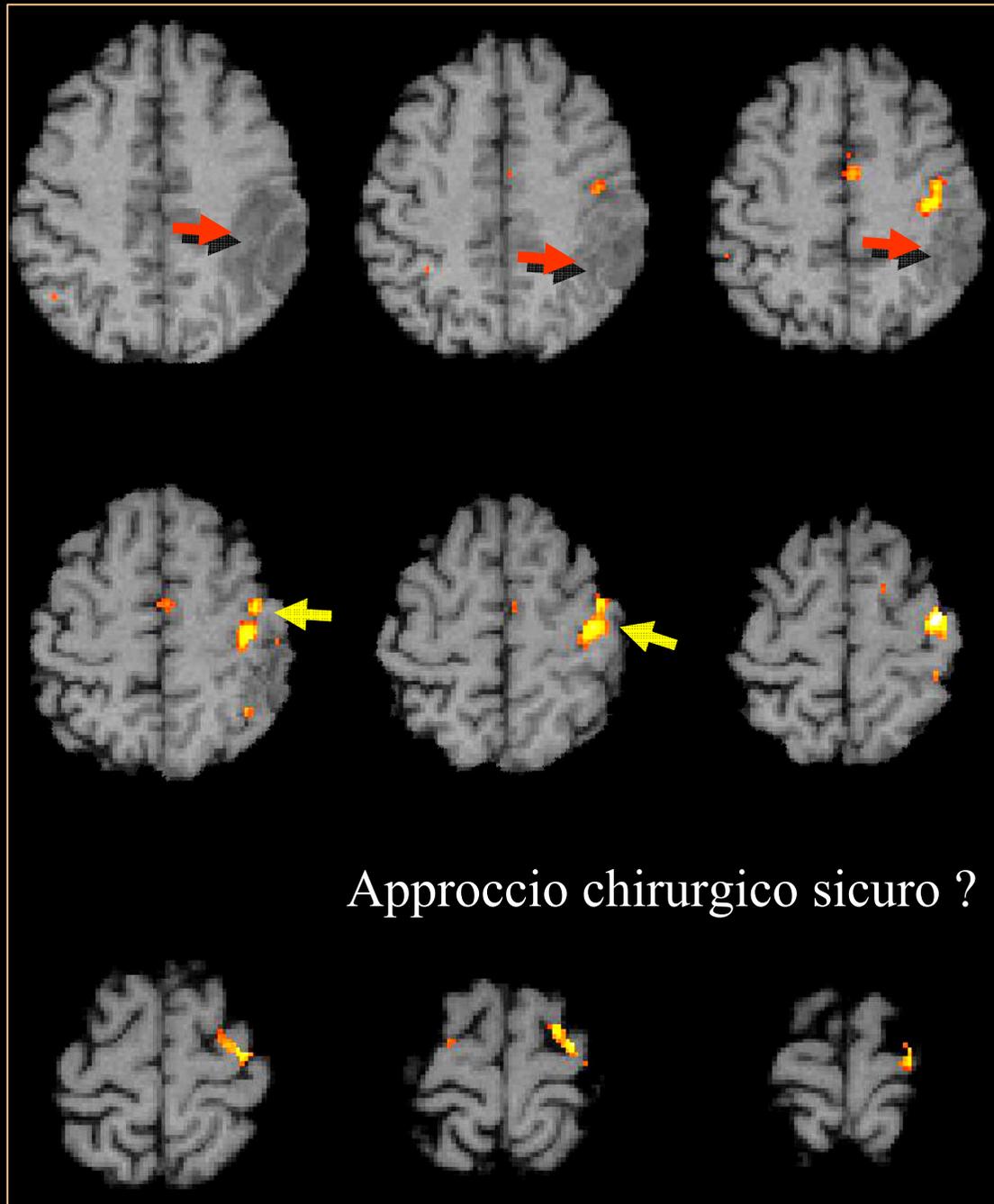
## Identificazione corteccia motoria

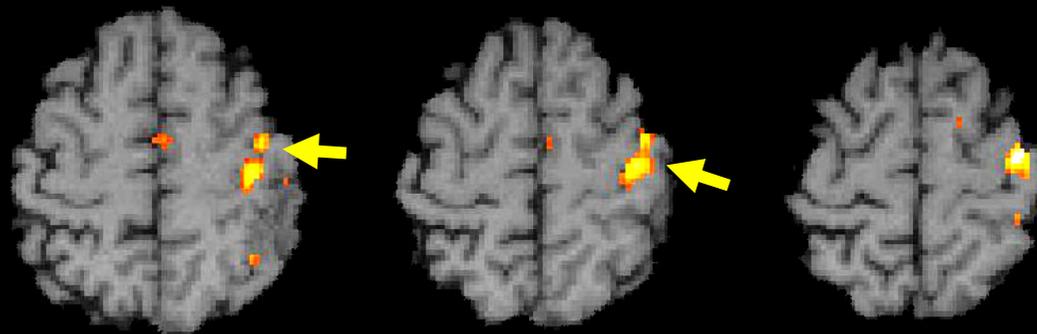
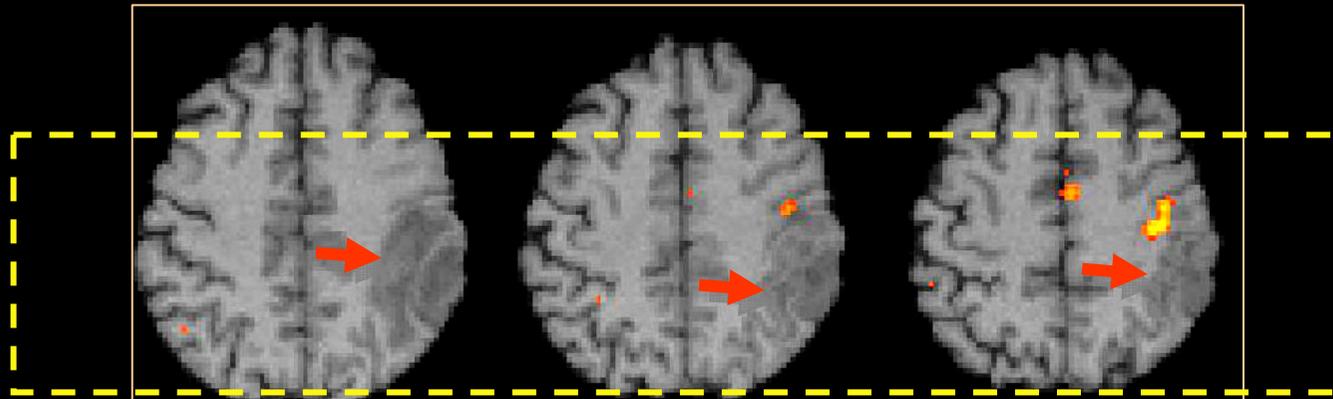
- criteri anatomici
- effetto massa



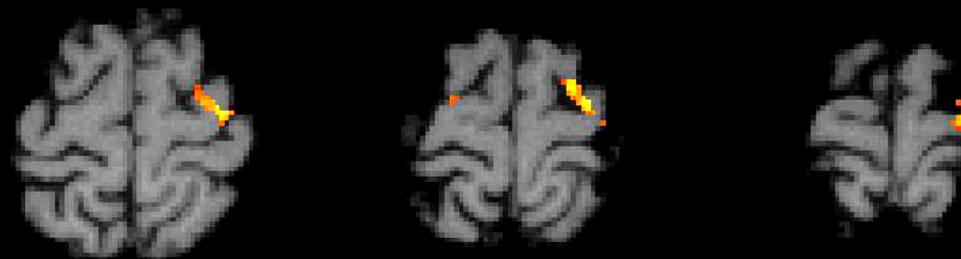
# Quesiti più frequenti (FAQ) ———

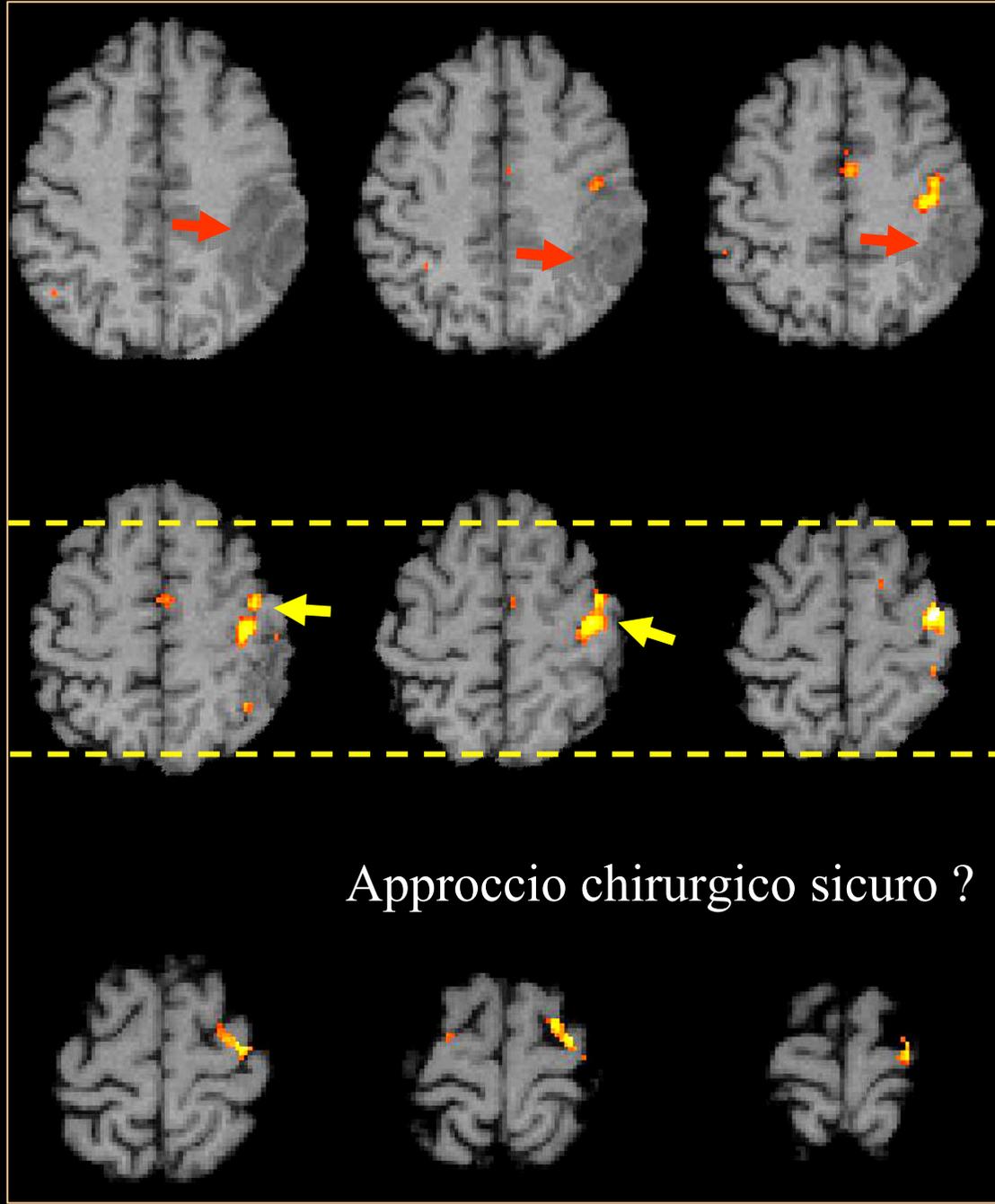
- M1 & S1: localizzazione
  - funzione verbale
    - dominanza emisferica
    - dove sono le aree del linguaggio
    - approccio chirurgico sicuro
    - rischi e conseguenze intervento
  - funzioni cognitive
-



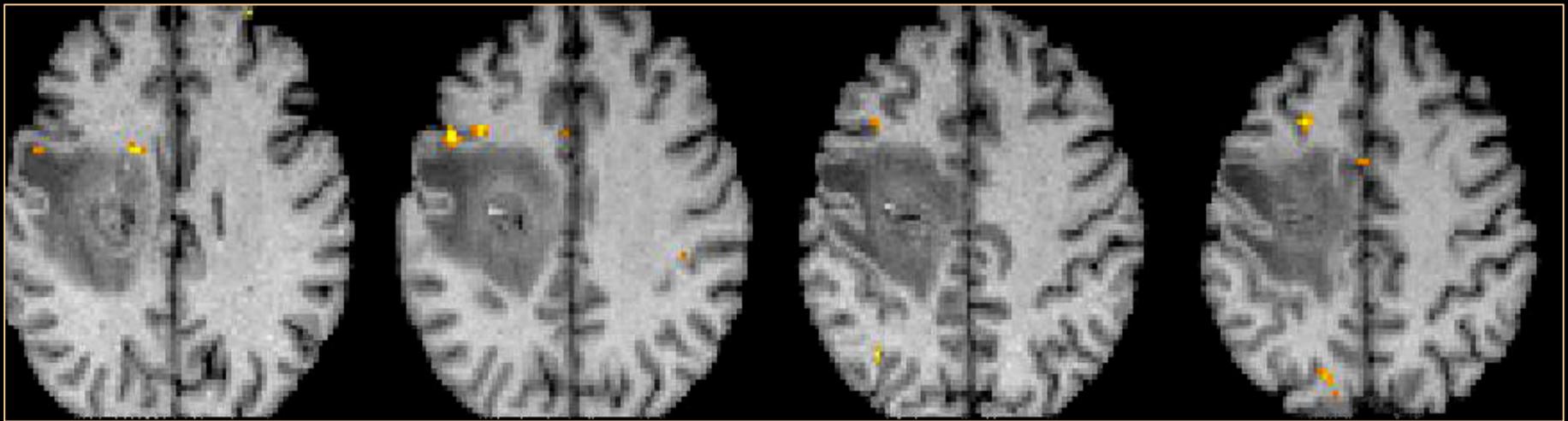


Approccio chirurgico sicuro ?

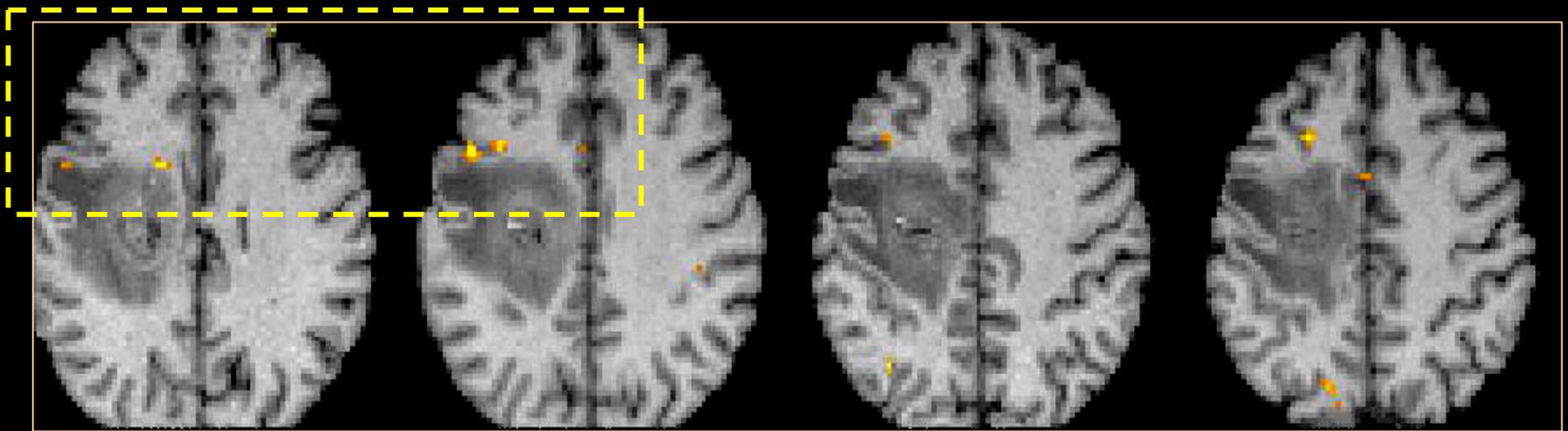




Approccio chirurgico sicuro ?



La lesione è operabile?



Quali sono i rischi?

# Paradigmi

## Funzione motoria

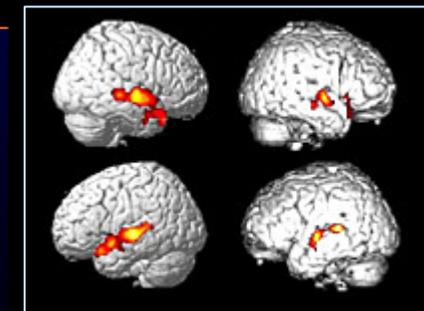
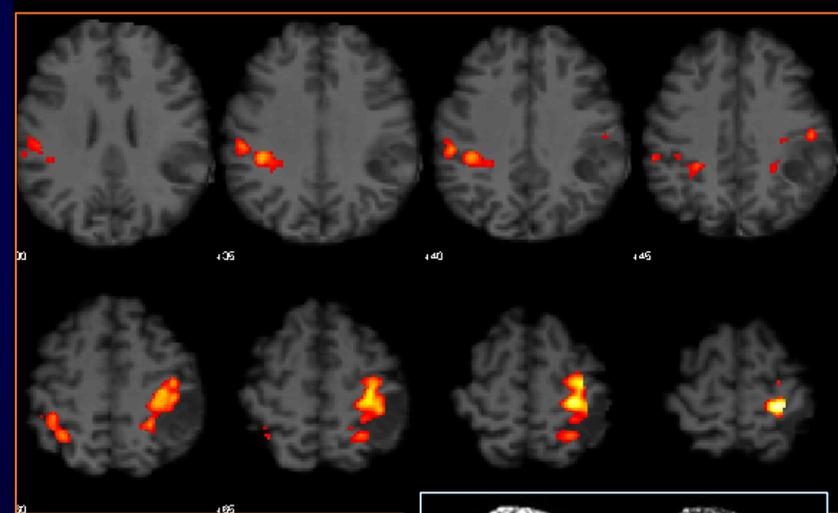
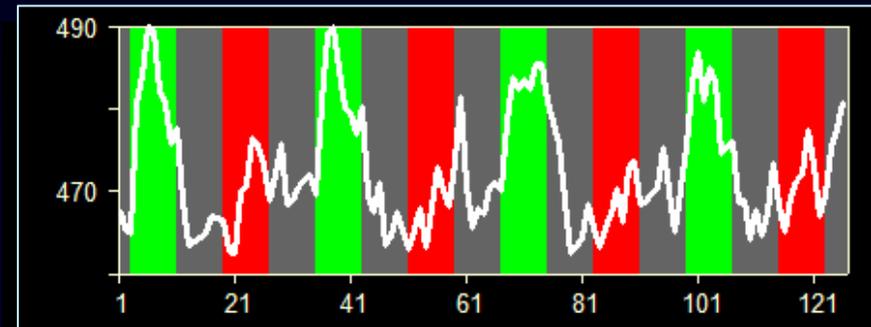
- “Finger tapping”
- Apertura-chiusura mano
- Flesso-estensione piede

## Funzione sensitiva

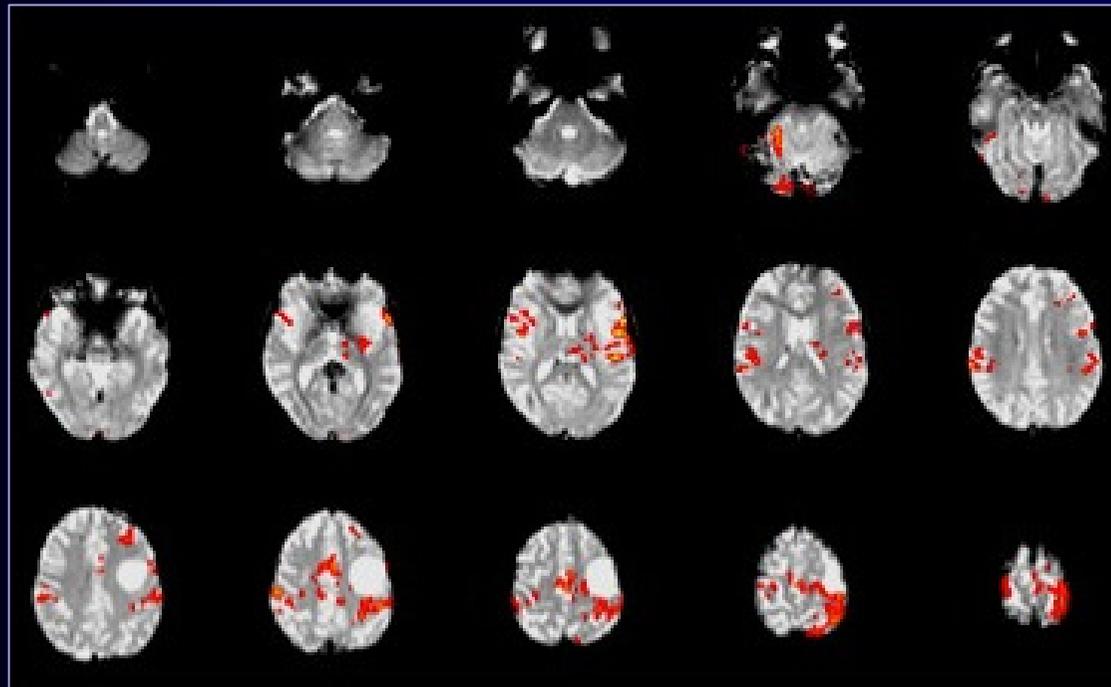
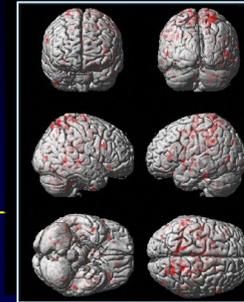
- stimolazione passiva mano

## Funzione verbale

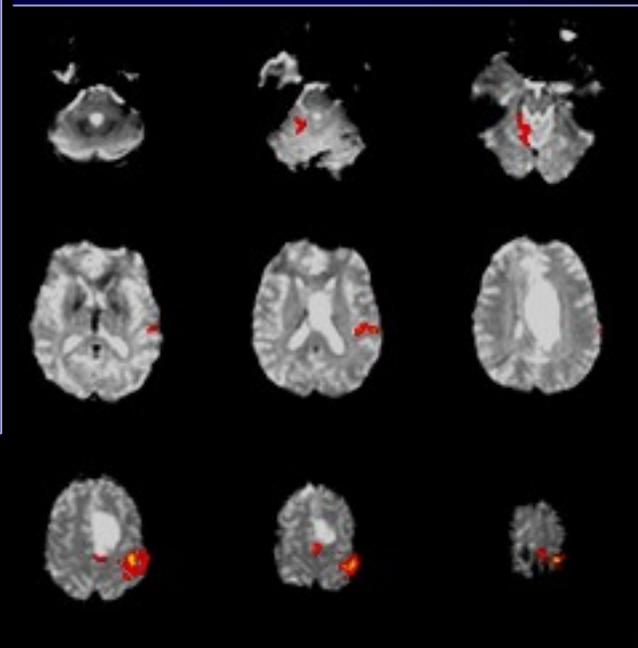
- Fluenza semantica
- Produzione di parole
- Lettura di parole
- Denominazione di oggetti



# Brain Mapping

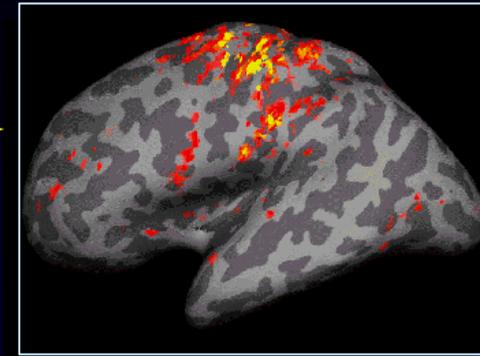


Funzione motoria



# Brain Mapping

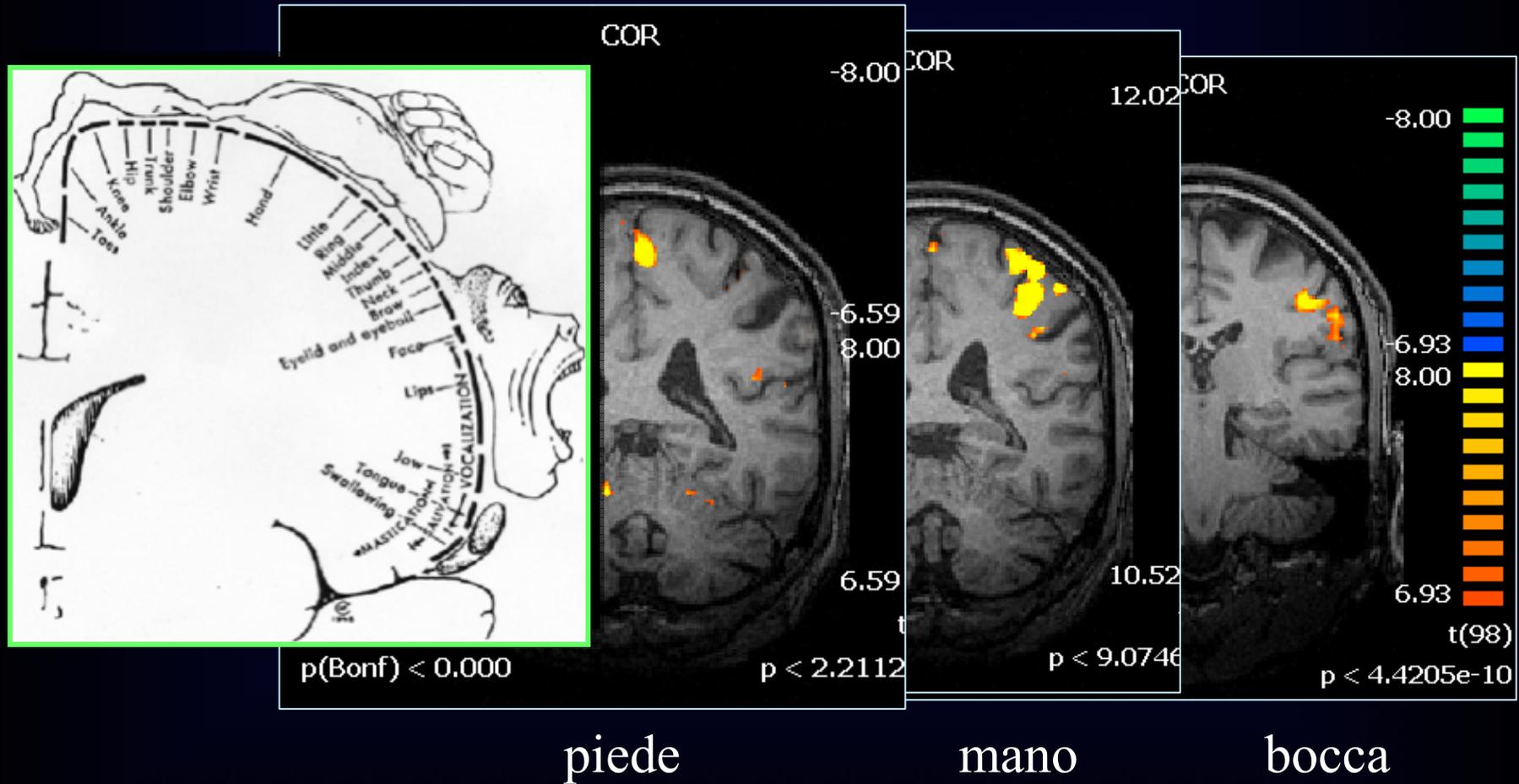
---



- Localizzazione M1 & S1
  - Imaging della somatotopia
  - Plasticità cerebrale
-

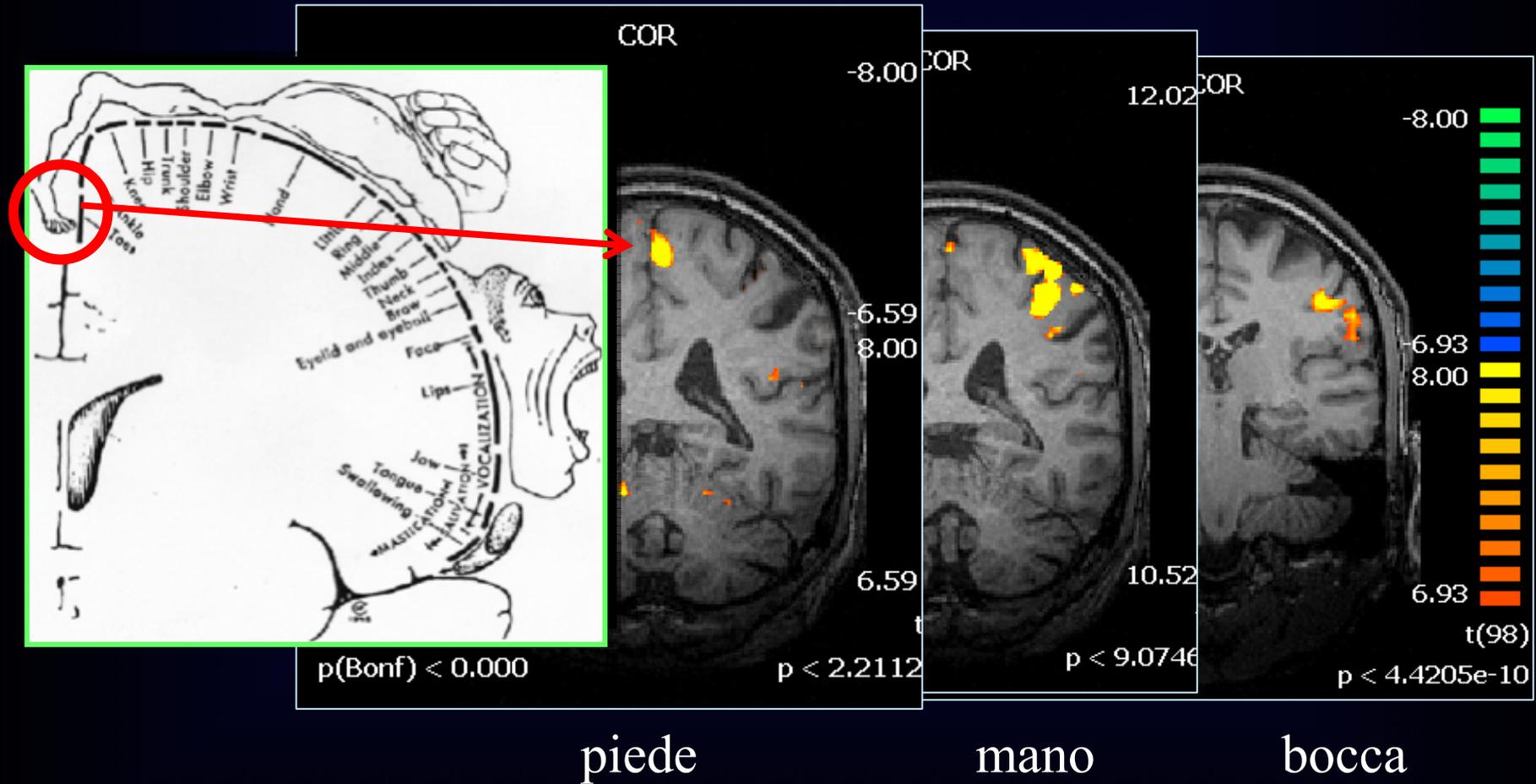
# fMRI: somatotopia

@ 3.0T



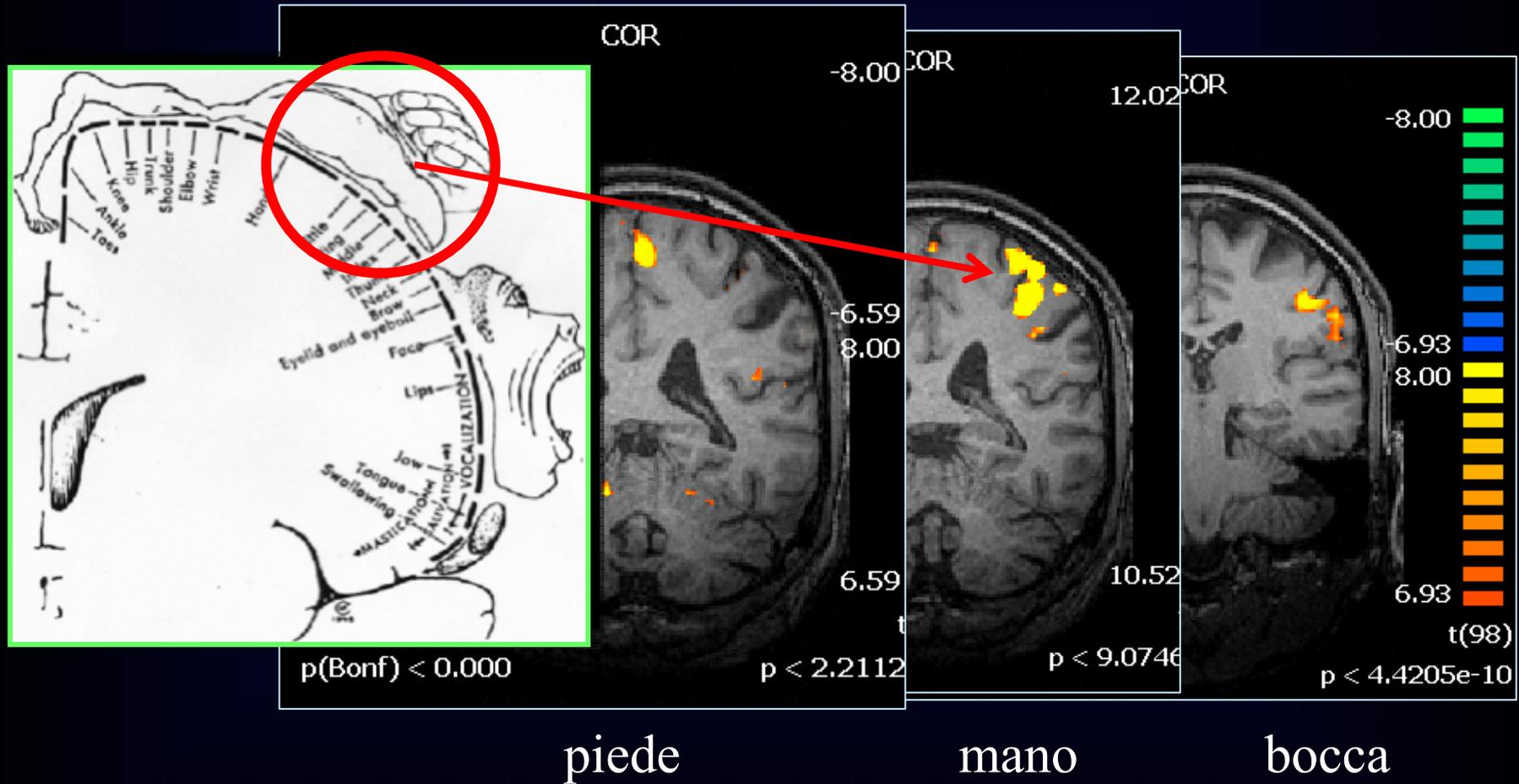
# *f* MRI: somatotopia

@ 3.0T



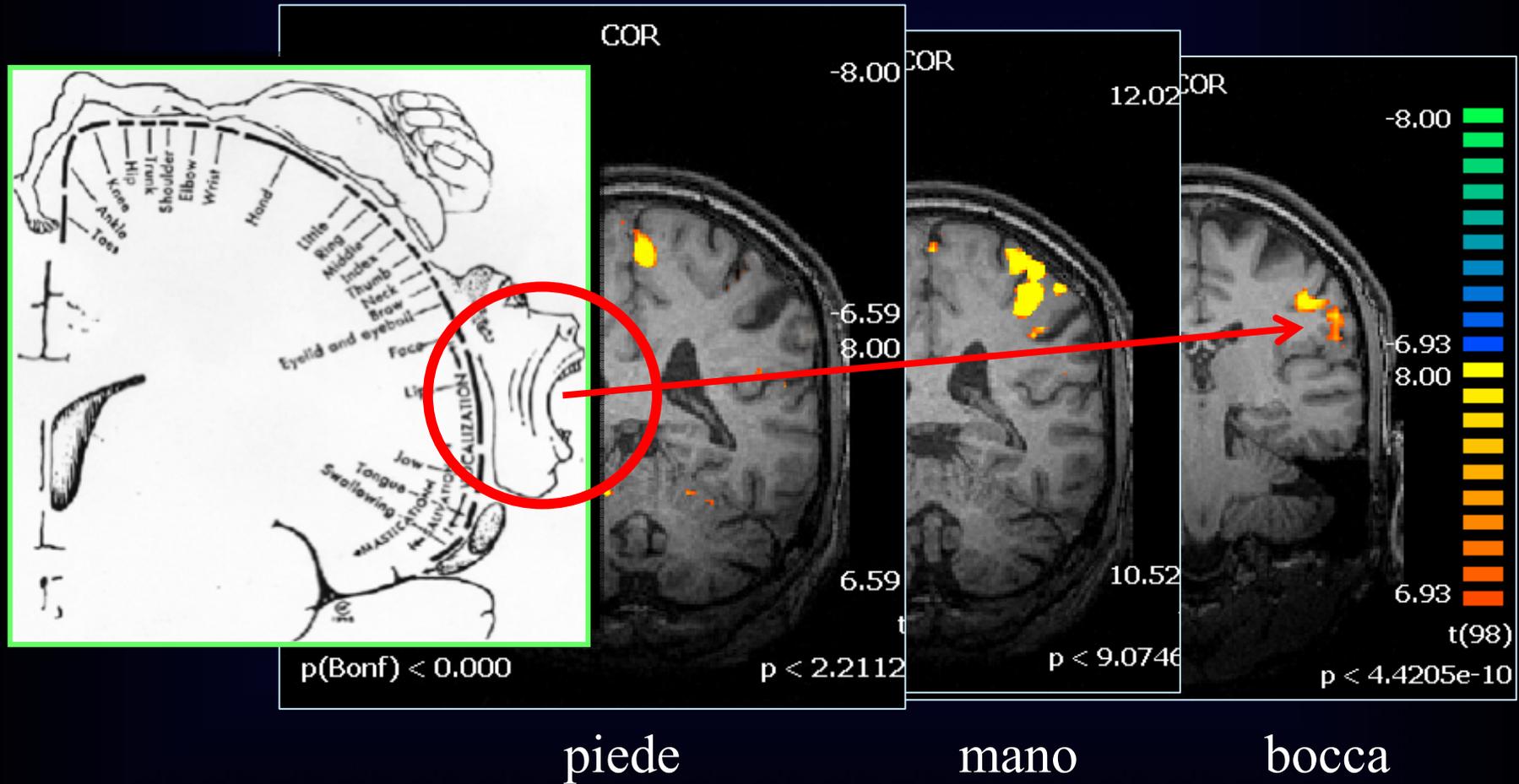
# *f* MRI: somatotopia

@ 3.0T

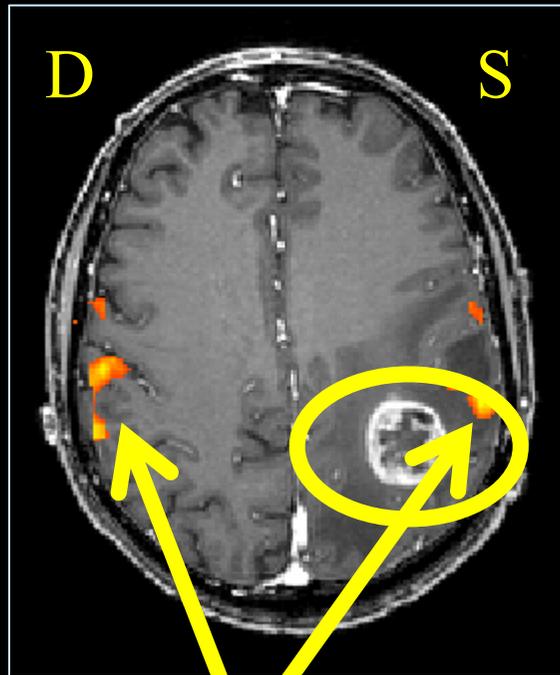


# fMRI: somatotopia

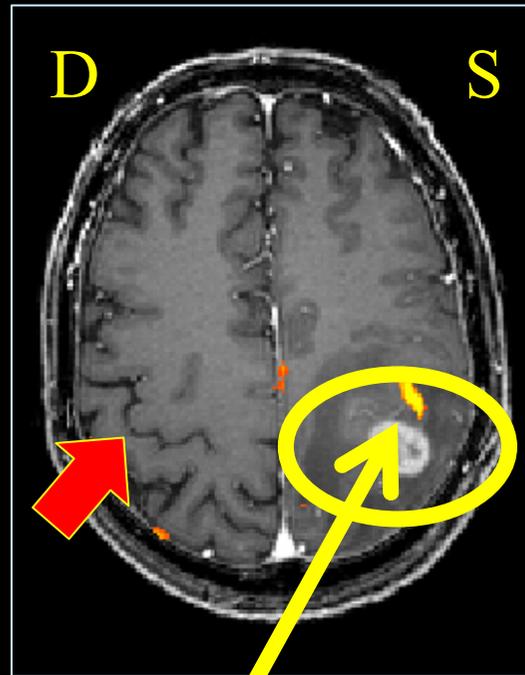
@ 3.0T



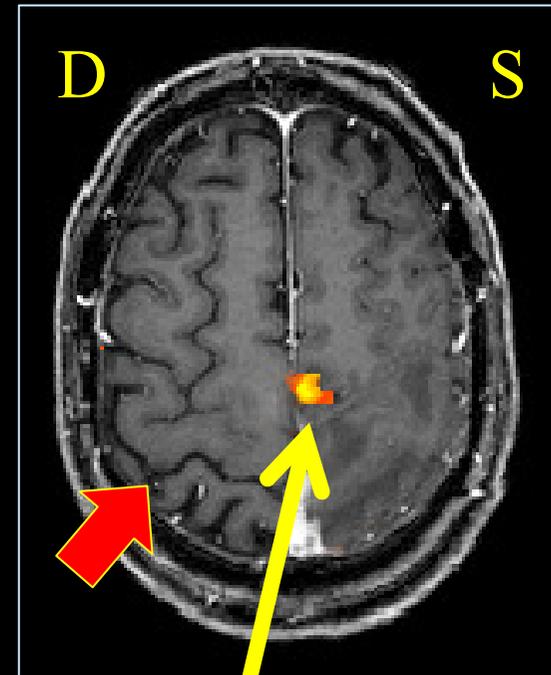
# M1 & S1: assenza di reperi anatomici RM



bocca



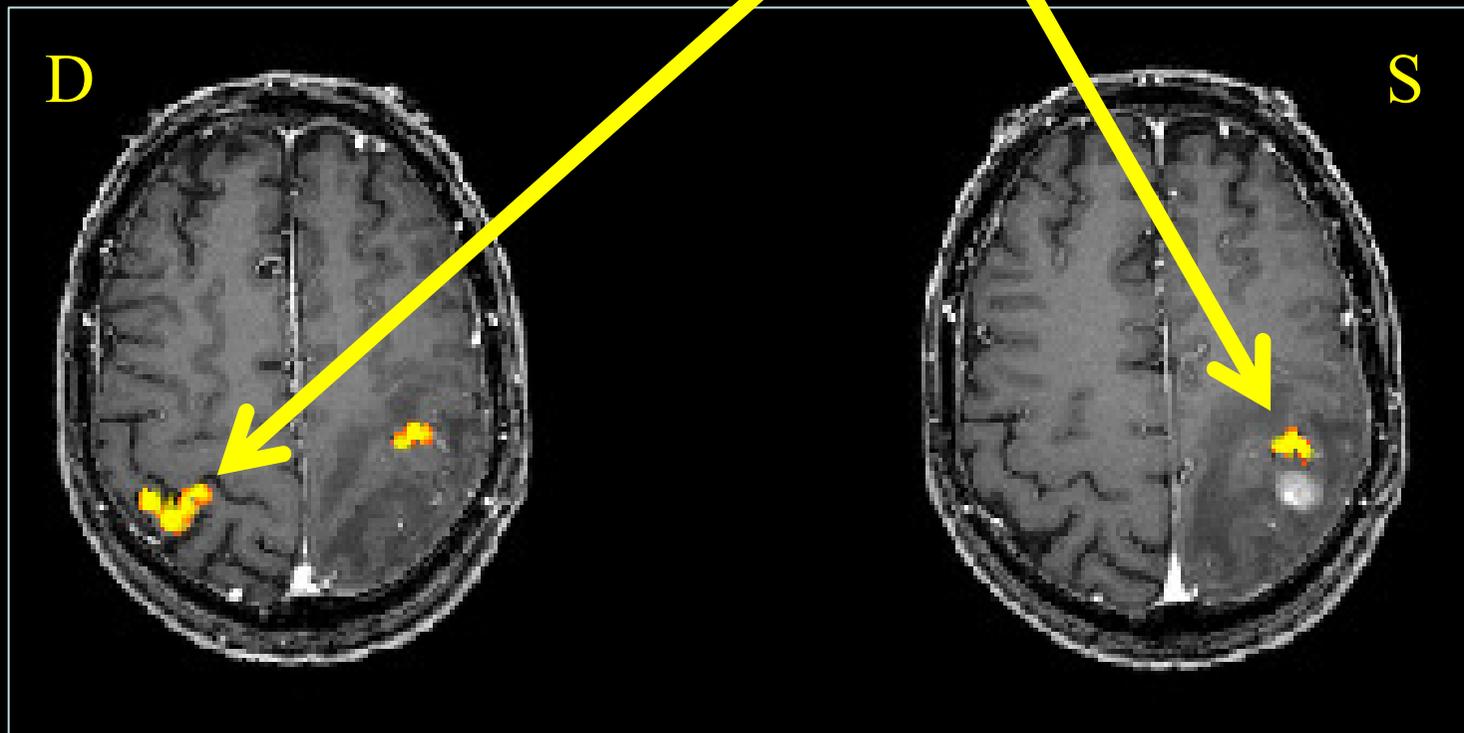
mano destra



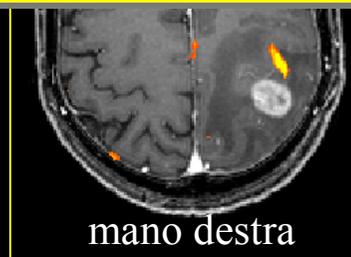
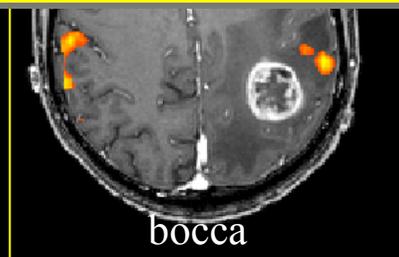
piede destro

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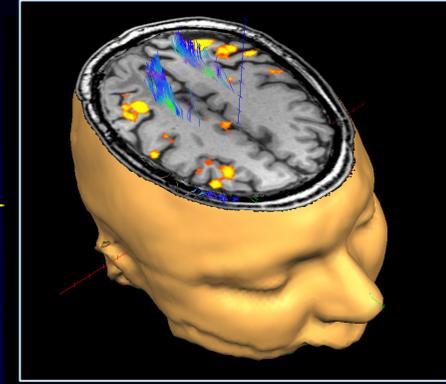
## stimolazione tattile mano destra & sinistra



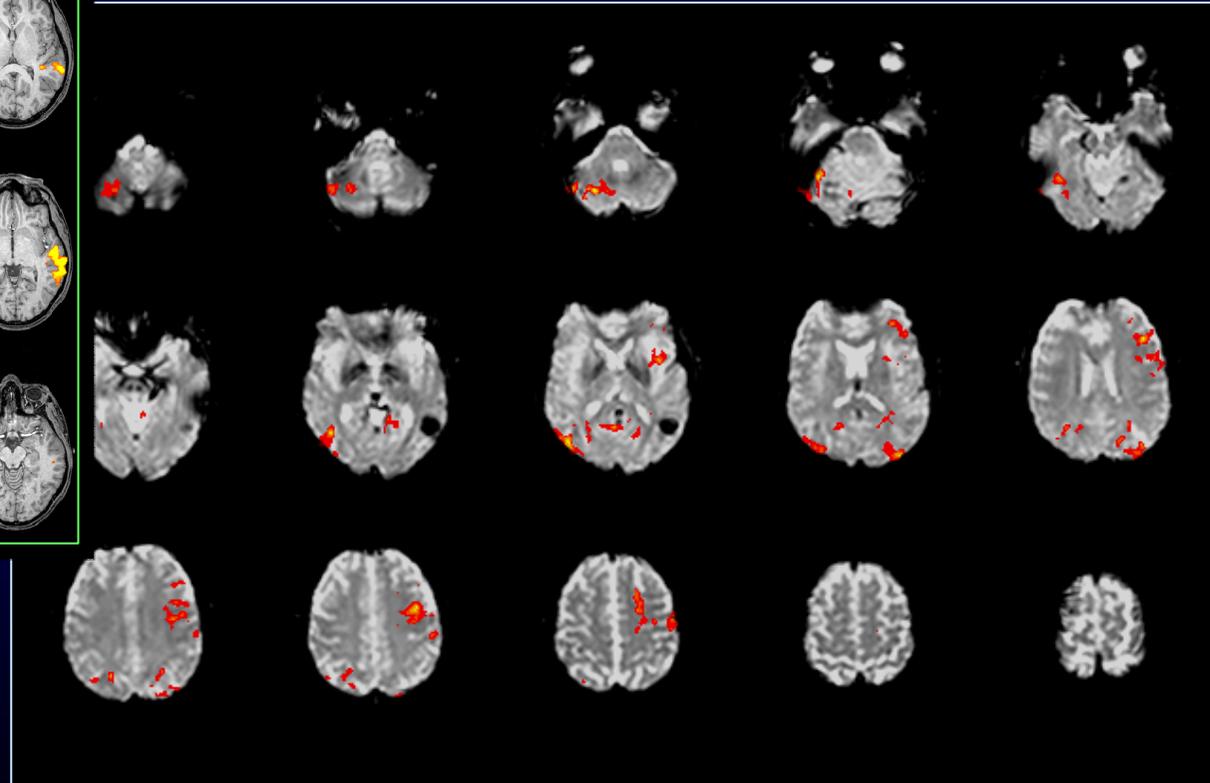
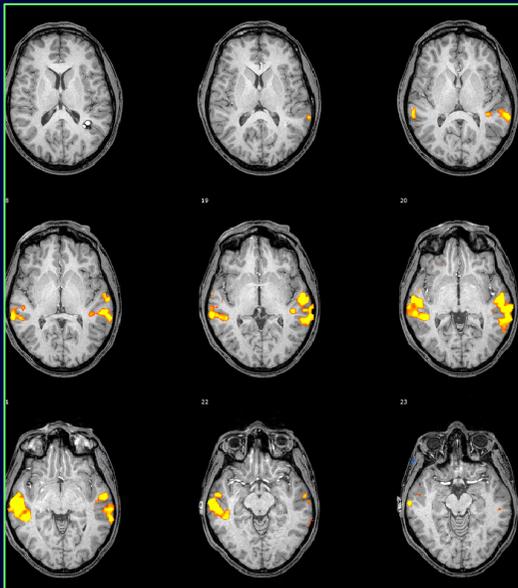
- Topografia M1 & S1
- Validazione intra-operatoria



# Brain Mapping

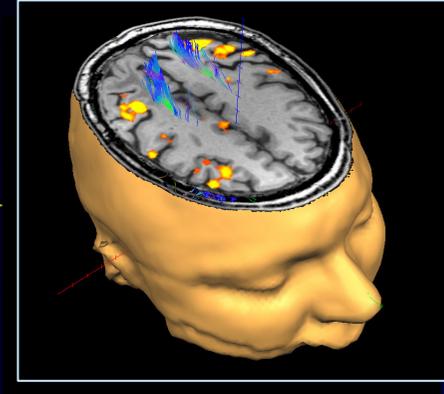


## Funzione verbale



# Brain Mapping

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## Funzione verbale

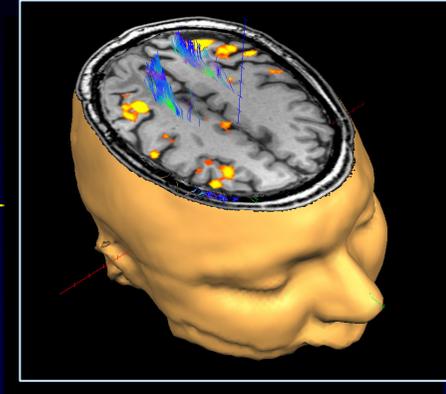
- complessità della rappresentazione del linguaggio
- difficoltà di implementazione (*costi dell'hardware*)
- variabilità (*paradigmi, presentazione degli stimoli*)
- validazione (*WADA test, ECoG*)

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Tumori

# Brain Mapping

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## Funzione verbale

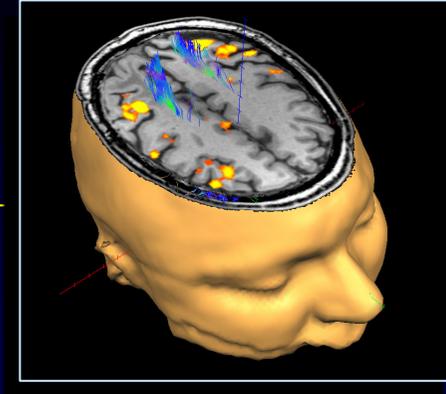
1. Localizzare le aree del linguaggio motoria (Broca) + sensoriale (Wernicke)
2. Determinare dominanza emisferica
3. Valutare plasticità e sue modificazioni

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Obiettivi

# Brain Mapping

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## Funzione verbale

1. Deficit della funzione verbale
2. Tumori emisfero sinistro & destro
3. Pazienti mancini
4. Pazienti multilingue

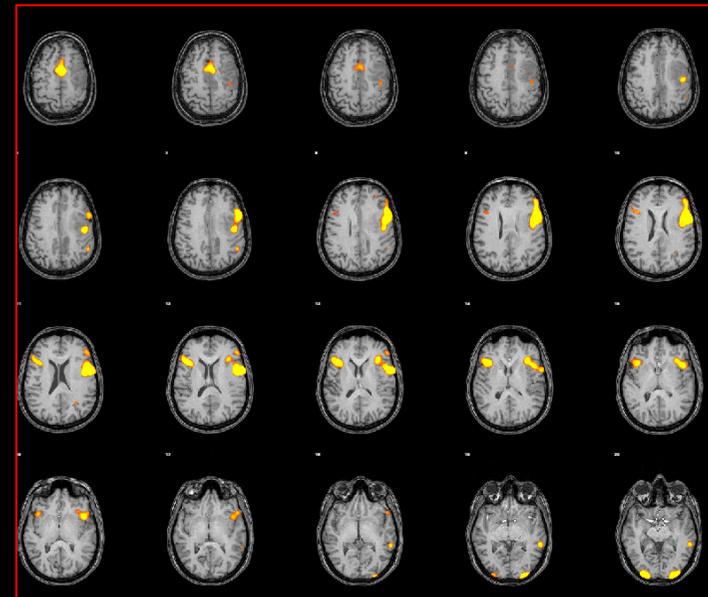
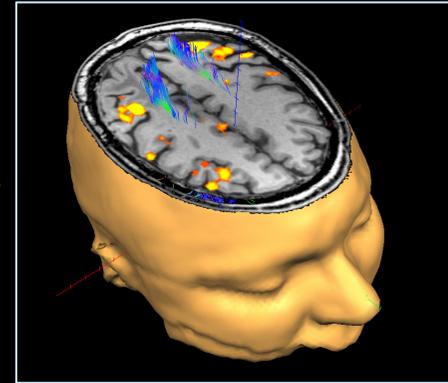
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Indicazioni

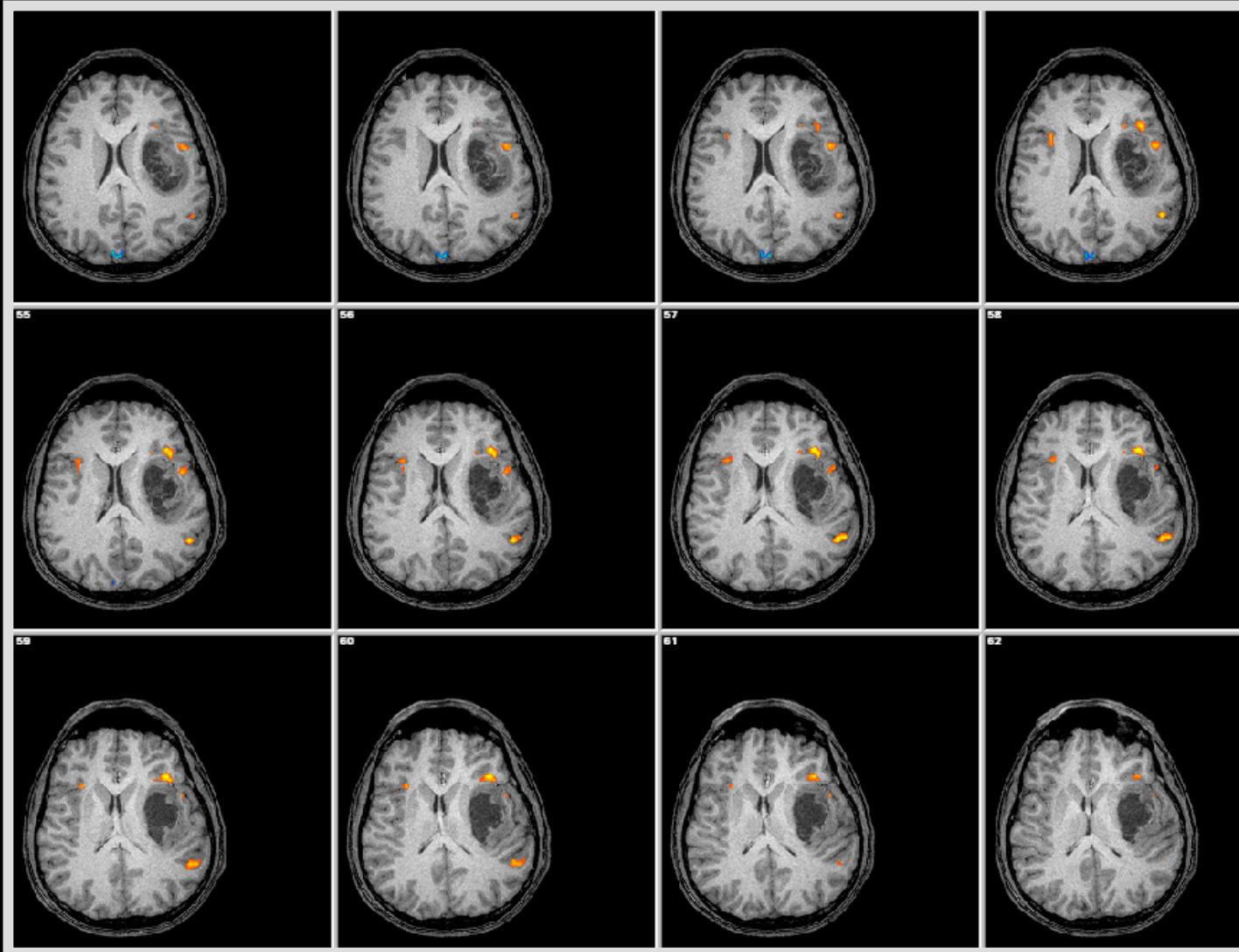
# Brain Mapping

## Paradigmi

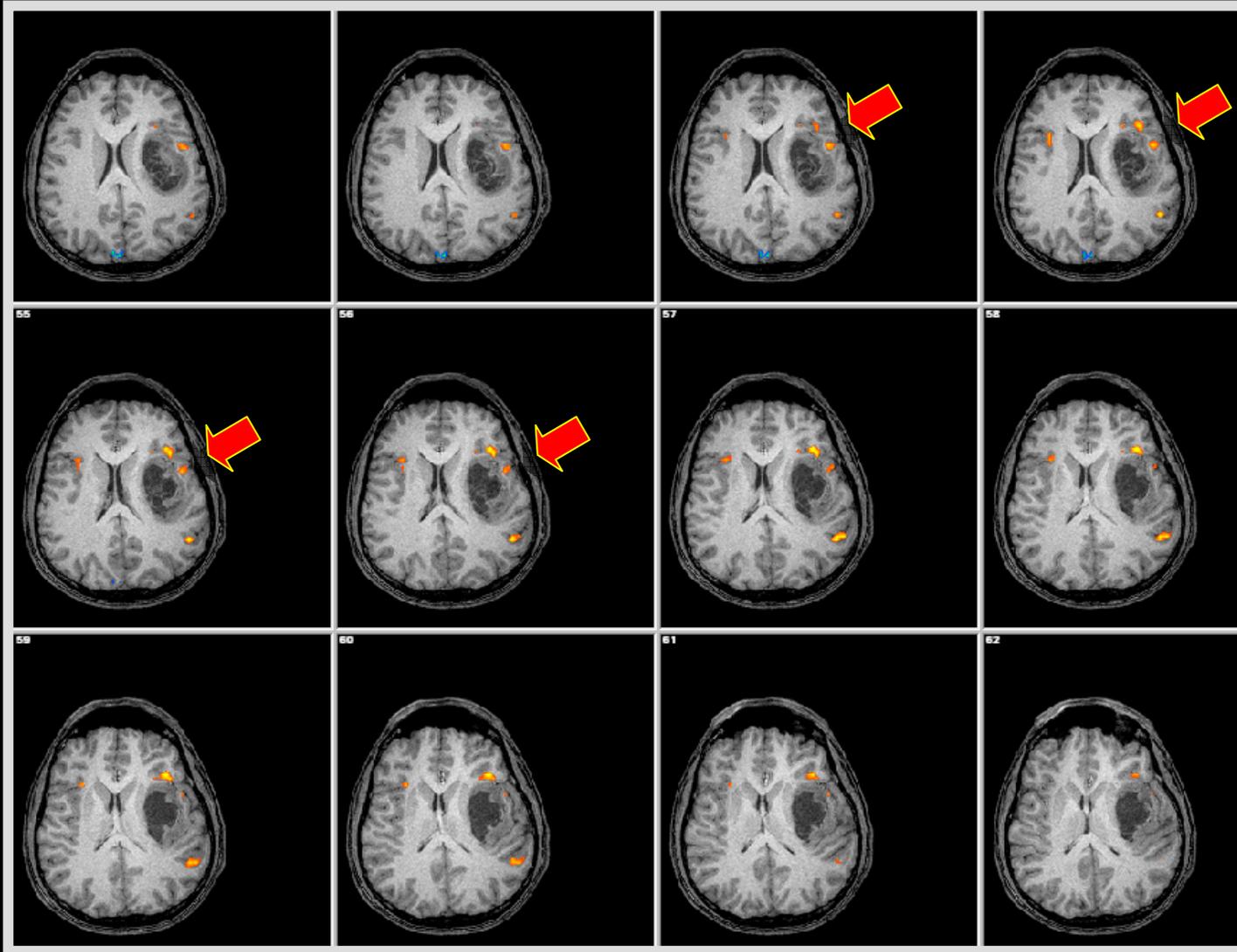
- Produzione verbale
- Lettura di parole
- Denominazione di oggetti
- Fluenza semantica



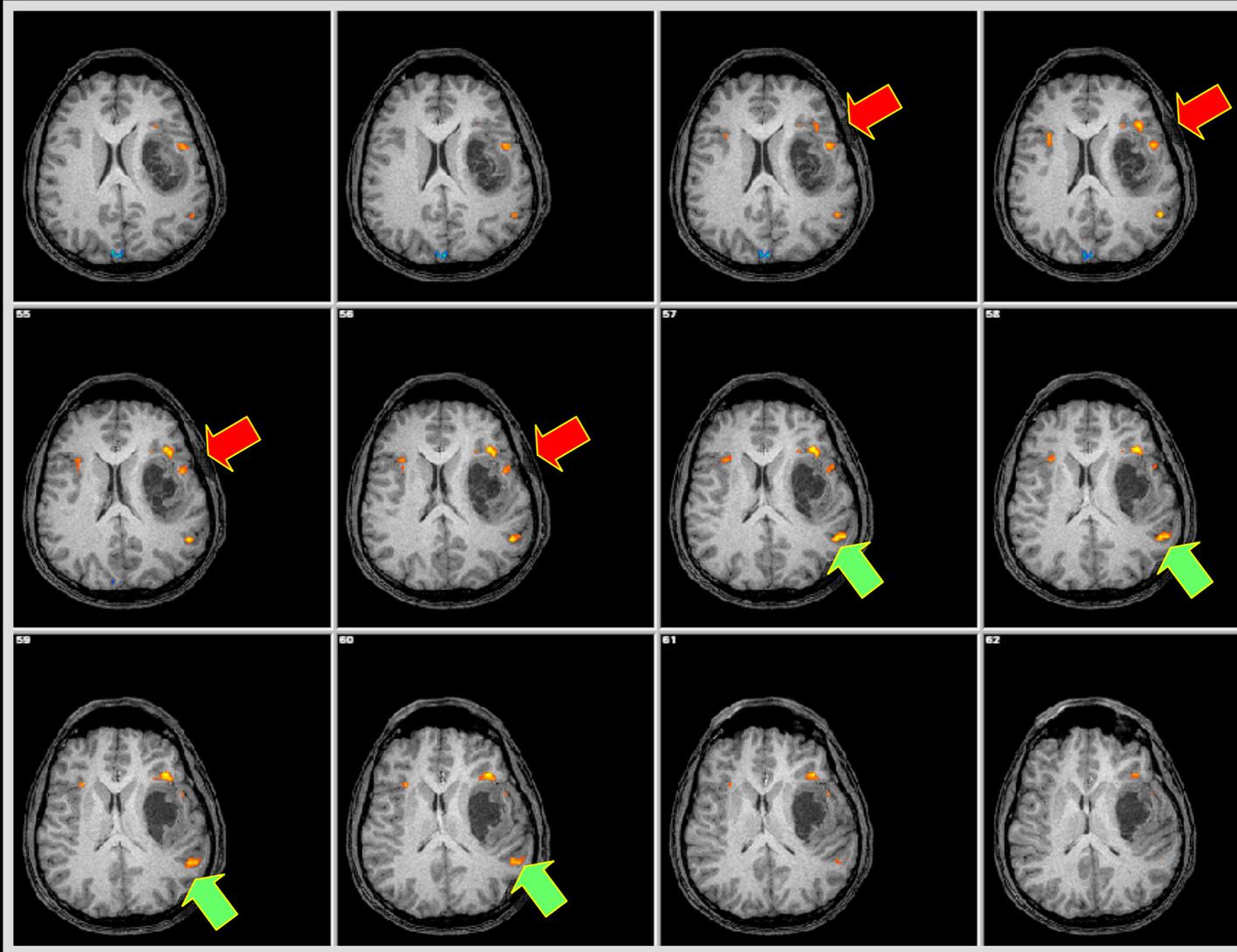
Funzione verbale



Funzione verbale

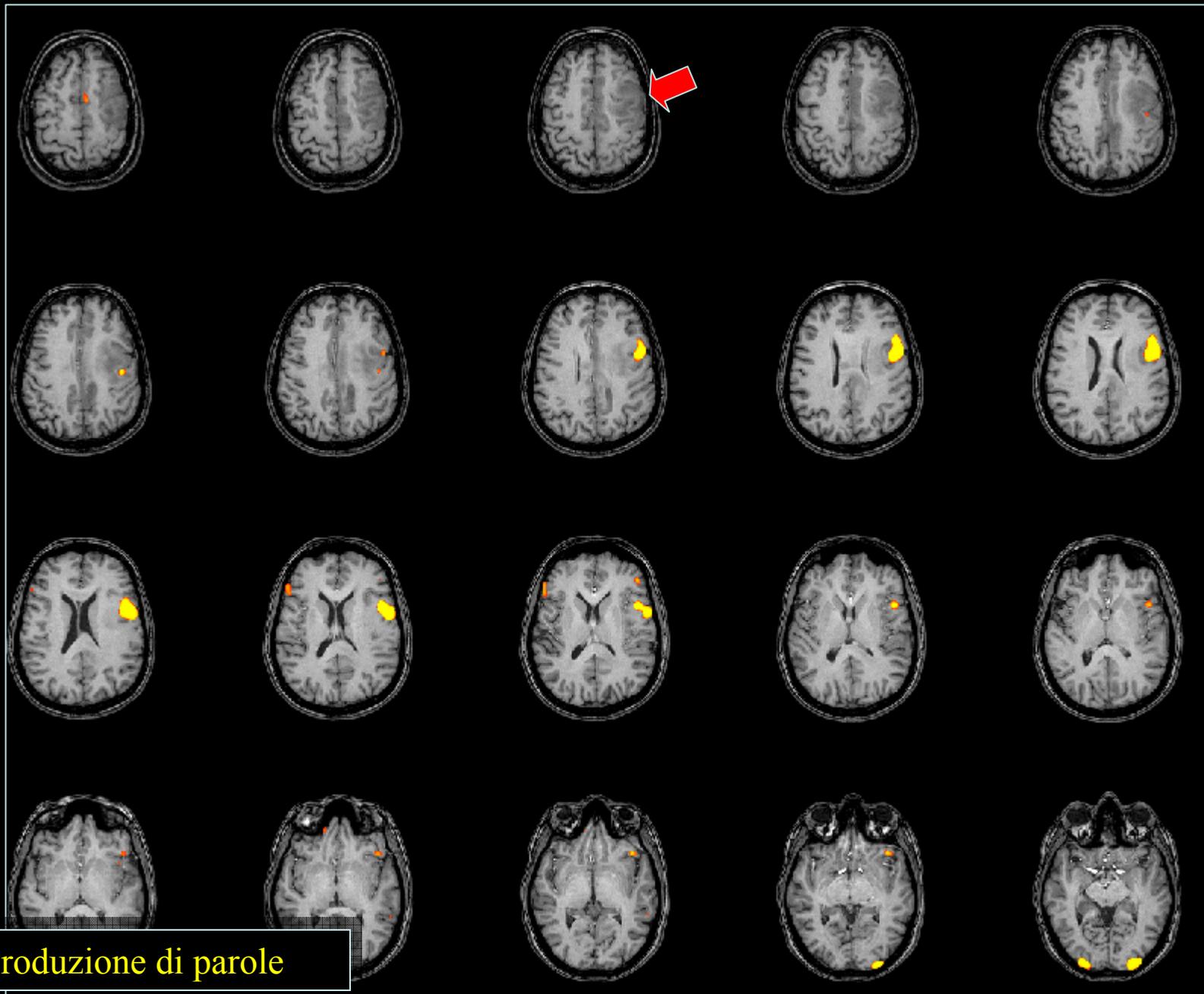


Broca



Broca

Wernicke



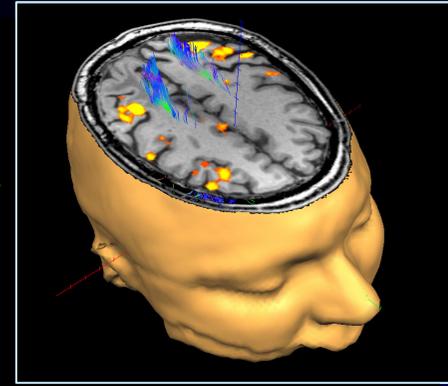
Produzione di parole

# Brain Mapping

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## Protocolli

- Funzione complessa: tanti paradigmi....
- Specificità diversa; task multipli
- Migliore segnale @ 3T
- Task non vocalizzati
- Target: principalmente Broca & Wernicke



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Funzione verbale

# Considerazioni



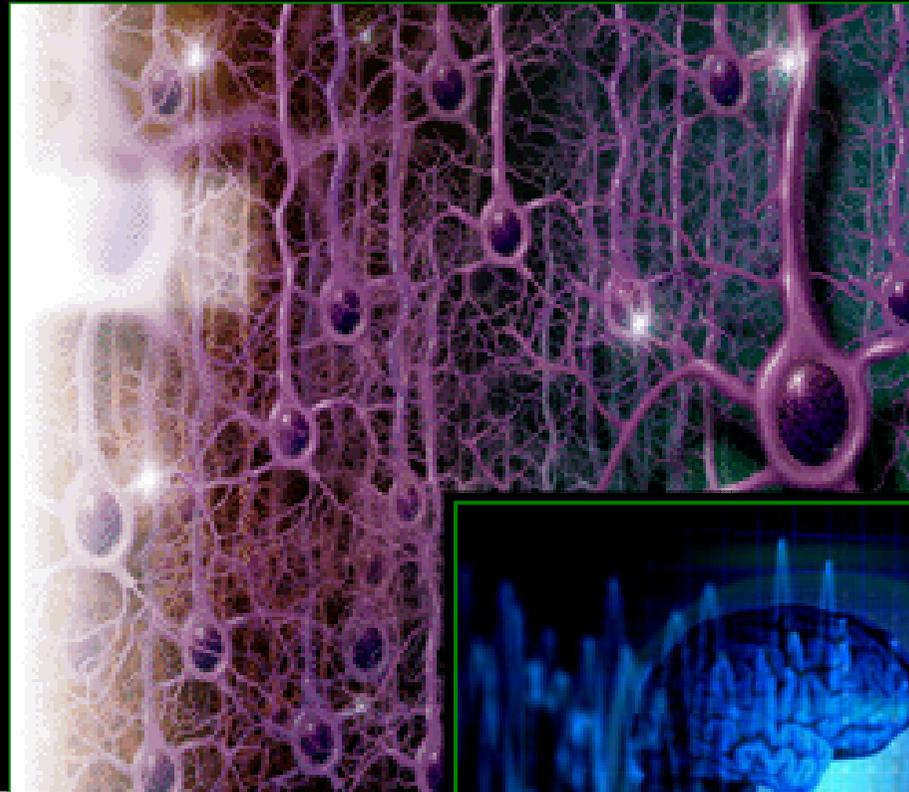
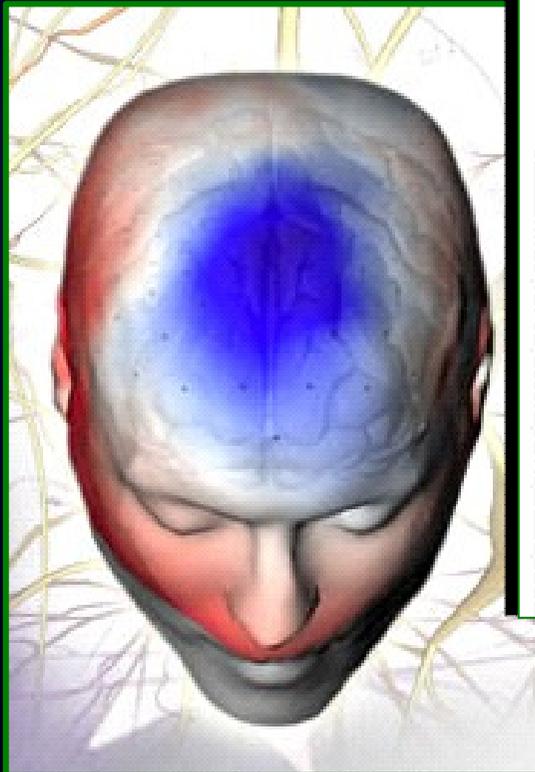
- Collaborazione del Paziente è essenziale
- “Training” pre *f*MRI intensivo
- Tests neuropsicologici
- Apparecchiature dedicate  
(stimolazione visiva, acustica ...)

Funzione verbale

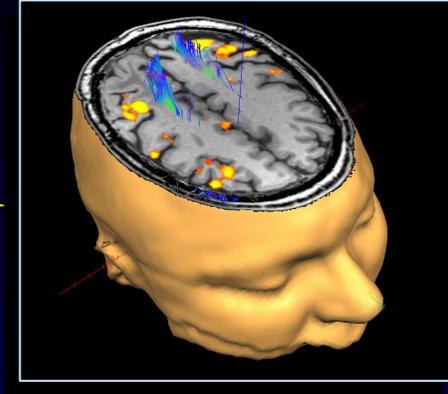


# S. Cognitivo

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## Brain Mapping



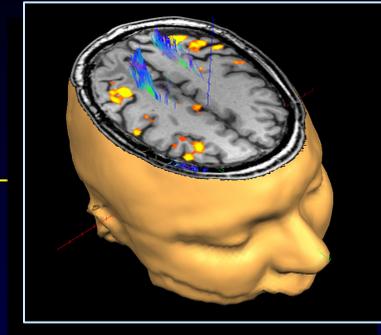
# Psichiatria

- limiti pre-*f*MRI: risoluzione temporale & uso isotopi
- studi attuali danno grande impulso alla ricerca
- analisi multiparametrica (MRS, PWI, DWI, DTI)
- dati predittivi di malattia e risposta terapeutica

*f*MRI

# *f*MRI in Psichiatria

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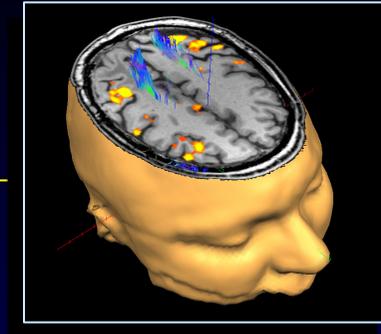
- Autismo
- Dipendenze
- Schizofrenia
- Depressione (disturbo bipolare)
- Demenza

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Applicazioni

# *f*MRI in Psichiatria

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## Autismo

Riduzione volumetrica amigdala (neuroanatomia)



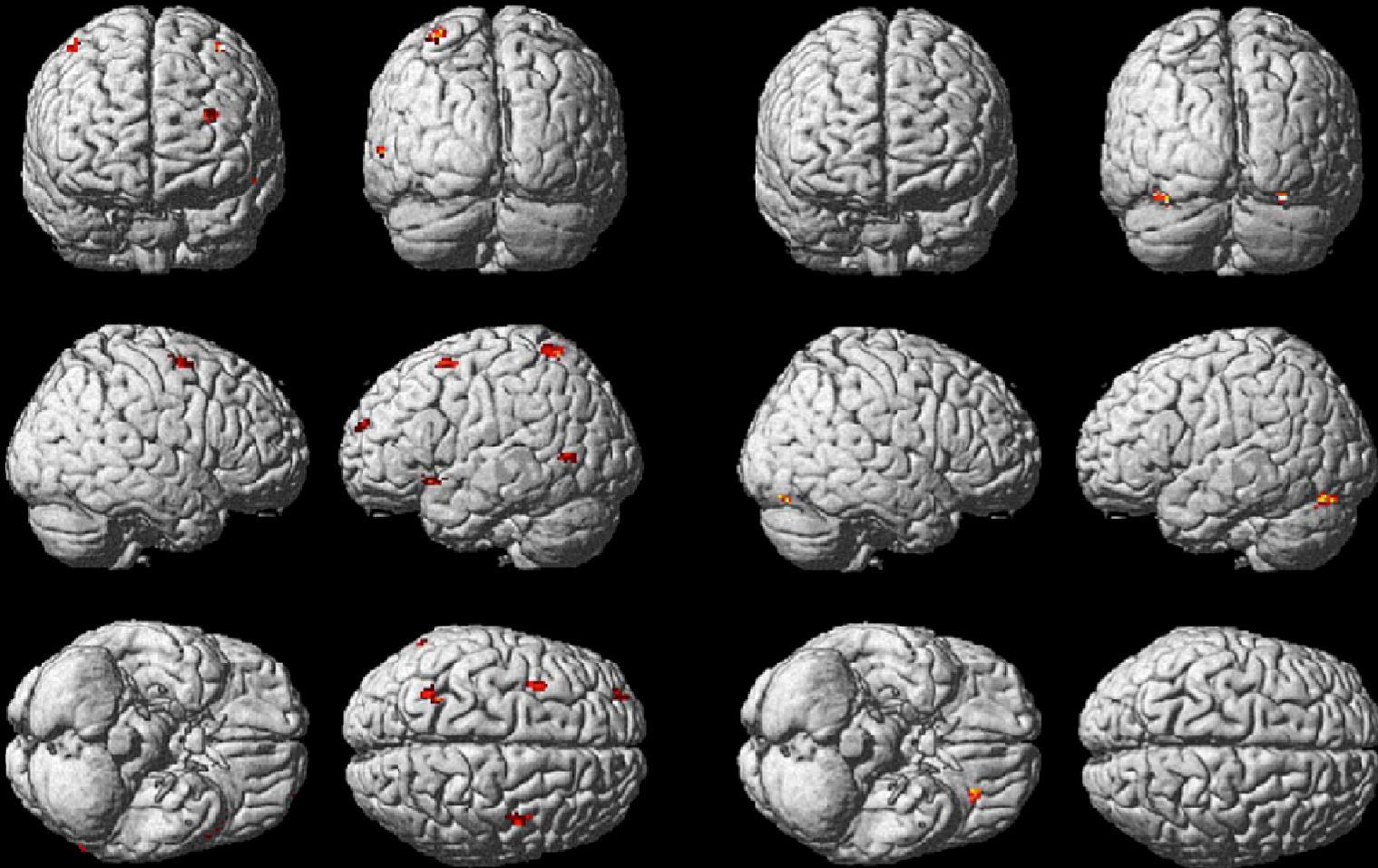
RUOLO DELL'AMIGDALA CON *f*MRI

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Applicazioni

**Normal**

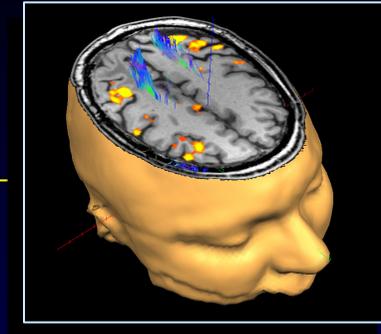
**Autistic**



Ridotta attivazione g. fusiforme & amigdala

# *f*MRI in Psichiatria

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## Schizofrenia

- grande interesse della comunità scientifica
- paradigmi motori e sensitivi semplici (stimol. visiva)
- *f*MRI e terapia farmacologica



Alterata attivazione corticale

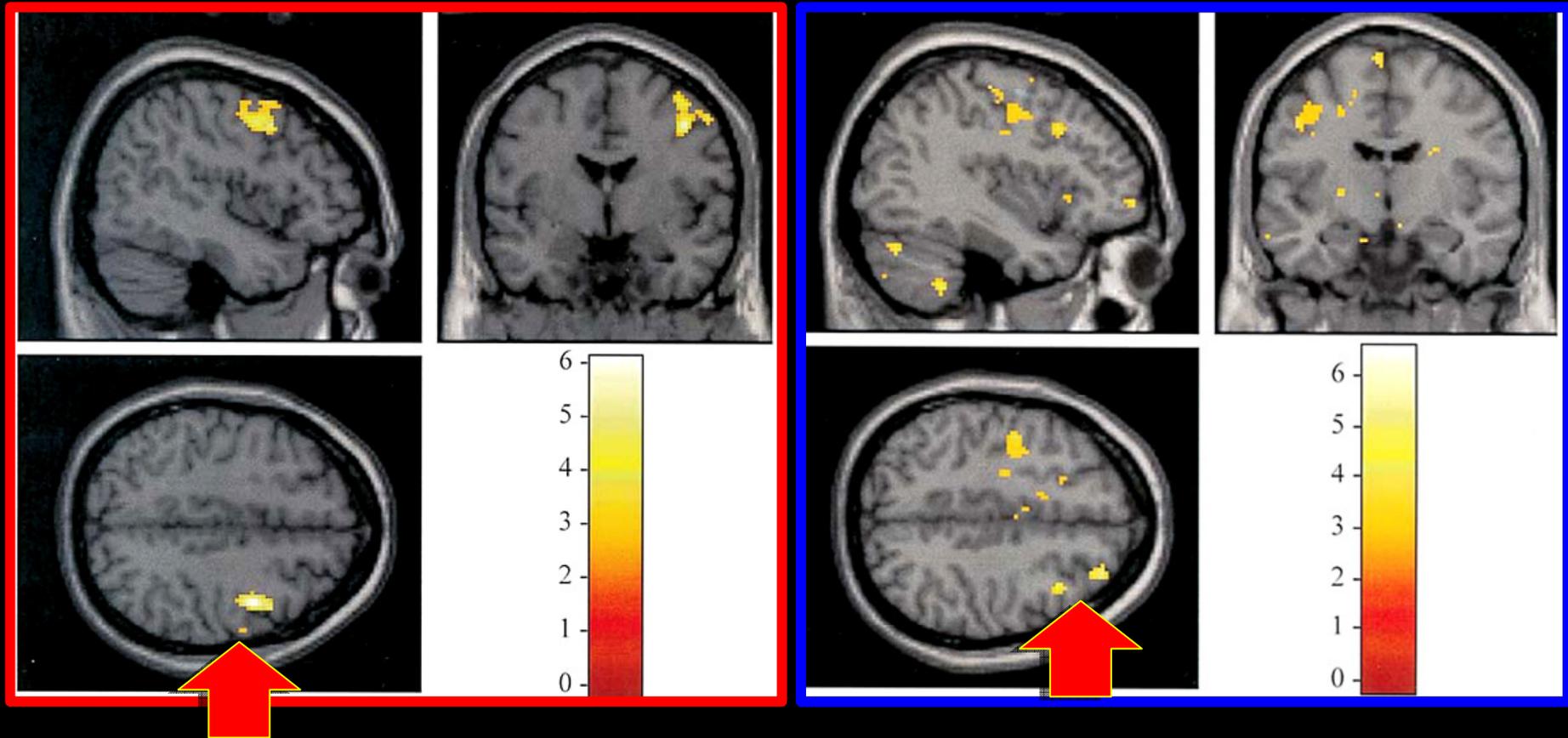
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**Applicazioni**

# Task: "finger tapping"

Mano sinistra

Mano destra



Alterata attivazione corticale

Table 8.3C. Summary of fMRI Research Pertaining to Schizophrenia Using Working Memory Task Paradigms

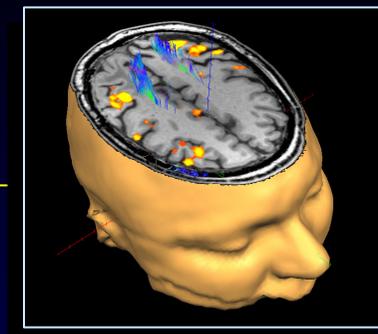
Authors	Subjects	fMRI paradigm	Results
Ramsey et al., 2002 <sup>42</sup>	Medicated schizophrenic patients; medication-naïve schizophrenic patients; healthy controls	XT-Task—Executive function task requiring logical reasoning alongside a closely matched control task	After correction for performance, deductive-reasoning brain activity (Brodmann's Areas) did not differ between controls and medicated schizophrenics, but did remain different between controls and medication-naïve schizophrenics.
Manoach et al., 2001 <sup>41</sup>	Schizophrenic patients; normal controls	Scanned twice during a working memory task	Overall, no group activations or performance differences were found between the two scans. In schizophrenics, however, individual differences in activation were significant from first scan to the next.
Manoach et al., 2000 <sup>40</sup>	Schizophrenic patients; normal controls	Working memory task (Modified Sternberg Item Recognition Task)	Before and after correction for performance, schizophrenics showed activation in the basal ganglia and thalamus, whereas controls did not. Schizophrenics showed decreased working memory performance and differential dorsolateral prefrontal cortex activation.
Callicott et al., 2000 <sup>39</sup>	Schizophrenic patients; healthy controls	Working memory task	Exaggerated and inefficient cortical activity in the dorsolateral prefrontal cortex.
Manoach et al., 1999 <sup>38</sup>	Schizophrenic patients; normal controls	Reward performance on working memory task (Modified Sternberg Item Recognition Task)	Schizophrenics had increased activation in the left dorsolateral prefrontal cortex, which was inversely correlated with task performance (measured by errors).

Table 8.3F. Summary of fMRI Research Pertaining to Hallucinatory Symptoms in Schizophrenia

Authors	Subjects	fMRI paradigm	Results
Lawrie et al., 2002 <sup>49</sup>	Schizophrenic patients; healthy controls	Visually presented sentences with last word missing; patient was instructed to think of last word	Correlation coefficients between the left temporal cortex and left dorsolateral prefrontal cortex were inversely correlated with severity of auditory hallucinations in patients.
Lennox et al., 2000 <sup>50</sup>	Medicated schizophrenic patients	Scanned while having hallucinations in scanner	During hallucinations, all subjects showed activation in the temporal cortex and prefrontal cortex.
Woodruff et al., 1997 <sup>48</sup>	Male schizophrenic patients with a history of auditory hallucinations but were not actively hallucinating; male schizophrenic patients with no history of auditory hallucinations; non-psychiatric males	Auditory perception of externally presented speech	Patients (both with and without hallucinations) showed a decrease in left temporal lobe activation, and as a combined group also showed an increase in right temporal activation when compared to controls.

# *f*MRI in Psichiatria

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## Tossico dipendenze

- Droga: deficit cognitivi cronici
- Cocaina: euforia e successivamente “craving”

## Cocaina & *f*MRI

1. Autosomministrazione

→ attivazione DLPFC  
ACC

2. Video-tape

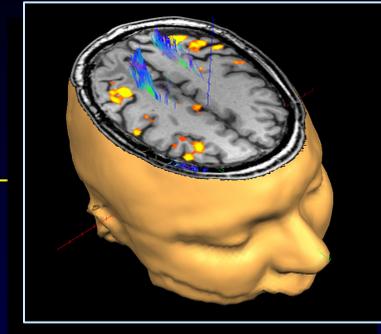
ridotta attivazione lobo frontale

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## Applicazioni

# fMRI in Psichiatria

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## Craving

### Aree attivate

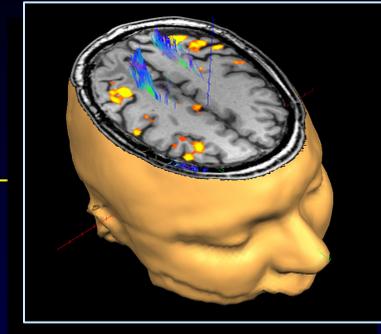
- Corteccia limbica (motivazioni & emozioni)
- ACC
- Amigdala
- N. accumbens
- Insula

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## Applicazioni

# *f*MRI in Psichiatria

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## Demenza

- Alterazione degenerativa della connettività cerebrale
- *f*MRI & test comportamentali: diagnosi preclinica

## Demenza & *f*MRI

1. “Resting state”
2. Compiti mnemonici

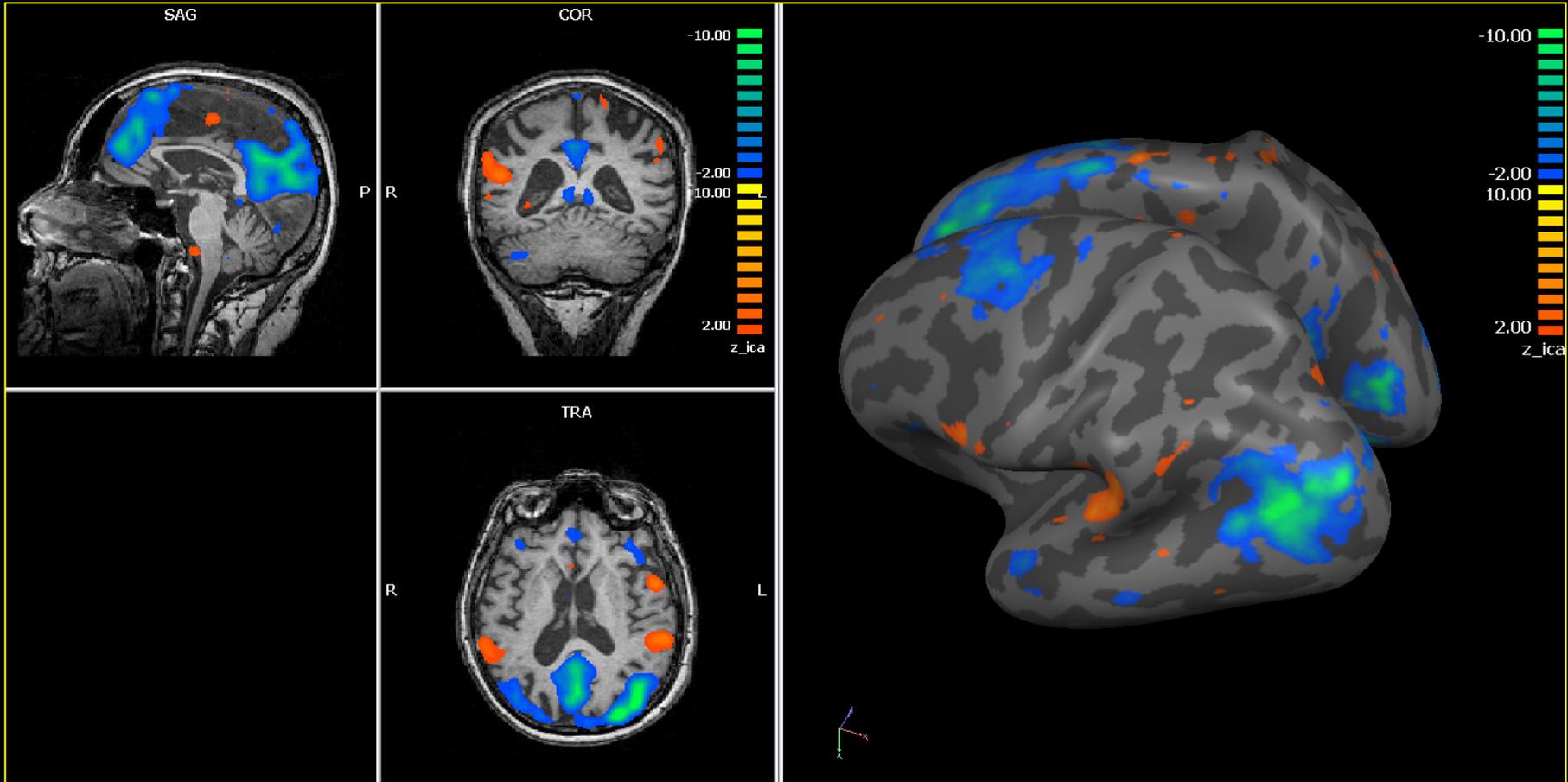
Fluttuazioni segnale BOLD

DMN: Default mode network

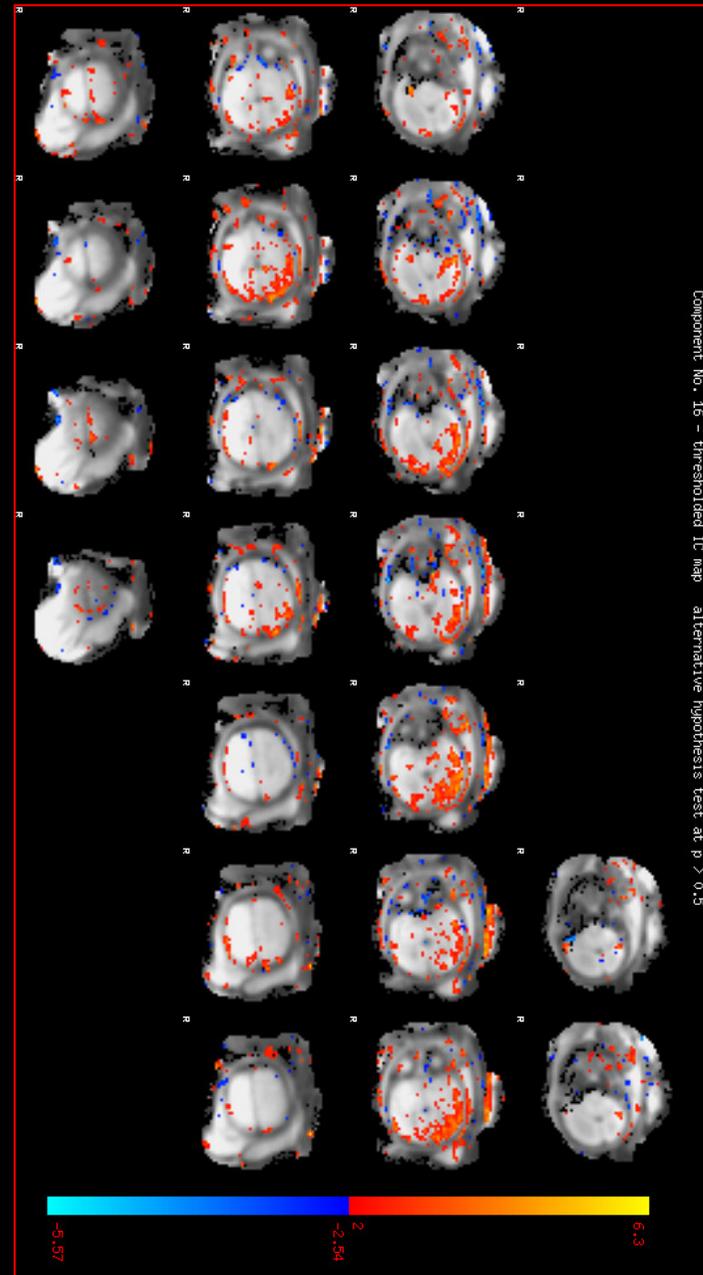
Ridotta attivazione ippocampo

Deattivazione c. post-mediale

AD: atrofia & alt. strutturali



# fMRI (ICA) fetale



# Conclusioni

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- Importanza della RMN
- Imaging ultrastrutturale (molecolare)
- Teams multidisciplinari
- Supporto della ricerca

