

UNIVERSITÉ
DE GENÈVE
FACULTÉ DE MÉDECINE

HUG
Hôpitaux Universitaires de Genève



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Caratterizzazione della zona epilettogena mediante co-registrazione EEG-fMRI

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ZONA EPILETTOGENA: Area corticale necessaria e sufficiente perché le crisi insorgano e la cui rimozione o disconnessione è necessaria per abolire le crisi (concetto neurofisiologico e “teorico”)

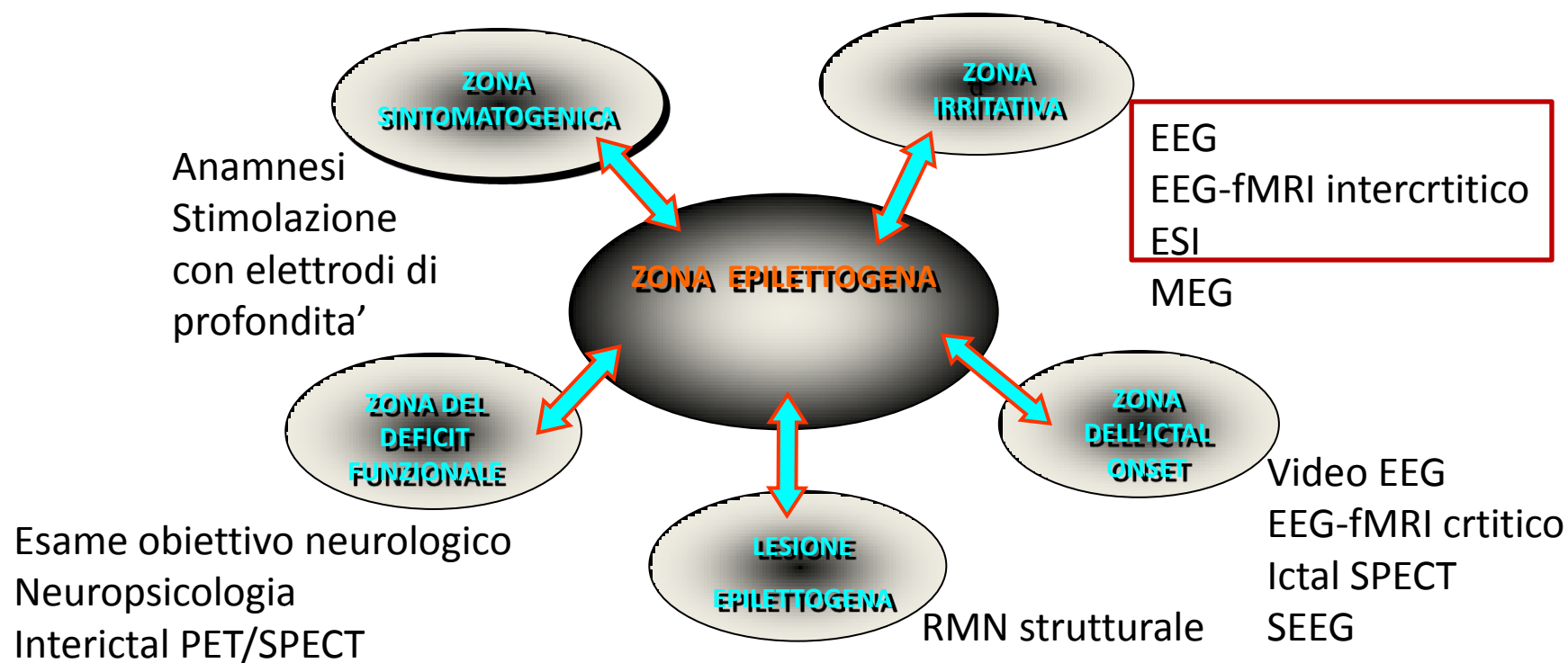
ZONA IRRITATIVA: Area corticale capace di generare anomalie intercritiche (la sua estensione dipende dal metodo neurofisiologico usato)

ZONA DELL'ICTAL ONSET (SOZ): Area corticale dalla quale le crisi hanno origine sull' EEG

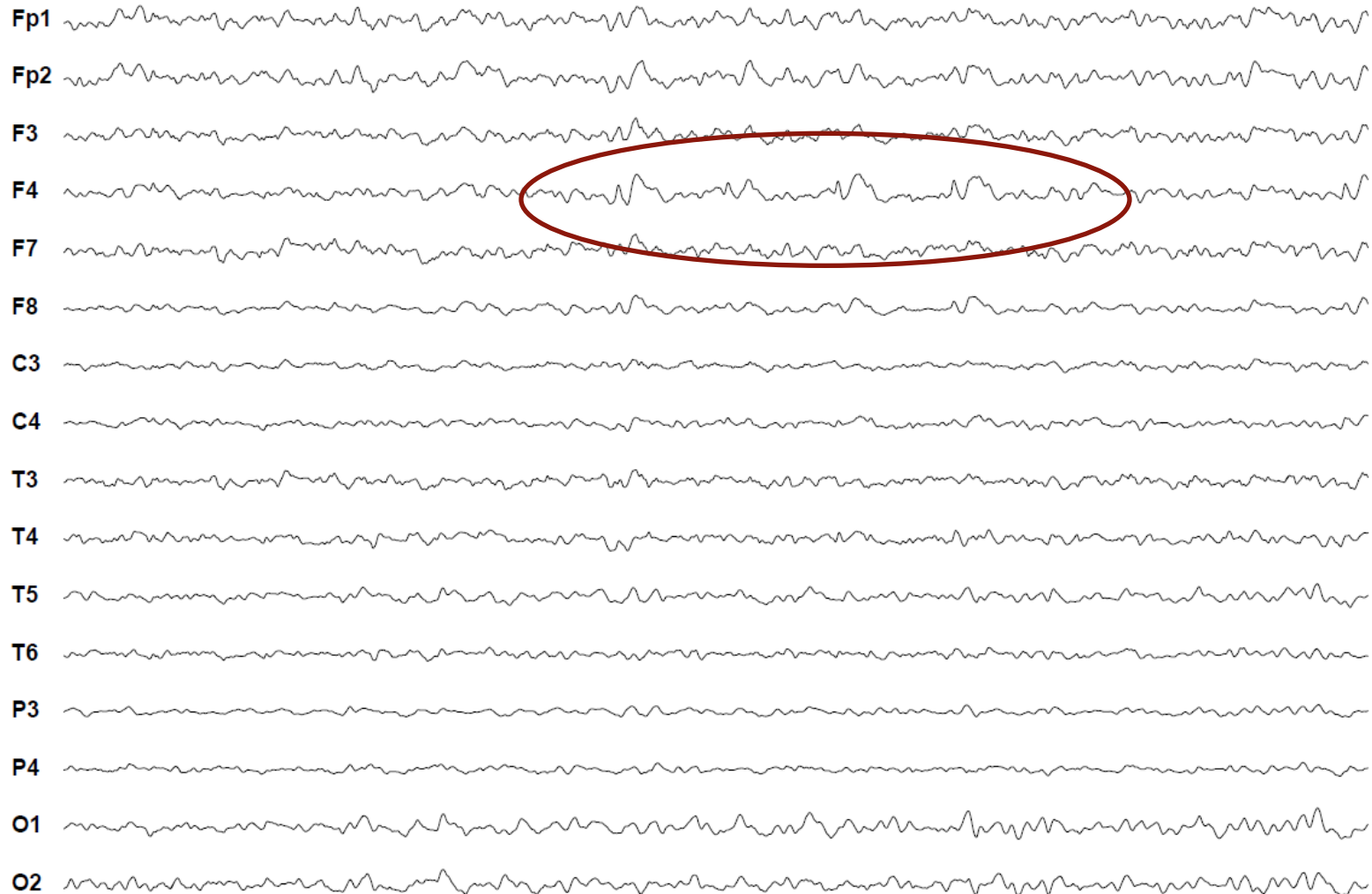
LESIONE EPILETTOGENA: Area cerebrale strutturalmente alterata che presumibilmente causa l'epilessia

ZONA DEL DEFICIT FUNZIONALE: Area responsabile delle disfunzioni intercritiche non epilettiche

ZONA SINTOMATOGENICA: Area corticale che, attivandosi, produce i sintomi critici iniziali



Quali strutture cerebrali generano queste punte?



EEG 93045

Short communication

Monitoring the patient's EEG during echo planar MRI

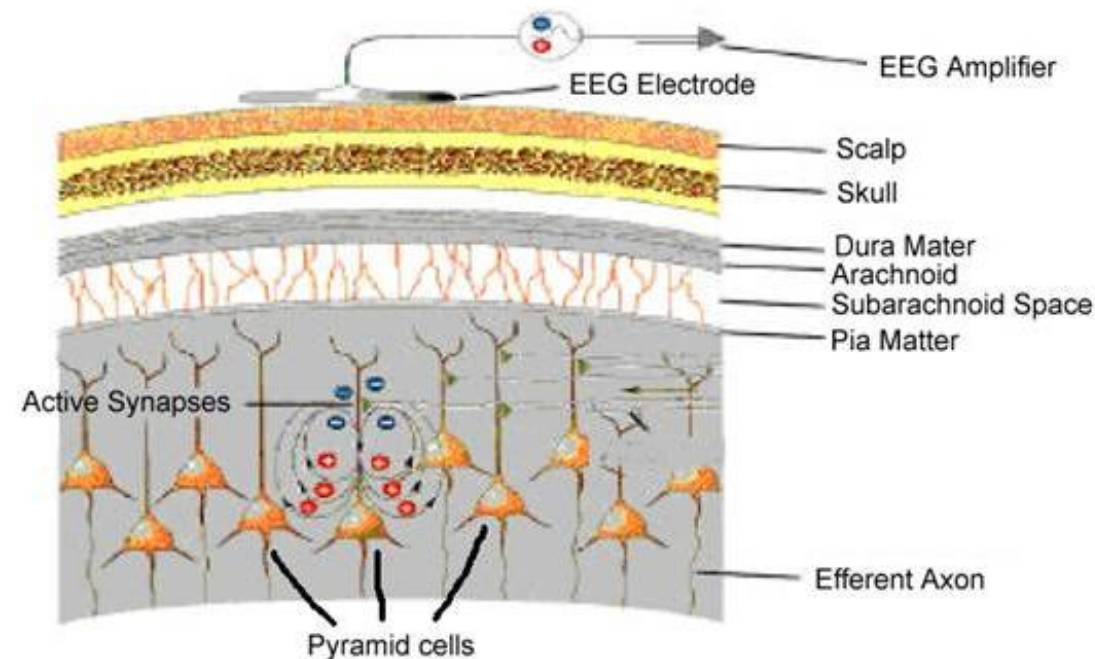
J.R. Ives ^{a,*}, S. Warach ^{a,b}, F. Schmitt ^c, R.R. Edelman ^b and D.L. Schomer ^a

Departments of ^a Neurology (DA-807) and ^b Radiology, Beth Israel Hospital, Harvard Medical School, 330 Brookline Ave., Boston, MA 02215 (USA), and ^c Siemens Medical Systems, Erlangen (Germany)

(Accepted for publication: 27 August 1993)

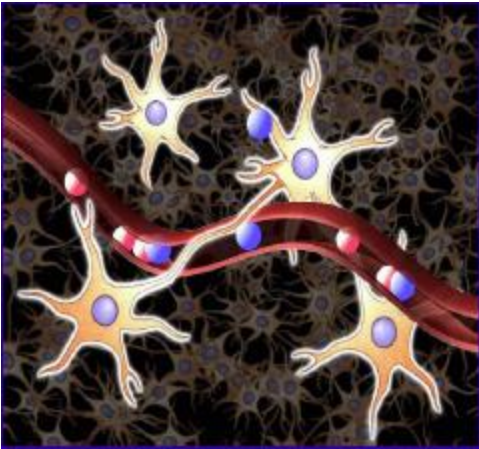
EEG

- Misura la differenza di potenziale fra due punti dello scalpo
- Riflette l'attività di un alto numero di cellule piramidali sincronizzate
- EPSPs & IPSPs (10-250ms), no PA (1-2ms)!

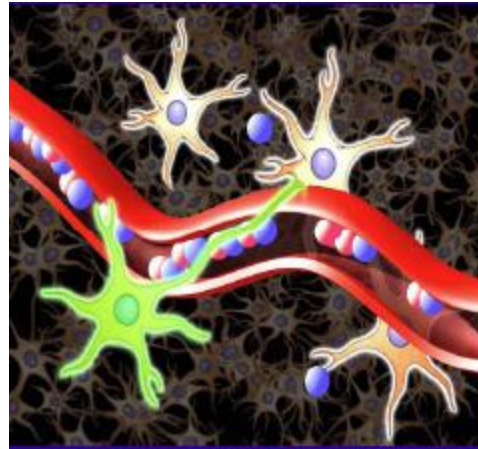


fMRI

- L'attivazione funzionale di una regione cerebrale determina:
 - Aumento dell'attività neuronale, seguita da:
 - Aumento della **quantità** di deossiHb nel sangue venoso come risultato dell'aumentato consumo di ossigeno neuronale, seguito da:
 - Aumento del flusso e del volume di sangue.
 - Questa combinazione porta a una diminuita **concentrazione** di deossiHb nel sangue venoso.

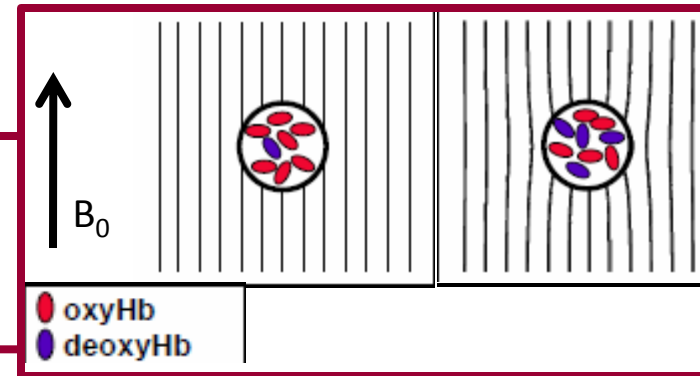


Riposo

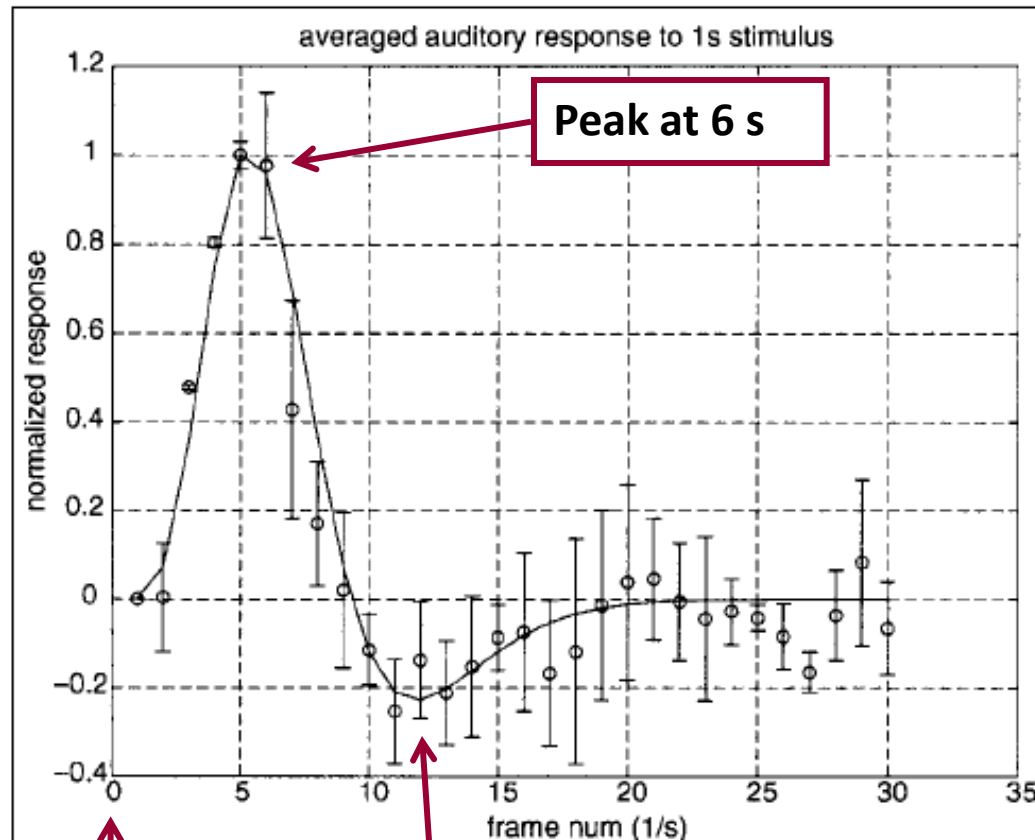


Attivazione

Effetto BOLD (**B**lood **O**xygenation **L**evel **D**ependent), che può essere misurato dalle sequenze $T2^*$ perché la deossiemoglobina è paramagnetica



HRF: Hemodynamic Response Function

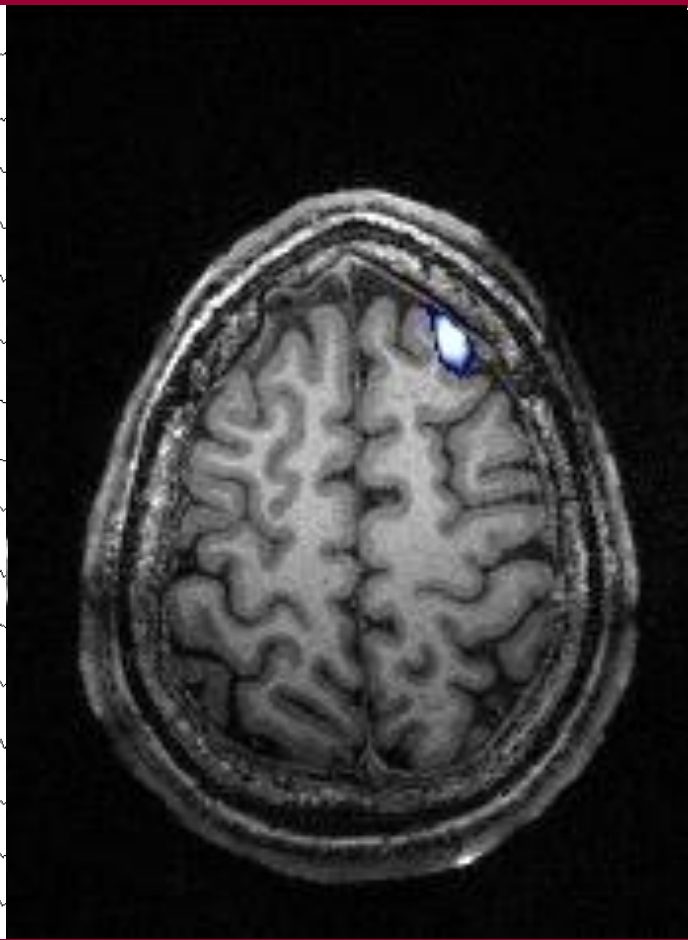
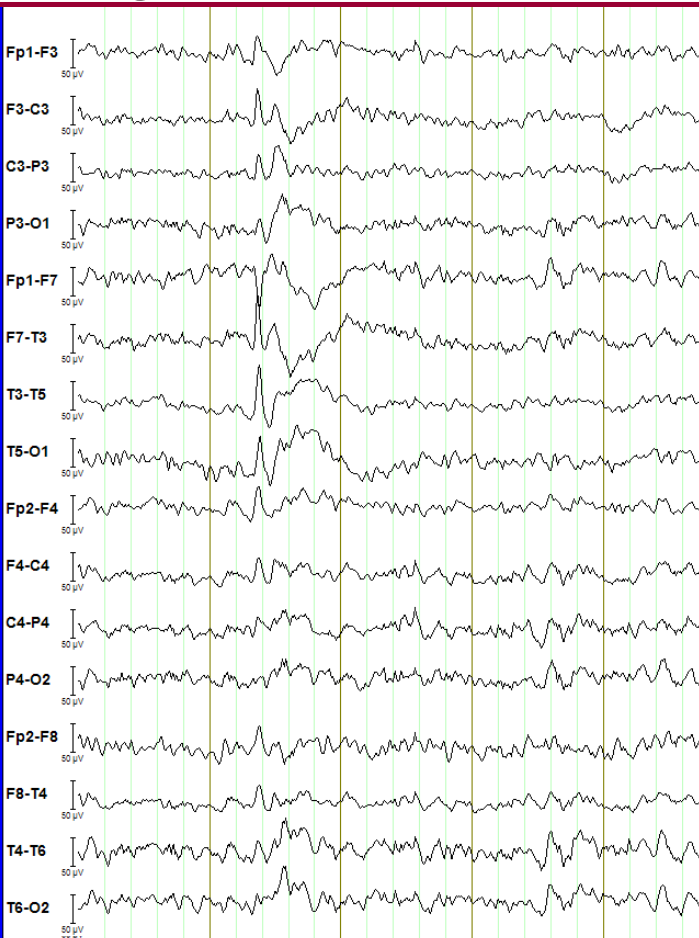


Neuronal activation

Undershoot at 12 s

EEG-fMRI

- Rileva in quali regioni cerebrali è presente un aumento di metabolismo in seguito a un evento critico o intercritico marcato sull'EEG di scalp. Queste e altre regioni



significativa

ativa

attività sinaptica)

a attività sinaptica)

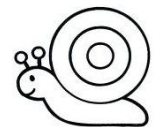
- **Segnale elettrico:**

- Si propaga con una velocità di ms (10 ms per andare da un emisfero all'altro)
- Le nostre attuali macchine misurano variazioni di segnale elettrico in tempo reale
- “An epileptiform discharge would need to involve at least *10 cm² of synchronous cortex* to be visible on the scalp” (Tao et al., 2007).



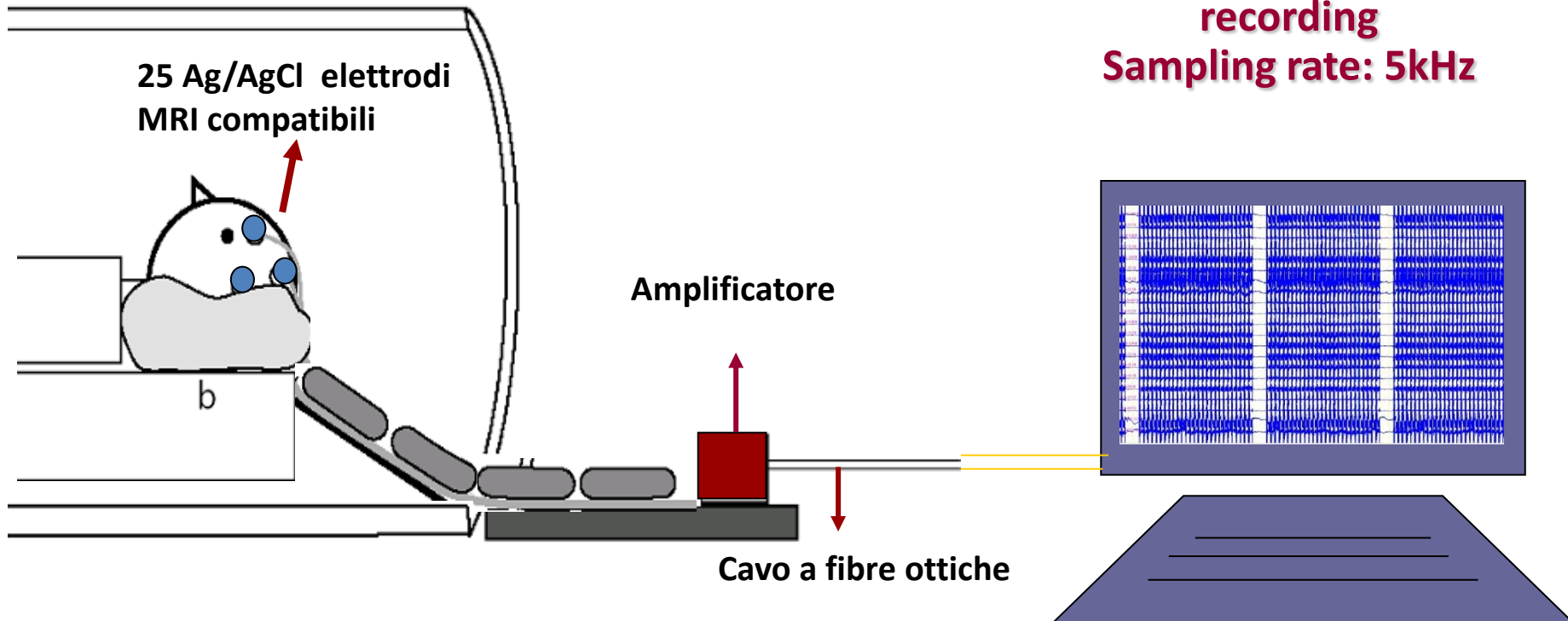
- **Segnale BOLD:**

- Misura le variazioni di metabolismo con una risoluzione spaziale che al momento è di 2-3 mm.
- La risposta metabolica a un evento ha un picco a 6 secondi dall'evento
- Le nostre attuali macchine sono capaci di misurare variazioni BOLD ogni 2 secondi

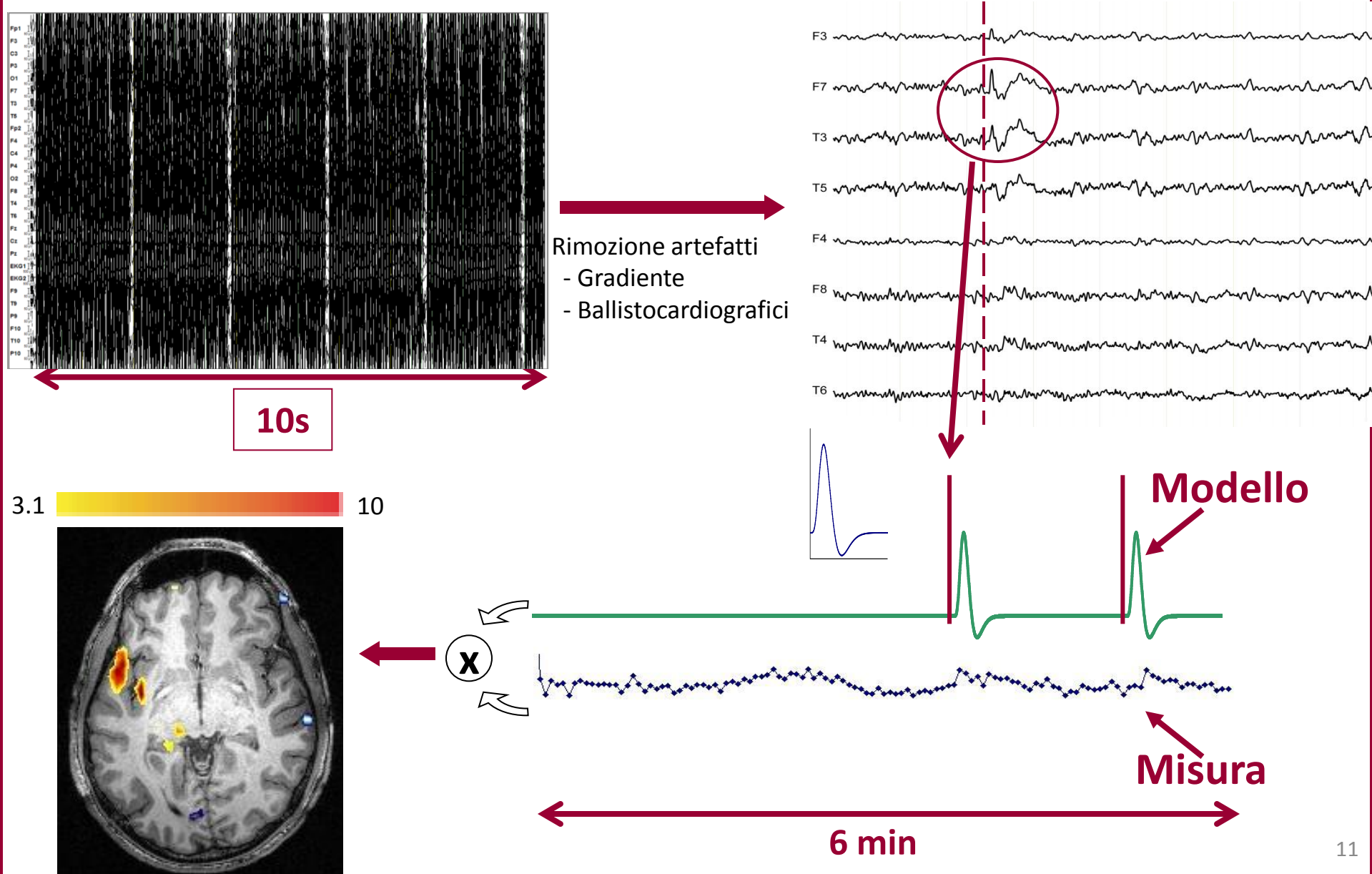


EEG-fMRI: acquisizione EEG

MRI scanner room



EEG-fMRI processing

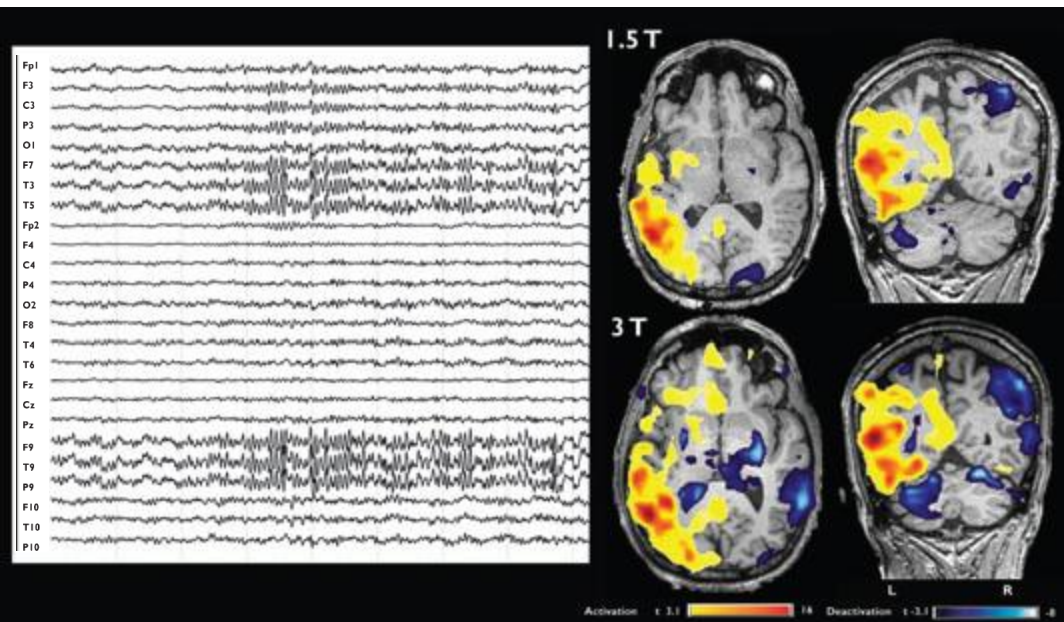
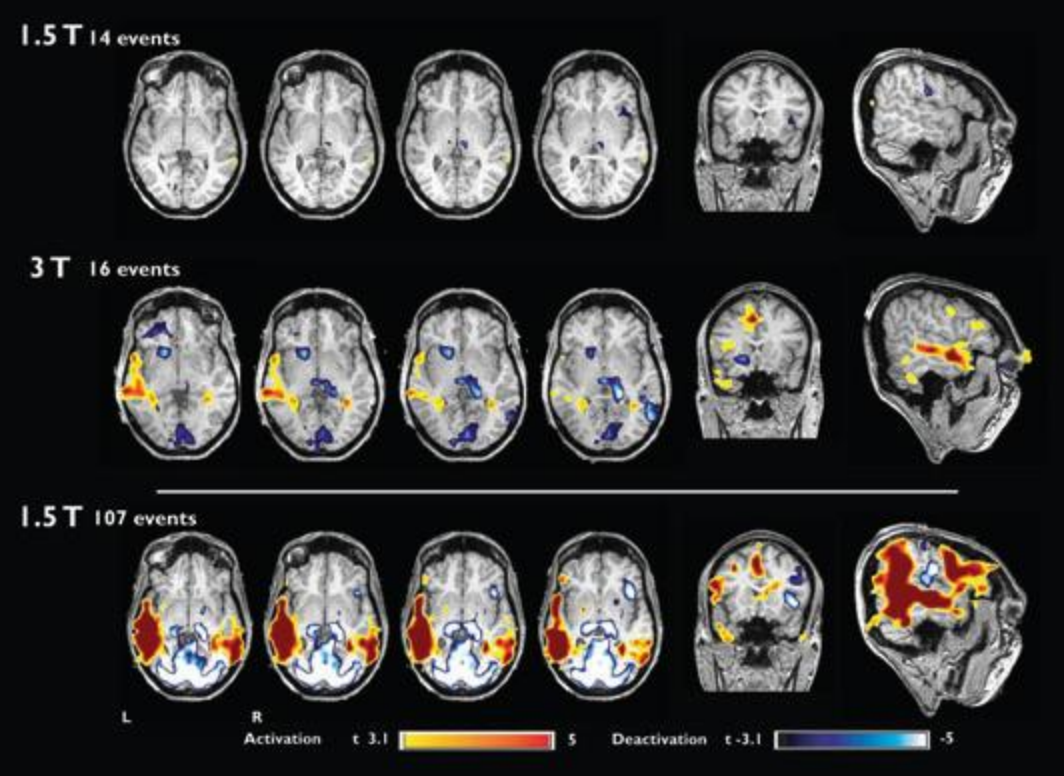


La mappa BOLD di una punta

- Paziente specifica e riproducibile
 - *Gholipour et al., 2010; Moeller et al., 2008; Flanagan et al., 2009*
- Validata con gold standard
 - Intracranial EEG: *Thornton et al., 2011; Grouiller et al., 2011*
 - Post-OP: *Thornton et al., 2010; Grouiller et al., 2011; An et al., 2013*
- Contribuisce a localizzare il focus epilettico
 - *Pittau et al., 2012; Zijlmans et al., 2007*

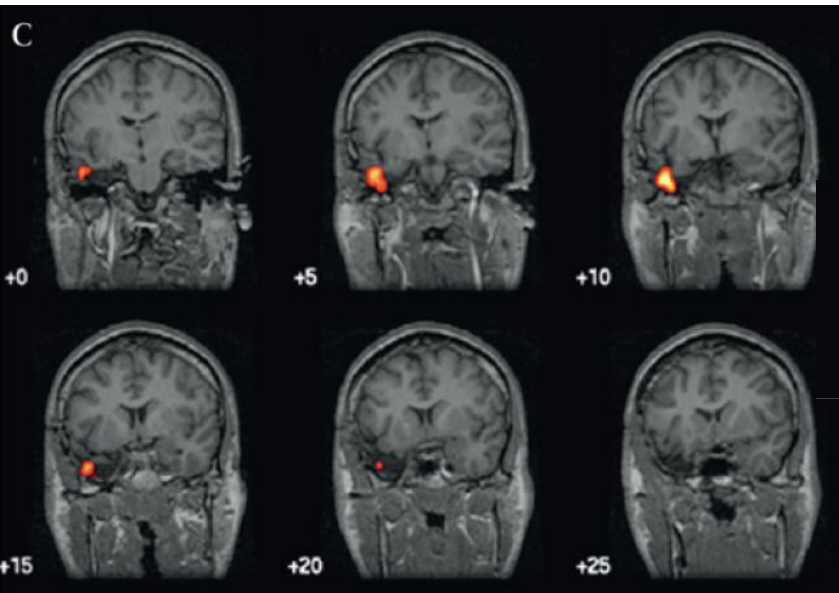
Paziente specifica e riproducibile

- Valore statistico $\uparrow$ col numero di eventi
- Al pari di numero di eventi, la risposta $\uparrow$ con l'intensità del campo magnetico

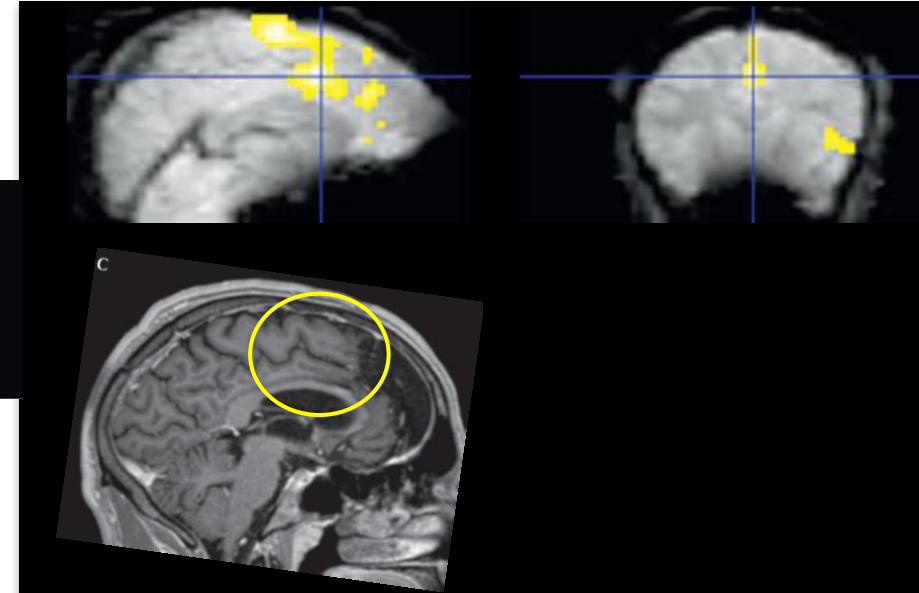


Validazione: confronto con follow-up post-resezione

Concorde → Engel I



Discorde → Engel > 1



Zona Epilettogena:

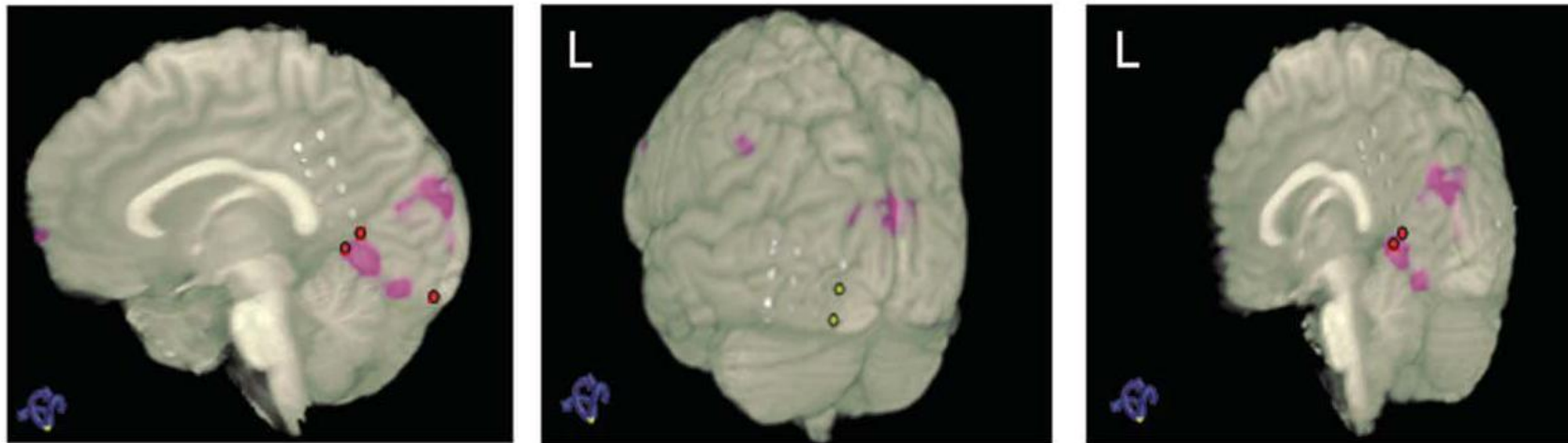
64: EEG-fMRI - 52 operati

10: risposte BOLD & intervento

Concordanza in 6/7: Engel I

Discordanza in 3/3: Engel > 1

Stessi risultati in popolazione con FCD



Seizure onset zone (icEEG):

Displasia corticale focale (N=23)

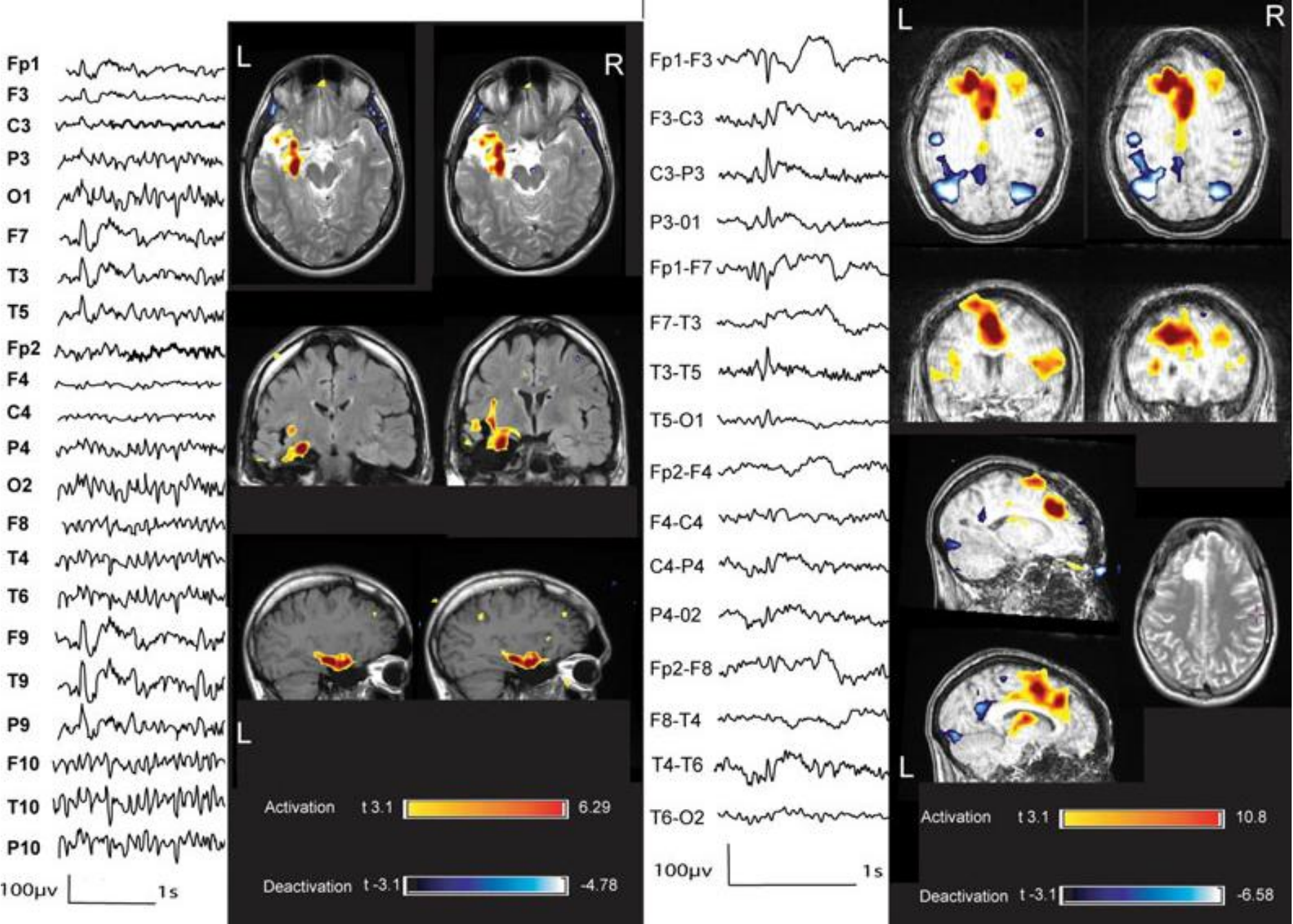
11/23 con risposte BOLD

BOLD concorde: 4/5 Engel I

BOLD discorde / diffuso: 5/6 Engel > I o non operabili

Predittivo di outcome

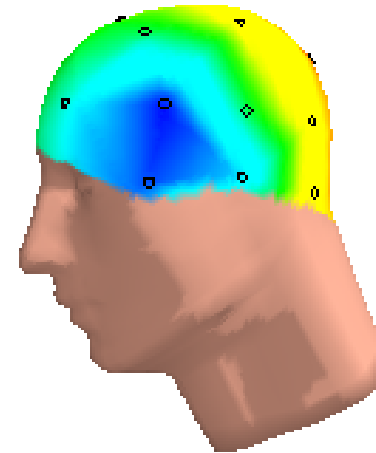
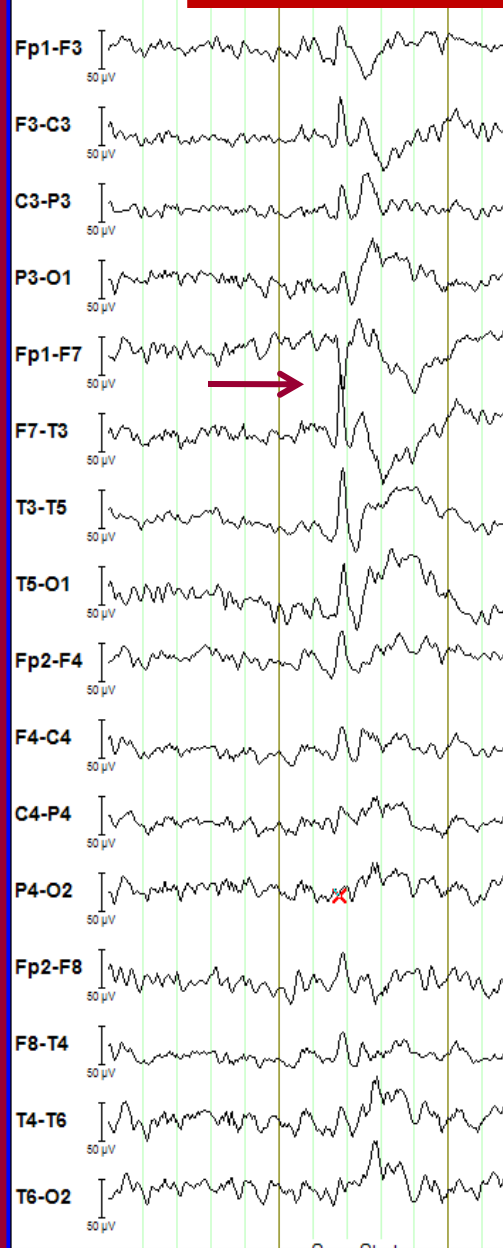
- 35 pazienti con EEG-fMRI e intervento (12 mesi follow-up)
- 4 gruppi:
 - Completamente concorde → 7/10 Engel I
 - Parzialmente concorde → 4/9 Engel I
 - Parzialmente discorde → 3/5 Engel I
 - Completamente discorde → 1/11 Engel I
- Sensibilità: 87.5%
- Specificità: 76.9%
- Valore prognostico positivo: 70%
- Valore prognostico negativo: 90.9%



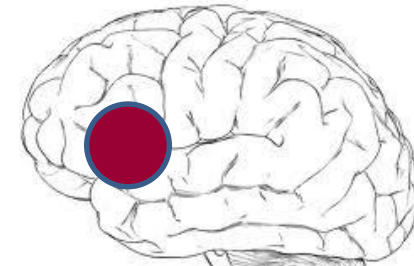
Contribution of EEG/fMRI to the definition of the epileptic focus

Francesca Pittau, François Dubeau and Jean Gotman

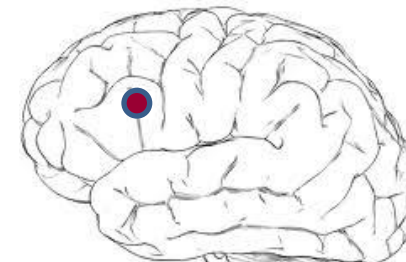
Neurology 2012;78:1479-1487 Published Online before print April 25, 2012



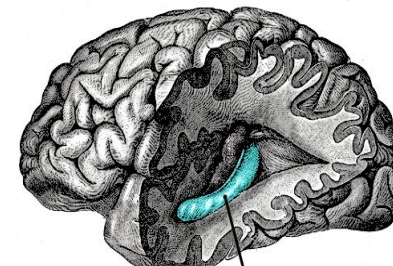
7370 - 7372 ms



Not contributory

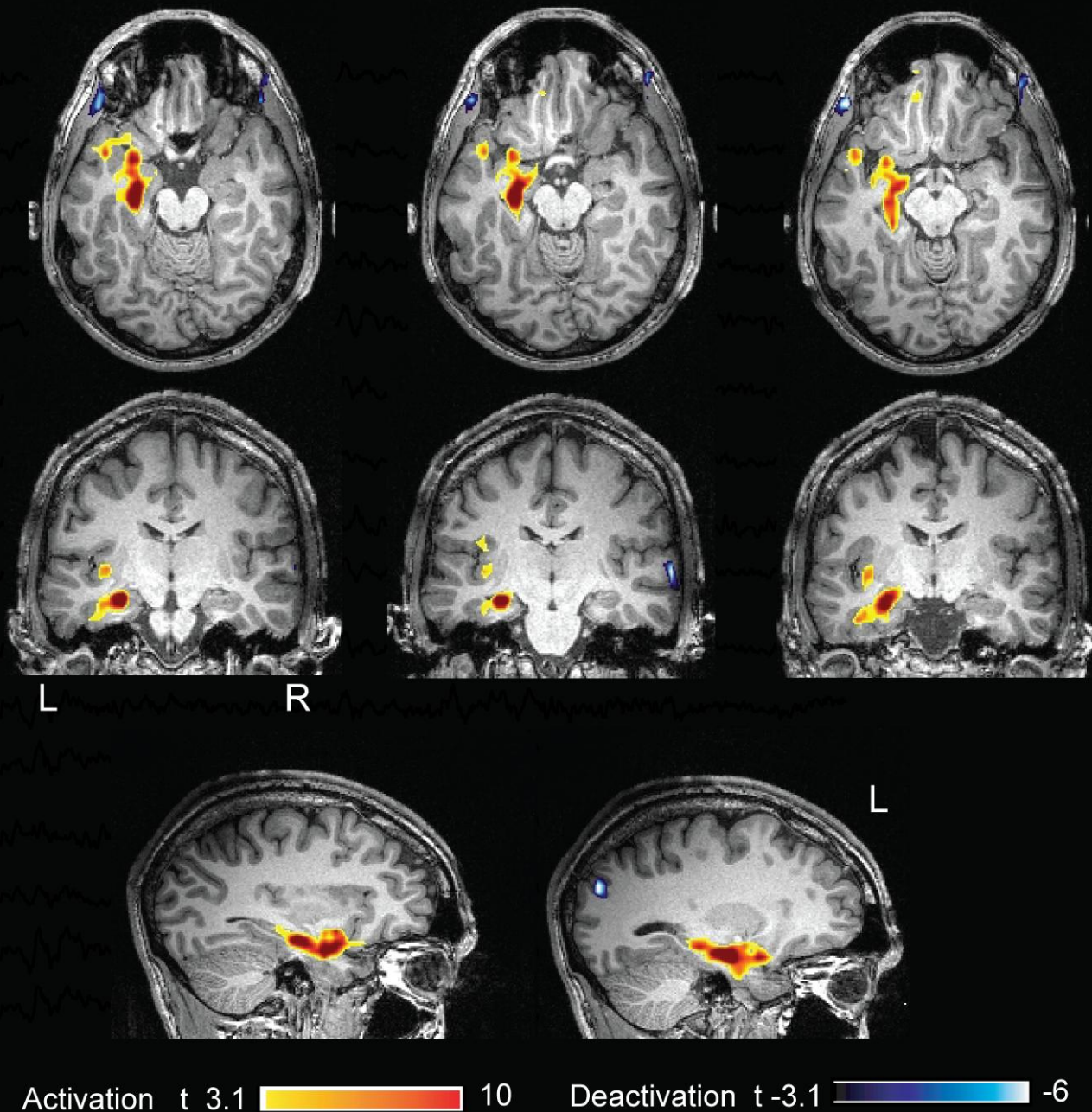
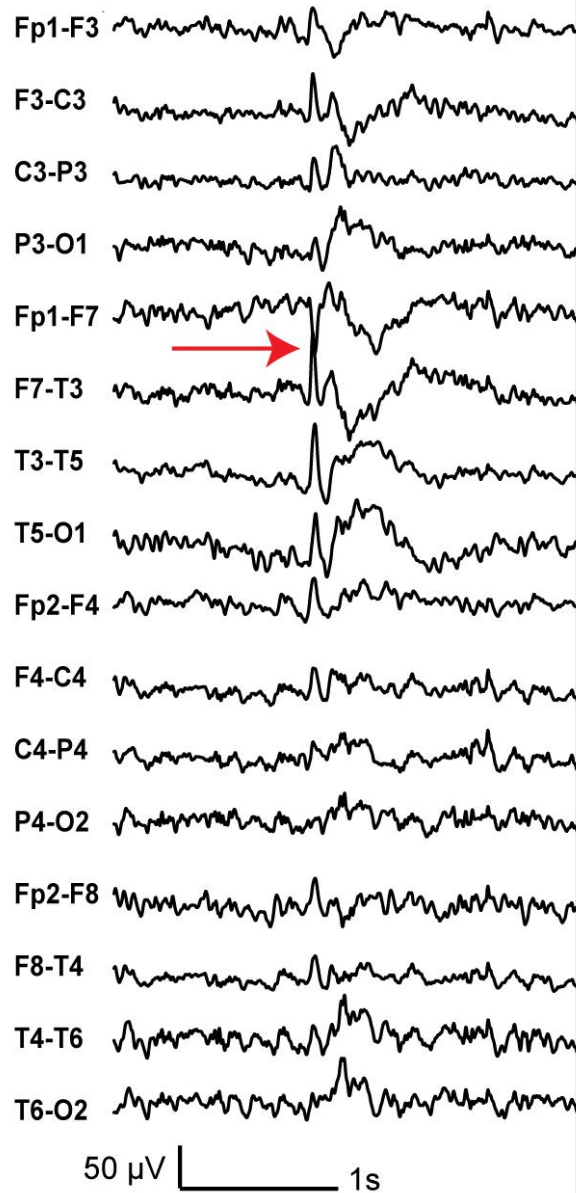


Contributory

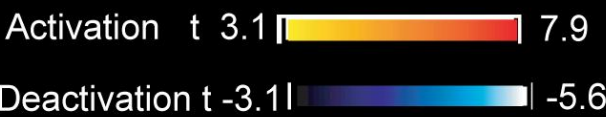
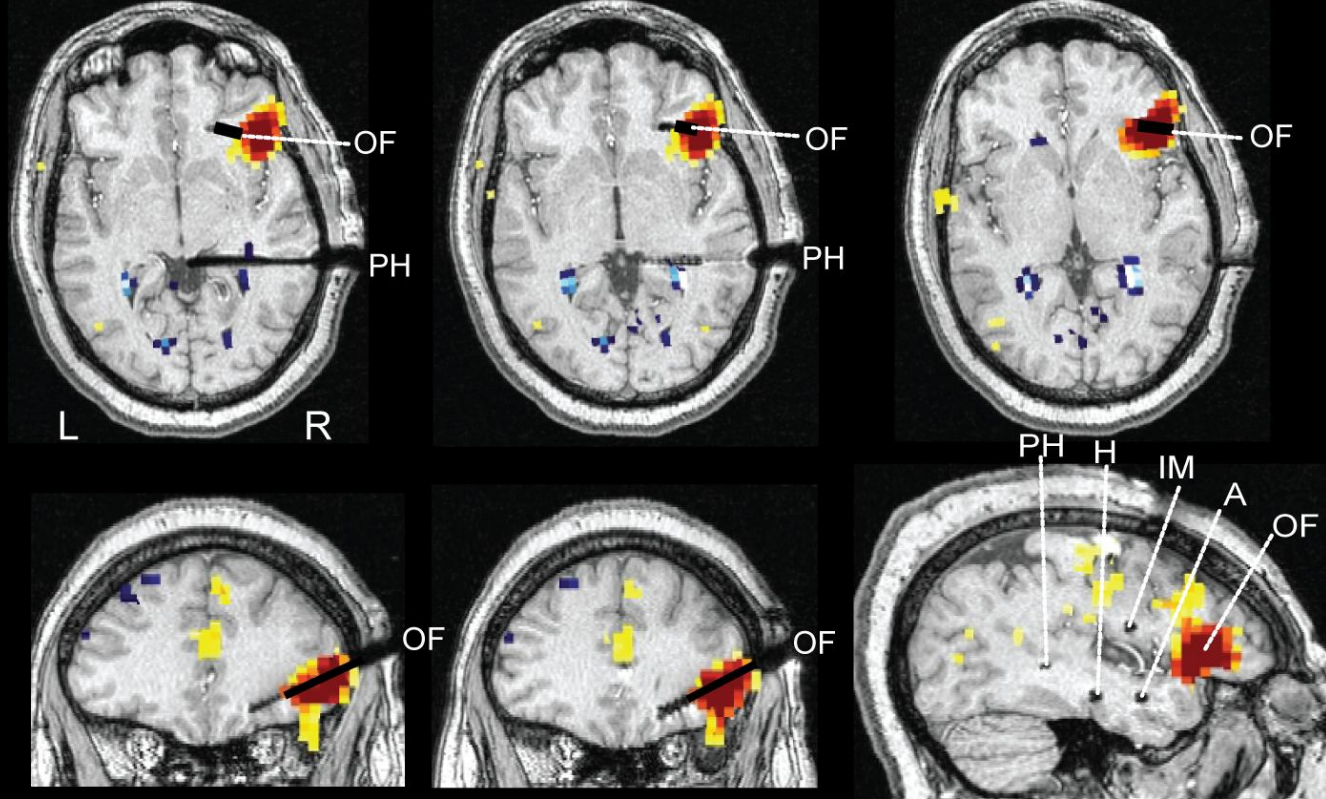
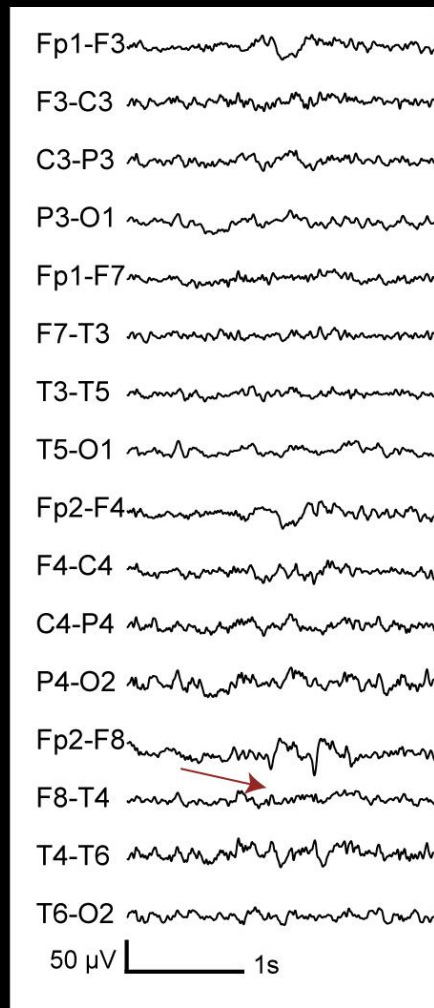


Contributory

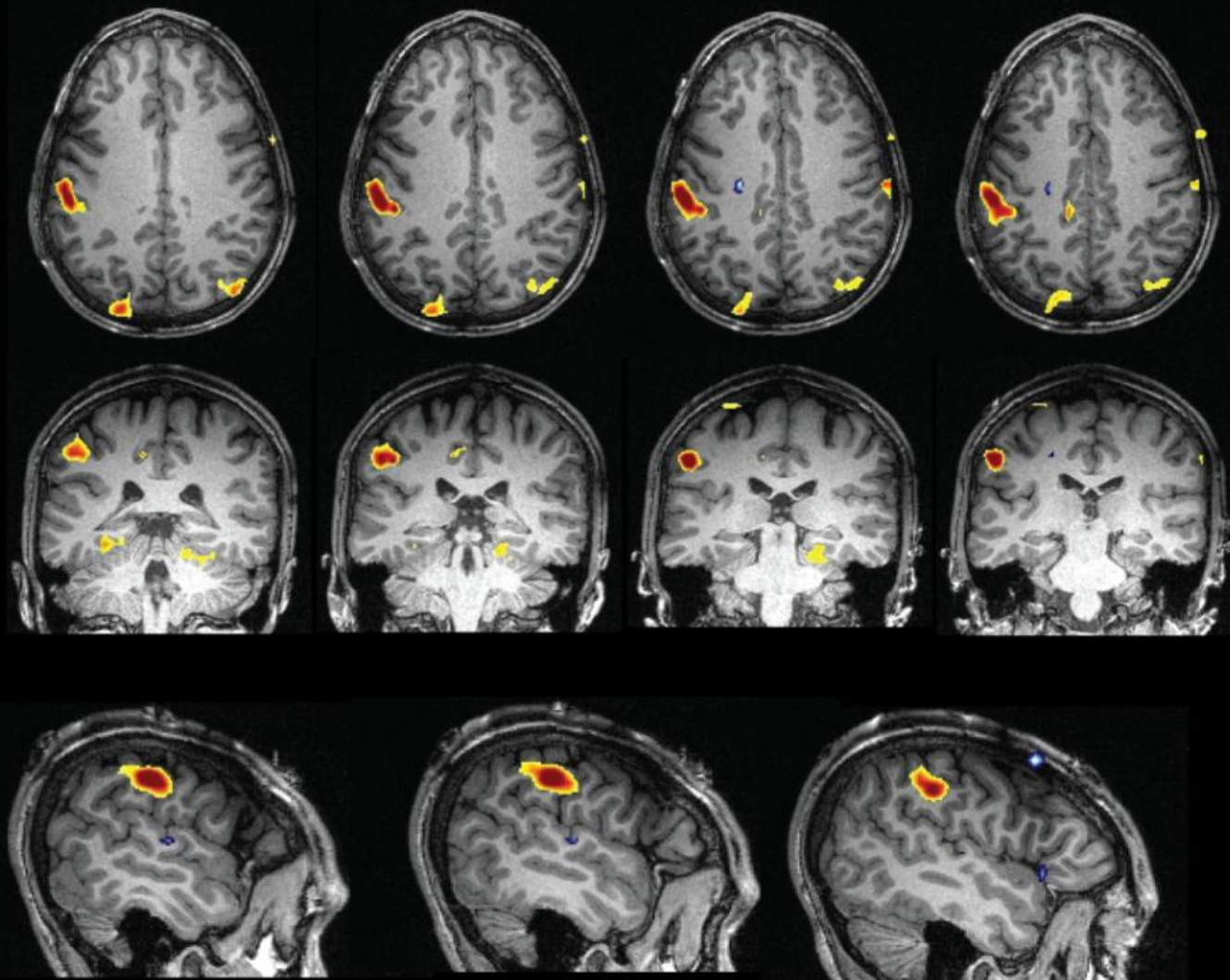
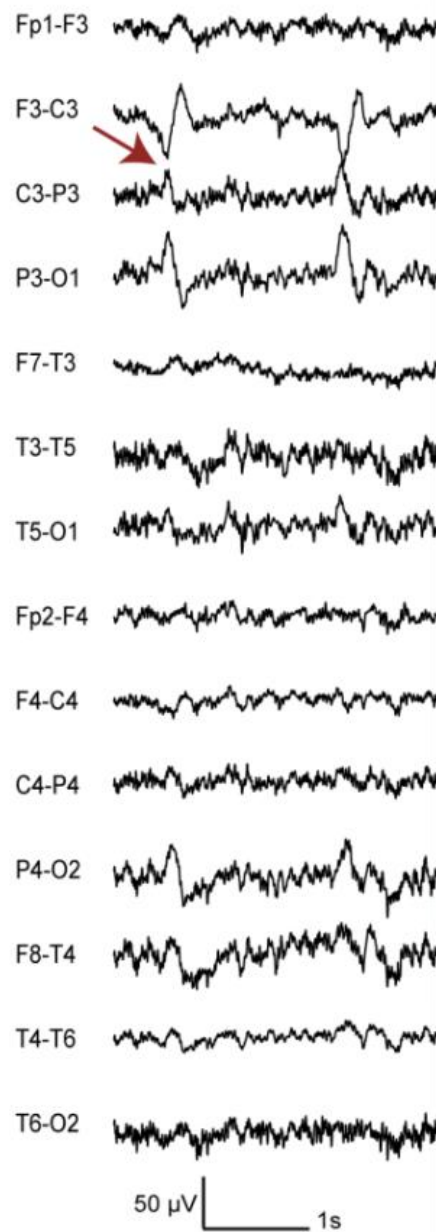
Additional localization information
21/43 (invasive validation N=10)



Concordant, Contributory, Validated (focal lesion)



Concordant, Contributory, Validated (focal lesion)



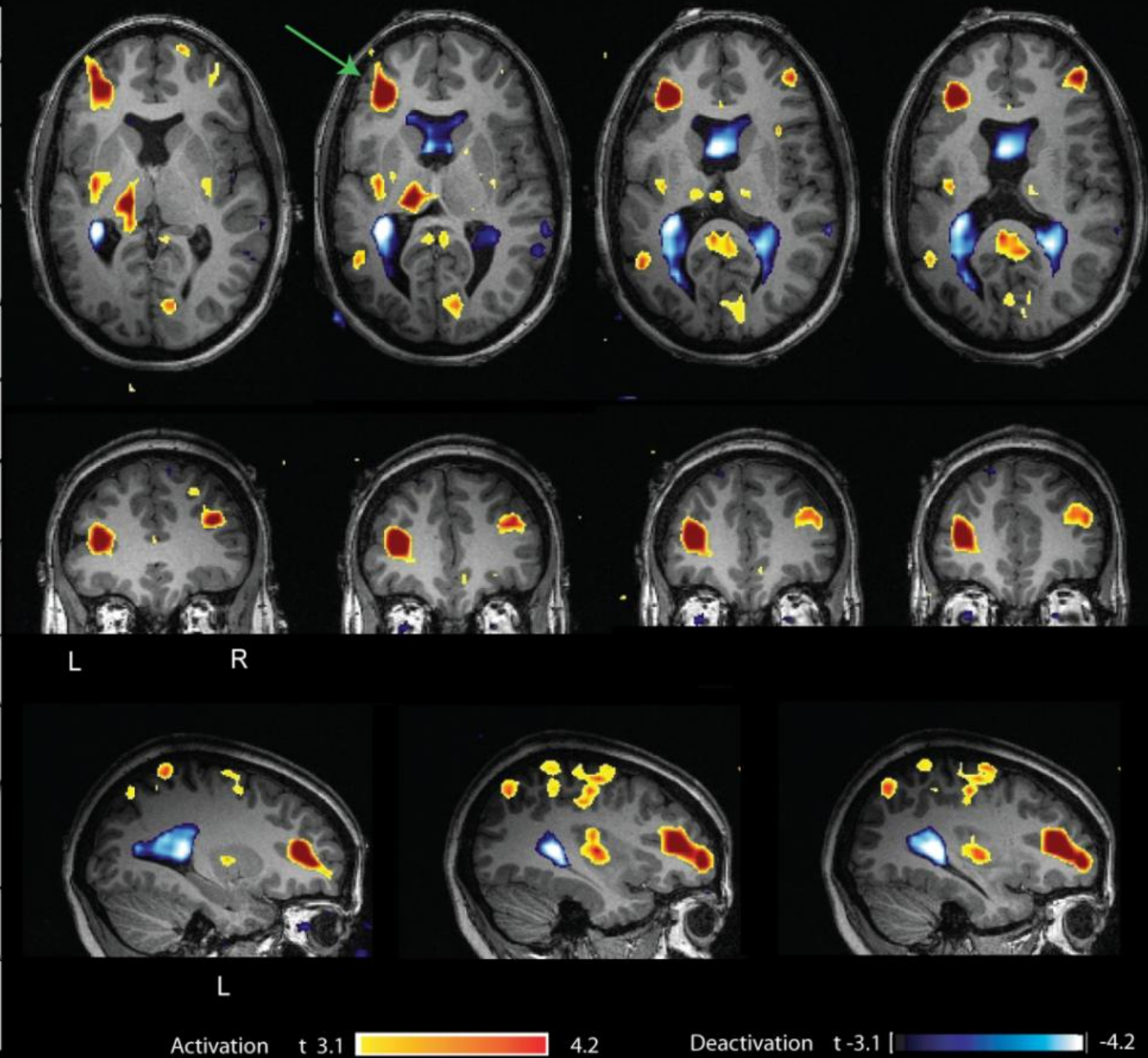
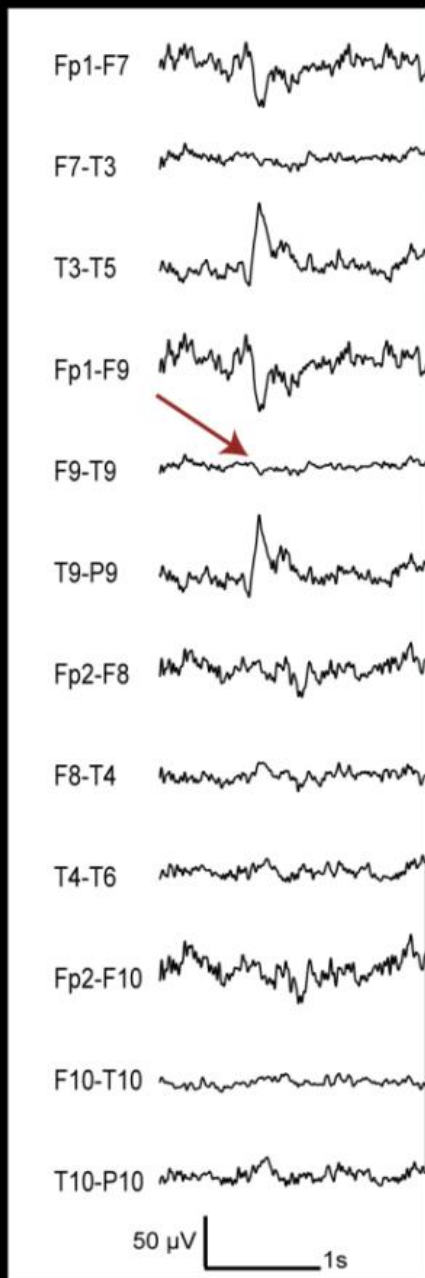
Activation t 3.1



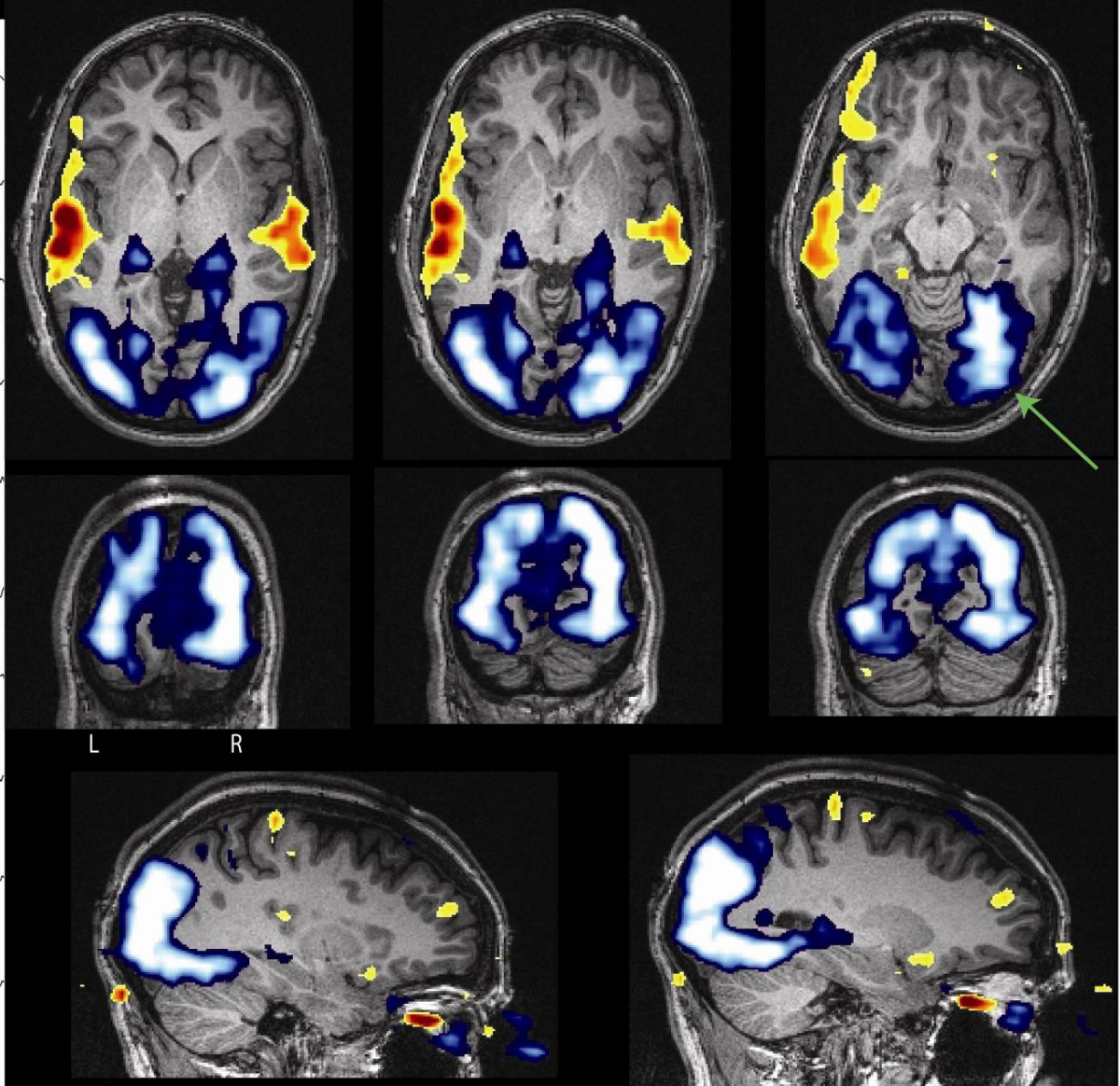
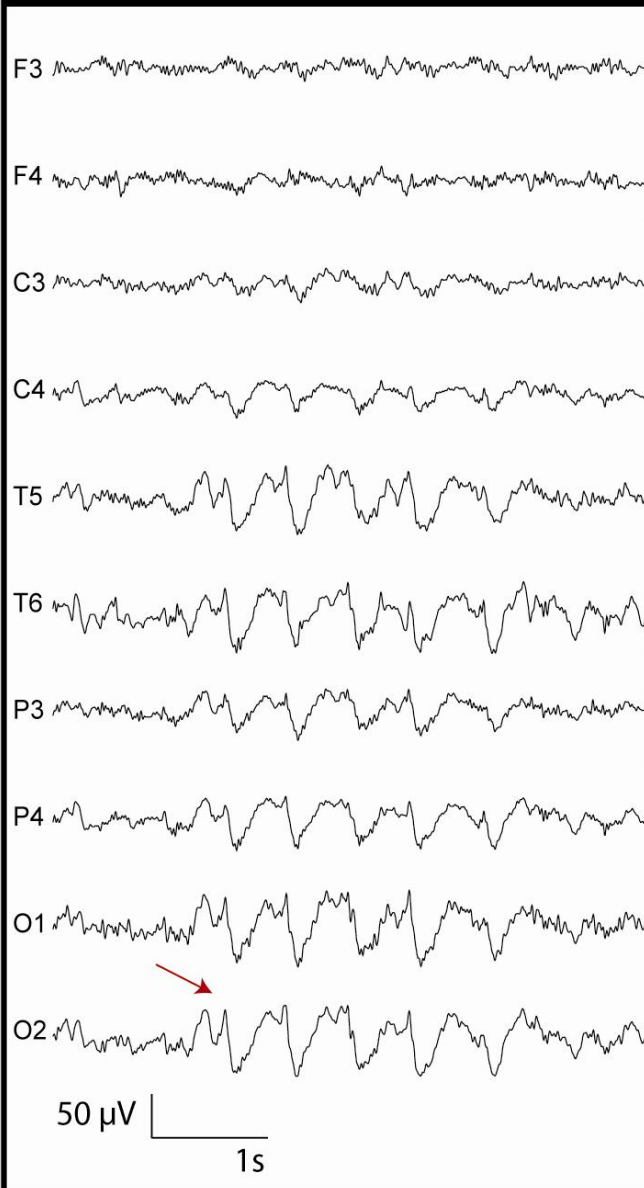
Deactivation t -3.1



Concordant, Contributory, Validated (grid)



Concordant, Contributory, Validated (SEEG)



Activation t 3.1



5.8

Deactivation t -3.1



-17.2

Concordant, not Contributory, Validated (SEEG)

Risultati negativi: perché?

- **Non si vede niente:**

- Aumentata concentrazione di GABA in
- Modello matematico: variabilità di morfologia e distribuzione delle punte
- No punte durante la registrazione
- Focus molto attivo (→ non è possibile avere una baseline)

Individual Variability in the Shape and Amplitude of
the BOLD-HRF Correlates with Endogenous
GABAergic Inhibition

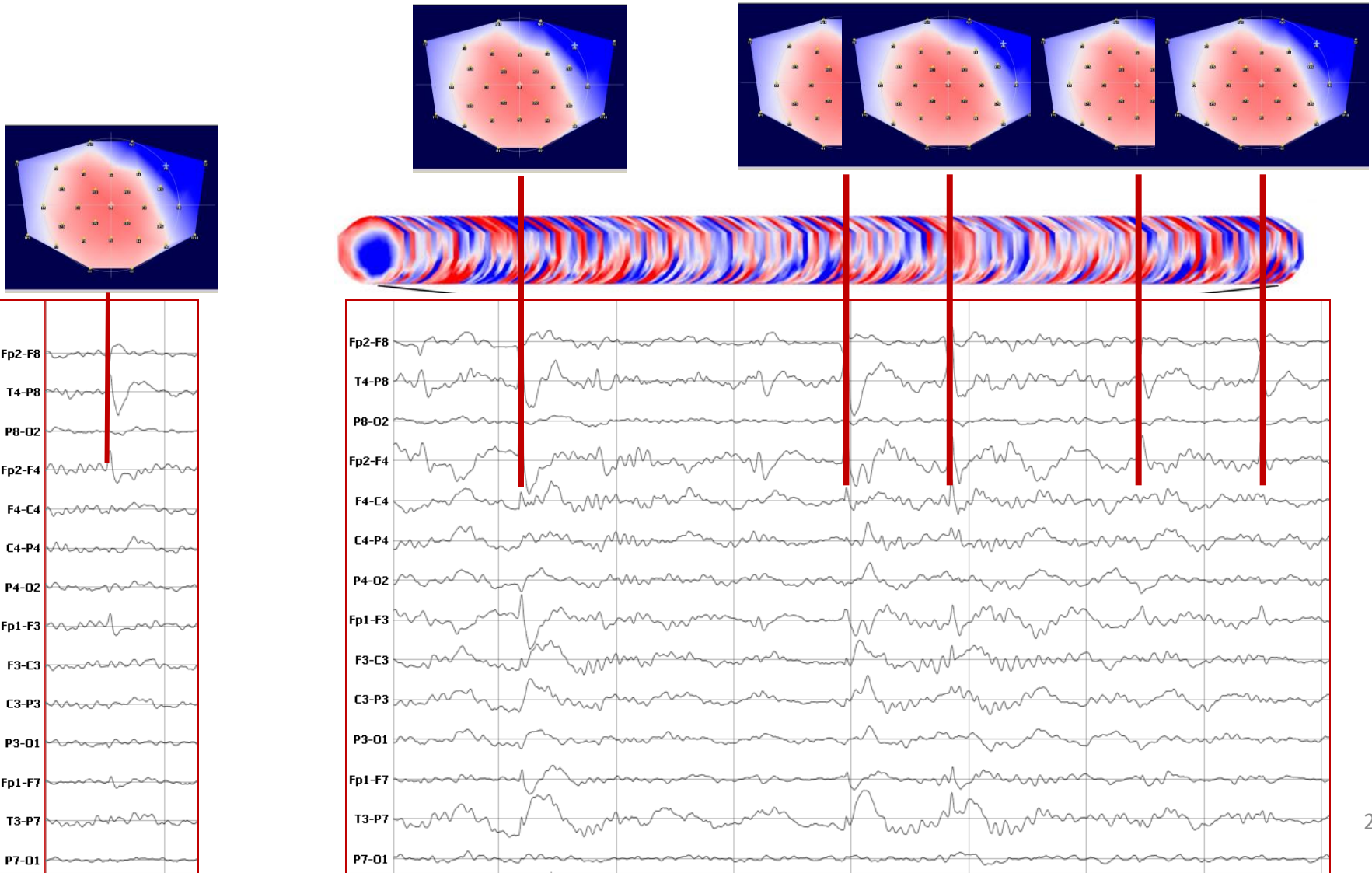
Suresh D. Muthukumaraswamy,^{1,*} C. John Evans,¹ Richard A.E. Edden,^{2,3}
Richard G. Wise,¹ and Krish D. Singh¹

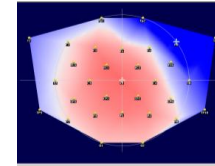
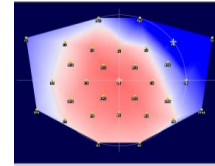
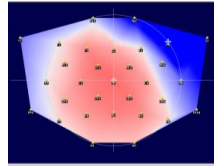
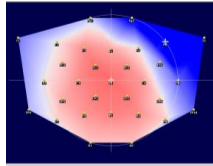
- **Si vede troppo:**

- Oltre il focus altre aree.... Significato?
 - Artefatto? → necessità di occhi esperti e di integrazione con altri esami
 - Modulazione di networks funzionali
 - Attivazione di networks « epilettici »

L'EEG standard in termini di mappe di voltaggio

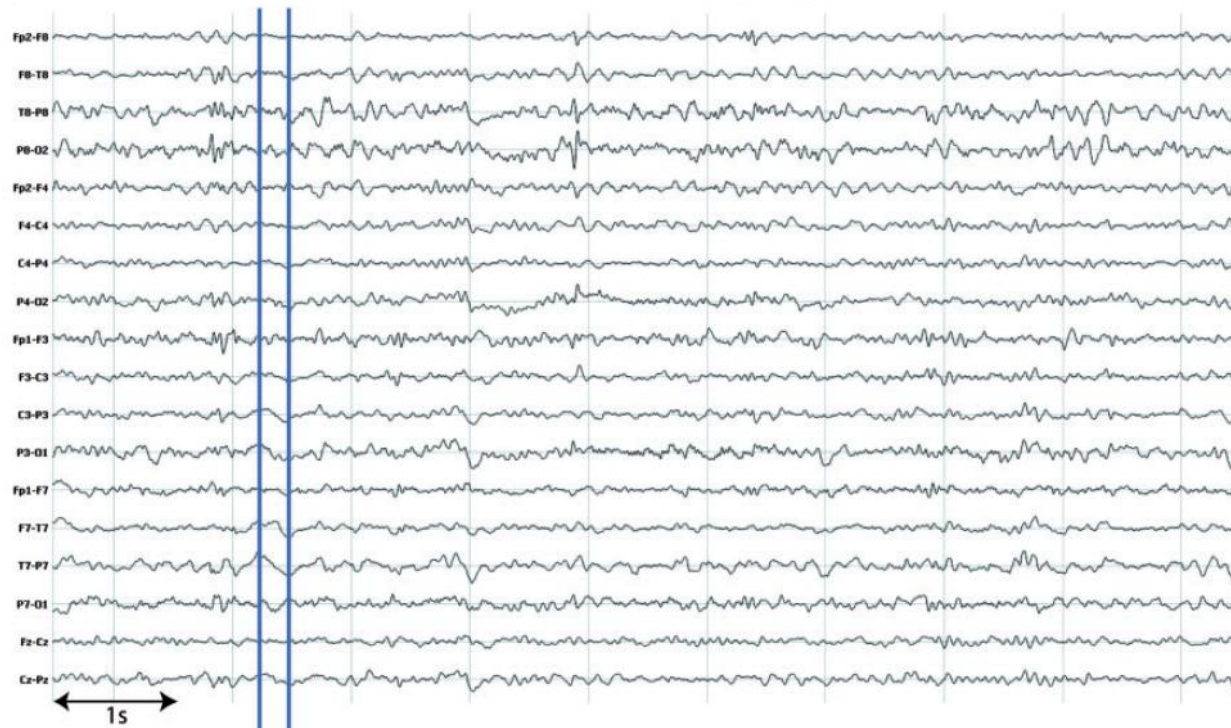
Michel et al., 2004





A

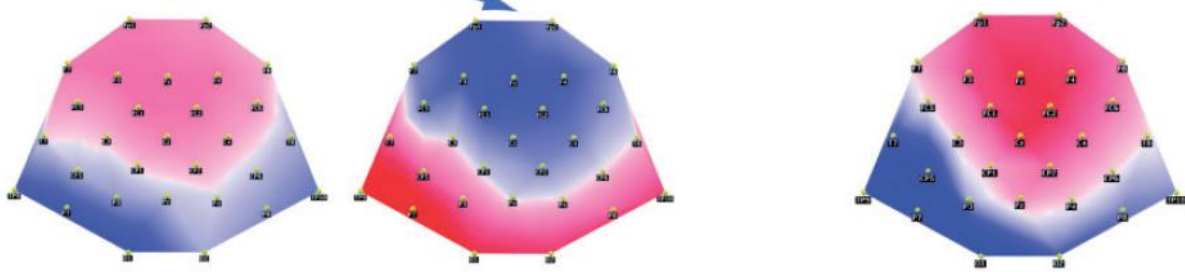
Intra-MRI EEG recording

**B**

Spatial correlation with the epileptic map

**C**

Epileptic map



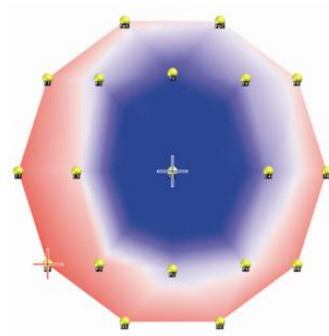
With or without spikes: localization of focal epileptic activity by simultaneous electroencephalography and functional magnetic resonance imaging

Brain 2011; 134; 2867–2886

Frédéric Grouiller,¹ Rachel C. Thornton,² Kristina Groening,³ Laurent Spinelli,¹ John S. Duncan,² Karl Schaller,⁴ Michael Siniatchkin,^{3,5} Louis Lemieux,² Margitta Seeck,¹ Christoph M. Michel¹ and Serge Vulliemoz^{1,2}

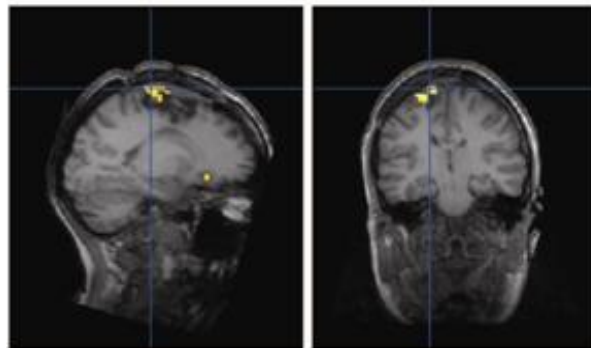


Long-term clinical EEG:
midline spikes

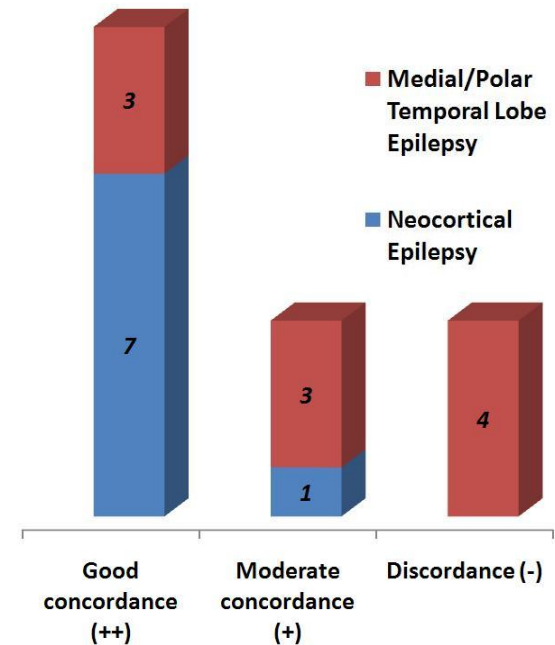


Averaged
EEG spike map

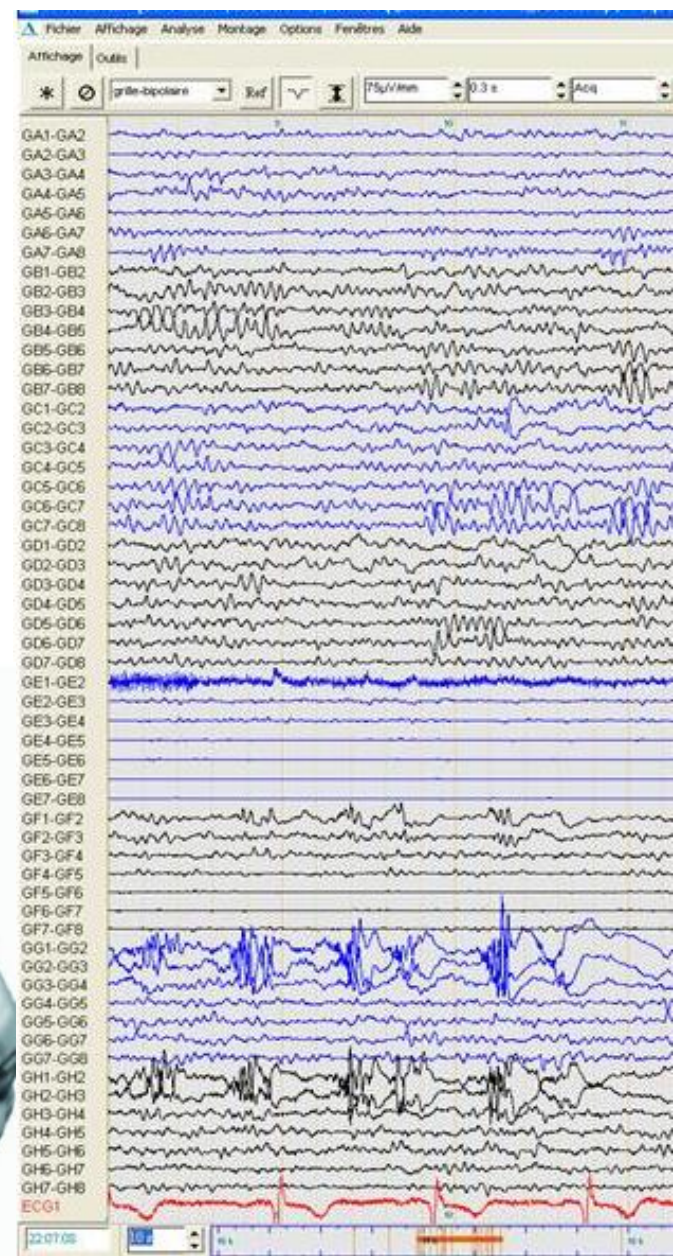
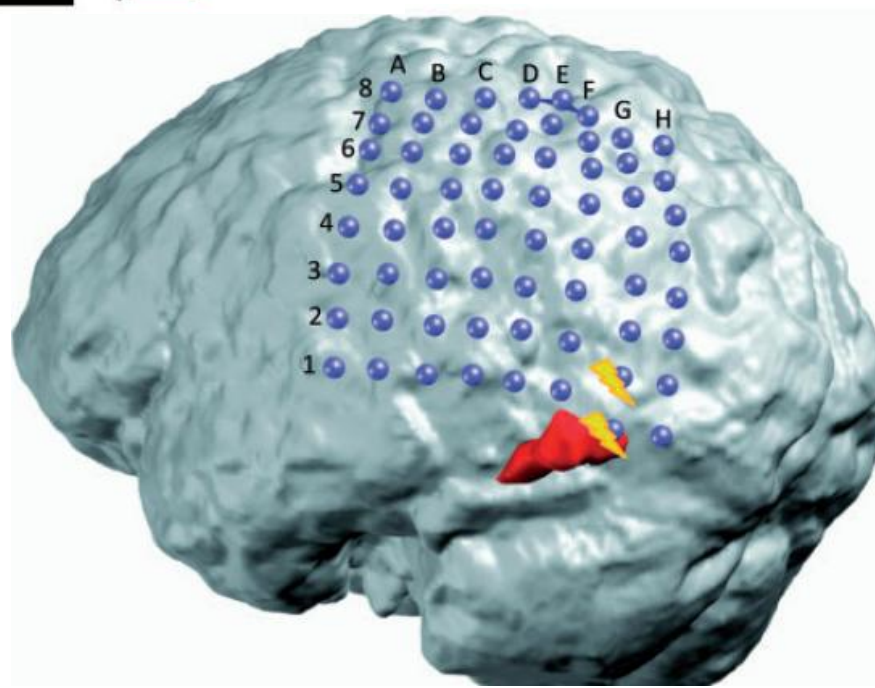
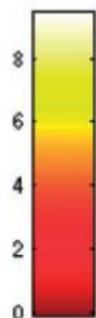
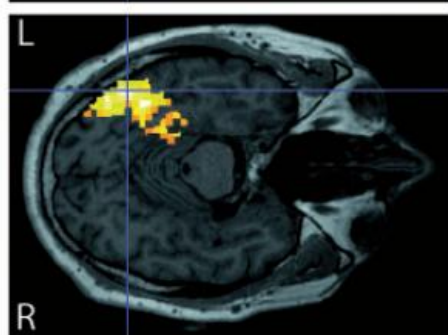
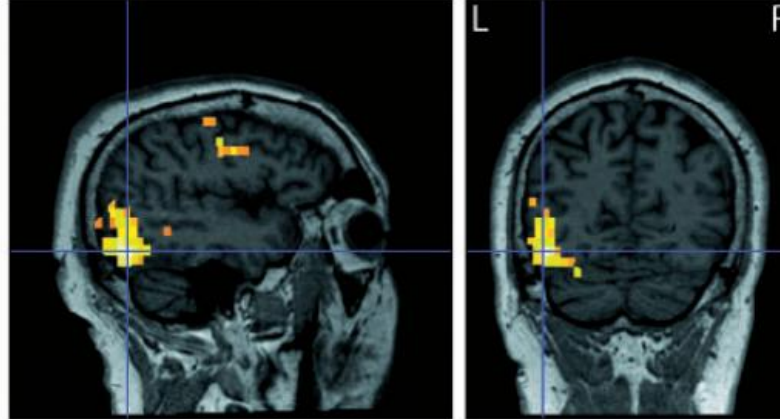
Map-correlated
BOLD changes



78% (14/18):
concordant localisation
invasive validation



fMRI analysis informed by EEG topography improves the localisation of focal epileptic activity in difficult cases.



Risultati negativi: perché?

- **Non si vede niente:**

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- Modello matematico: variabilità di morfologia e distribuzione delle punte
- No punte durante la registrazione
- Focus molto attivo (→ non è possibile avere una baseline)

Individual Variability in the Shape and Amplitude of the BOLD-HRF Correlates with Endogenous GABAergic Inhibition

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 - Attivazione di networks « epilettici »

EEG-fMRI critico

- Pochi studi hanno riportato modificazioni BOLD correlati a brevi crisi con manifestazioni cliniche minime o assenti.
- Le crisi generano modificazioni BOLD molto più diffuse rispetto alle anomalie inter-critiche (Tyvaert et al., 2008).
- Metodi di analisi dinamica possono dare informazioni sulla regione di inizio crisi e le regioni di propagazione (Murta et al., 2012) → network di propagazione della scarica

Dynamic Causal Modelling of epileptic seizure propagation pathways: A combined EEG-fMRI study

Referenze bibliografiche I

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- Zijlmans M, Huiskamp G, Hersevoort M, et al. EEG-fMRI in the preoperative work-up for epilepsy surgery. *Brain* 2007;130:2343-2353.
- Tao JX, Baldwin M, Hawes-Ebersole S, et al. Cortical substrates of scalp EEG epileptiform discharges. *J Clin Neurophysiol* 2007;24:96-100.
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Referenze bibliografiche II

- Gholipour T, Moeller F, Pittau F, et al. Reproducibility of interictal EEG-fMRI results in patients with epilepsy. *Epilepsia* 2011;52:433-442.
- Grouiller F, Thornton RC, Groening K, et al. With or without spikes: localization of focal epileptic activity by simultaneous electroencephalography and functional magnetic resonance imaging. *Brain* 2011;134:2867-2886.
- Gotman J, Pittau F. Combining EEG and fMRI in the study of epileptic discharges. *Epilepsia* 2011;52 Suppl 4:38-42.
- Thornton R, Vulliemmoz S, Rodionov R, et al. Epileptic networks in focal cortical dysplasia revealed using electroencephalography-functional magnetic resonance imaging. *Ann Neurol* 2011;70:822-837.
- Pittau F, Dubeau F, Gotman J. Contribution of EEG/fMRI to the definition of the epileptic focus. *Neurology* 2012;78:1479-1487.
- Muthukumaraswamy SD, Evans CJ, Edden RA, et al. Individual variability in the shape and amplitude of the BOLD-HRF correlates with endogenous GABAergic inhibition. *Hum Brain Mapp* 2012;33:455-465.
- An D, Fahoum F, Hall J, et al. Electroencephalography/functional magnetic resonance imaging responses help predict surgical outcome in focal epilepsy. *Epilepsia* 2013;54:2184-2194.
- Pittau F, Grouiller F, Spinelli L, et al. The role of functional neuroimaging in pre-surgical epilepsy evaluation. *Front Neurol* 2014;5:31.
- Pittau F, Megevand P, Sheybani L, et al. Mapping epileptic activity: sources or networks for the clinicians? *Front Neurol* 2014;5:218.