FSL Course 2016

Clinical (Presurgical) Applications of FMRI & Tractography using FSL

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Outline of the Talk

- Clinical Challenge –> Clinical Relevance –> Solution *(Is there any?, How can FSL help?)*
- Focus on Language Networks, Auditory System & Pyramidal Tract: FMRI-Mapping & DW-Tractography *(with Xing fibres modeling)*
- Case-based Illustrations
  - *FMRI / Tractography prior to 'bionic' (cochlear) implantation*
  - *Assessing Interhemispheric Dominance ("Lateralisation") prior to Epilepsy Surgery*
  - *Presurgical Planning / Intraoperative Neuro-navigation for Resection of Intraaxial Lesions*

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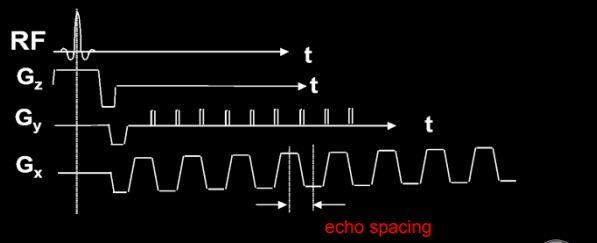
Challenge: Echo-Planar Imaging (EPI) is LOUD



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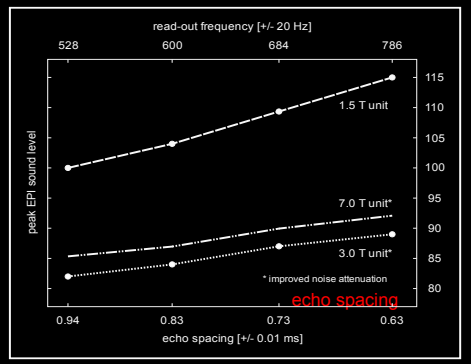
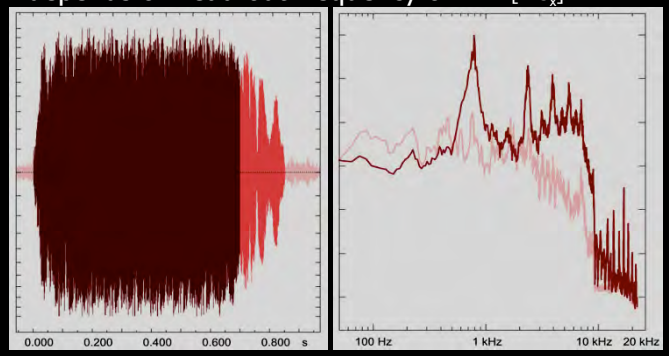


Fundamental Frequency Peak of EPI

- depends on read-out frequency of EPI [± G_x]

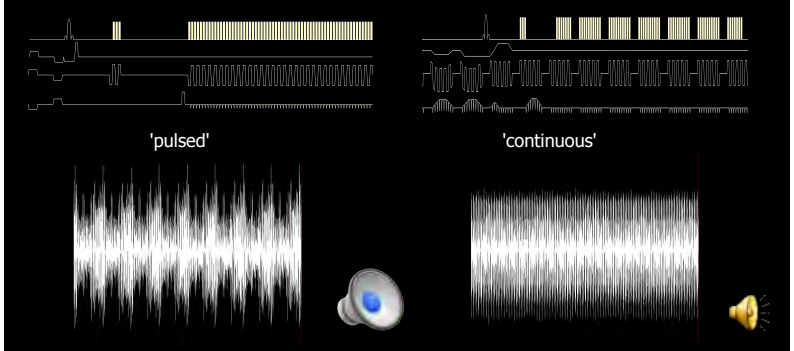


Bartsch et al., *NeuroImage 2007*

EPI is LOUD: Clinical Consequence

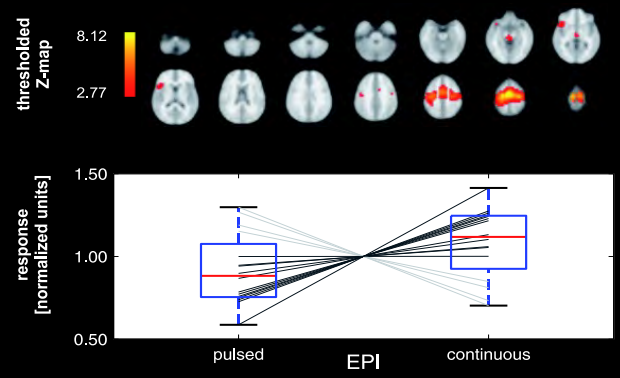
- Reduced patient comfort
- Startle movements
- Impaired audio transmission
- Recuded FMRI-activations

Solution 1: Low Impact Noise Aquisition or 'Continuous' EPI



Seifritz et al., *NeuroImage 2006* (courtesy of K. Scheffler)

... can increase FMRI-Responses

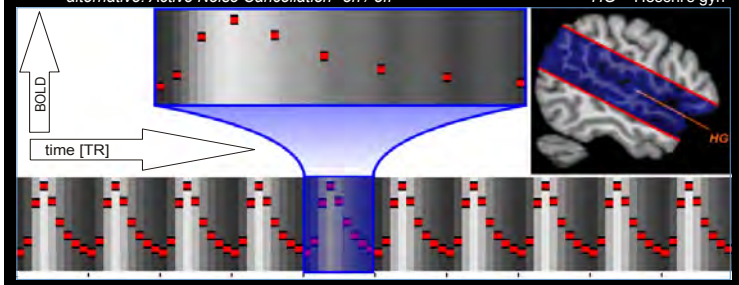


Haller et al., *Brain Res 2009*

Can Acoustic EPI Noise be useful?FMRT-Audiometry by Read-Out Omissions

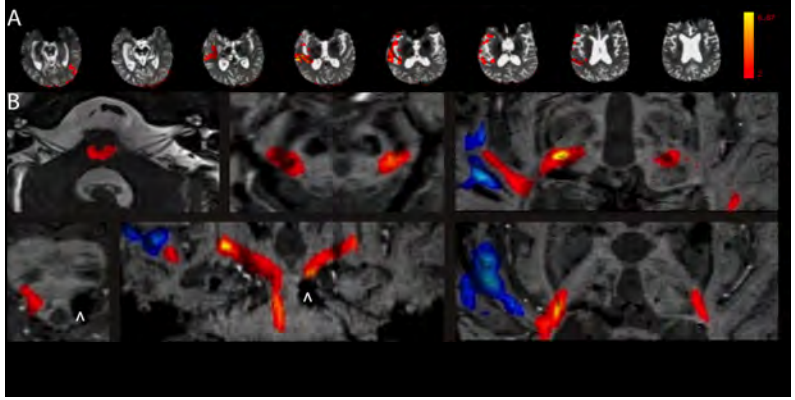
- EPI Read-Out [■] evokes auditory activations*
- omissions of [■] yield detectable BOLD-fluctuations#

alternative: Active Noise Cancellation° on / off — *HG* = Heschl's gyri

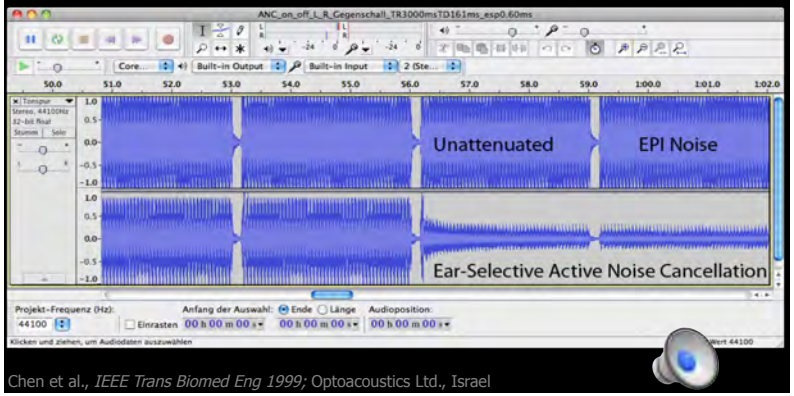


Bartsch et al.,**Riv Neuroradiol* 2003/#*NeuroImage* 2007; °Chen et al., *IEEE Trans Biomed Eng* 1999

FMRT-Audiometry, -Promontory Testing & Tractography of the Auditory Radiation prior to CI in TBI (diffuse axonal shearing injury)



Solution 2 (to reduce EPI Noise): Active Noise Cancellation (ANC)

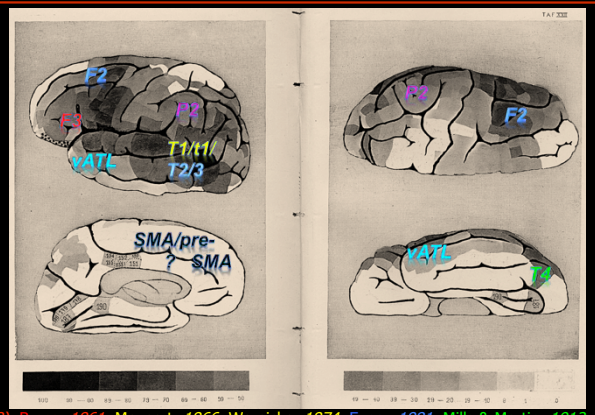


Chen et al., *IEEE Trans Biomed Eng 1999;* Optoacoustics Ltd., Israel

Challenge *Before* You Start Mapping

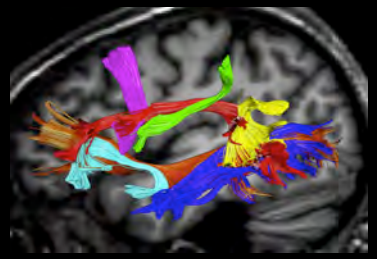
- ***detect*** the lesion *(if there is any)*
  & establish its location with respect to the presumed components of the functional network(s) of interest (FNOI; e.g. speech / language)
- ***detect*** even subtile deficits of the patient
- ***select*** the best paradigm

"Relative" Language Areas



Dax, *1836 (?);* Broca, *1861;* Meynert, *1866;* Wernicke, *1874;* Exner, *1881;* Mills & Martin, *1912*

Ventral & Dorsal Fibre Pathways implied in Speech & Language



Meynert, *1884;* Catani & Budisavljevic, *2014;*
cf. Rolheiser et al., *J Neurosci 2011;* Duffau et al., *J Neurosurg 2008*

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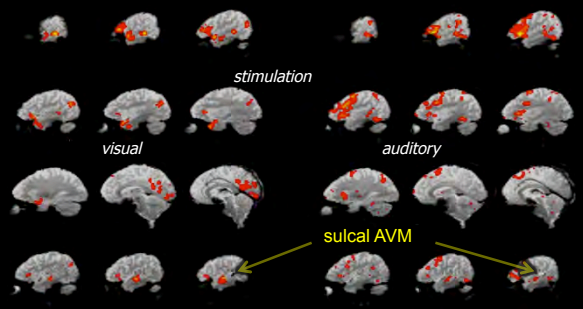
FMRI-Activations are variable and should be evoked optimally

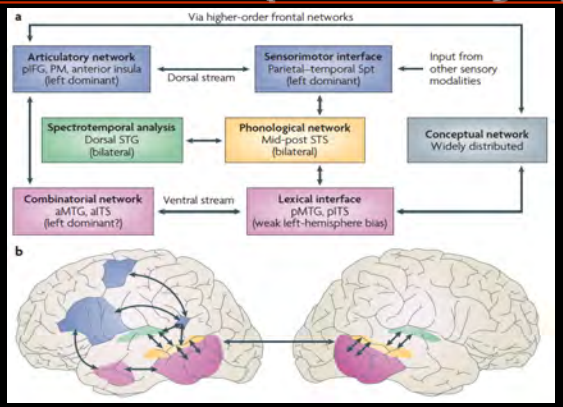
speech mapping: same patient, different paradigms

Reading nonfinal embedded clause sentences vs. Auditory description-cued covert naming



Bartsch et al., *JMRI 2006*

Just "Messy Maps" ? Dual Stream for Speech & Language !



Hickok & Poeppel, *Nat Neurosci 2007;* Ueno et al., *Neuron 2011*

Lateralisation in Auditory-Motor (Phonological) Activations

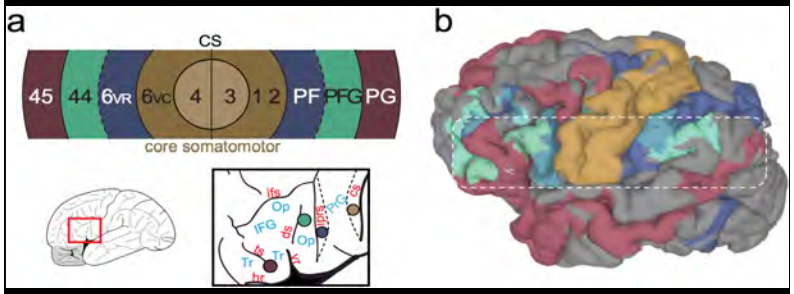
Spt…Sylvian Fissure / parietotemporal boundary = iSMG, STS…Sulcus temporalis superior
Hickok et al., *Behav Brain Sci 2003*

"Messy Maps" – Revisited: Different Components of the FNOI

speech mapping: same patient, different paradigms

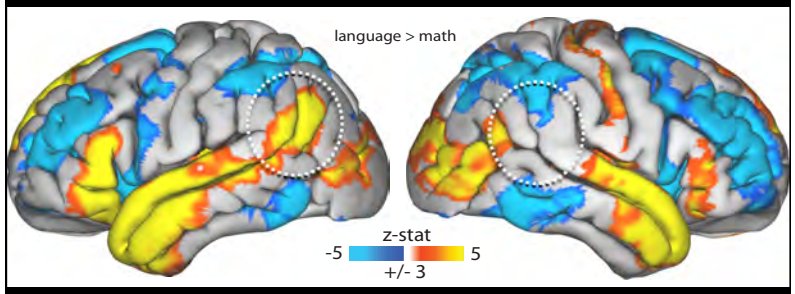
Reading nonfinal embedded clause sentences vs. Auditory description-cued covert naming

Speech/Language-Lateralisation & Mirror Connectivity around the CS



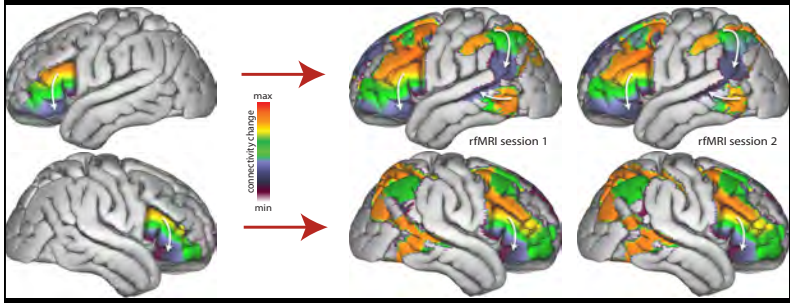
Margulies & Petrides, *J Neurosci 2013 – n=6 subjects*

Speech/Language-Lateralisation in Resting State-FMRI ? Task-FMRI Reference Results



Haak et al., *HBM 2015 – n=60 HCP subjects, 8 min*

Speech/Language-Lateralisation in Resting State-FMRI ? Connectivity Gradients (ConGrads)



Haak et al., *HBM 2015 – n=60 HCP subjects, 30 mins*

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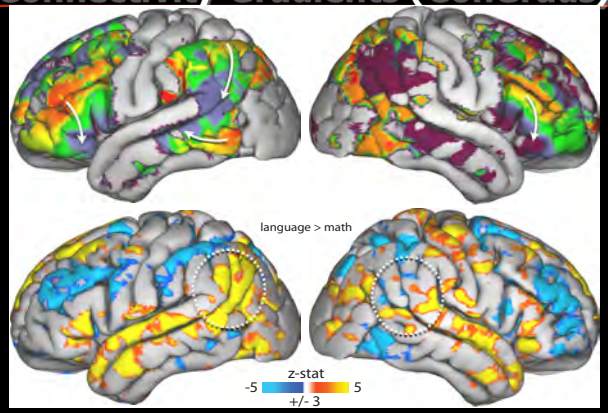
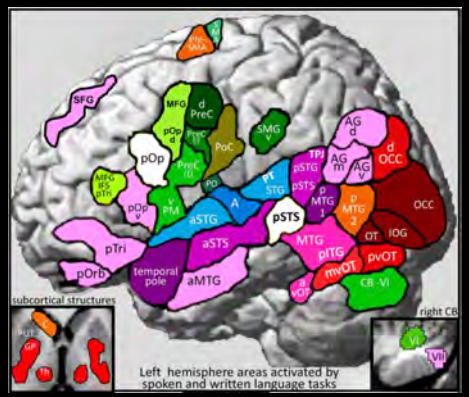


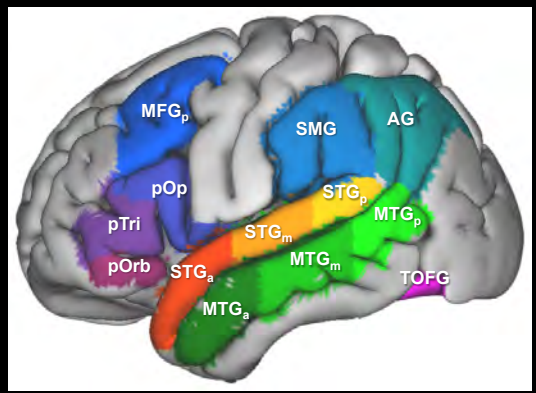
Haak et al., *HBM 2015 – single subject* # 100307 / session 1

Cortical Areas involved in Speech & Language



Price, *NeuroImage 2012*

Cortical Areas involved in Speech & Language – A Simplification



Why Graph Theory ?

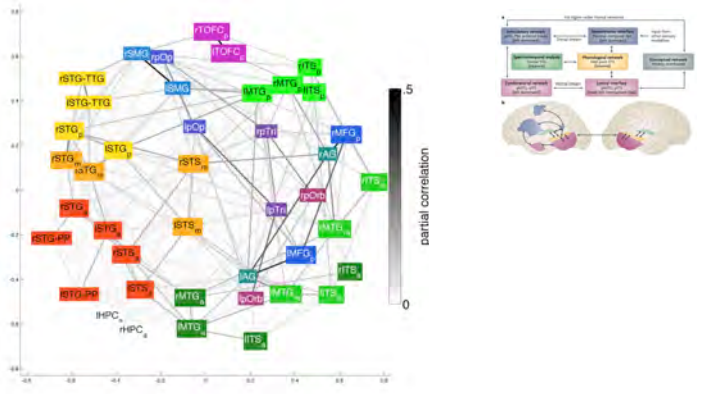
Wir weisen also die Annahmen zurück, daß der Sprachapparat aus gesonderten Zentren bestehe...

Die "Zentren" [erscheinen] als die Ecken des Sprachfelds...

Freud, *1891*

BOTH HEMISPHERES **Dual stream model for speech processing**

Hickok and Poeppel (2007)



Results from Multidimensional Scaling (MDS) of Resting State-FMRI Data (n=470 HCP subjects; courtesy of Izabela Przezdzik & Koen Haak)

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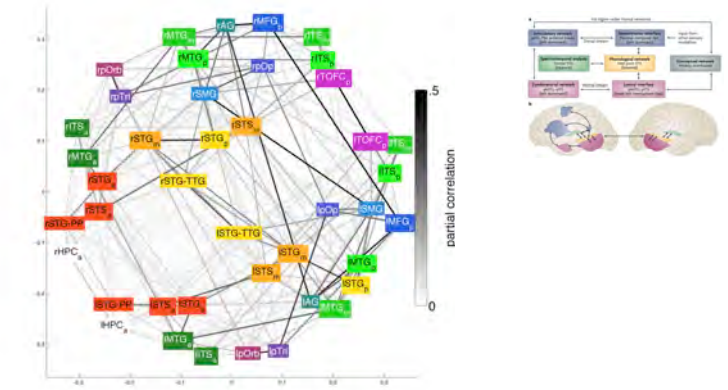

Results from Multidimensional Scaling (MDS) of Task-FMRI Data (n=470 HCP subjects; courtesy of Izabela Przezdzik & Koen Haak)

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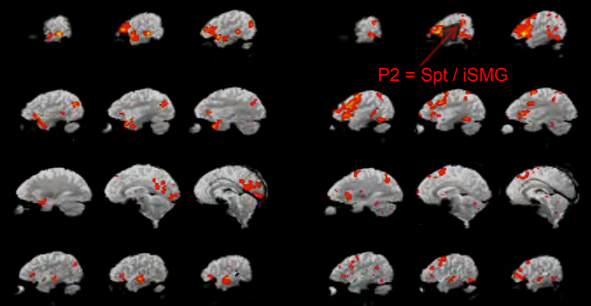
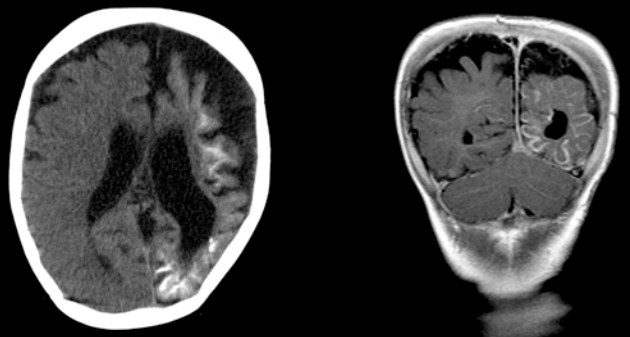


Solution

Based upon detailed neuropsychological examination:

- Visual vs. auditory stimulation
- Performance-adjusted presentation speed
- Task-based vs. -free *(=passive)* paradigm
- Event-related vs. blocked design

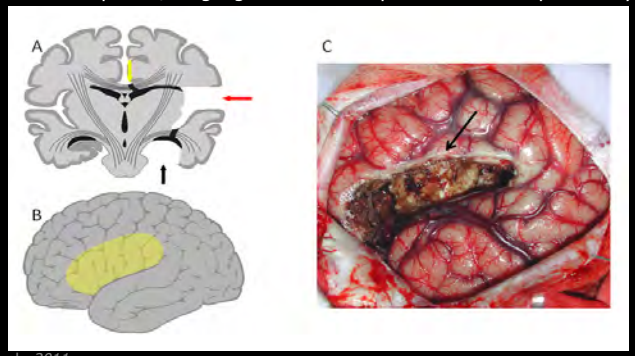
AUDIENCE CASE 1:
9-yo Boy, Refractory (Lesional) Epilepsy



right hemiparesis & -anopsia, glaucoma,
speech slow & slurred but preserved during seizures (3rd grade, inclusion)

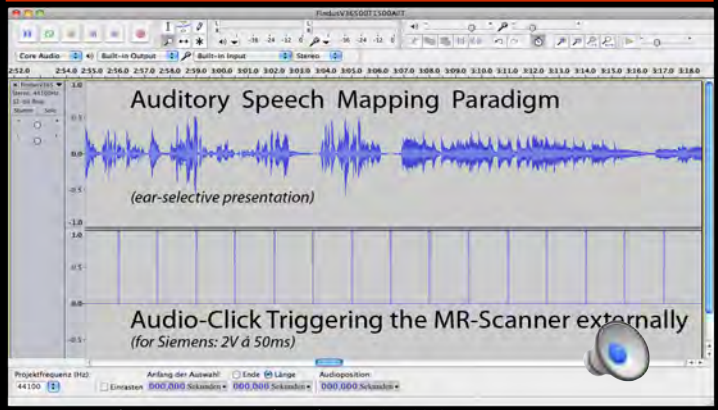
What is the Diagnosis, why is an FMRI requested ?

encephalotrigeminal angiomatosis (Sturge-Weber syndrome);
establish speech / language lateralization prior to left hemispherotomy*



*Terra et al., *2011*

How do we map this patient BEST ?



Audio-Trigger: Bartsch, *DGNR 2012;* Homola et al., *PLoS One 2012*

CHALLENGE:

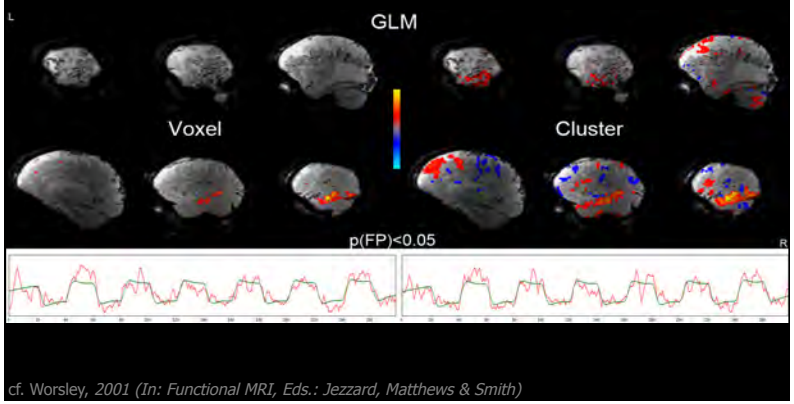
How do we analyze the data ?

What do we test for ?

CLINICAL RELEVANCE:

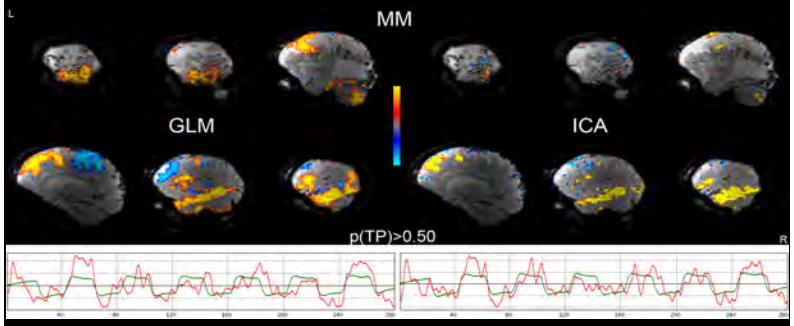
What we are going to find will vary !

Hypothesis-driven Analysis, Family-wise Error Rates (FWER) <5%



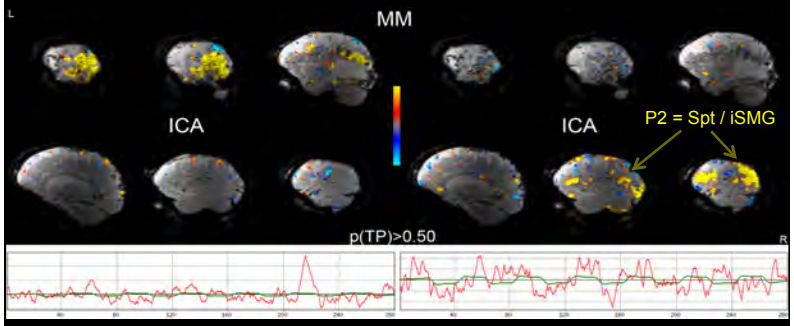
cf. Worsley, *2001 (In: Functional MRI, Eds.: Jezzard, Matthews & Smith)*

Hypothesis- vs. Data-driven Analysis, (De-)Activation Probabilities >50%



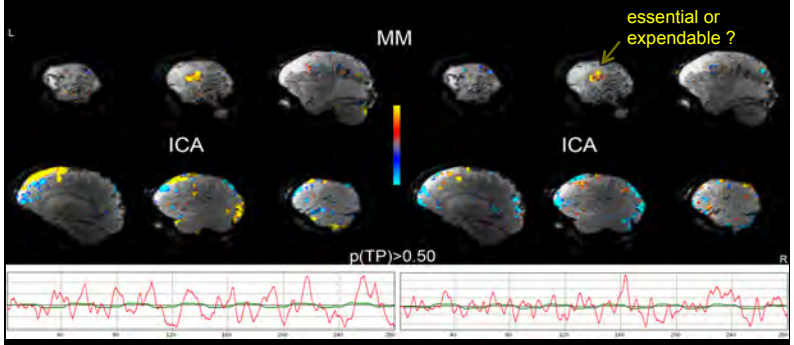
Mixture Modeling (MM) & H(1)-Testing: Beckmann et al., *HBM Conf. 2003*; Beckmann & Smith, *IEEE TMI 2004*; Everitt & Bullmore, *HBM 1999*; Hartvig & Jensen, *HBM 2000*; Woolrich et al., *IEEE TMI 2005*; Durnez et al., *CABN 2013*; Johnson et al., *Stat Methods Meds Res 2013*

Data-driven Analysis (ICA), (De-)Activation Probabilities >50%



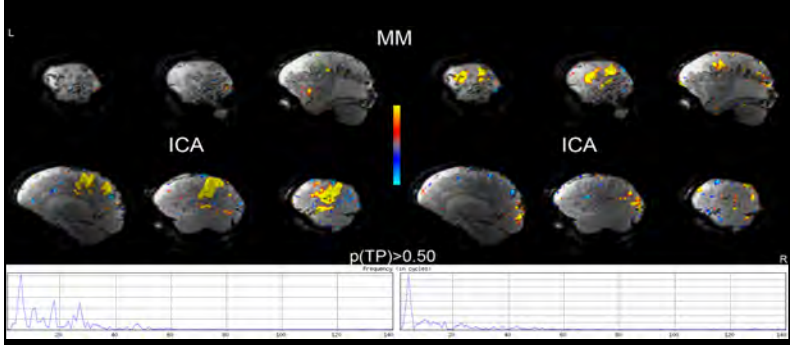
Independent Components (ICs) *also* significantly correlated with the paradigm
-> Is left hemisphere "silent"? - speech dissociates in pSTG/vAPL-ICs*
*cf. Simmonds et al., *HBM 2013*

Solution: Use GLM & ICA, Alternative Hypothesis Testing



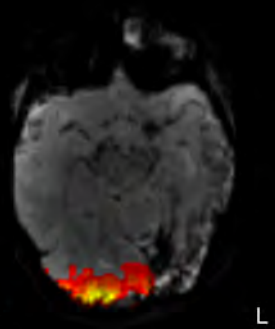
Independent Components (ICs) *also* significantly correlated with the paradigm
-> left hemisphere is not "silent": left lower precentral gyrus is "eloquent"

Data-driven Analysis (ICA), (De-)Activation Probabilities >50%



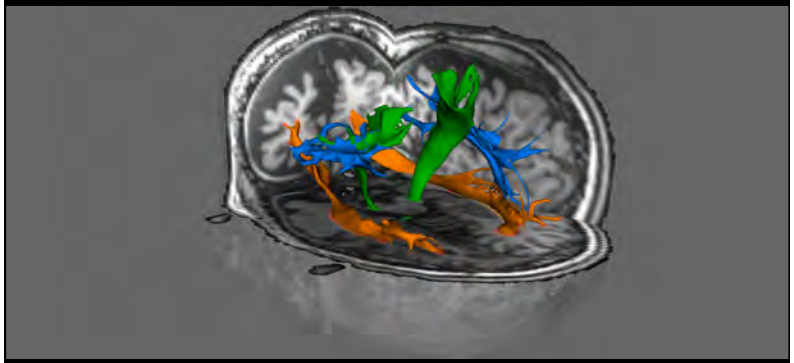
ICs *un*correlated with the speech & language paradigm
-> "Resting-State" Networks (right sensorimotor & left frontoparietal)

Data-driven Analysis (ICA), (De-)Activation Probabilities >50%



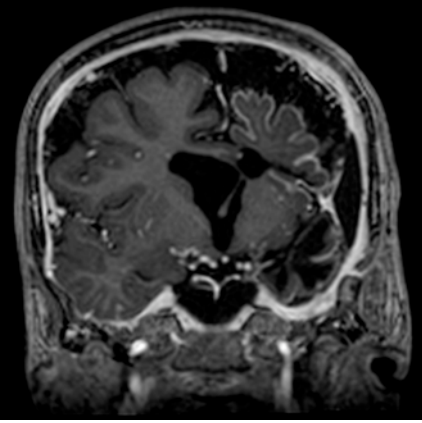
ICs *un*correlated with the speech & language paradigm
-> visual RSN (corresponding to the hemianopsia!)

and Diffusion Tractography ?



Arcuate (posterior right >> left), inferior fronto-occipital fasciculus (laregely intact) and pyramidal tract (right>left)

Hemispherectomy and Outcome



CHALLENGE:

Which Blobs / Tracts are (in-)dispensible ?
How far do they extend ?

CLINICAL RELEVANCE:

Huge – our clinical decisons will vary !

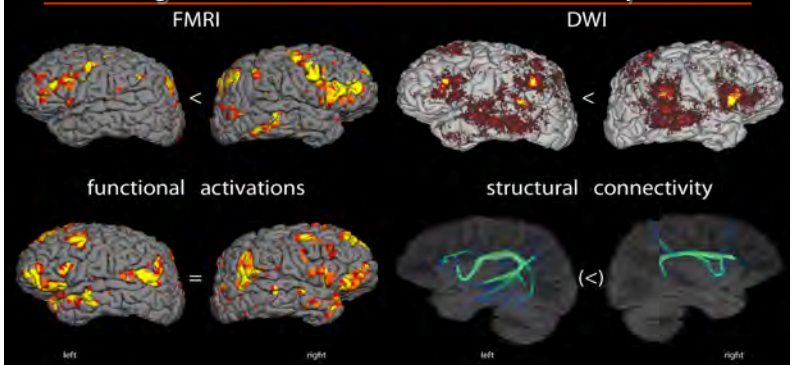
SOLUTION:

NONE *(yet)* ☹

but maybe there is hope...

COMPANION CASE 2: 13-yo Boy, Refractory *Non*lesional Epilepsy

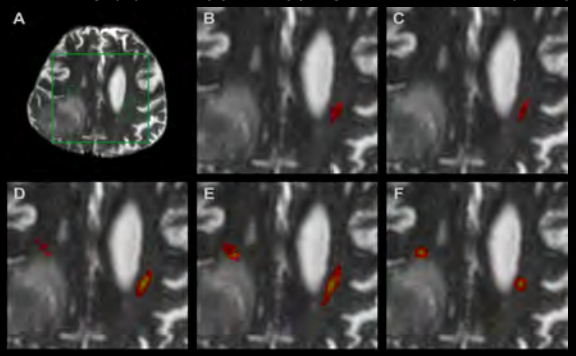
Matching Functional & Structural Connectivity Profiles



Left-Hander, hypermotor left frontotemporal seizures with aggressive behaviour & preserved speech
Question: speech / language lateralization prior to invasive electrocorticography

Challenge: Tracking in Perifocal Edema increases False-Negatives

right retro-Rolandic glioblastoma (A), simple (B) vs. interpolated (B) streamlining, probabilistic tractography without (D) & with (E) Xing fibres + constrained Bayesian (F)



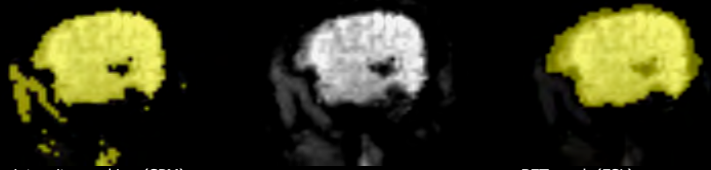
Bartsch et al., *2014 (In: Diffusion MRI, Eds.: Johansen-Berg & Behrens)*

CHALLENGE: EPI suffers from LOCAL SIGNAL LOSS

- bleedings, flow-void, drilling abrasions, calcinations etc. altering the EPI signal

→ *Make sure lesion is covered by analysis mask! Always look at original EPI* *(not just stats-overlays on highres anatomical)* *!*

arteriovenous malformation (AVM; hypointense flow-void)

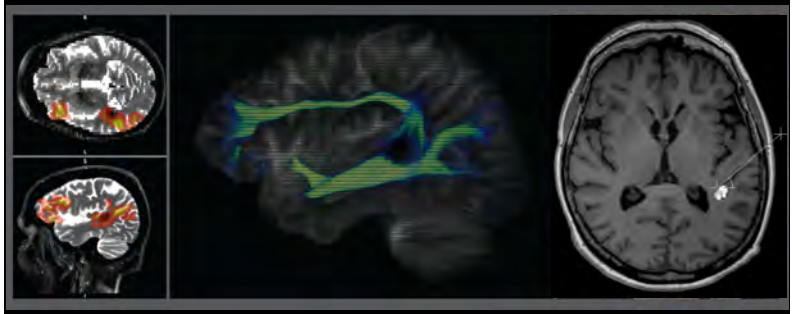


intensity-masking (SPM)

BET-mask (FSL)

Haller & Bartsch, *Eur Radiology 2009*

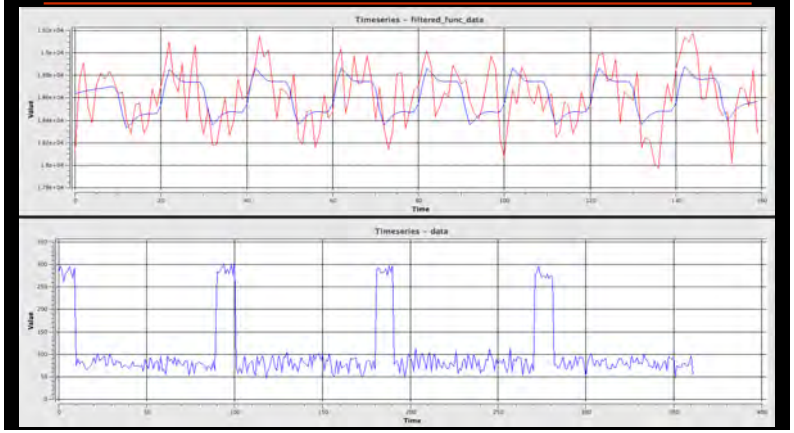
CLINICAL RELEVANCE: No Signal – No Activations / Tracts



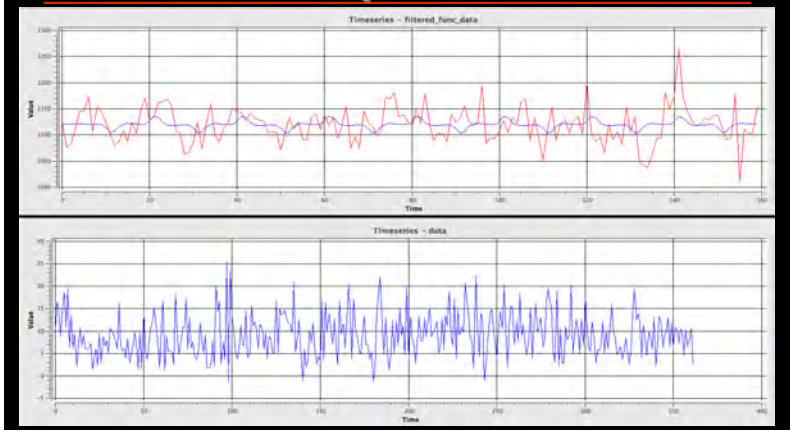
left temporal cavernoma (Zabramski type I; intracellular MetHb)

Bartsch et al., *2014 (In: Diffusion MRI, Eds.: Johansen-Berg & Behrens)*

FMRI- & Diffusion-EPI *SIGNAL*



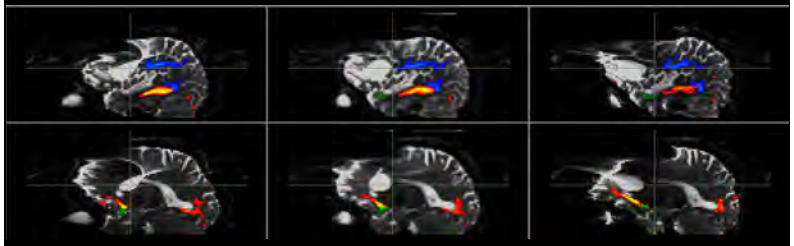
FMRI- & Diffusion-EPI *SIGNAL LOSS:* No easy solution !



CHALLENGE: DISTORTIONS

CHALLENGE: EPI suffers from GEOMETRIC DISTORTIONS...

A -> P | topup-corrected | A <- P

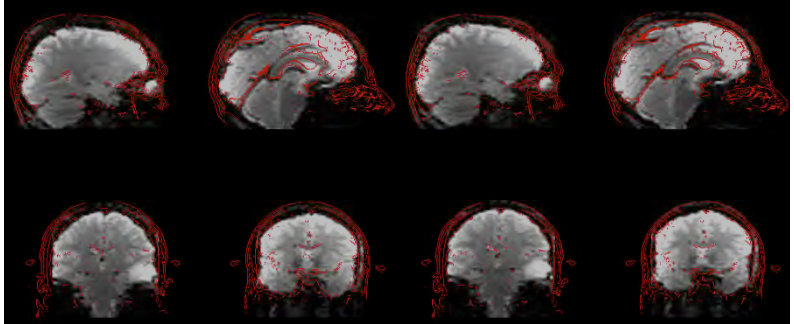


Arcuate, inferior fronto-occipital and uncinate fasciculus
in a ganglioglioma patient with craniofix & a Ommaya reservoire

Anderson, *2014 (In: Diffusion MRI, Eds.: Johansen-Berg & Behrens)*; Choli et al., *MAGMA 2013*

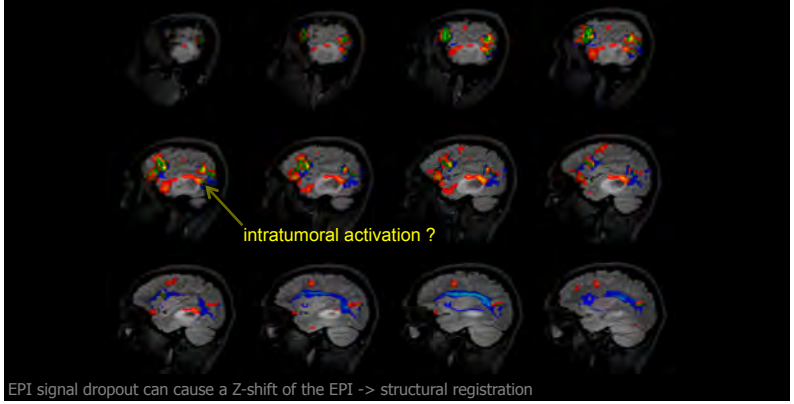
...and, for GE-EPI, SIGNAL DROPOUTS can cause REGISTRATION ERRORS

rigid body (6 DoF) | boundary-based*



*Greve & Fischl, *NeuroImage 2009*

CLINICAL RELEVANCE - CASE 3: Incidental left T2/3-Astrozytoma °III



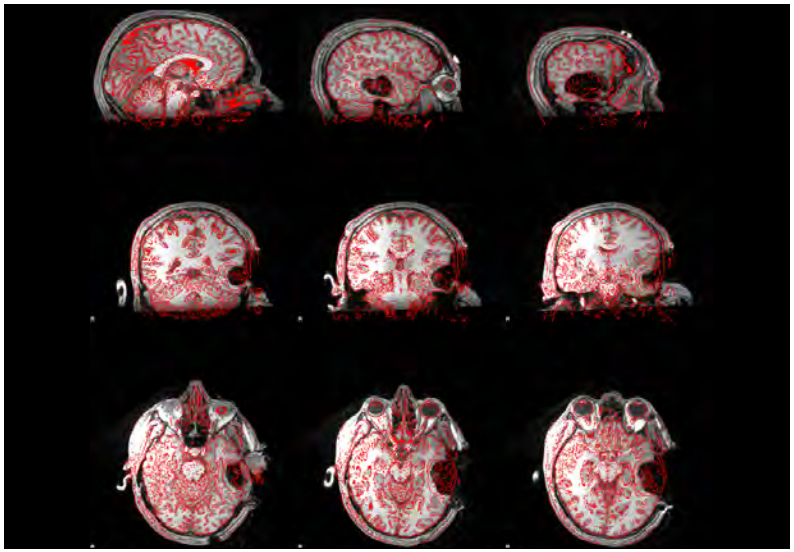
EPI signal dropout can cause a Z-shift of the EPI -> structural registration

SOLUTION: Optimal Distortion Correction & Registration for Presurgical Planning

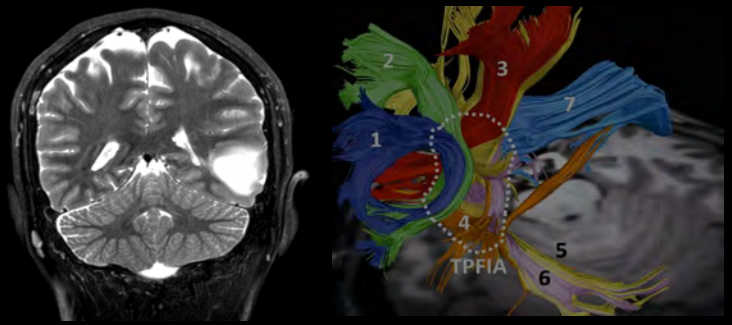
paradigm: reading non-final embedded clause sentences

and Intraoperative Neuronavigation !

... but what about brain shift ?
Here is none!



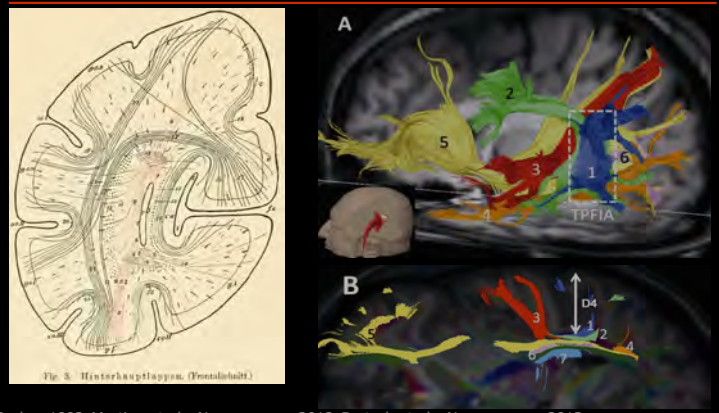
Gross Tumor Resection (GTR) – Is the Deficit predictable ?



Martino et al., *Neurosurgery 2012*

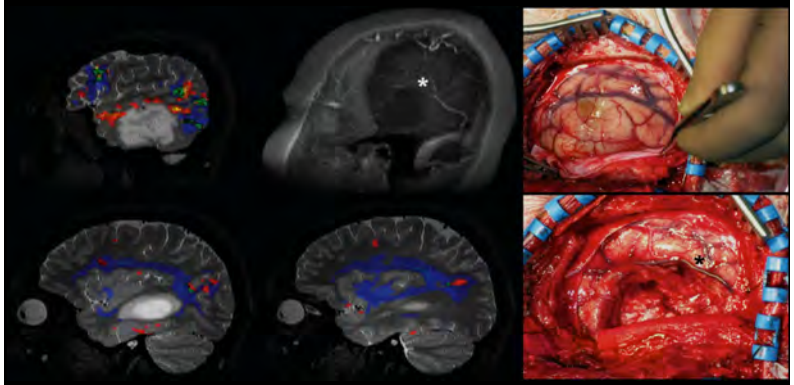
1 - ?, 2 – AF, 3 – MLF, 4 – ILF, 5 – IFO, 6 – OR, 7 – Tp

"Temporoparietal Fiber Intersection Area"



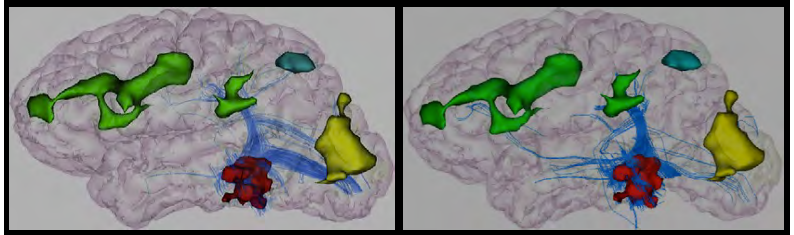
cf. Sachs, *1892*; Martino et al., *Neurosurgery 2012*; Bartsch et al., *Neurosurgery 2013*

Which Deficit Would You Expect ?



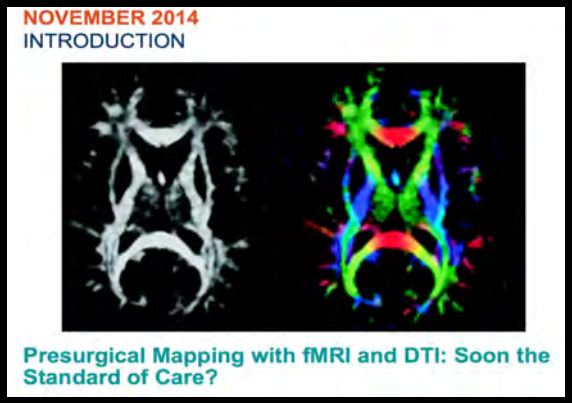
"No Ifs, Ands, or Buts!"

Transient Pure Alexia without Agraphia or Hemianopsia



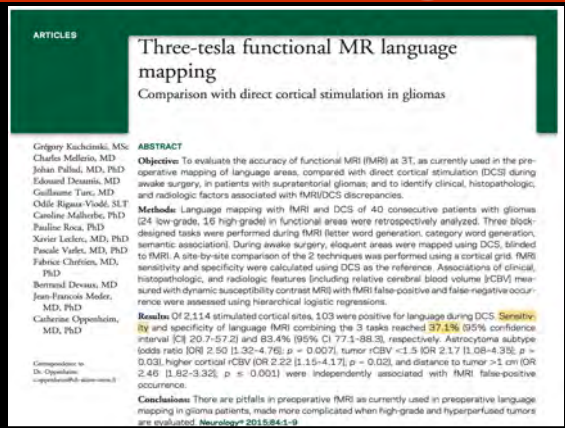
Epelbaum et al., *Cortex 2008*
Kussmaul, *1877*; Charcot, *1890*; Dejerine, *1892*; Greenblatt, *1976-90*) cf.

FMRI and Tractography: Clinically Valuable or Useless ?

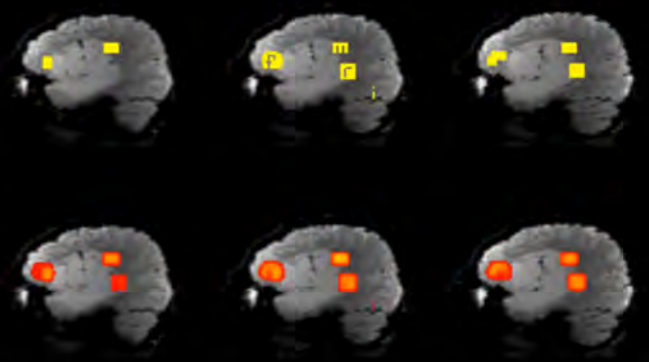


AJNR, *2014*

Smoothing > 7x of the Voxel Size can result in False-Negatives

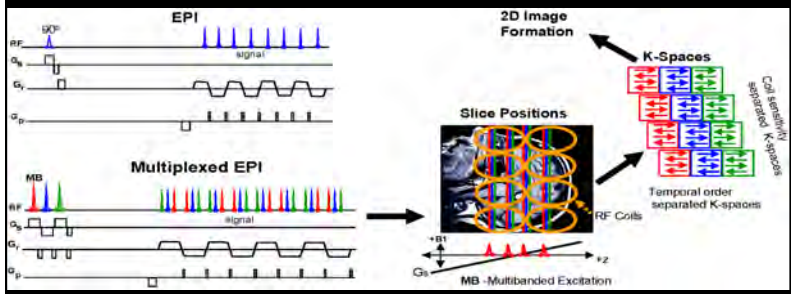


Why / When is Spatial Smoothing "bad" ?



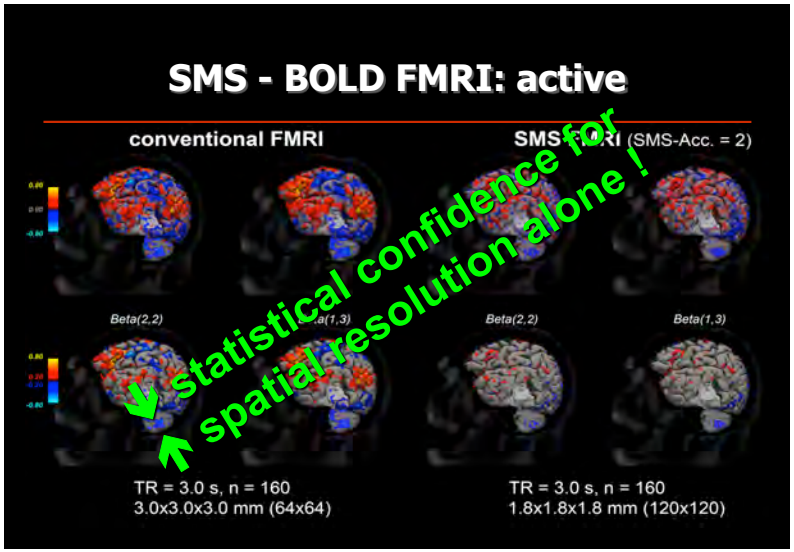
4.5 mm FWHM, spatial resolution: 1.8x1.8x2.1mm

Increase the Spatiotemporal EPI Resolution ? Simultaneous Multi-Slice !

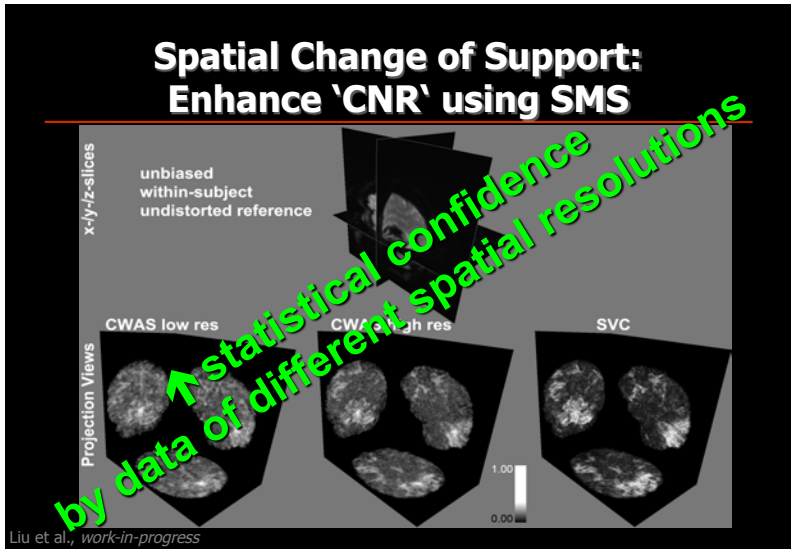


Feinberg et al., *PLoS One 2010*

SMS - BOLD FMRI: active

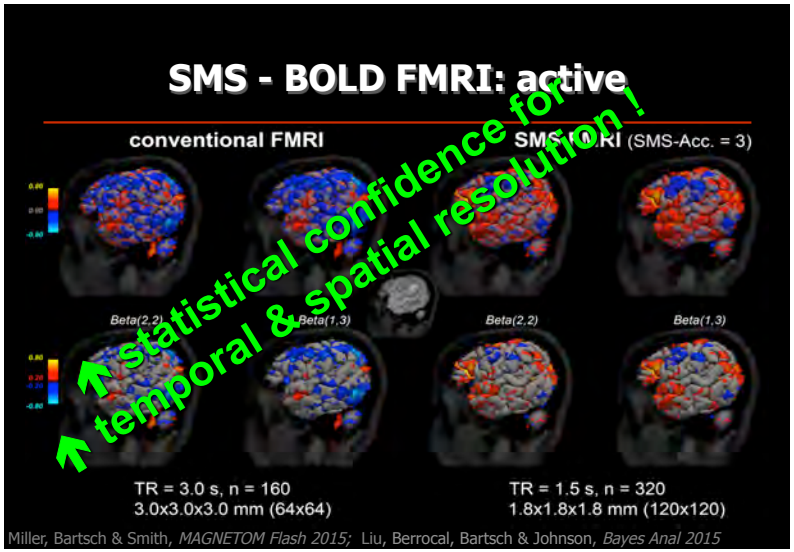


Spatial Change of Support: Enhance 'CNR' using SMS



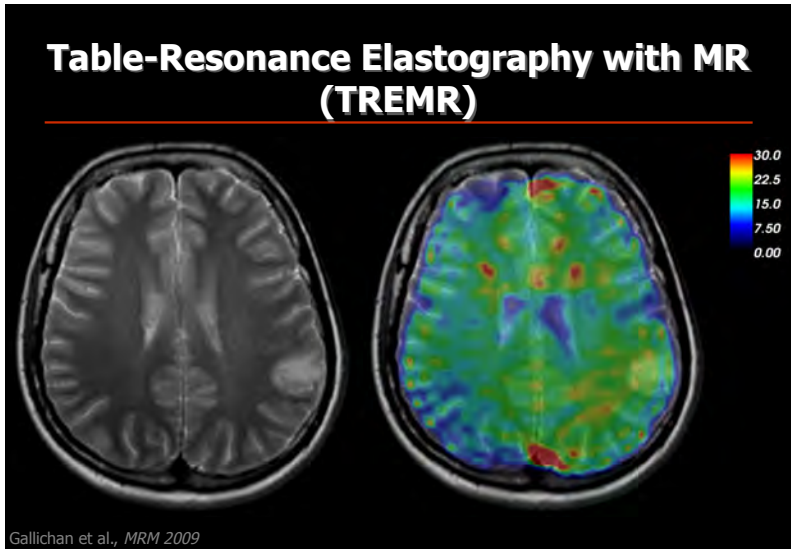
Liu et al., *work-in-progress*

SMS - BOLD FMRI: active



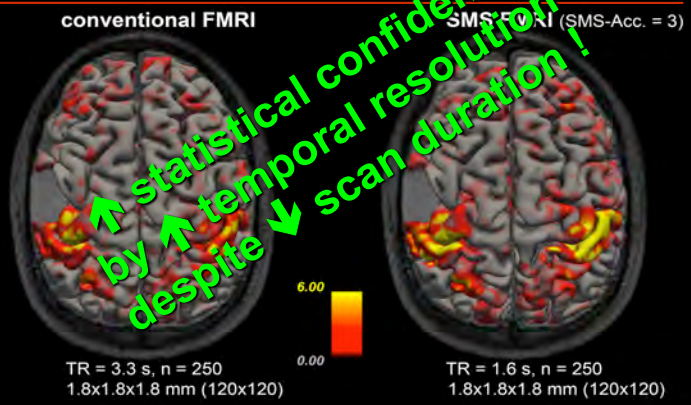
Miller, Bartsch & Smith, *MAGNETOM Flash 2015;* Liu, Berrocal, Bartsch & Johnson, *Bayes Anal 2015*

Table-Resonance Elastography with MR (TREMR)

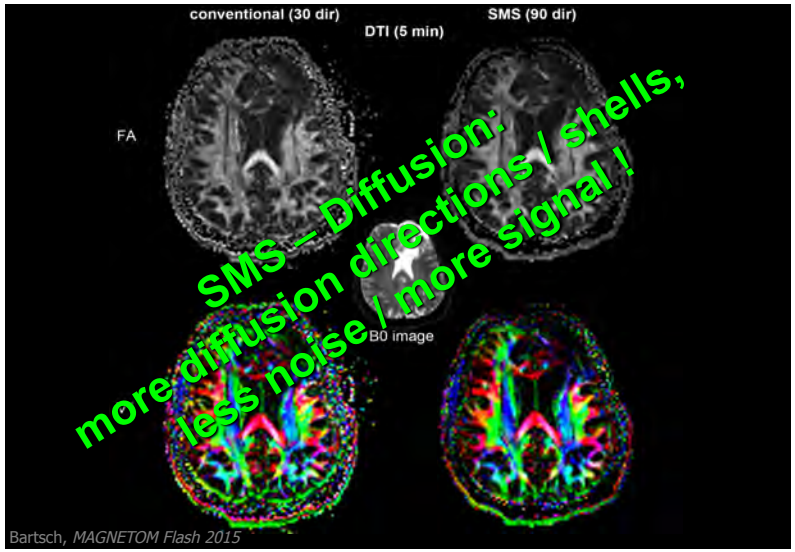


Gallichan et al., *MRM 2009*

SMS - BOLD FMRI: Resting State

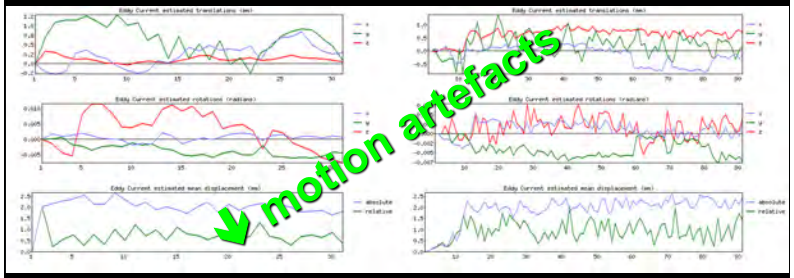


Miller, Bartsch & Smith, *MAGNETOM Flash 2015*



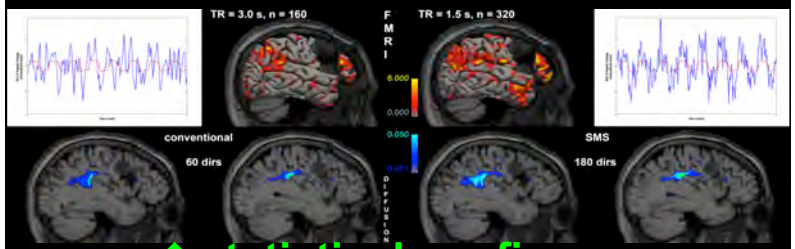
Bartsch, *MAGNETOM Flash 2015*

Without vs. with SMS (factor 3)



Bartsch, *MAGNETOM Flash 2015*

SMS - BOLD FMRI and Diffusion



↑ statistical conficence
by ↑ temporal resolution !

Bartsch, *MAGNETOM Flash 2015*; r = 0.2 vs. 0.7

Take Home

- Preoperative patient condition matters:

  epilepsy surgery - patients with no presurgical deficits or brain pathology are at high risk

  tumor surgery - patients with no presurgical deficits and the small pathologies tend to fare best

- There is no uniform mapping / tracking procedure:

  paradigms, seeds / targets etc. need to be tailored to the individual patient performance, deficits & pathology

- Current limitations and future challenges:

  FMRI & tractography i) measure only epiphenomena of neuronal acitivity & axonal integrity -> false-negative risk, ii) can't discriminate essential from dispensable activations / tracts, iii) spatial extent is probabilistic

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Thank You !