Electrical Source Imaging in Epilepsy

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Electric Source Imaging (ESI)

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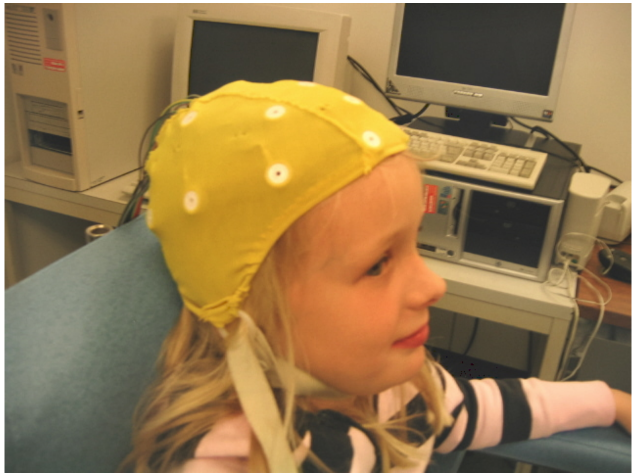
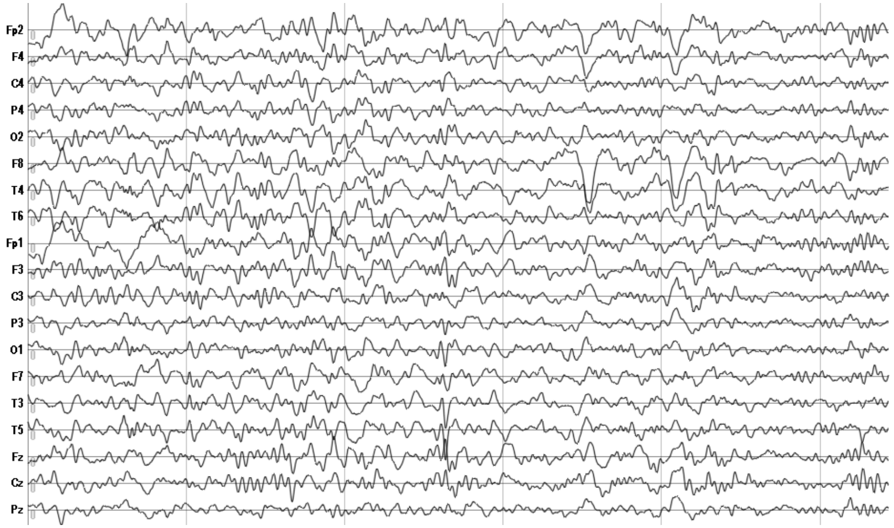
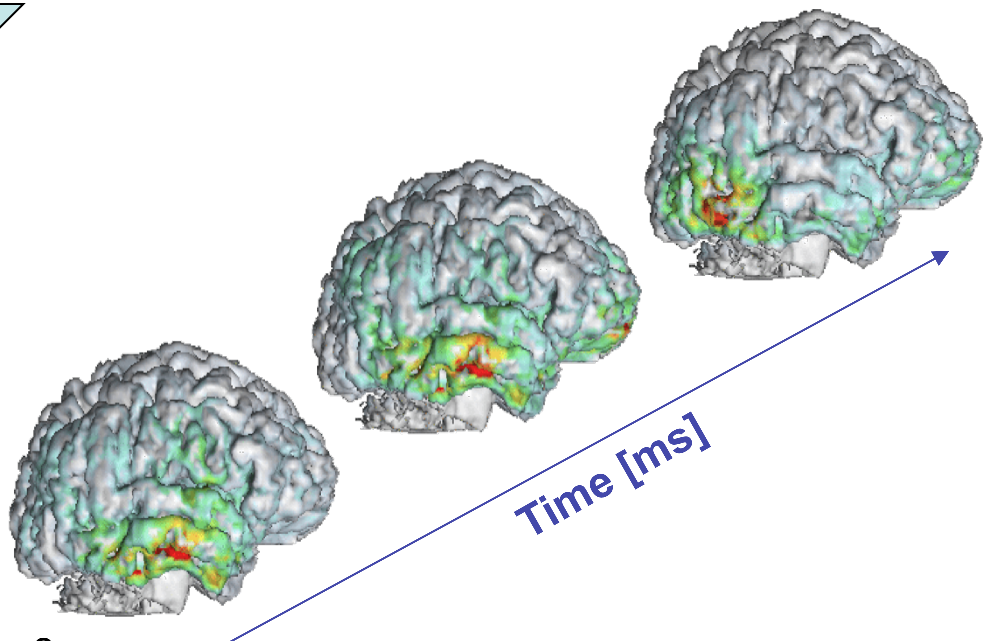


EEG



ESI



Layout

- **Method** — Head and source models
- **Spatial resolution** — Number of electrodes
- **Temporal resolution** — Propagation
- **Multimodal imaging** — ESI / fMRI combination

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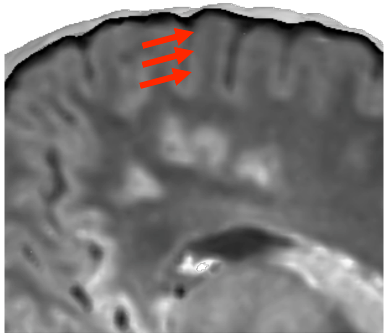
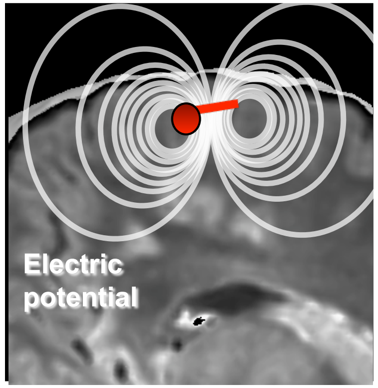
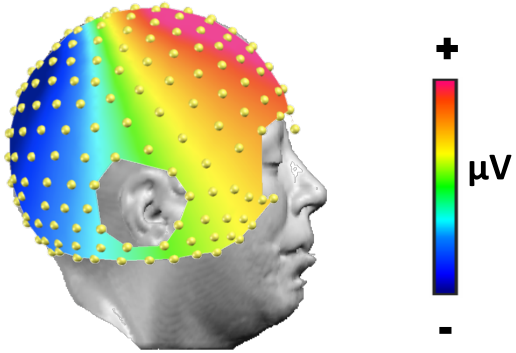
The forward problem: from active neurons to scalp EEG

Equivalent current dipole | *Volume conduction* | *Scalp potential field*

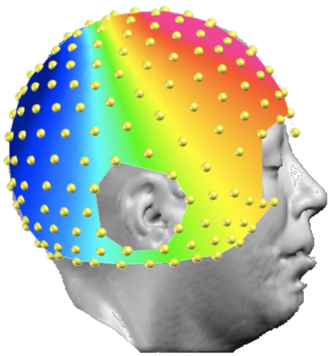






The inverse problem: from scalp EEG to active neurons

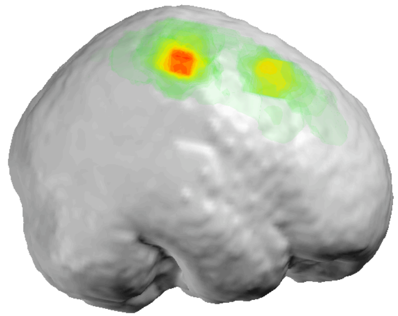
Scalp potential field



No unique solution

Infinite number of source configurations can produce the same surface map

Current density distribution



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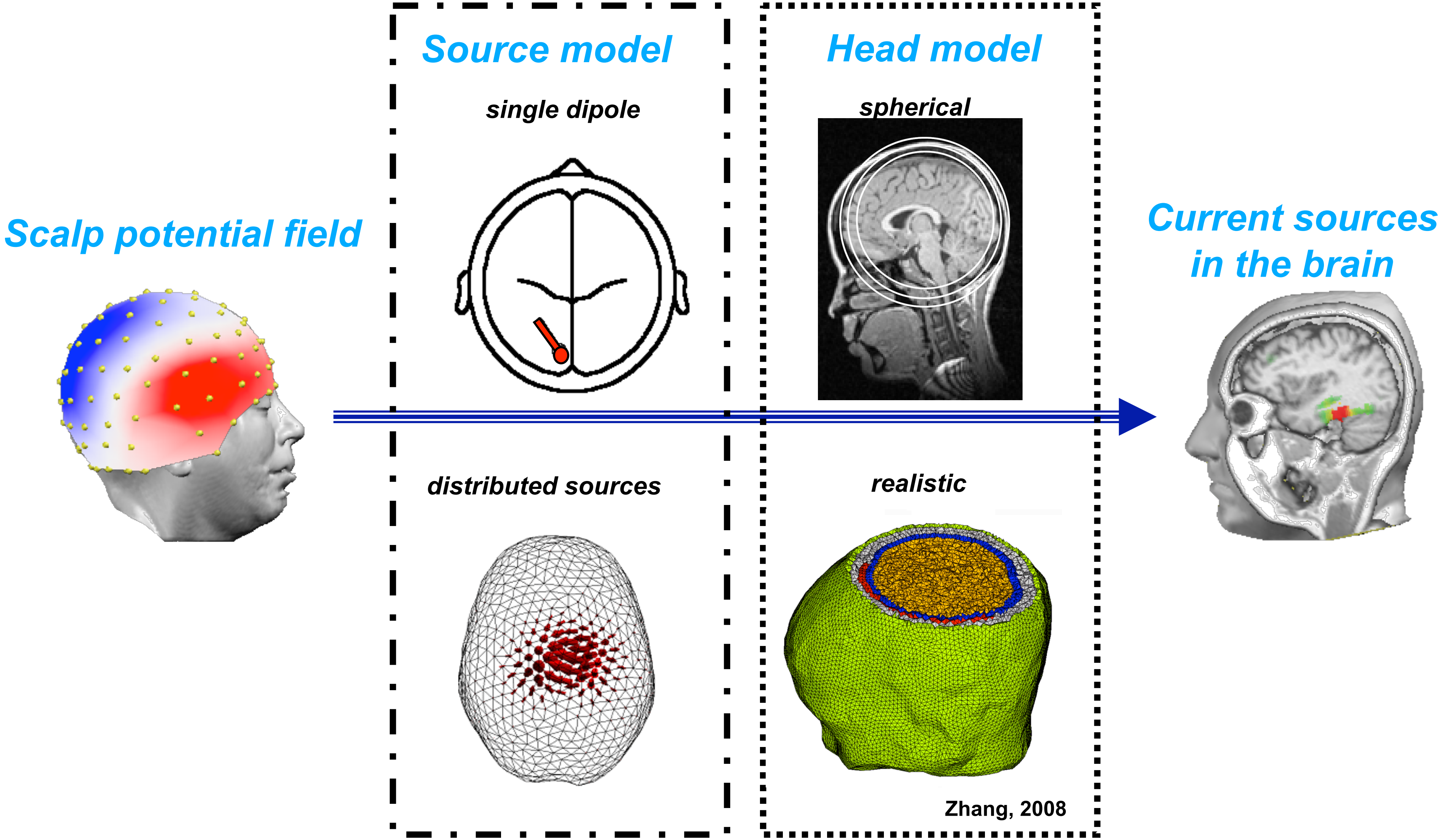
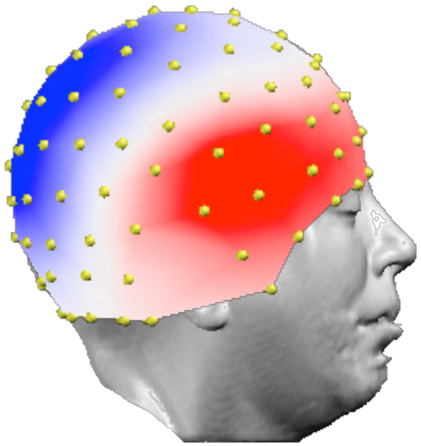
The inverse problem: from scalp potential to active neurons

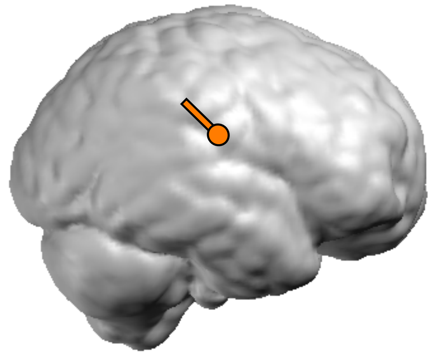


Michel et al., Clin. Neurophysiol., 2004

ESI : Source Models

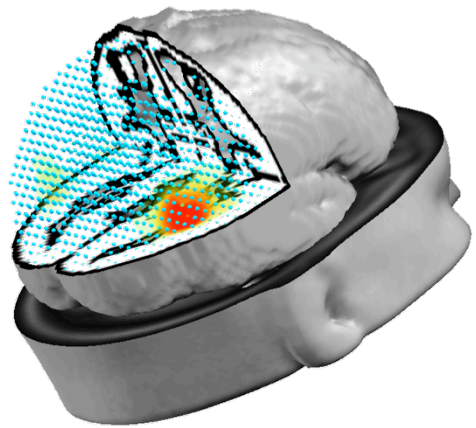


Search for one or a few equivalent dipoles



Number of dipoles must be known.
Solution by Least Square Methods
(Non-linear iterative optimization)

Calculation of a 3D current distribution



Underdetermined system
→ A priori constraints needed

ESI : Distributed linear inverse solutions

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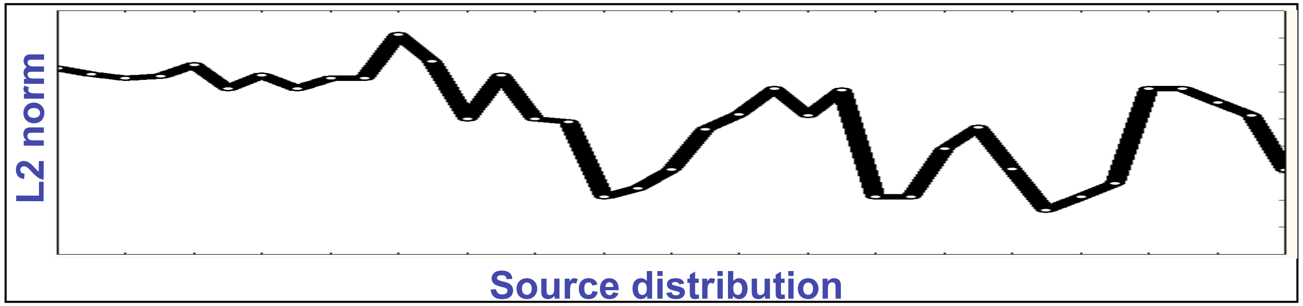
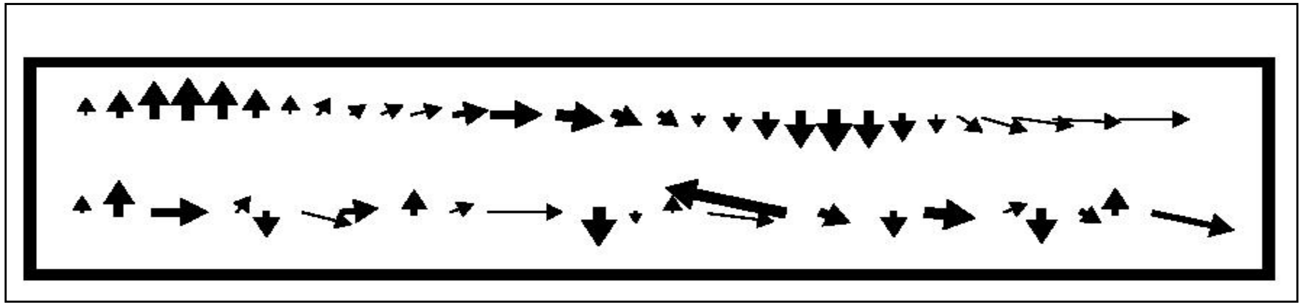
Underdetermined system → A priori constraints needed

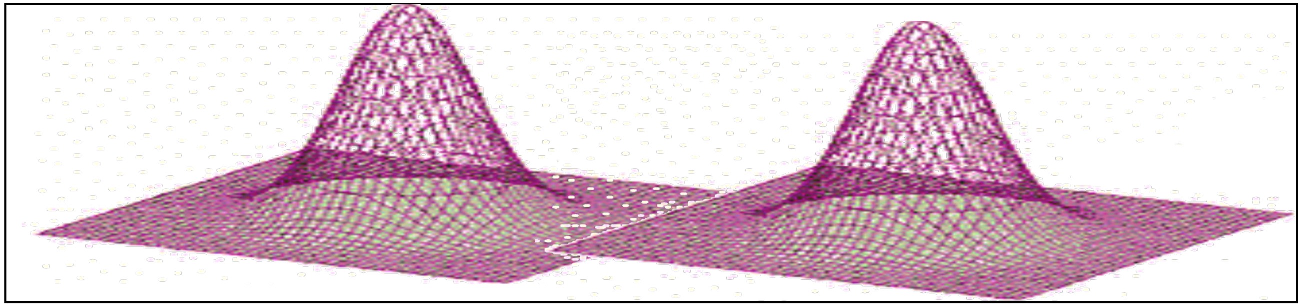
Distribution with minimal use of energy
= *Minimum Norm Solution*
Hamalainen & Illmoniemi, 1985



Distribution with maximal smoothness
= *Laplacian Minimization*
LORETA, Pascual-Marqui, 1994



Spatial attenuation of the current
= *Local autoregressive average*
LAURA, Grave de Peralta, 2001



Michel et al., Clin. Neurophysiol., 2004

ESI : Distributed linear inverse solutions

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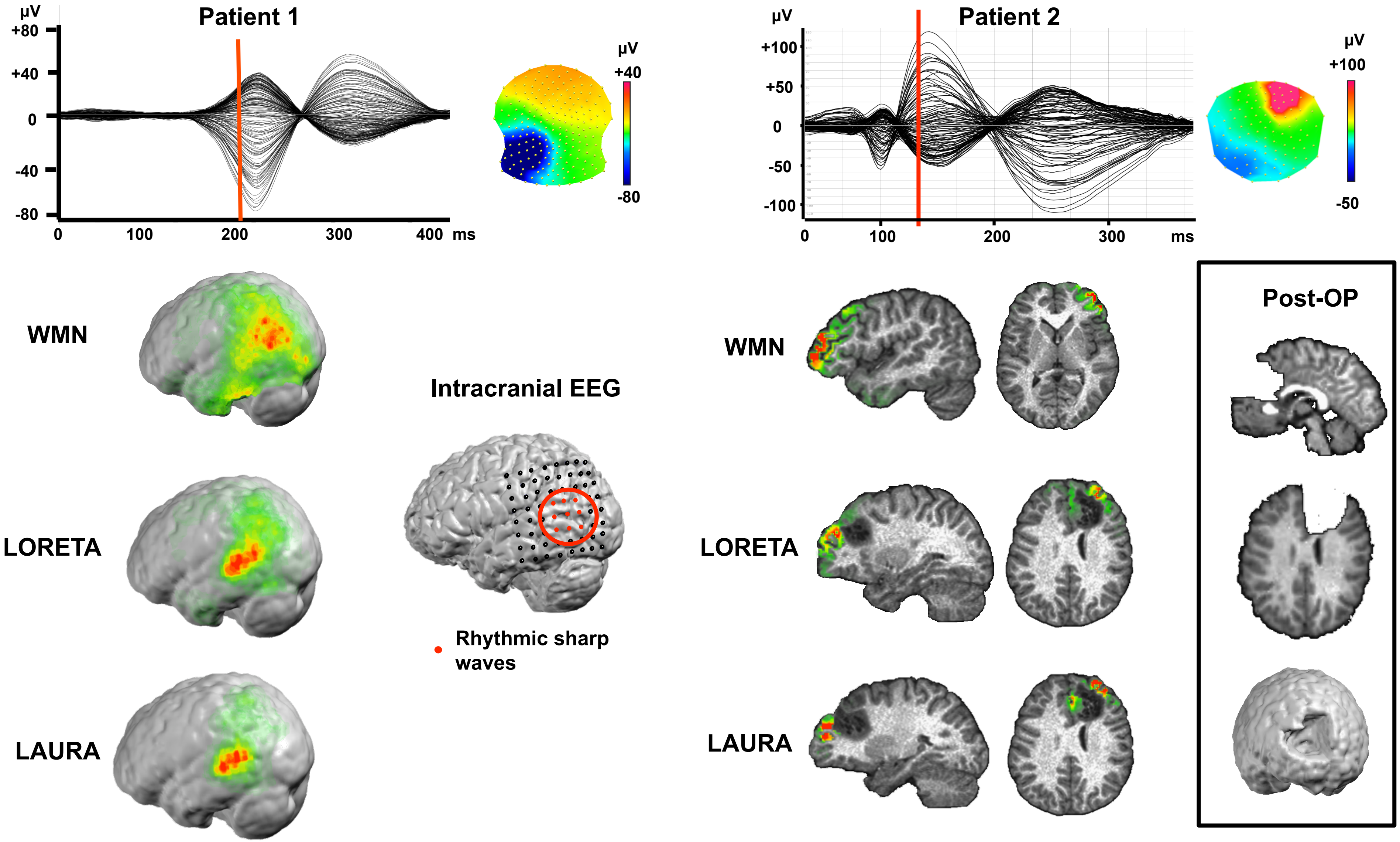
Comparison of different algorithms



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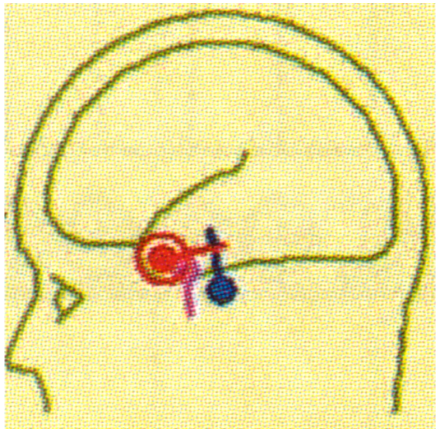
Spherical model



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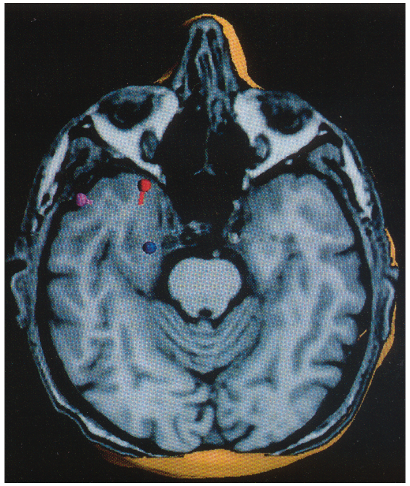
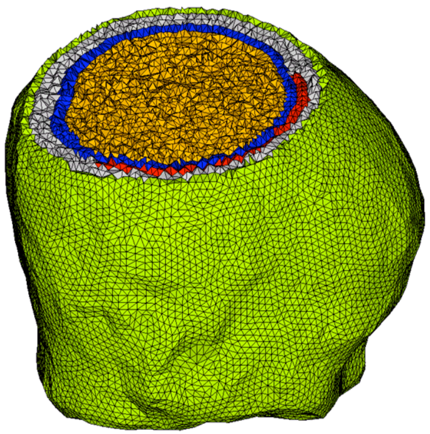
Anatomical Projection



Does not consider individual anatomy

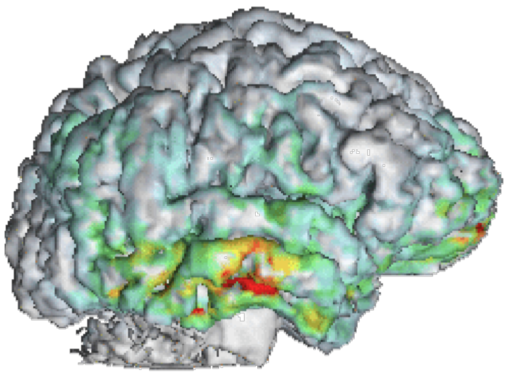
Analytical solution

Realistic head model (BEM, FEM)



Zhang et al., 2008

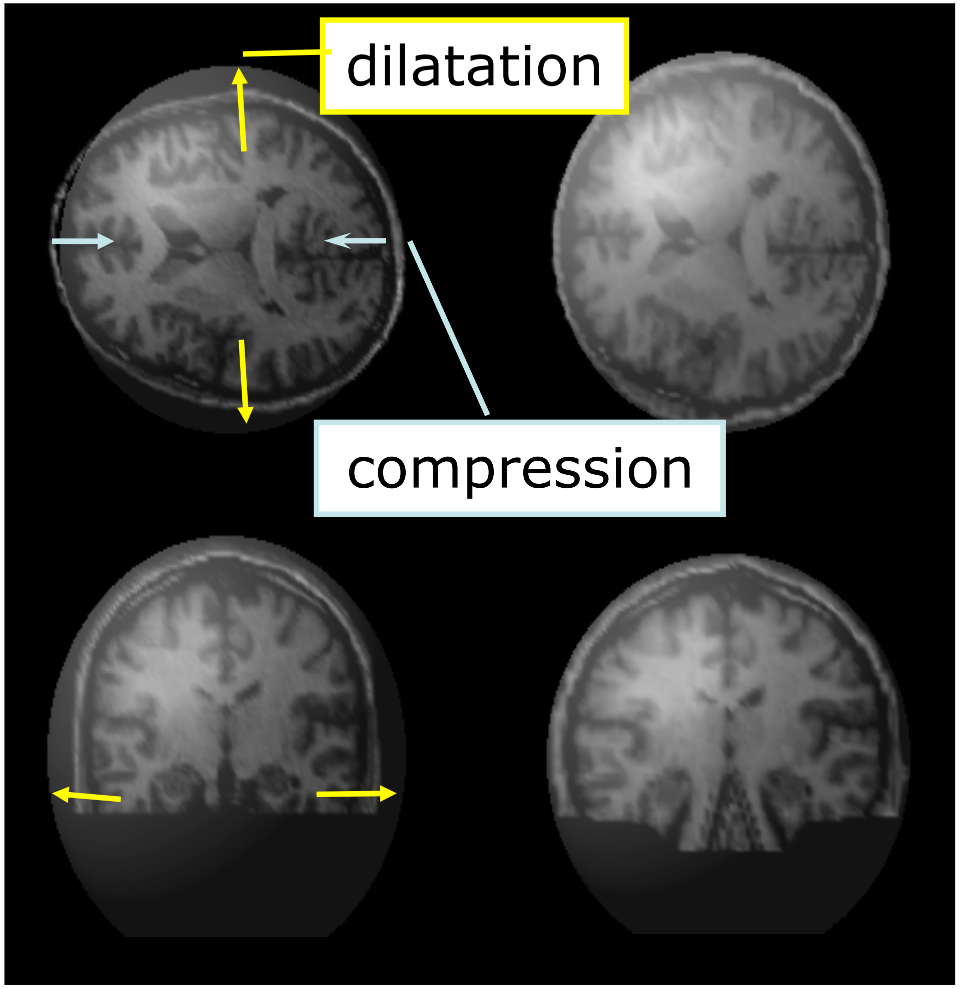
Anatomically constrained solution



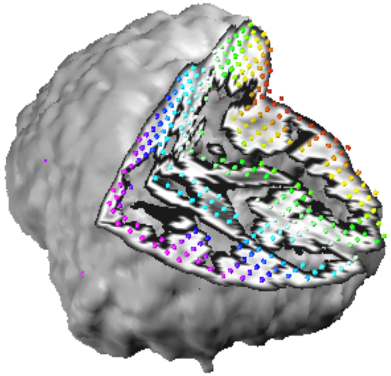
Complex, needs detailed segmentation of the MRI including the interfaces of the different head compartments

Numerical solution

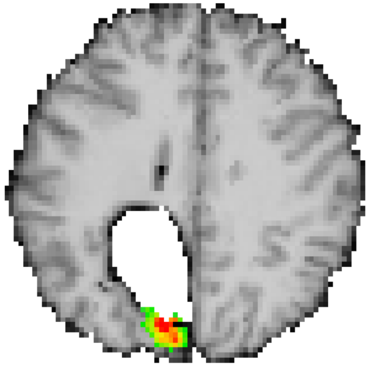
ESI : The SMAC Head Model



ESI in anatomically constrained spherical head models (SMAC)



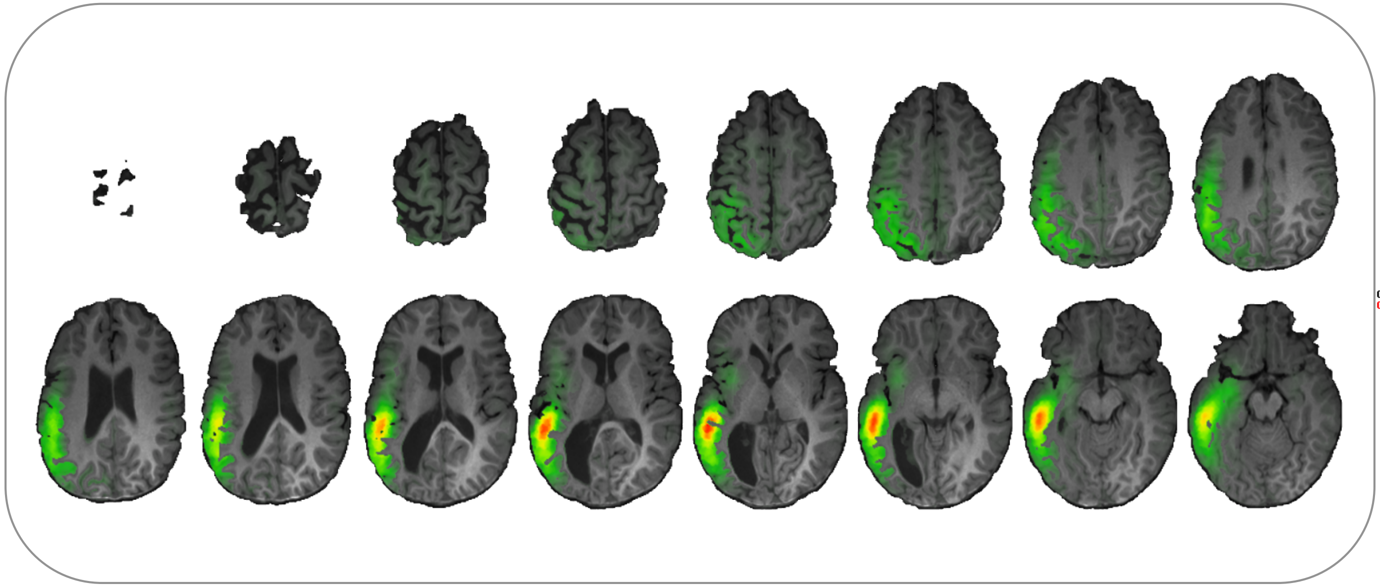
Solution points restricted to the gray matter

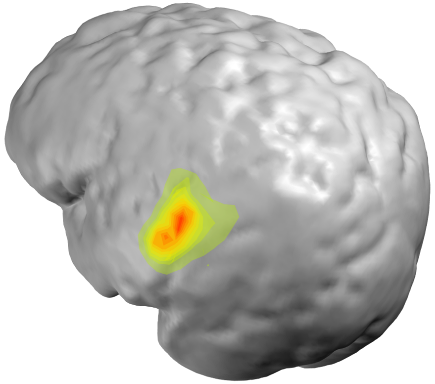


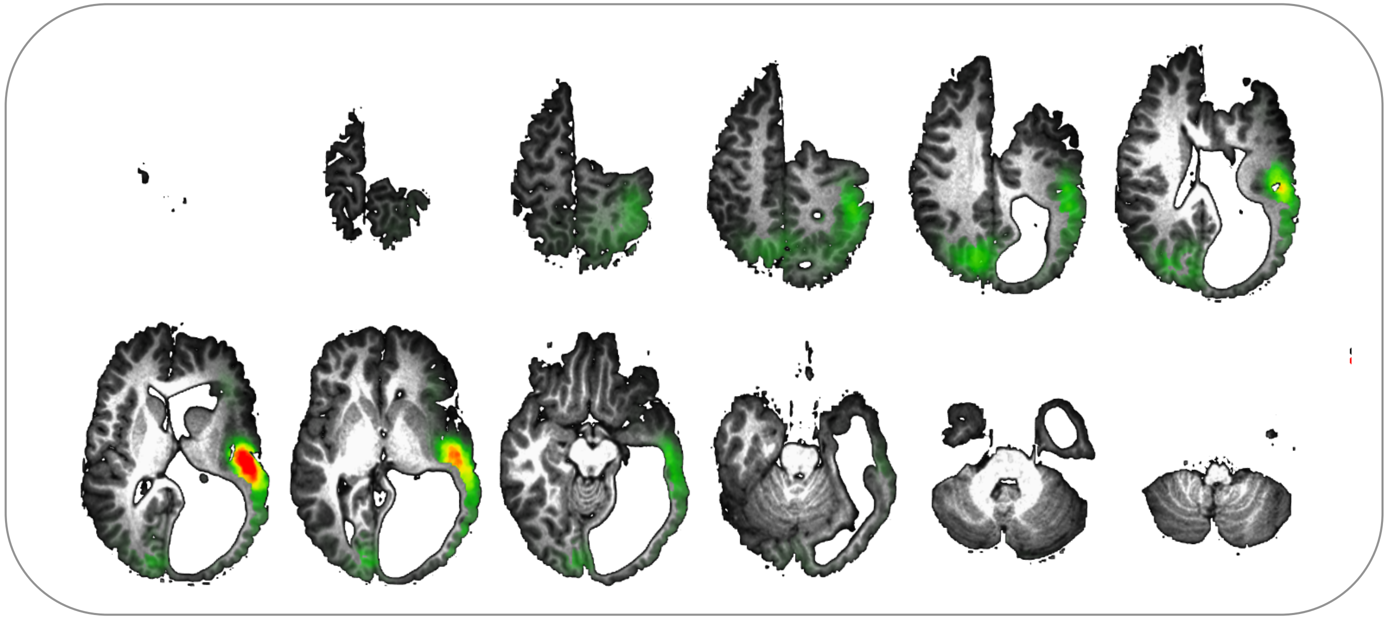
Source localization in the individual brain

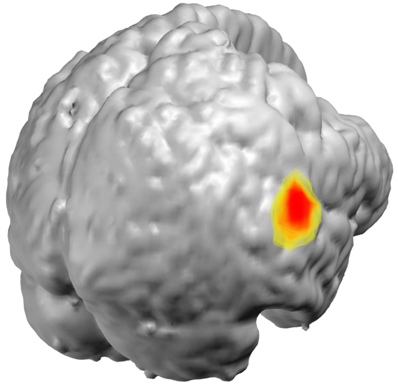
Spinelli et al., Brain Topogr., 2000

ESI in individual MRI



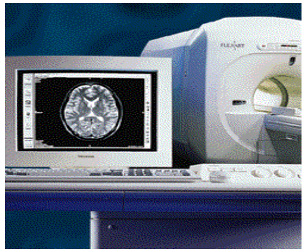






ESI in Epilepsy: the Method

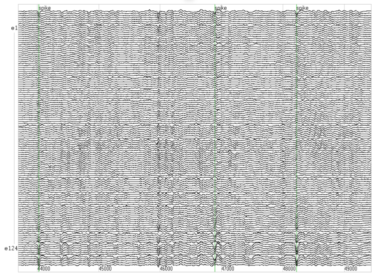
High resolution EEG recordings



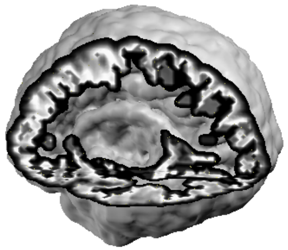
Recording of the structural MRI

Recording of the 3D sensor positions

Segmentation of the brain surface



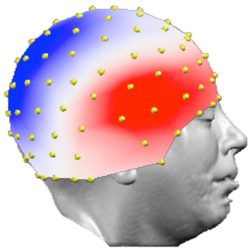
Selection of Spikes



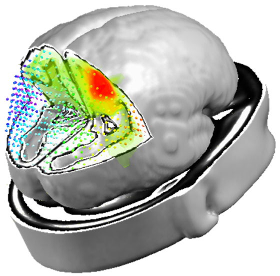
Definition of the grey matter

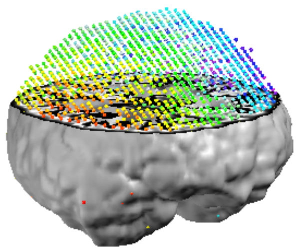
$$\Phi = G\,L\,J_v + n$$

Inverse solution calculation



Mapping of the scalp electric field





Definition of the solution space within the gray matter

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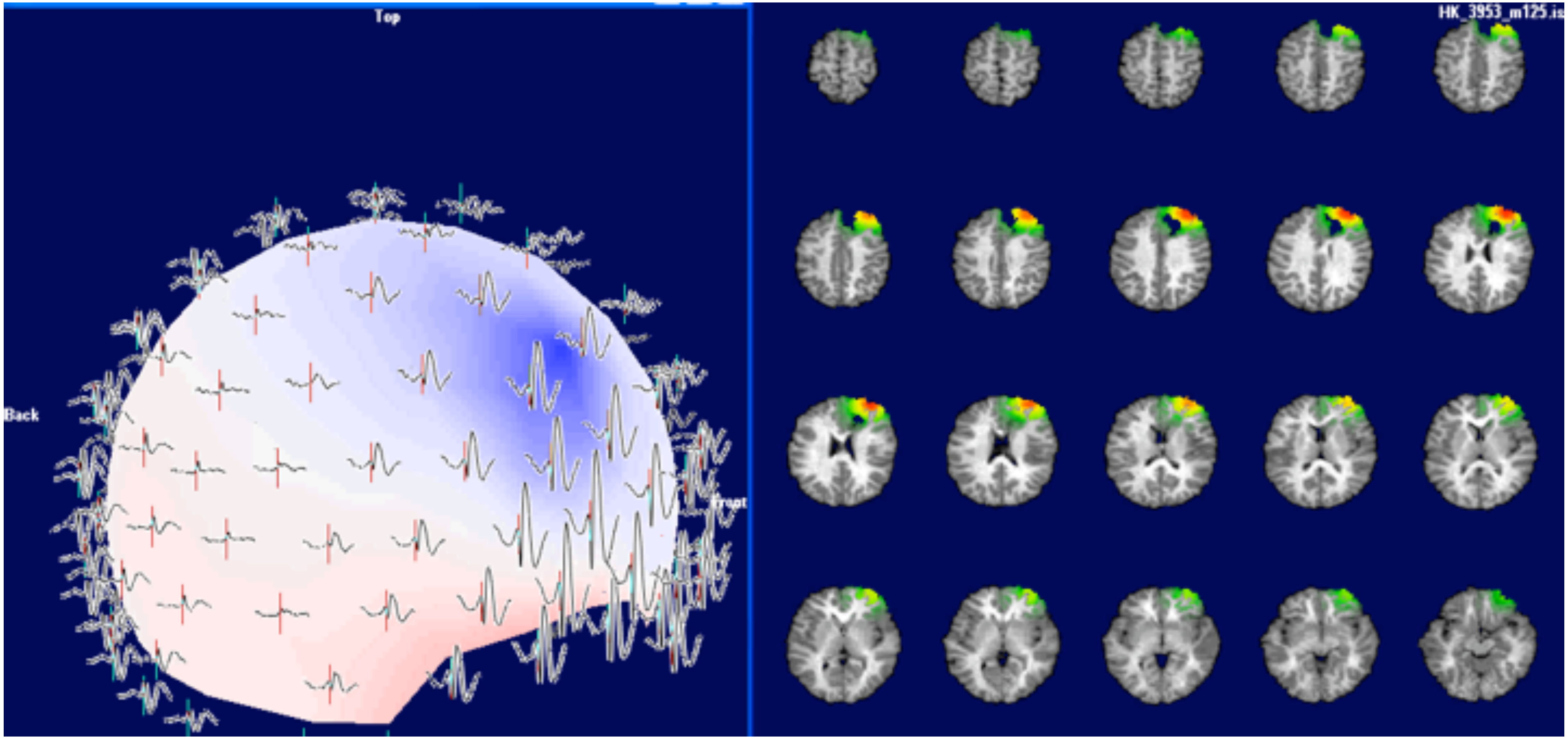
Averaged Spike (128 channel recording)



Study 1: ESI in children

30 patients (11 male, 19 female); age range: 1-20 years, mean age 10.6 years

<u>All but one patient had abnormal MRI</u>

- **6 hippocampal sclerosis (HS) w/wo temporal lobe atrophy.**
- **18 cases with different kinds of cortical lesions**
- **2 tuberous sclerosis (TS)**
- **5 hemispheric atrophy (HA).**

<u>All patients had epilepsy surgery (24 resections, 6 hemispherotomies)</u>

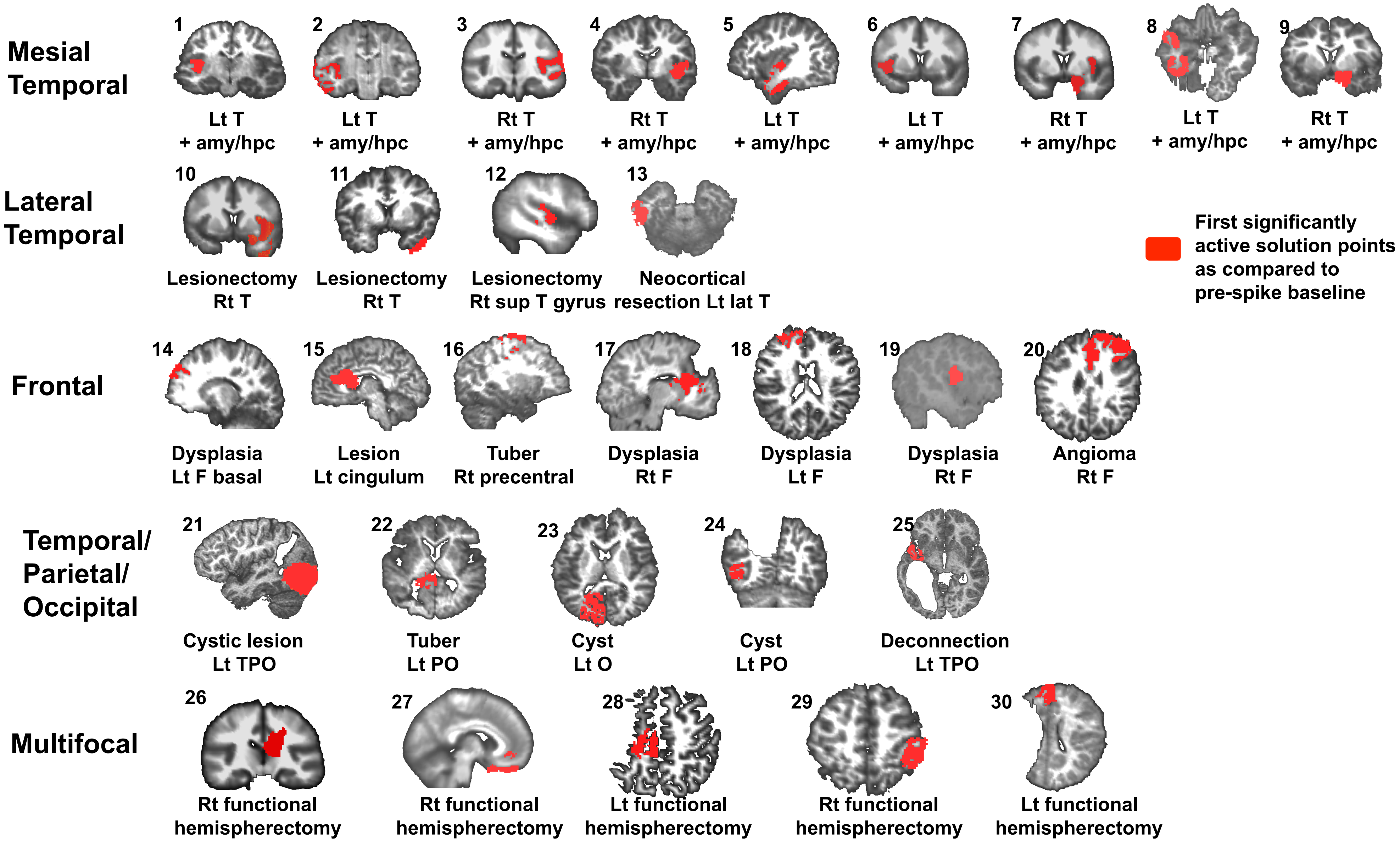
Follow up: 27 of the patients were seizure free 2-60 (mean 13) months after surgery
1 patient had 2 short seizures 3 months postoperatively
2 patients without follow up information, although no indications of remaining seizures.

Recordings: 21-32 channel standard clinical EEG recordings

Analysis:
- Selection of 20-60 spikes with similar topography
- Alignement to time point of maximal Global Field Power
- Statistical parametric mapping in the inverse space
- Concordance with respect to the resected area

Sperli et al., Epilepsia, 2006

Study 1: ESI in children



Sperli et al., Epilepsia, 2006

Study 1: ESI in children

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Concordance of different imaging methods with resected area

	PET	SPECT	ESI
Temporal *13 pat.*	8/11 73%	8/10 80%	10/13 77%
Frontal *7 pat.*	6/7 86%	3/6 50%	7/7 100%
Parieto-Occ *6 pat.*	4/5 80%	2/3 67%	5/5 100%
Hemispheric *5 pat.*	5/5 100%	3 / 4 75%	5/5 100%
TOTAL *31 pat.*	**23/28** **82%**	**16/23** **70%**	**27/30** **90%**

Sperli et al., Epilepsia, 2006

ESI : How many electrodes are needed ?

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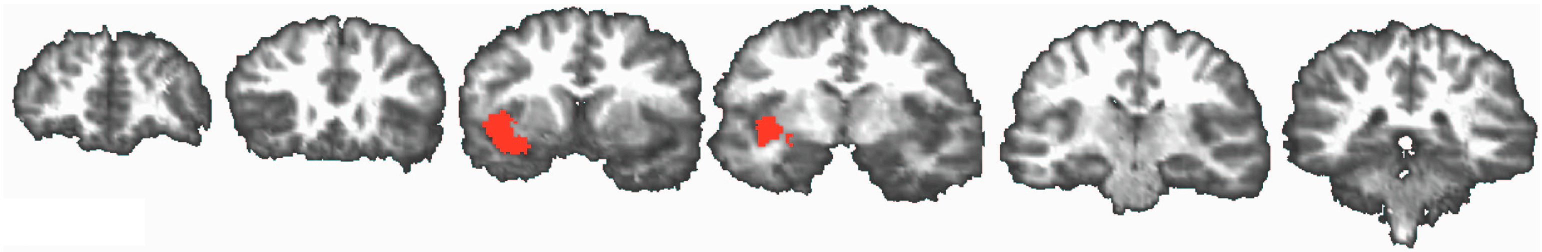
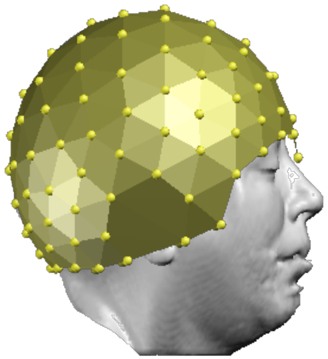
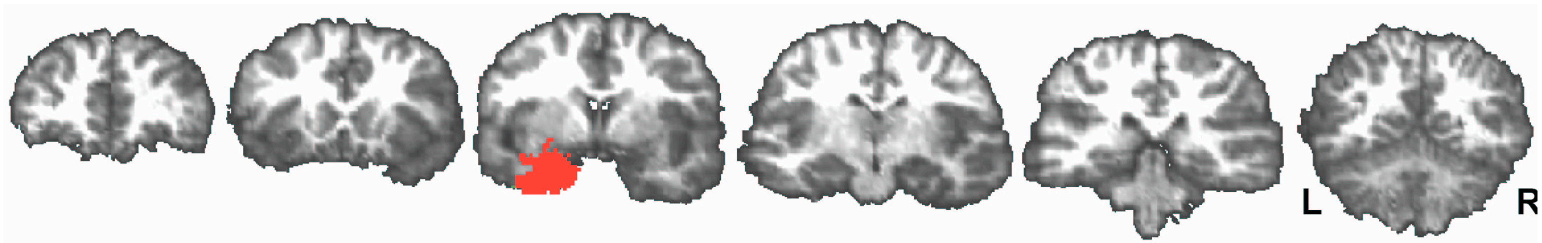
Pat. 1: mesial temporal lobe epilepsy

21 electrodes



128 electrodes





Sperli et al., Epilepsia, 2006

ESI : How many electrodes are needed ?

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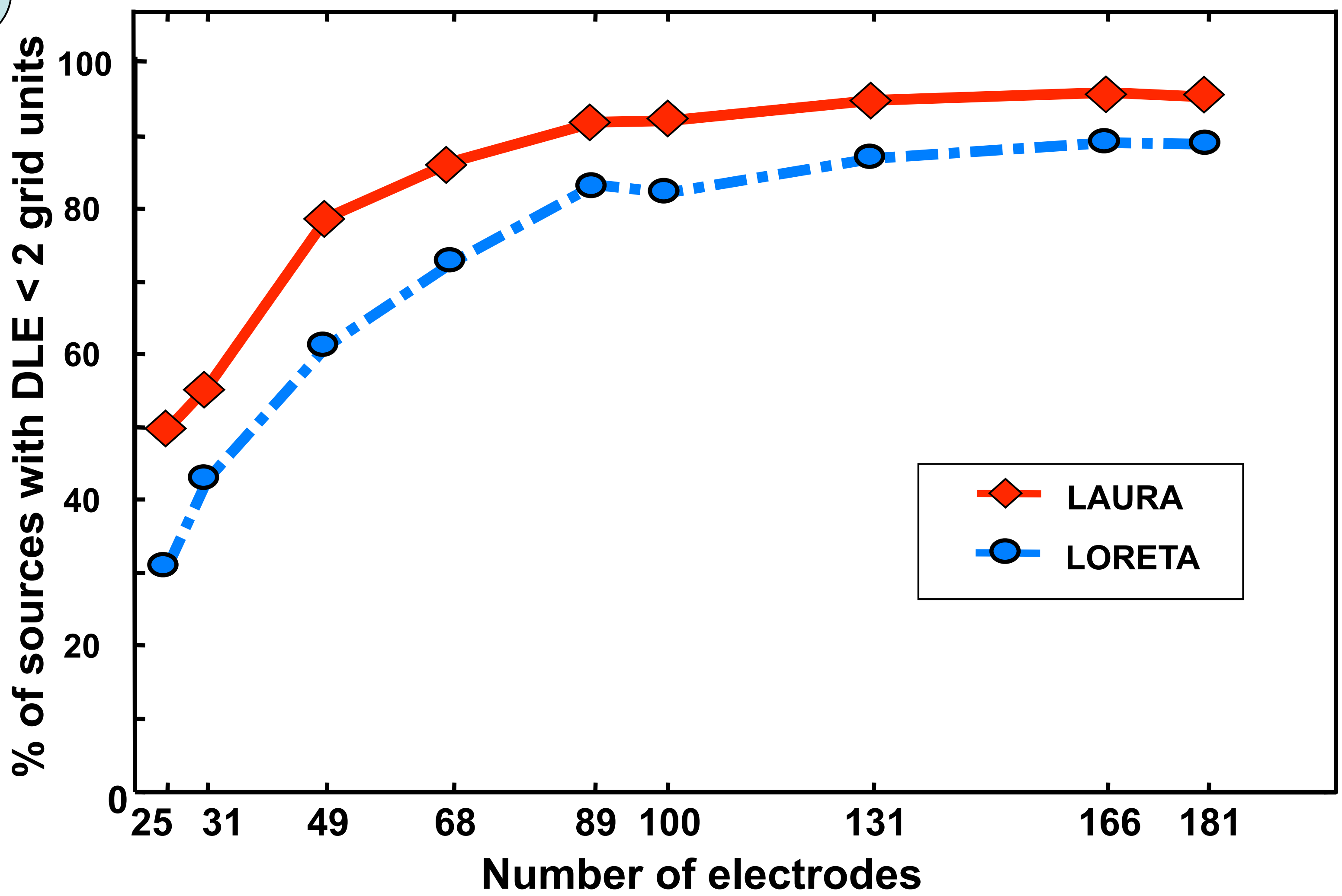
Effect of the number of electrodes on the source localization precision (simulation study)

4



Michel et al., Clin. Neurophysiol., 2004

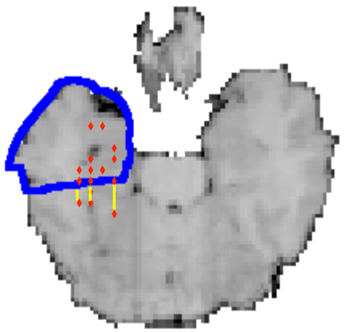
Study 2: Number of electrodes for ESI

5

Epileptic source localization with high density EEG: how many electrodes are needed ?

14 patients with partial epilepsy. Seizure-free after surgery

- **Recording of 123-channel interictal EEG and selection of ~30 spikes.**
- **Down-sampling of the data to 63 and to 31 electrodes.**
- **Source reconstruction separately for 123, 63, and 31 electrodes**
- **Delineation of the epileptogenic lesion in the MRI (MRI lesion in 12, iEEG recording in 2)**
- **Calculation of the distance of the source maximum to the epileptogenic lesion for each single spike.**



Lantz et al., Clin. Neurophysiol., 2003

Study 2: Number of electrodes for ESI

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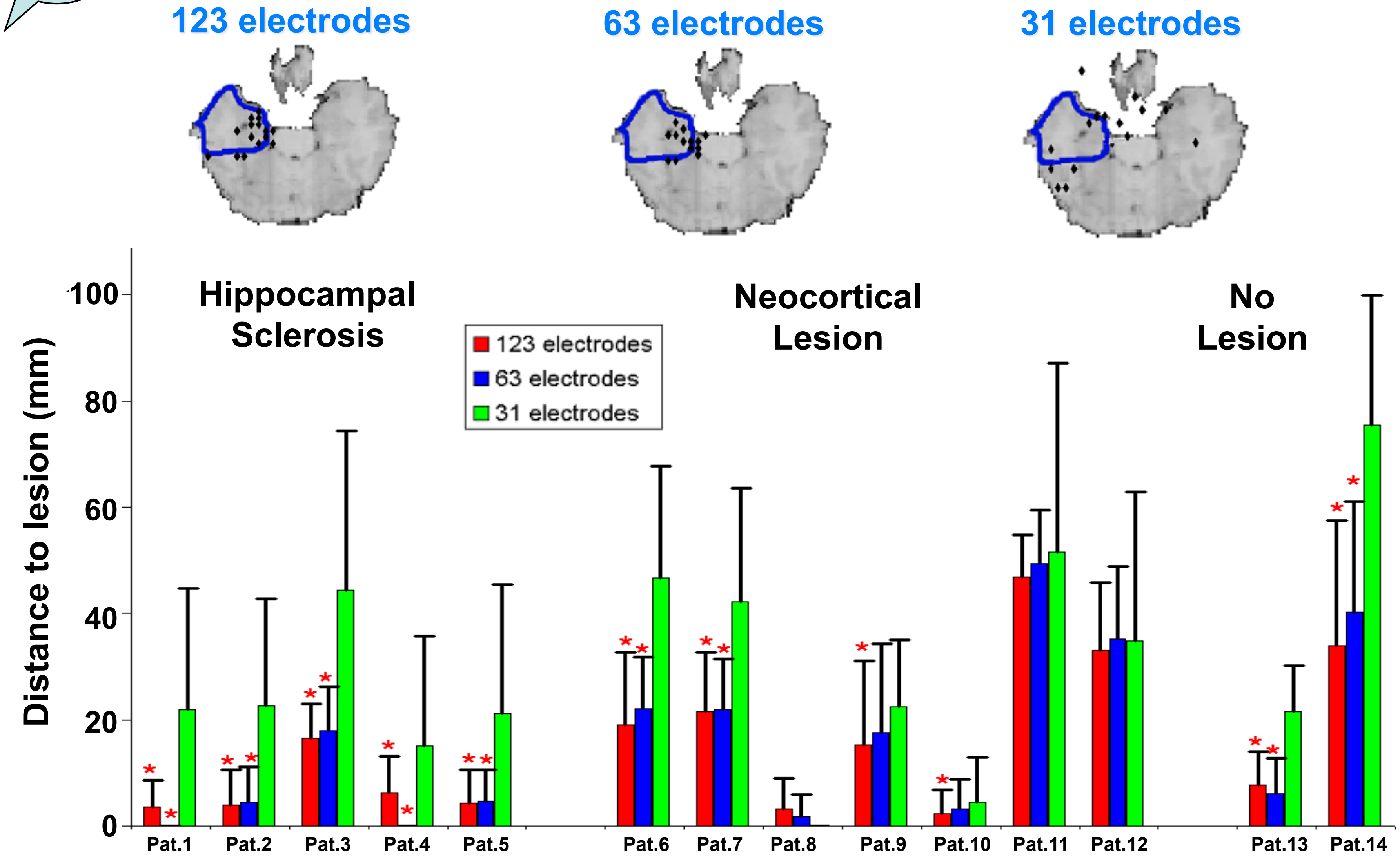
Effects of the number of electrodes on the localization of individual spikes



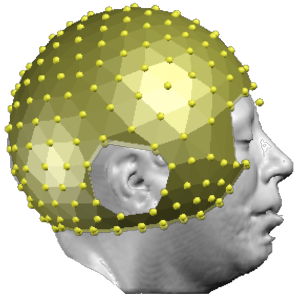
Lantz et al., Clin. Neurophysiol., 2003

ESI : How many electrodes are needed ?

1

Spatial frequency of the surface electric field < 3 cm

→ More than 100 electrodes are needed on a adult head



- *Spitzer et al., 1989*
- *Gevins et al., 1990*
- *Pflieger and Sands, 1995*
- *Babiloni et al., 1996*
- *Srinivasan et al., 1996, 1998*
- *Lantz et al., 2003*

2

Impedance of the skull is lower than assumed (1:20 instead of 1:80)

→More than 256 electrodes needed at realistic noise levels

- *Ryynänen et al., 2004, 2006*
- *Lai et al., 2005*
- *Goncalves et al., 2003*

3

Impedance of the skull in newborns is lower than in adults

→More electrodes needed in children than in adults

- *Grieve et al., 2004*
- *Fifer et al., 2006*

High Density EEG

- 128 – 256 channel saline sponge net
  (Electrical Geodesics Inc.)
  mounting time: 10-20 minutes

-Electrode positions determined by Photogrammetry
  (Electrical Geodesics Inc.)
  recording time: 5 minutes

Study 3: 128-channel ESI

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consecutive series of 44 patients with intractable epilepsy

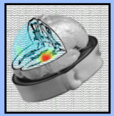
22 males, 22 females, mean age: 24.8 +/- 12.2 years.
15 patients <= 16 years, 5 patients <= 10 years.
Mean age of epilepsy onset: 9.9 years (s.d. 6.9).

Group 1 (24 patients)
focus was unambiguously localized and patients were operated.
13 mTLE, 4 neocortical TLE, 7 ETLE.
Intracranial iEEG in 5 patients. 21 patients seizure-free after surgery.

Group 2 (8 patients)
focus was strongly suggested but patients were not operated.
1 neocortical TLE, 7 ETLE, MRI normal in 5 patients, no iEEG.

Group 3 (12 patients)
No evidence for a discrete focus, indication for a predominant area in 5.
MRI normal in 10, diffuse abnormalities in 2, iEEG in 2 patients.

Michel et al., J. Clin Neurophysiol., 2004



Study 3: 128-channel ESI

Group 1 & 2 (N=32):

Evaluation of correct localization on a lobar level:
(subtemporal, lateral temporal, frontal, parietal, occipital)

Result:

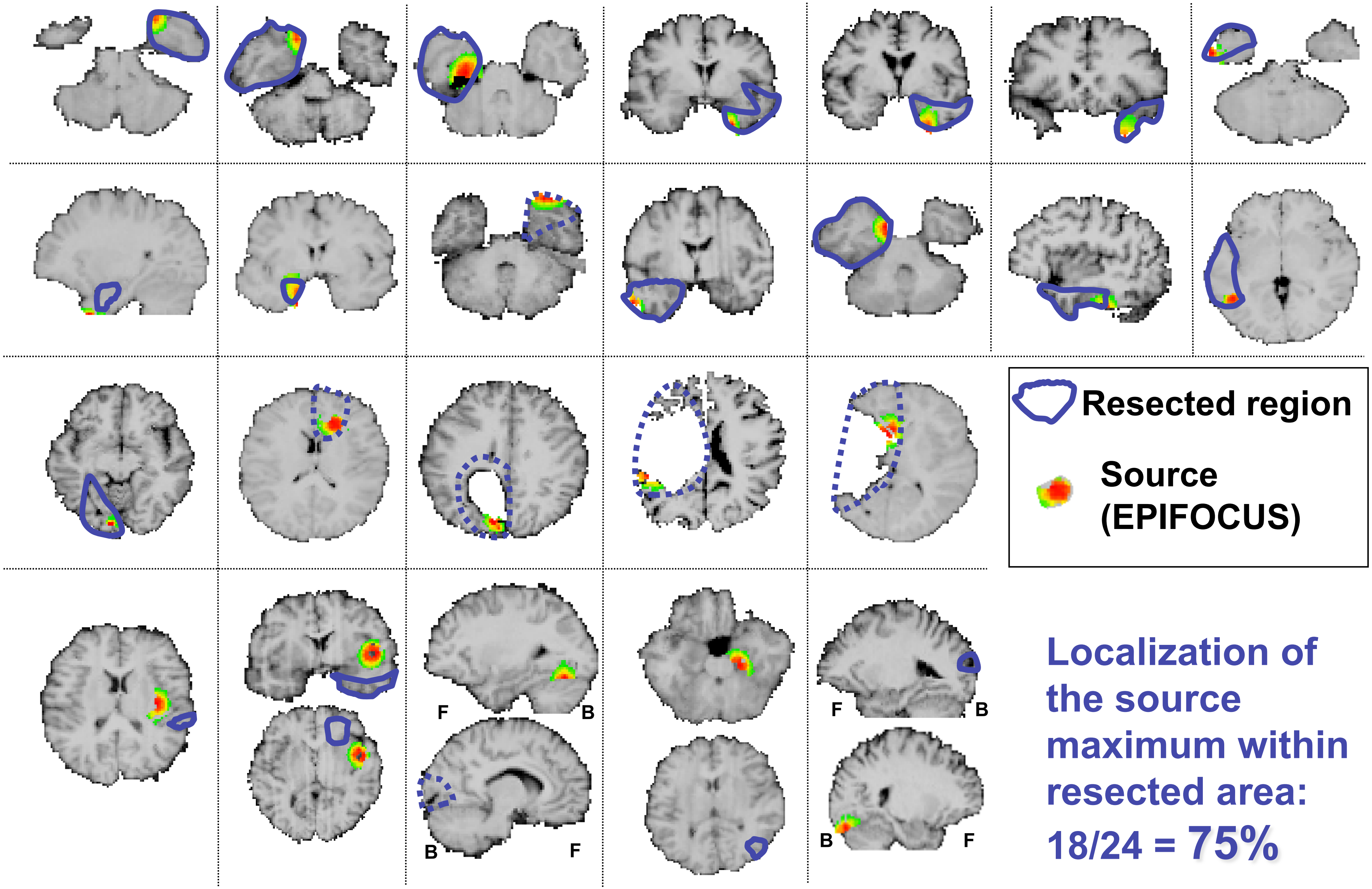
Correct Localization in 29/32 patients ***(90.6%)***

Incorrect localization in 3 patients:
1. Wrong side of a mesial occipital focus
2. Wrong side of a mesial occipital focus
3. A lateral temporal focus was localized mesial temporal
(Patient is not seizure free after DNET operation. Post-op control EEG suggested additional mesial focus → Source Localization correct ?)

→ ***Yield: 93.7%)***

Michel et al., J. Clin Neurophysiol., 2004

Study 3: 128-channel ESI

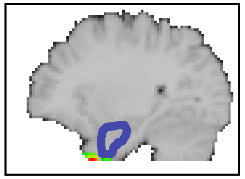


Localization of the source maximum within resected area: 18/24 = 75%

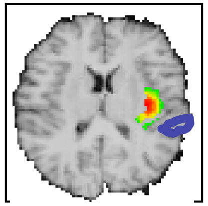
Michel et al., J. Clin Neurophysiol., 2004

Study 3: 128-channel ESI

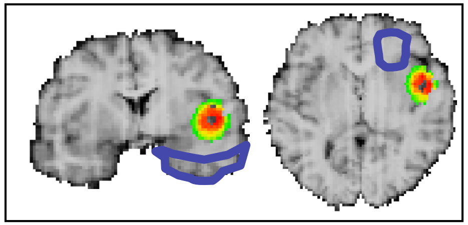
5/24 patients with incorrect localization



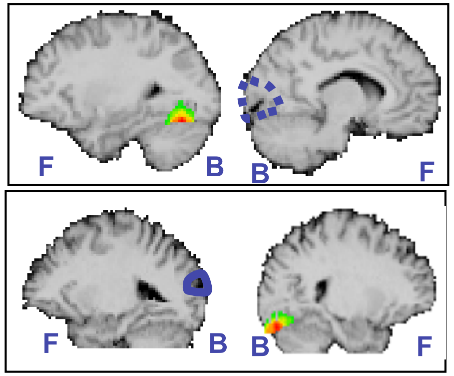
Hippocampus sclerosis with selective hippocampectomy
Source in the basal temporal cortex. Propagated spikes?



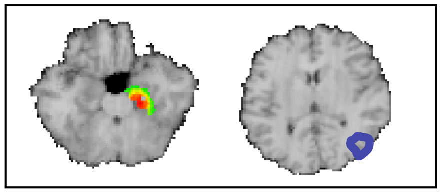
Only 4 low-amplitude spikes recorded.
Bad signal-to-noise ratio?



Multiple lesions (tubers) right frontal and temporal.
Spikes that were averaged were not homogenous?



Focus close to the interhemispheric fissure.
Incorrect assumption of electrode placement ?



Patient NOT seizure-free after DNET lesionectomy.
Post-op control EEG suggested additional mesial focus
→ Source Localization correct ? → *79%* correct localization

Michel et al., J. Clin Neurophysiol., 2004

Study 4: ESI in Patients with Large Lesions

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13 patients

- intractable epilepsy
- large lesions in MRI
- High resolution EEG ESI (128-256 channels)
- all underwent surgery

8 females, 5 males, mean age: 15.9 years (5-54).

Mean age of epilepsy onset: 6.6 years (0-31)..

N=12 with Engel Class I outcome
N= 1 with Engel Class III outcome

+ 1 patient not operated (with EEG / fMRI confirming ESI)

Brodbeck et al., J. Clin Neurophysiol., 2009

Study 4: ESI in Patients with Large Lesions

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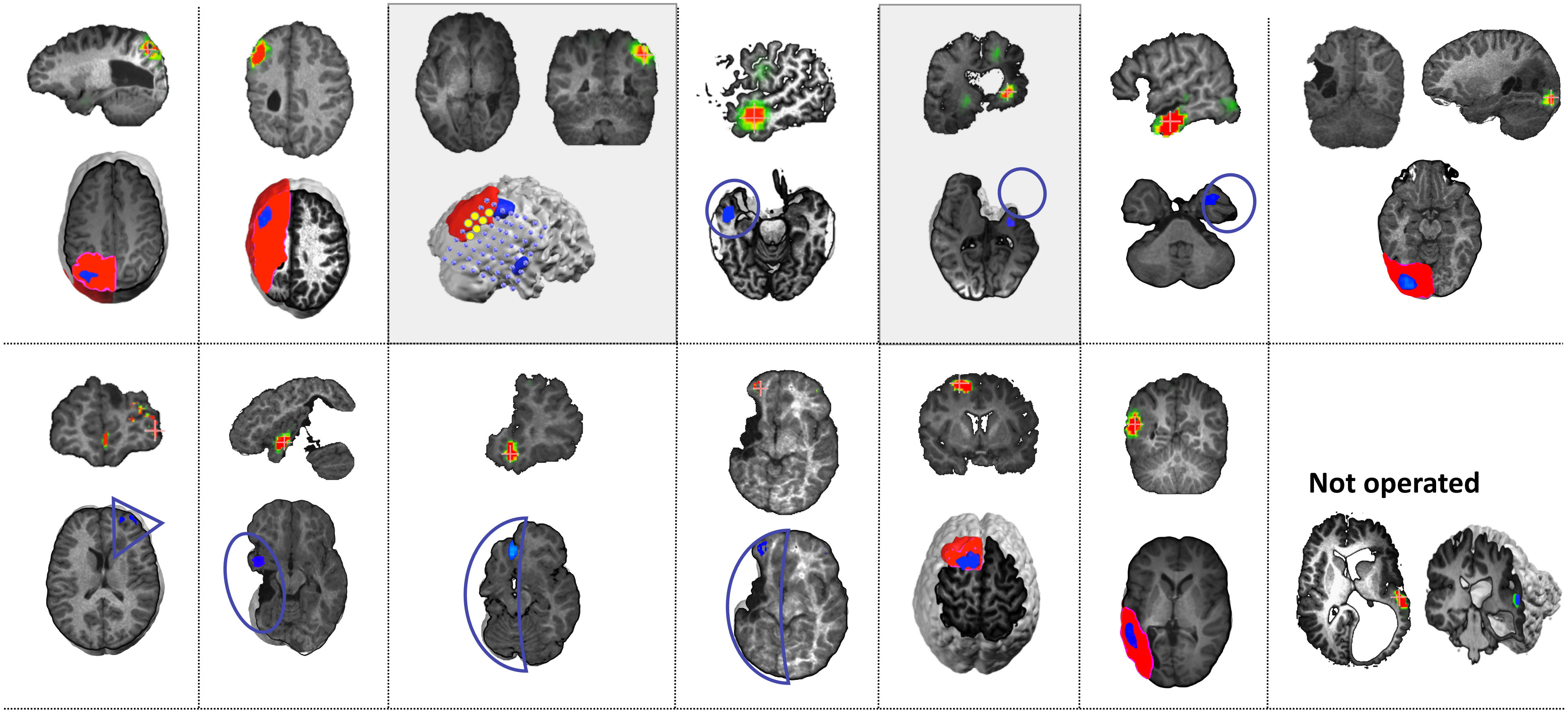

Post OP MRI verified resection

approximate resection

ESI (LAURA)

ESI outside resected region

N=13 +1

Localization of the source maximum within resected area: 11 of 12 seizure free patients = 91%

Brodbeck et al., J. Clin Neurophysiol., 2009

Study 4: ESI in Patients with Large Lesions

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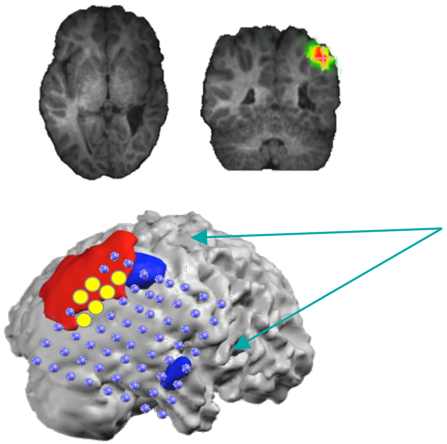
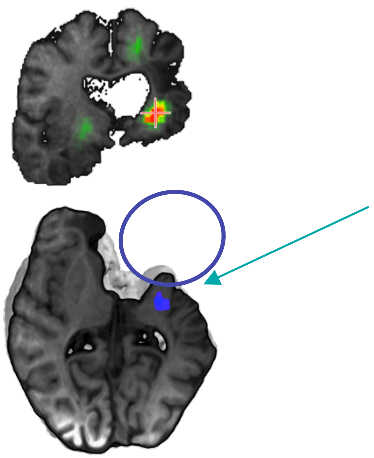
2 / 13 patients with incorrect localization



Case 1:

reduced seizure frequency (Engel Class III)
ESI: Imcomplete resection of epileptogenic area.
Source adjacent but anterior to resected area, close to somatosensory cortex + supplementary area temporal right



Case 2:

Seizure free after resection (Engel Class I)
ESI = Right Insular Source
Resection = Frontal not including the ESI indicated zone
(Post OP complications Haemorrhage in insular region with possible "antiepileptic effect"?)

Brodbeck et al., J. Clin Neurophysiol., 2009

Study 5: ESI in Non-Lesional Epilepsy

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10 patients

- intractable epilepsy
- no lesion detectable in high resolution MRI
- EEG ESI (19-256 channels)
- all underwent surgery

7 females, 3 males, mean age: 2.8 to 57.1 years (mean 23.7)
Mean age of epilepsy onset: 0.3 to 18 years (mean 8.7).

N= 9 with Engel Class I-II outcome
N= 1 with Engel Class III outcome

Brodbeck et al., submitted

Study 5: ESI in Non-Lesional Epilepsy

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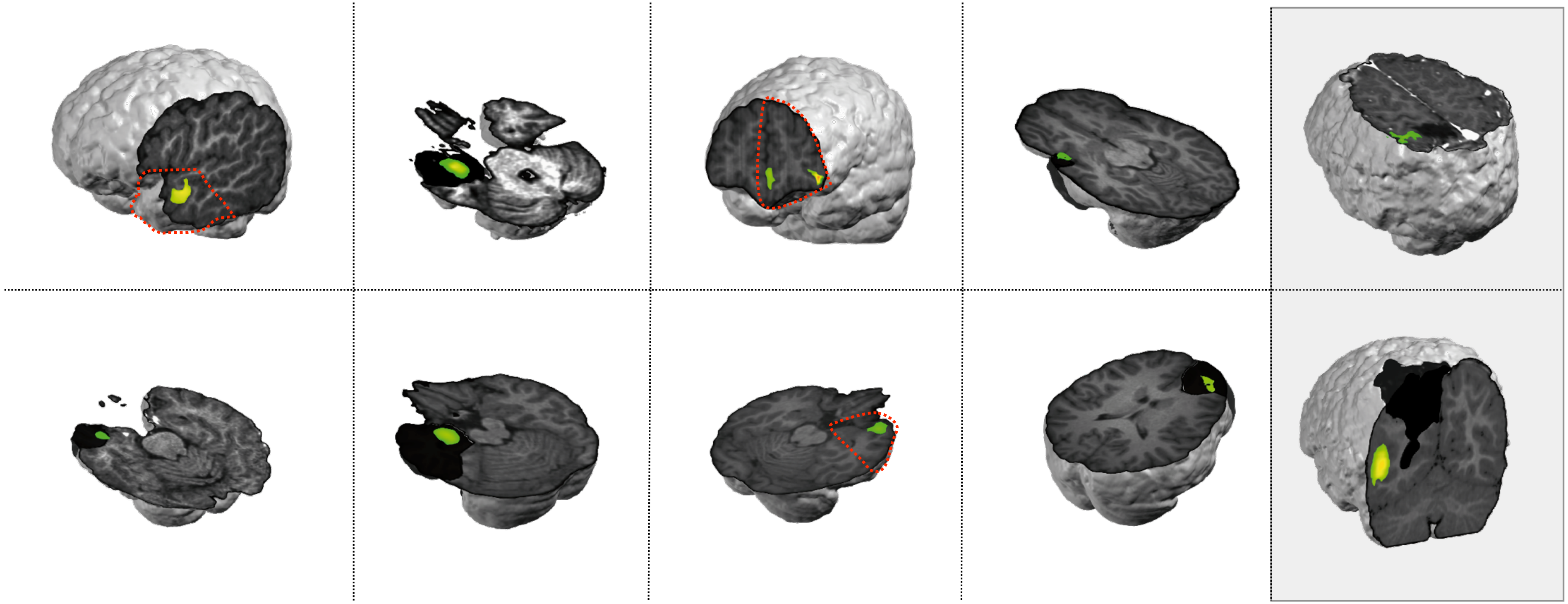

Post OP MRI defined resection

aproximate resected region

ESI (LAURA)

ESI outside resected region

N=10

Localization of the source maximum within resected area:
8 of 9 seizure free patients = 89 %

Brodbeck et al., submitted

Study 5: ESI in Non-Lesional Epilepsy

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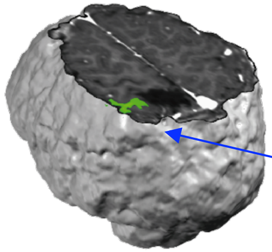
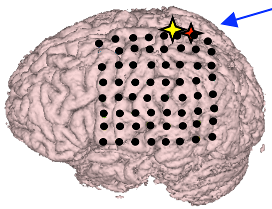
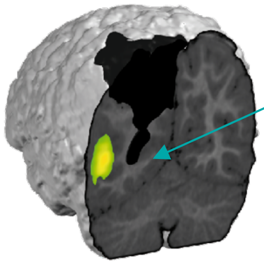
2 / 10 patients with incorrect localization





Case 1:
unchanged seizure frequency (Engel Class IV)
ESI: Source adjacent but lateral to resected area
Invasive ictal recordings suggested seizure onset in resected zone



Case 2:
Seizure free after resection (Engel Class I)
ESI = Left temporo-parietal Source
Resection = Parieto-Occipital, not including the ESI indicated zone

but: EEG for ESI with only 19 electrodes

Brodbeck et al., submitted

ESI: Temporal Resolution

Propagation of interictal epileptiform activity

Alarcon et al., 1994 — *Depth and surface EEG*

« Interictal epileptiform activity can propagate within several milliseconds to relatively remote cortex »

Engel, 1993 — *Depth and surface EEG*

« Secondary spike foci occur in areas that are well-connected by fiber tracts to the primary epileptogenic region »

Alarcon et al., 1997 — *Electrocorticography*

« Propagation and recruitment of neuronal activity along specific neural pathways »

Ebersole, 1999 — *Depth EEG*

« Spike propagation that is mesial to lateral and anterior to posterior temporal »

Merlet & Gotman, 1999 — *Depth EEG*

« Strong and time-locked interactions between temporal and orbito-frontal regions »

Scherg et al., 1999 — *EEG source modelling*

« Spike propagation to posterior and anterior temporal regions is typical »

Huppertz et al., 2001 — *EEG source modelling*

« Spike propagation to anterior, posterior, and partly to contralateral regions »

Merlet et al., 1996 — *EEG source modelling*

« Source propagation of interictal spikes in temporal lobe epilepsy »

ESI: Temporal Resolution

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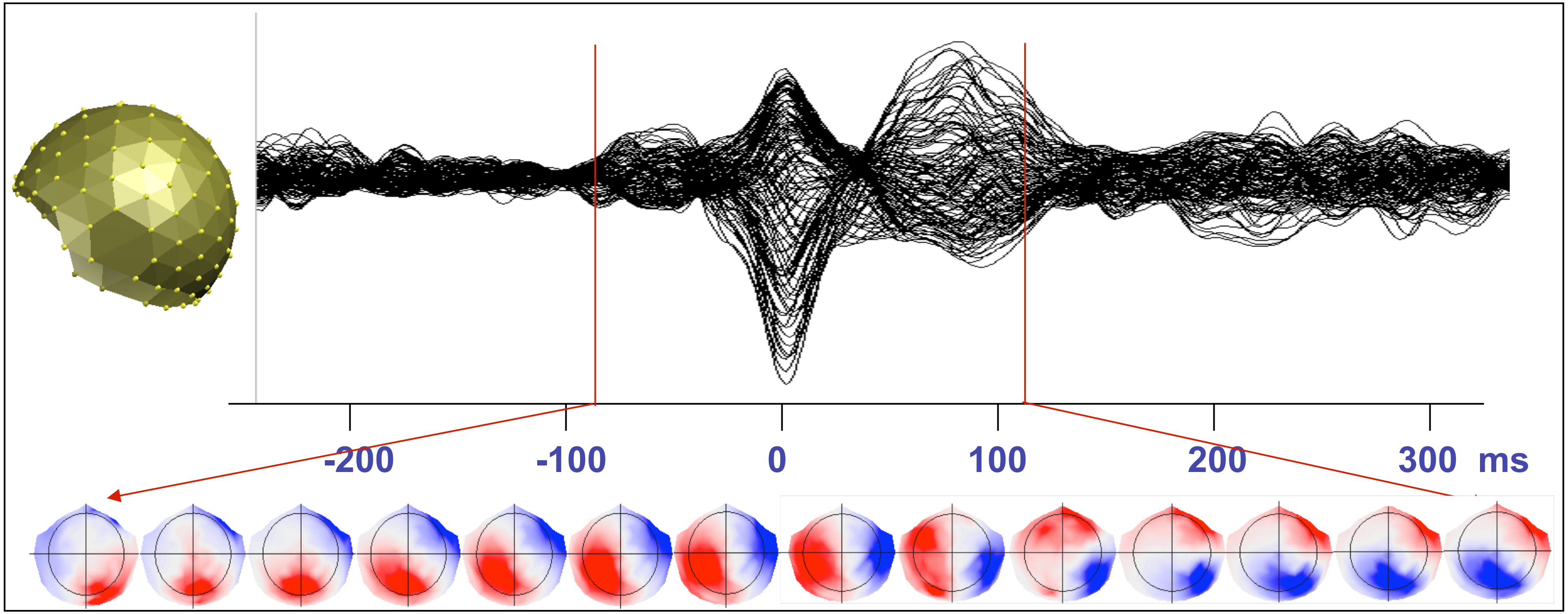
Propagation of interictal epileptiform activity



Duration of a spike-wave complex ~ 200 ms

Different scalp potential map topographies during this period

⇓

Different source configurations in the brain during this period

Study 6: Spike propagation

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Propagation of interictal epileptiform activity can lead to erroneous source localizations

16 patients with partial epilepsy, all with MRI lesion (10 temporal , 6 extratemporal). All seizure-free after surgery

- **Recording of 123-channel interictal EEG and averaging of ~25 spikes.**
- **Temporal segmentation with k-means spatial clustering method**
- **Source reconstruction using EPIFOCUS of each segmentation map using the patient's own brain as head model.**
- **Delineation of the epileptogenic lesion in the MRI**
- **Calculation of the distance of the source maximum to the epileptogenic lesion for each segmentation map.**

Lantz et al., J. Clin Neurophysiol., 2003

Study 6: Spike propagation

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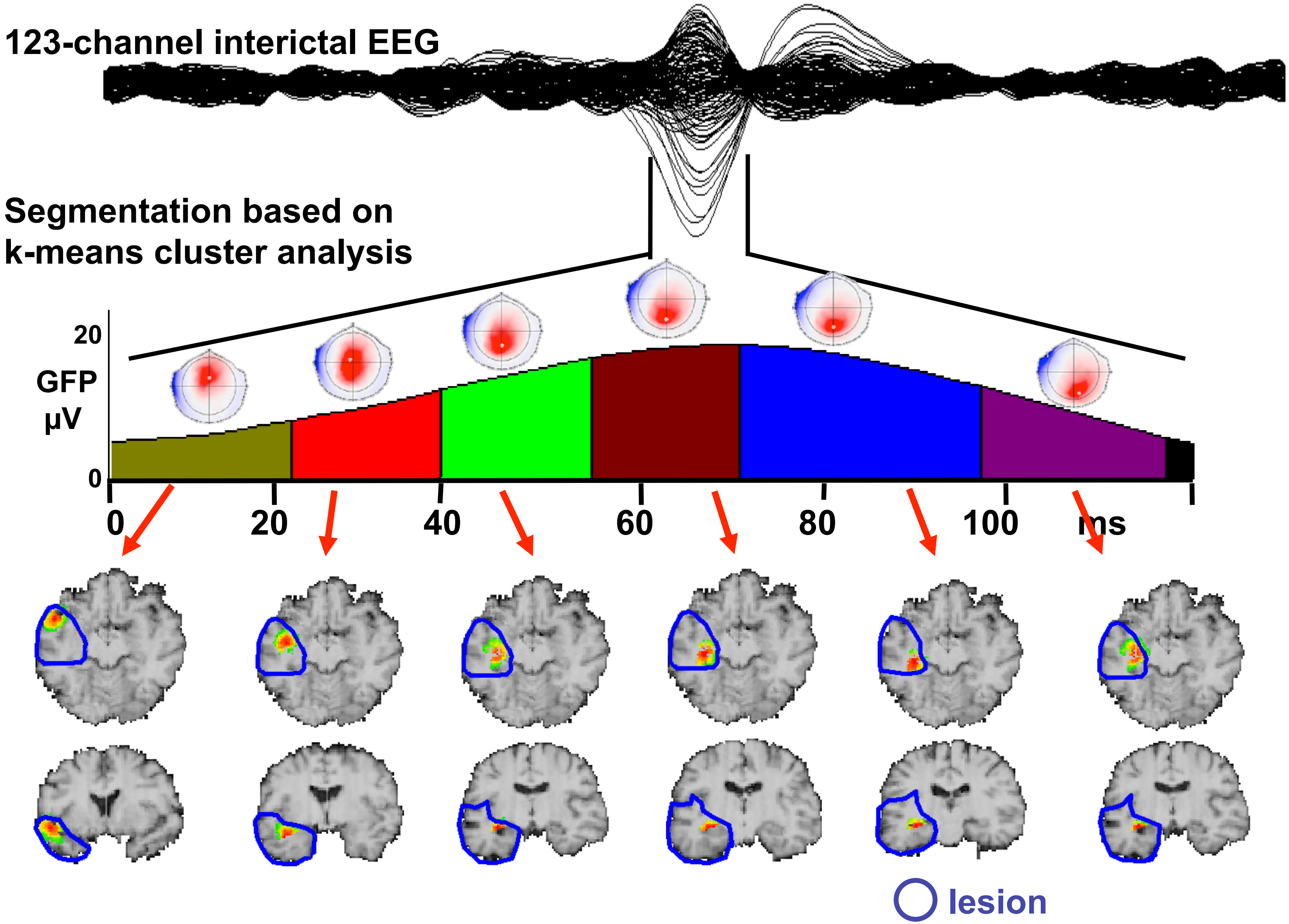
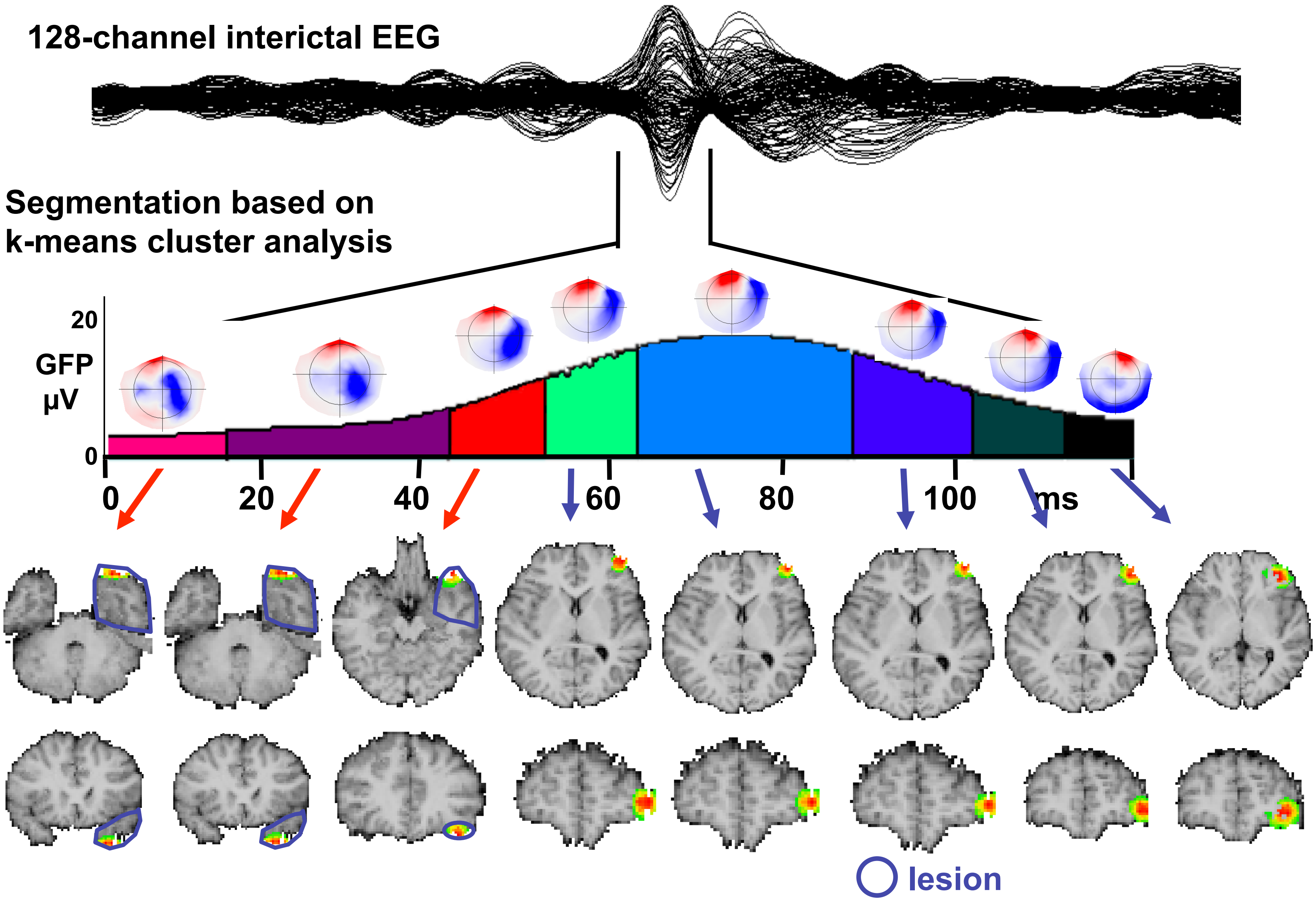


Lantz et al., J. Clin Neurophysiol., 2003

Study 6: Spike propagation

128-channel interictal EEG

Segmentation based on k-means cluster analysis



Lantz et al., J. Clin Neurophysiol., 2003

Study 6: Spike propagation

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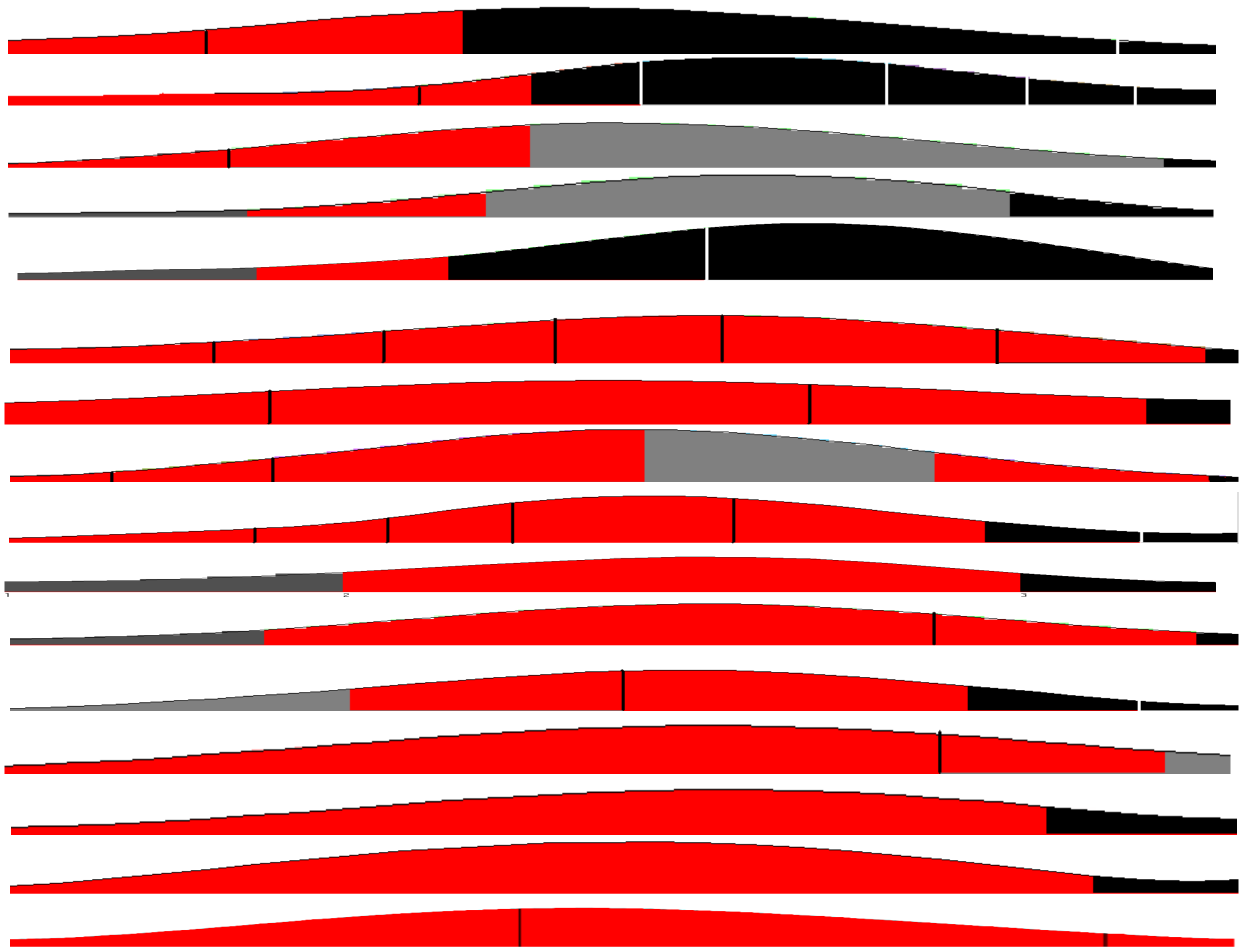
Pat.	Focus loc
1	rt ant T
2	rt ant T
3	rt ant T
4	lt TP
5	lt PTO
6	lt ant T
7	lt ant T
8	rt ant T
9	rt ant T
10	rt ant T
11	lt ant T
12	lt ant T
13	lt O
14	rt F
15	lt F + T
16	lt CP



Distance to lesion: 0 (red) 1 (grey) > 1 grid points (black)

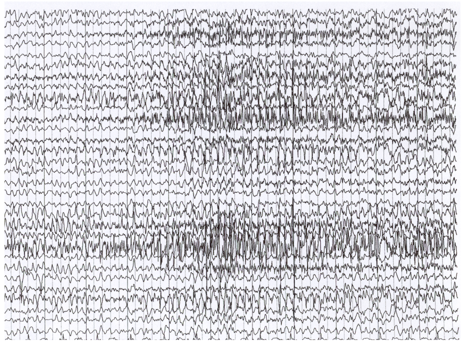
→ Correct localization at 50% rising time in all cases

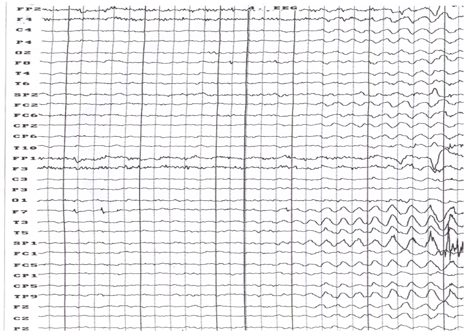
Lantz et al., J. Clin Neurophysiol., 2003

Metabolic / Haemodynamic Functional Imaging

SPECT

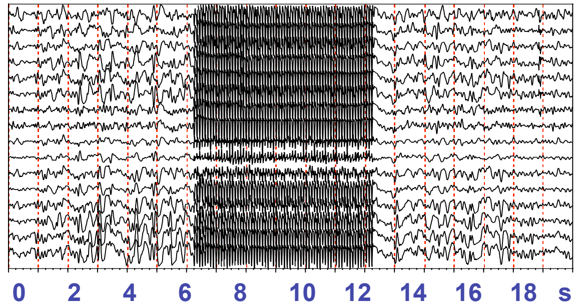
Ictal - interictal

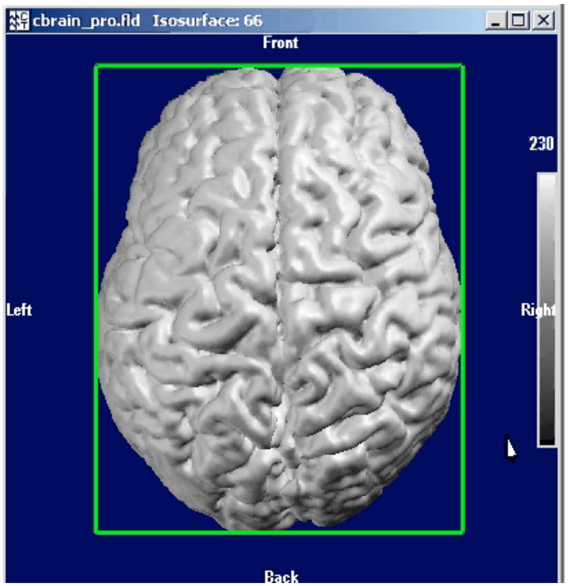


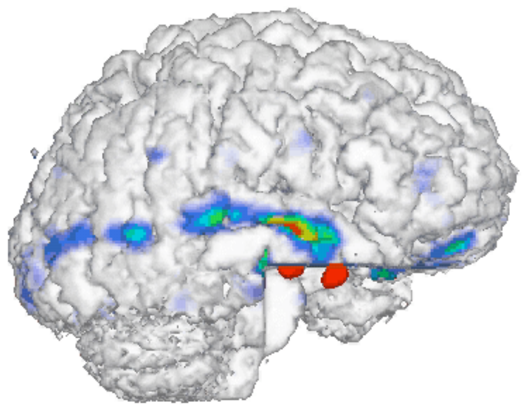


fMRI

spike–triggered vs. control







Multimodal Imaging

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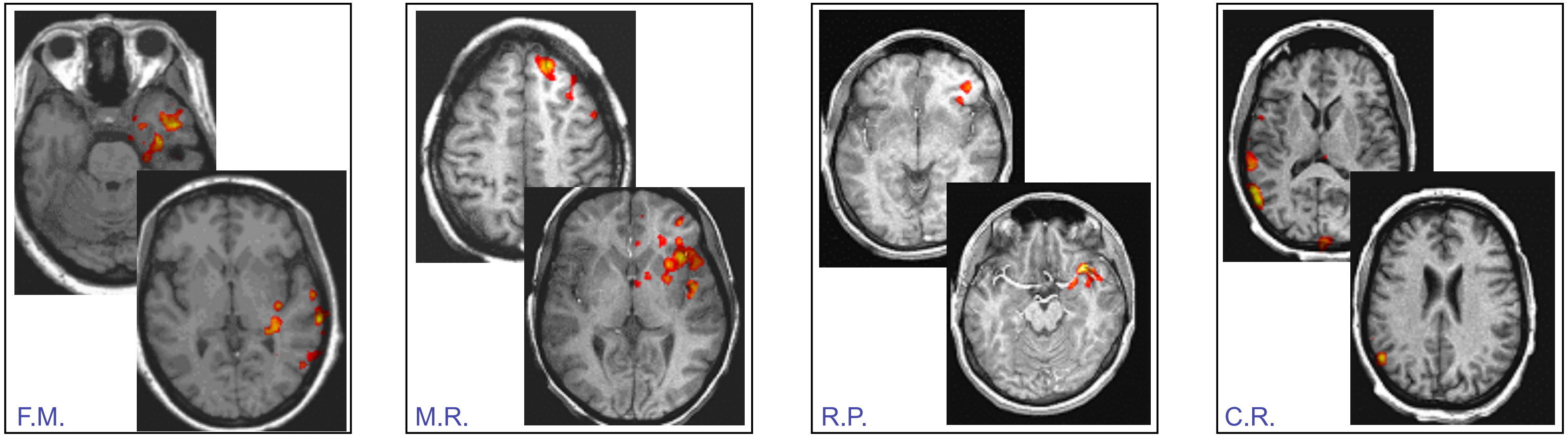
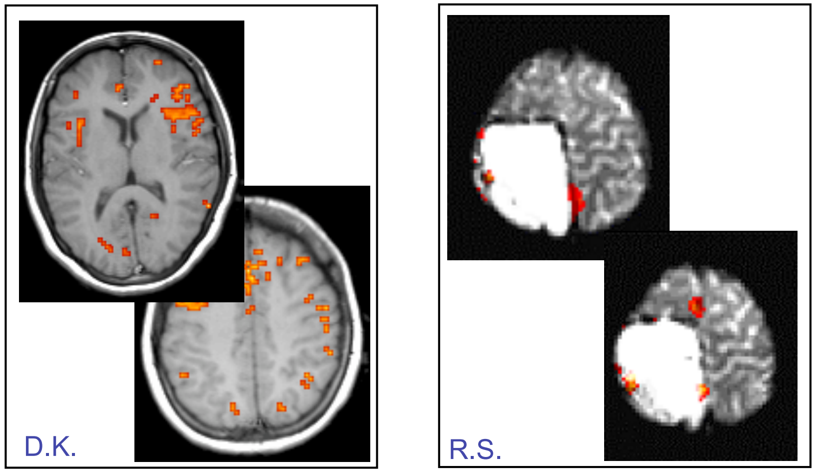
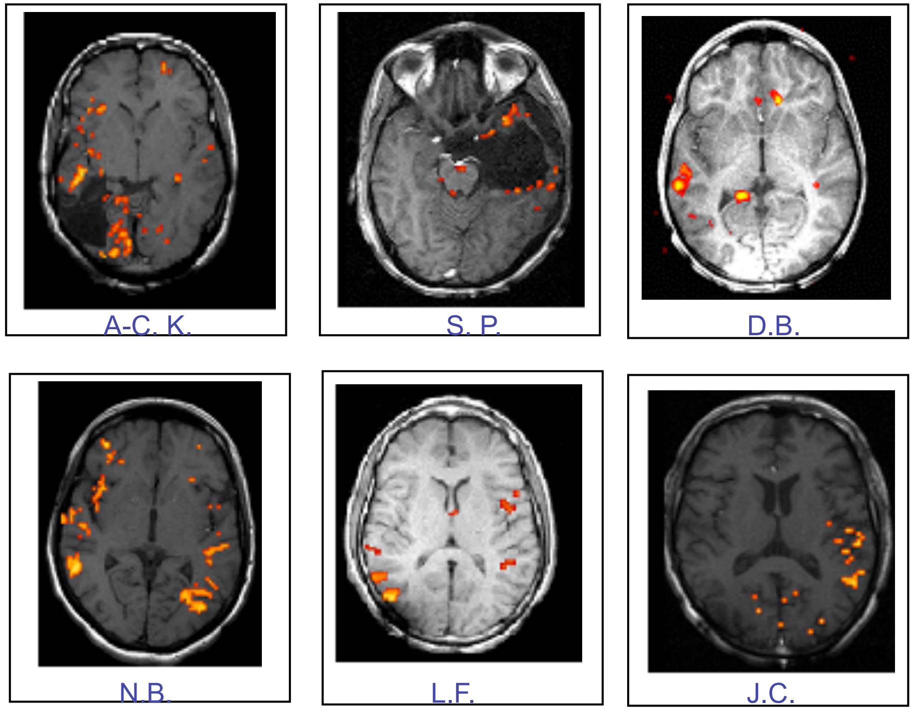
Spike-triggered functional MRI



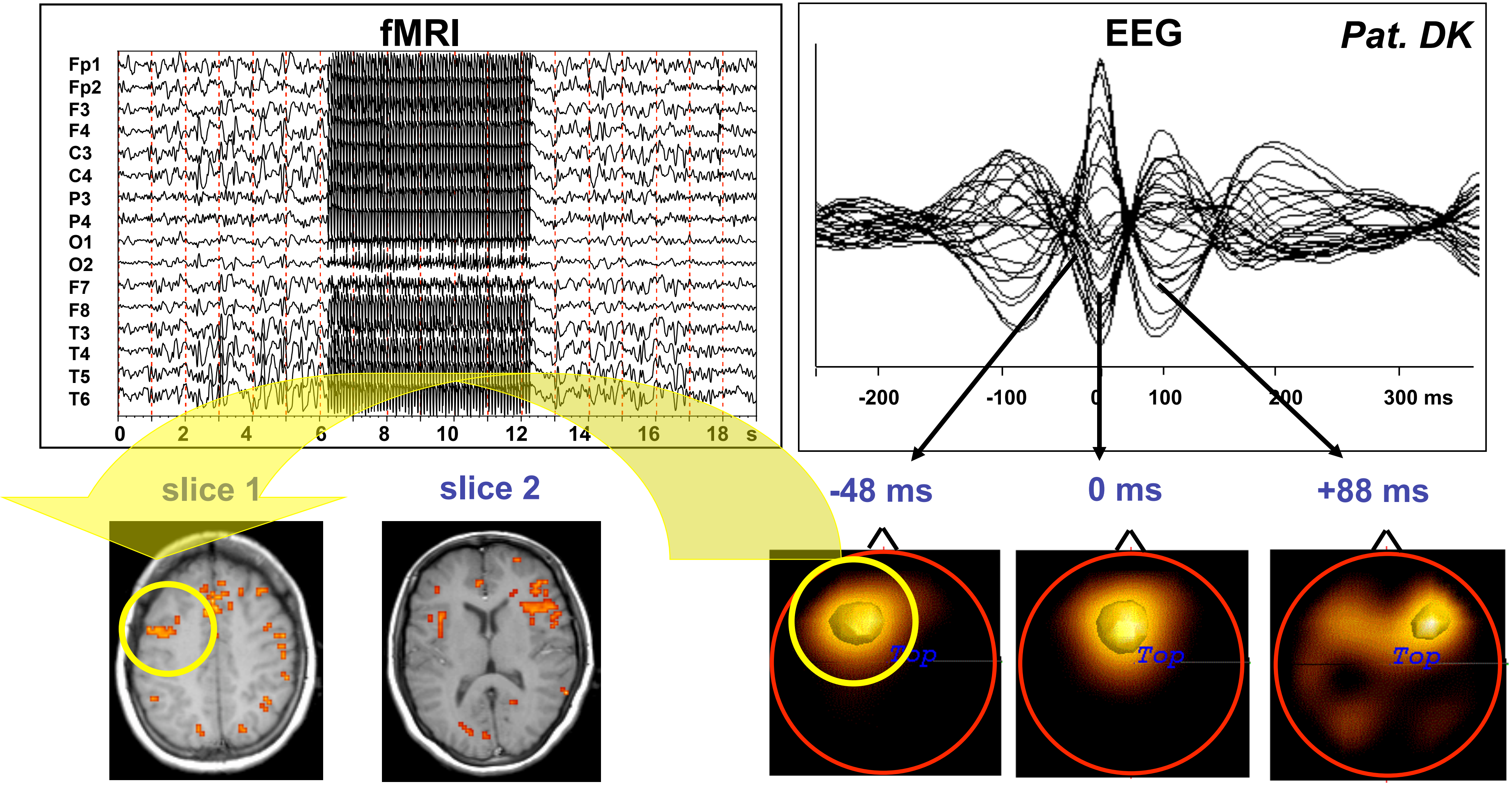




Several active areas !
Propagation ?

Combination of ESI and fMRI

Seeck, Lazeyras, Michel, et al., Electroenceph Clin Neurophysiol, 1998



SOURCE IMAGING OF THE EEG RECORDED OUTSIDE THE SCANNER

Combination of ESI and fMRI

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Two independent study of two different groups

Study 7: (Greoning et al., Neuroimage, 2009)

Group of M. Siniatchkin, Kiel, Germany

- 6 children with refractory focal epilepsy (4 with lesions, age range: 5.5 – 15.4)
- consistent focus localisation by EEG, PET and SPECT (and by MRI lesion in 4)
- 32-channel EEG in 3T MR scanner
- SOURCE IMAGING OF THE SAME SPIKES THAT WERE USED FOR fMRI ANALYSIS

Study 8: (Vulliemoz et al., Neuroimage, 2009)

Group of L. Lemieux, London, UK

- 9 adult patients with refractory focal epilepsy (8 cryptogenic in 8, 1 with dysplasia)
- Total 12 types of IED
- validation with intracranial EEG in 3 patients
- 32- or 64-channel EEG in 3T MR scanner
- SOURCE IMAGING OF THE SAME SPIKES THAT WERE USED FOR fMRI ANALYSIS

Combination of ESI and fMRI

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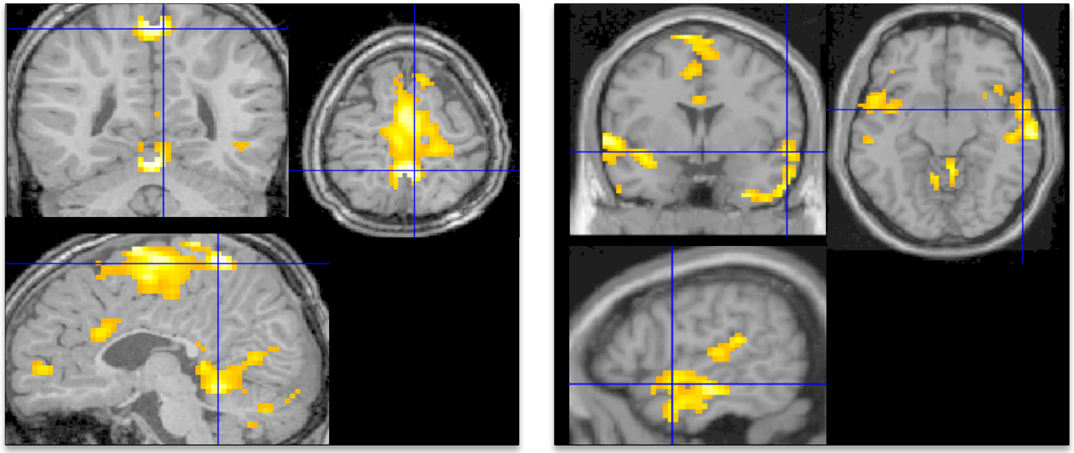
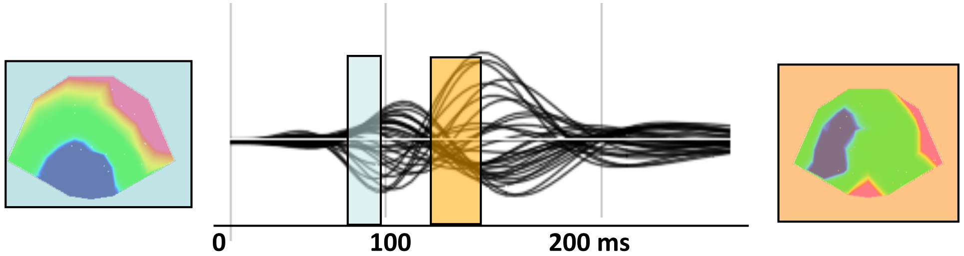
fMRI



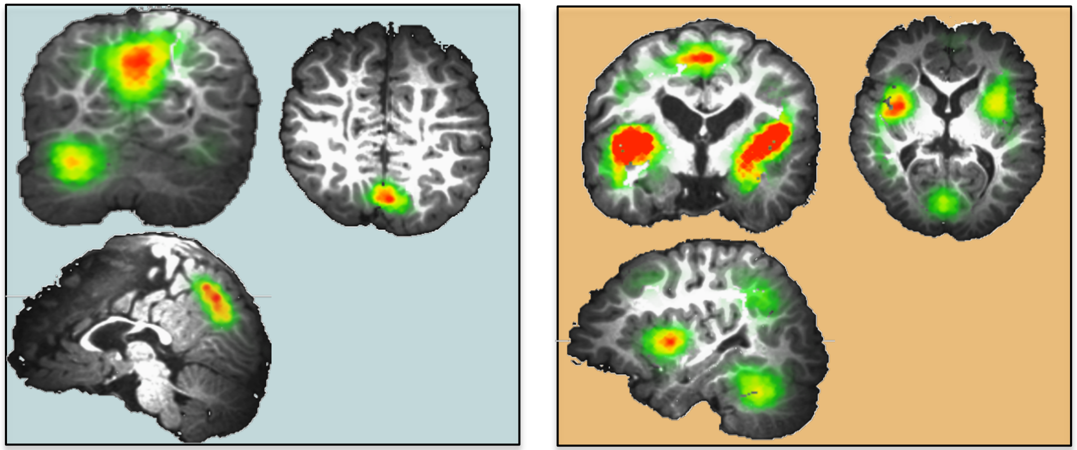
EEG



1st time period

2nd time period

ESI



Patient recorded in Kiel, Germany

Combination of ESI and fMRI

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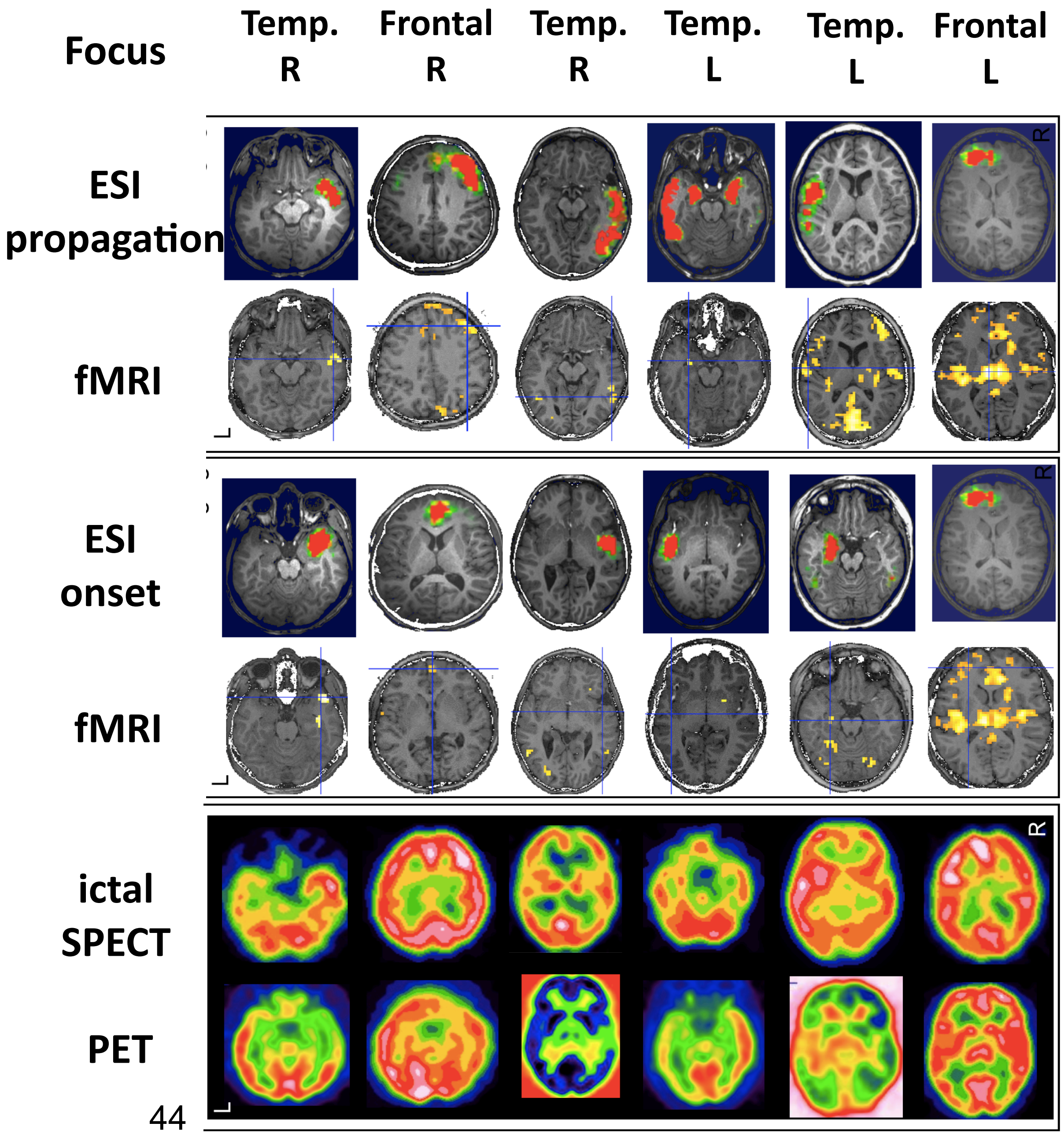
Study of Group 1:
Greoning et al., Neuroimage, 2009



Combination of ESI and fMRI

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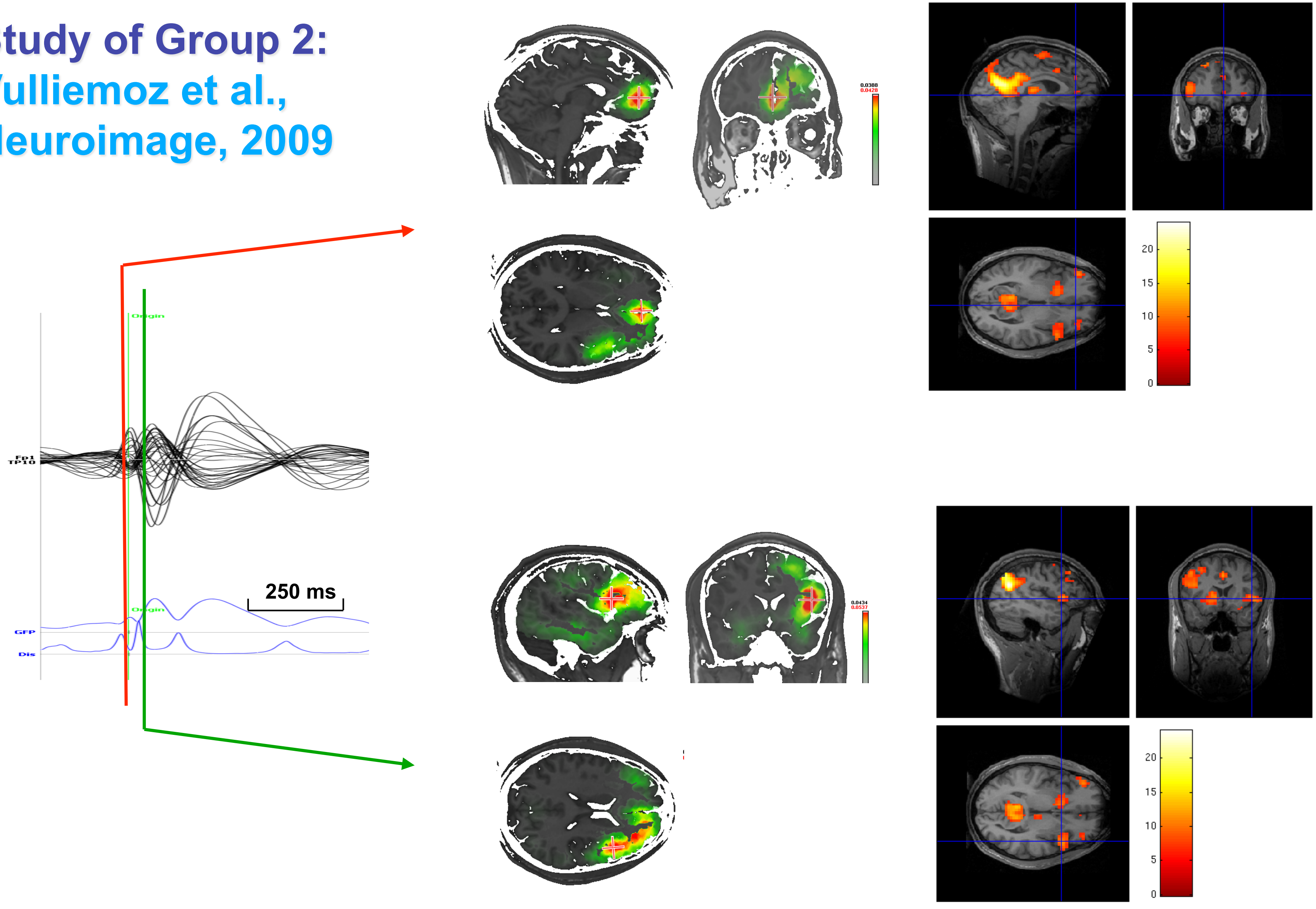
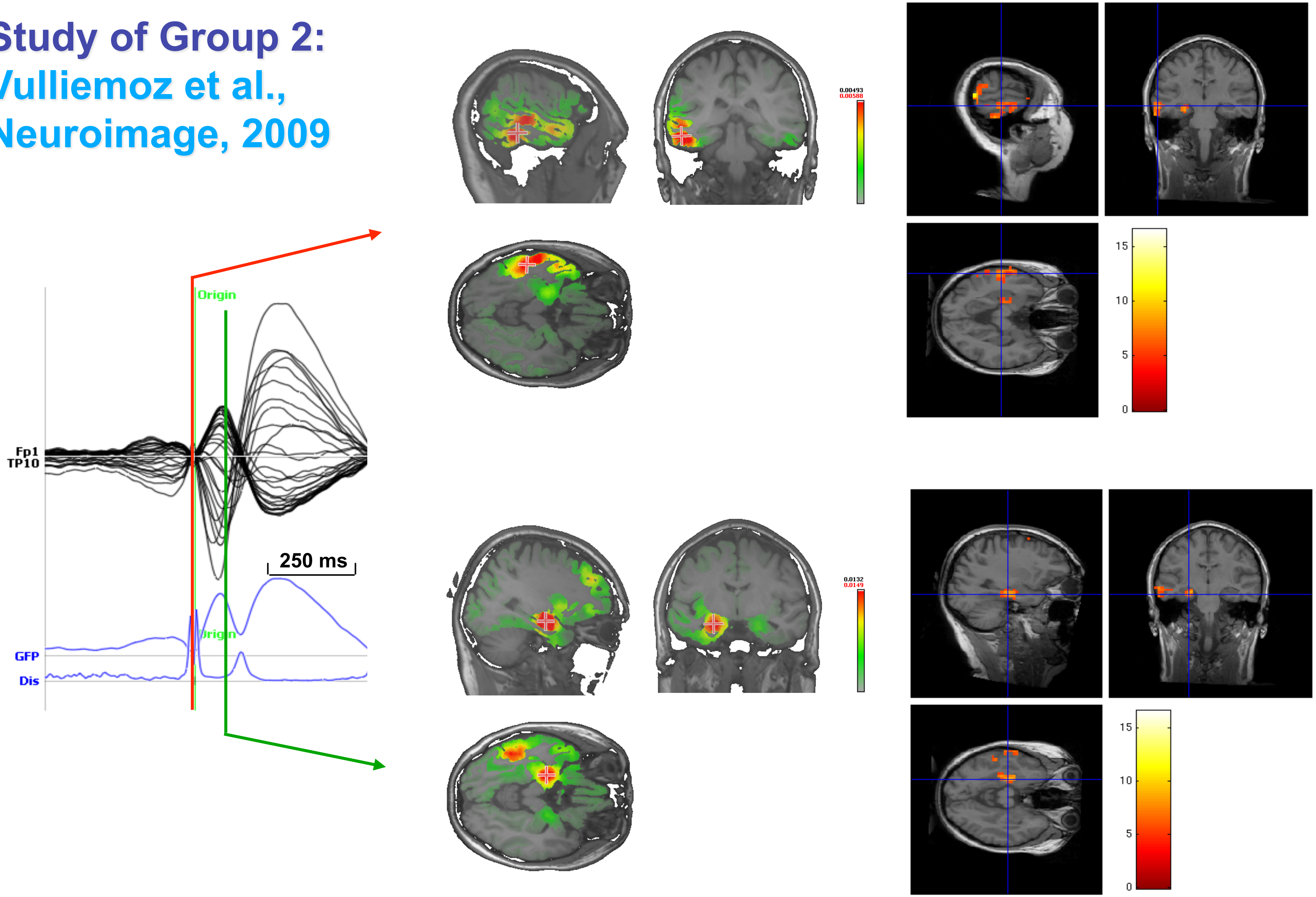
Study of Group 2:
Vulliemoz et al., Neuroimage, 2009



Intracranial EEG (9 depth electrodes): Mesial orbito-frontal IED onset

Combination of ESI and fMRI

Study of Group 2:
Vulliemoz et al., Neuroimage, 2009



Combination of ESI and fMRI

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Study of Group 1 (Kiel):
Greoning et al., Neuroimage, 2009

ESI:
- localization of spike onset correct in all cases
- Propagation in 5/6 cases

fMRI:
- significant BOLD in focus area in 4/6 cases
- other active areas in 5/6

ESI-fMRI correspondence:
at least one area in all cases

Study of Group 2 (London):
Vulliemoz et al., Neuroimage, 2009

ESI:
- localization of spike onset correct in 10/12 cases
- Propagation in all cases

fMRI:
- significant BOLD in focus area in 8/12 cases
- other active areas in all cases

ESI-fMRI correspondence:
- with positive BOLD in 4/12
- with negative BOLD in 4/12
- mean Euclidian distance between ESI and fMRI: 23 mm

Mapping of eloquent cortex with ESI

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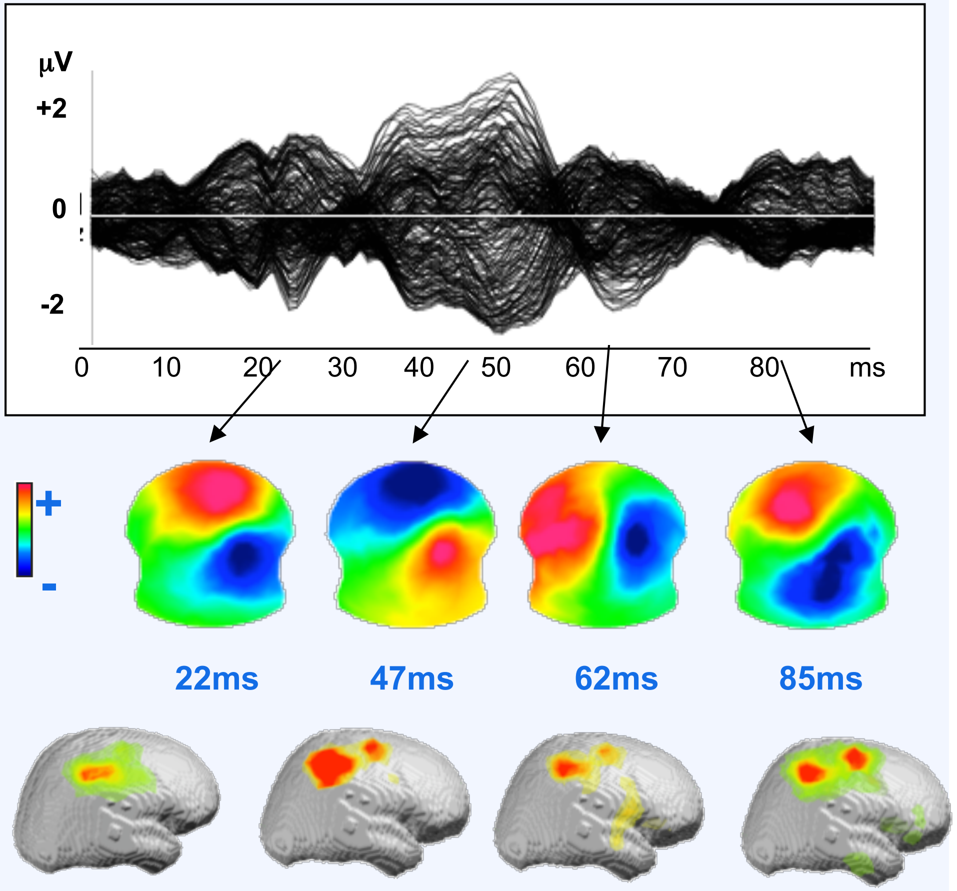
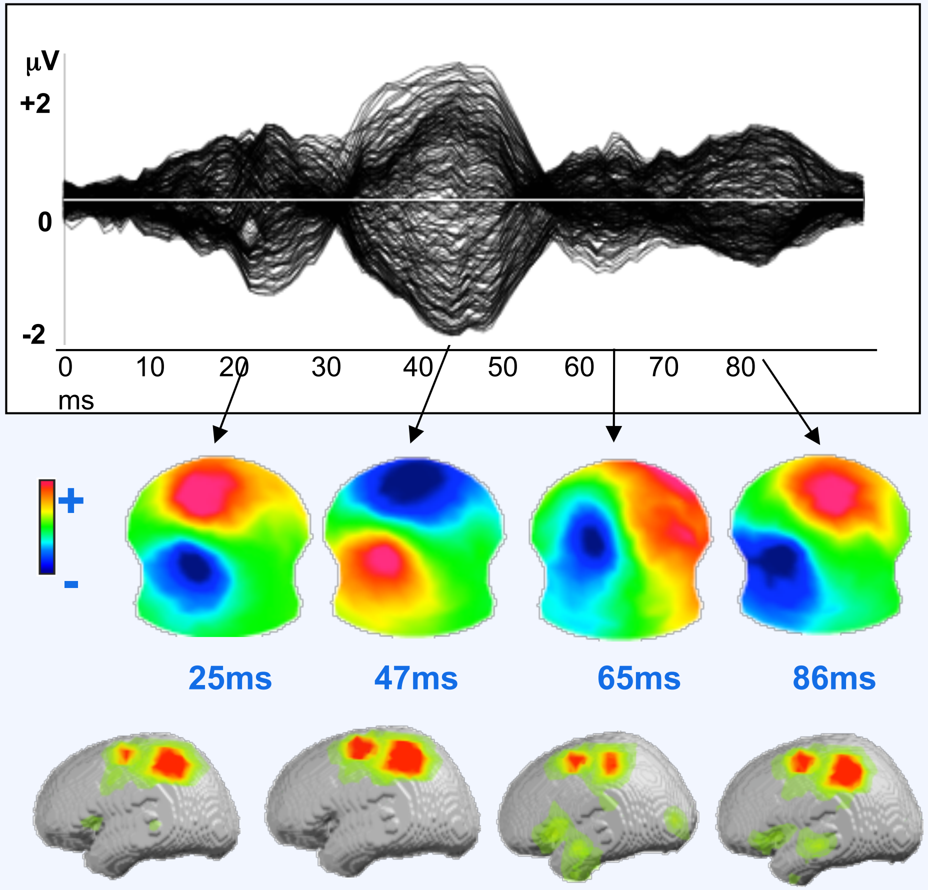
SSEP after
Pneumatic Stimulation

Left Thumb (N = 23)

Right Thumb (N = 23)





Pat. R. Multimodal Imaging

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The case:

- 12 year old boy, born prematurely at 33rd week, with cesarean section
- 1st seizure at age 3
- Normal schooling, best of his class
- Seizure semiology: feeling of vertigo (« head spins ») → pale, nauseous, LOC (1x/month)
- Neurostatus: normal, right-handed
- Ophthalmology: normal
- Neuropsychology: normal except discrete diminished verbal fluency.

- **MRI: *complex right hemispheric developmental malformation:* large voluminous cyst over the right frontal lobe, posterior ventricle enlargement with dysplastic gyri, 2 fronto-central schizencephalies, peri-insular dysplastic cortex.**

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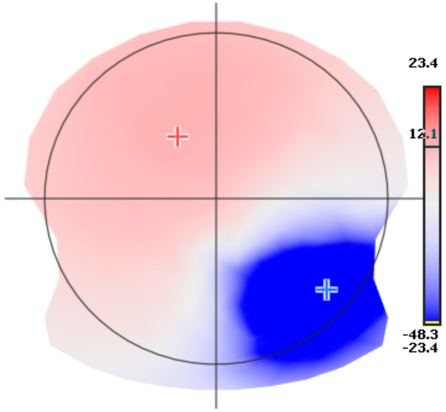
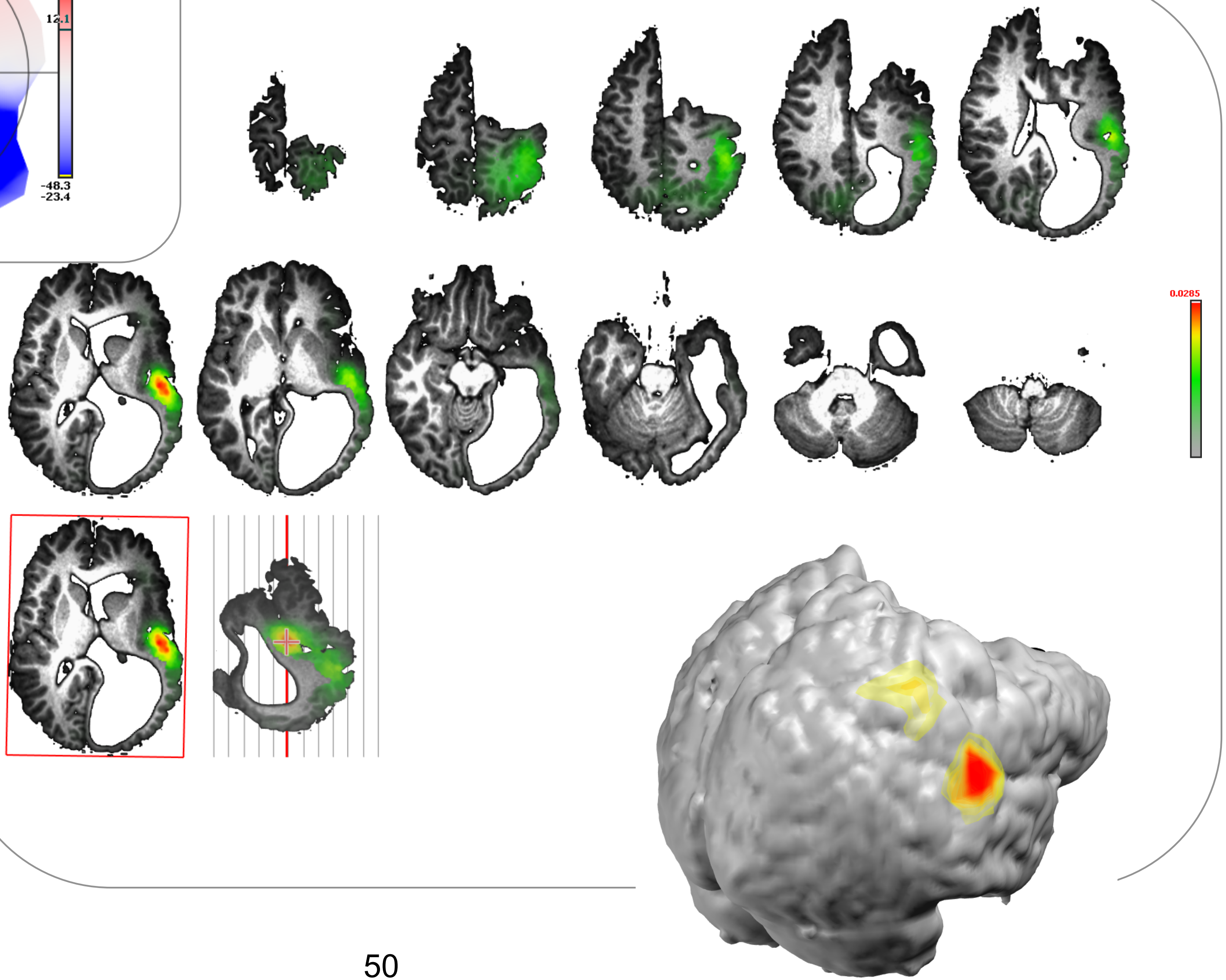


256 Channel ESI



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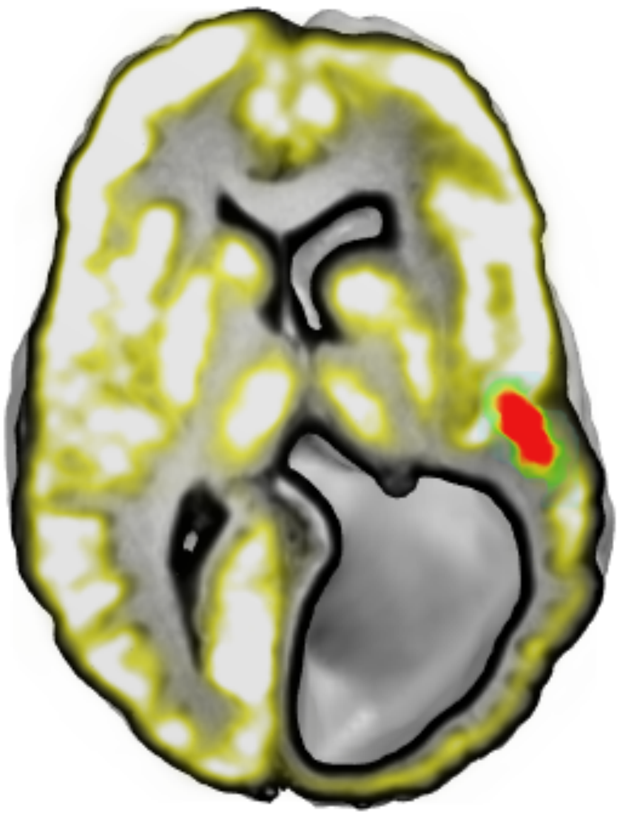
PET / ESI



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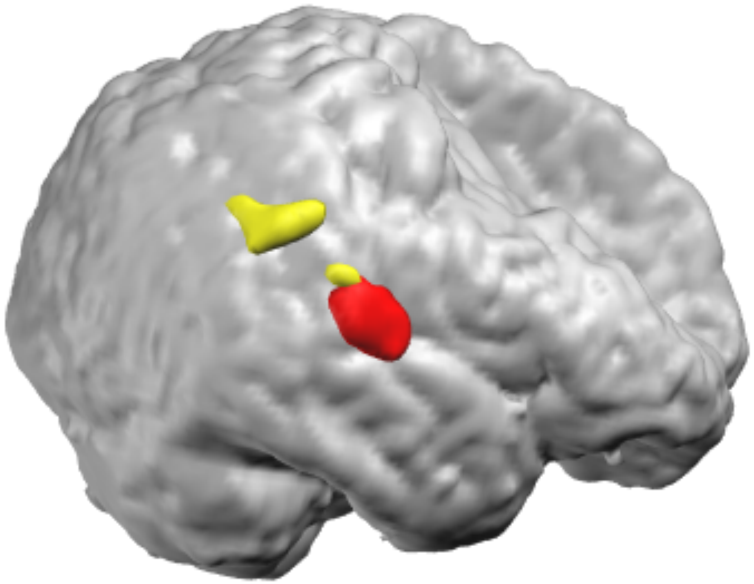
256-channel Spike ESI

EEG-controlled Spike fMRI



Pat. R. Multimodal Imaging

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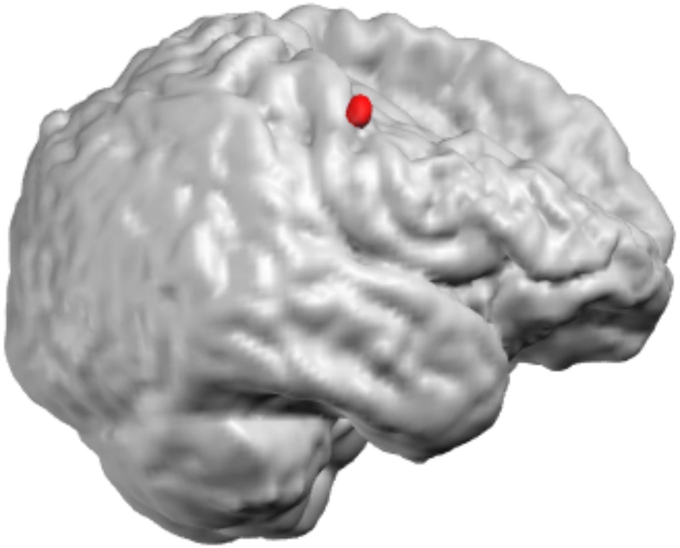
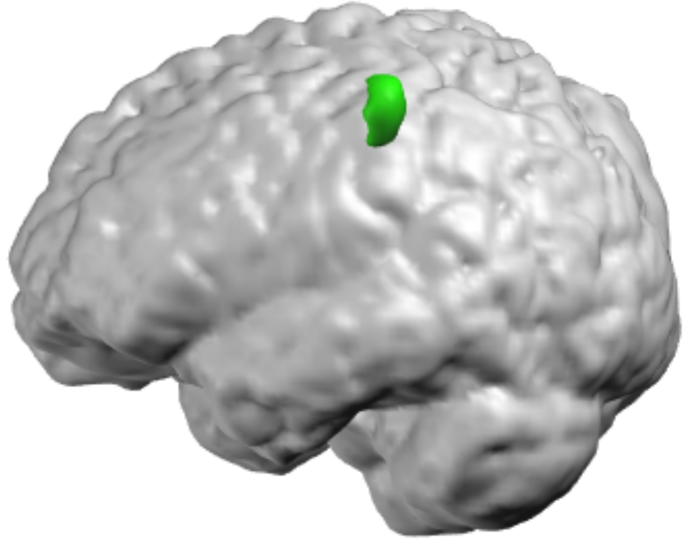
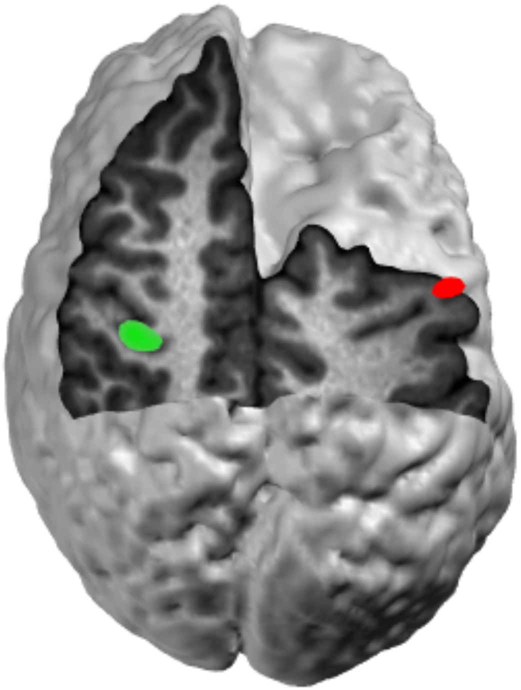
Motor fMRI

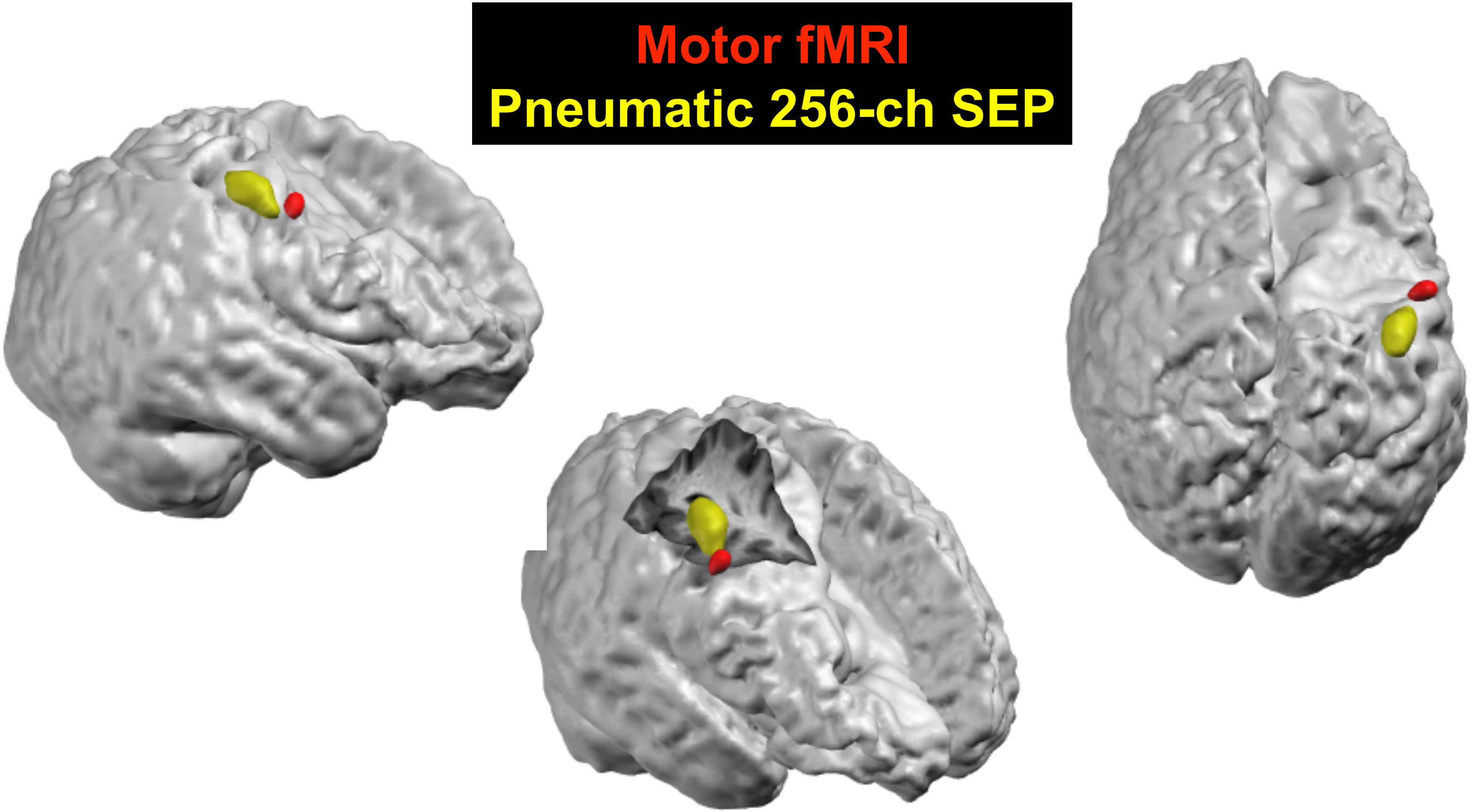
Left Hand
Right Hand



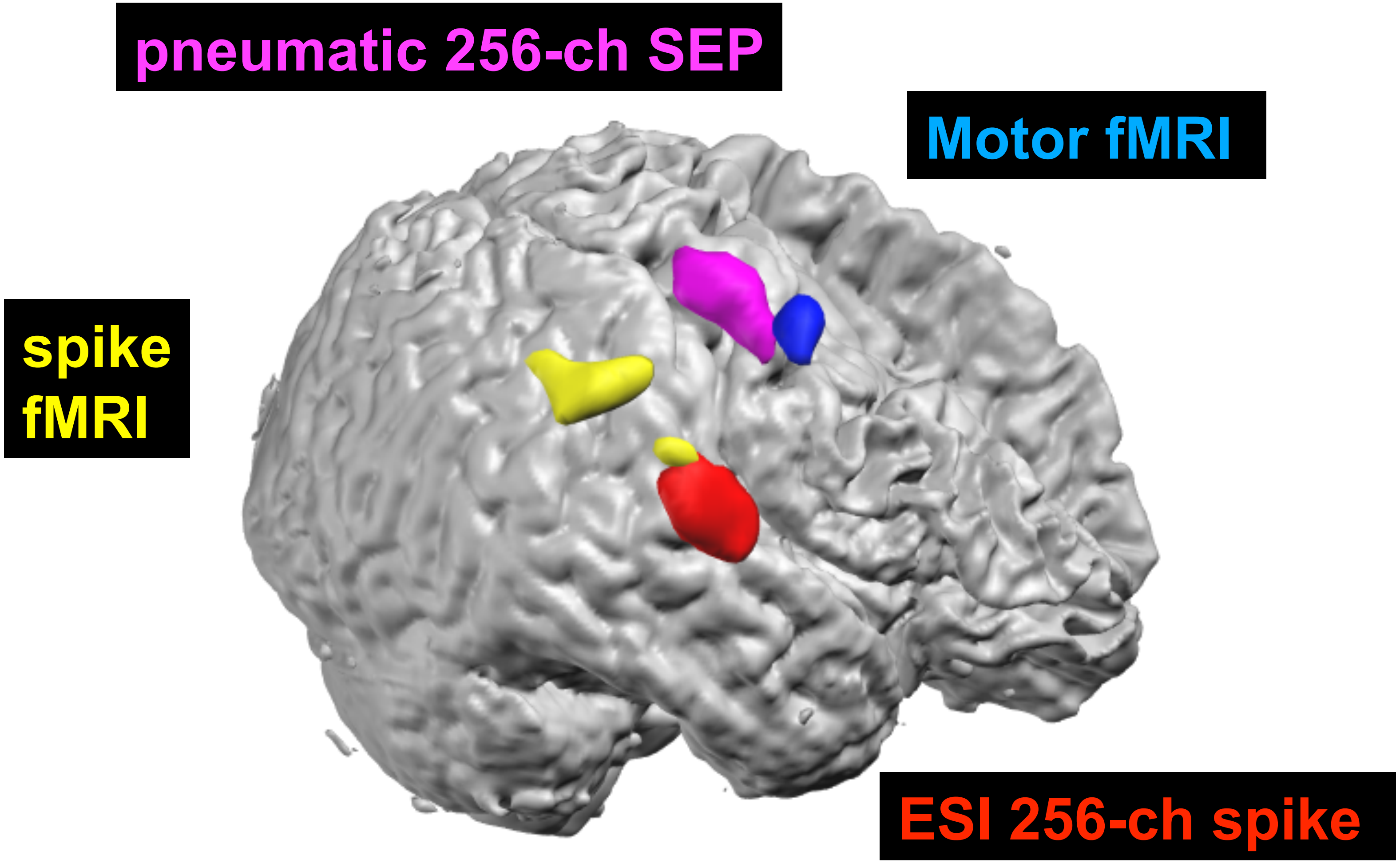




Left Hand



Pat. R. Multimodal Imaging



The Team

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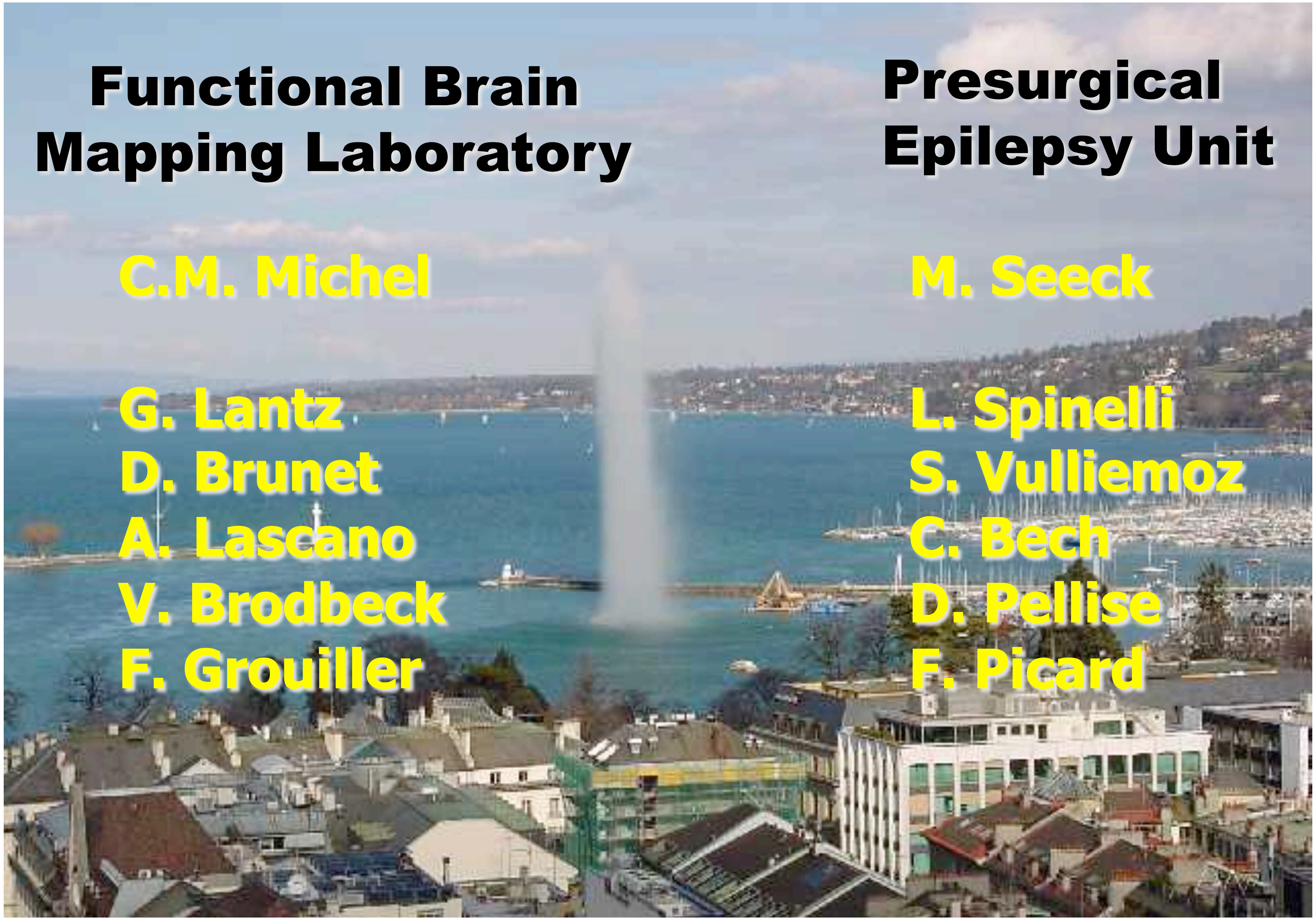

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