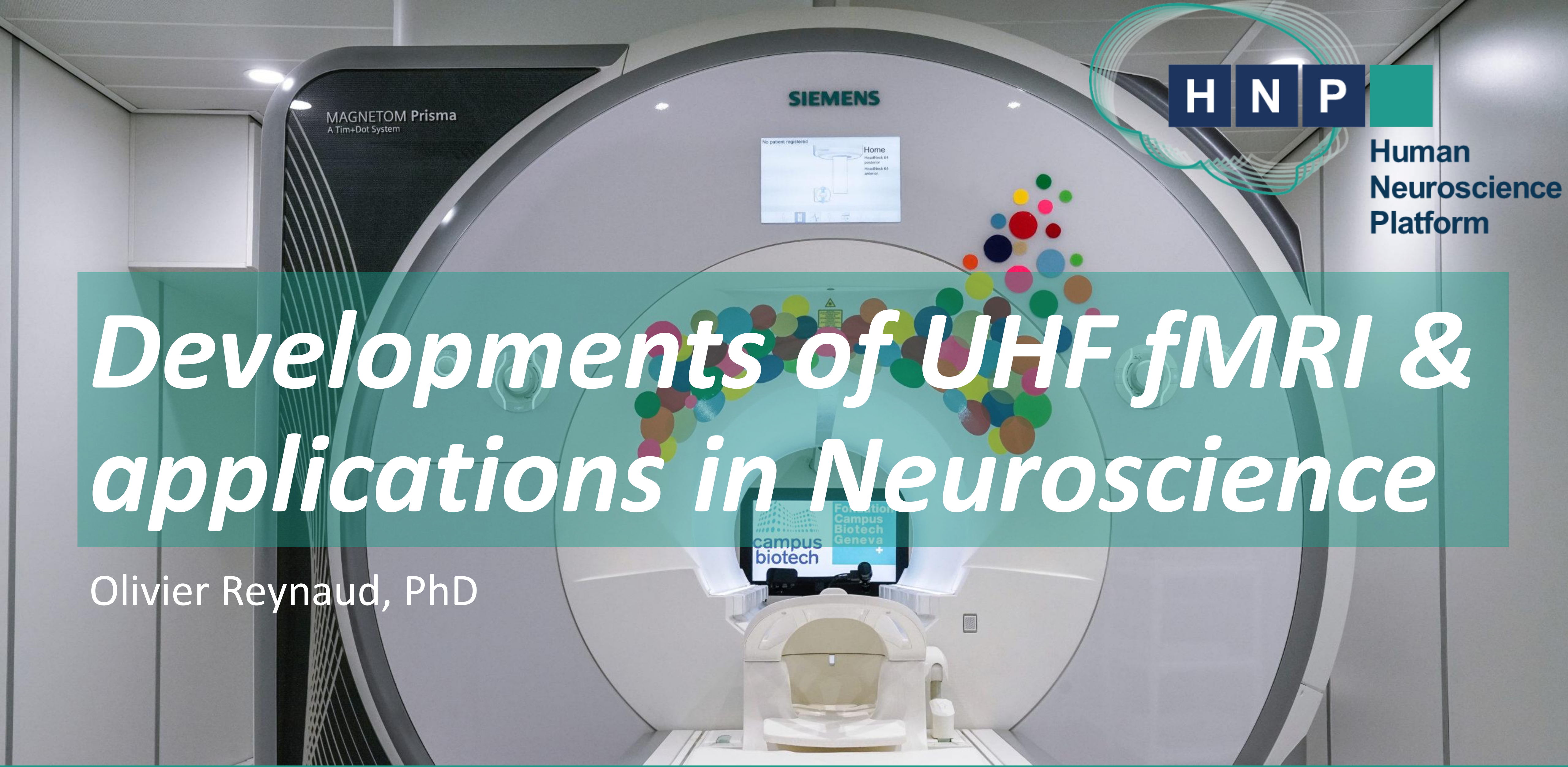


H N P
Human
Neuroscience
Platform

Developments of UHF fMRI & applications in Neuroscience

Olivier Reynaud, PhD

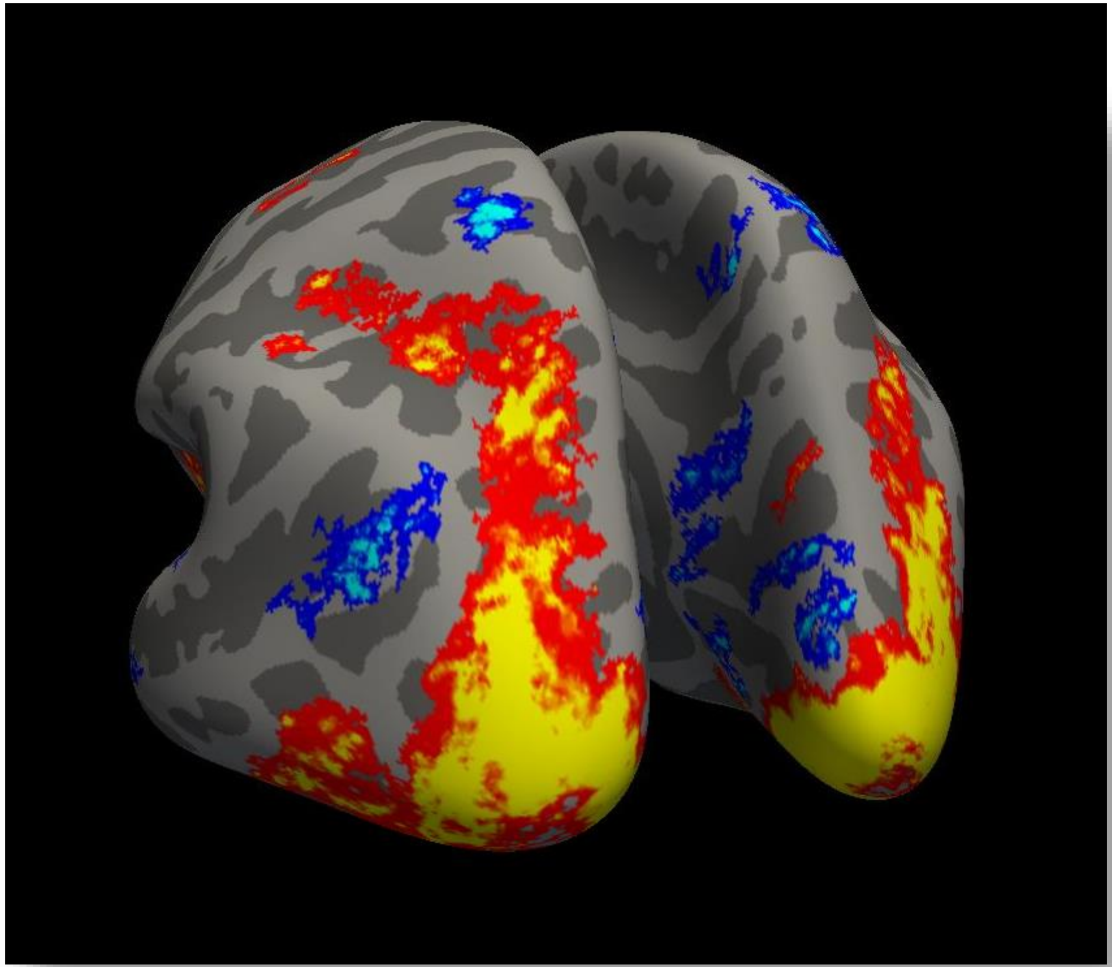
H N P
Human
Neuroscience
Platform

campus
biotech

Fondation
Campus
Biotech
Geneva

Outline

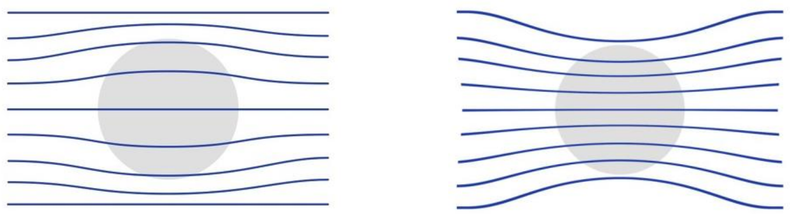
1. Why fMRI at 7 Tesla ?
2. 2D-EPI vs 3D-EPI
3. BOLD fMRI applications
4. 1H fMRS (Spectroscopy)
5. Perfusion fMRI & others



0. functional MRI

Diamagnetic materials
(oppose external field)

Paramagnetic materials
(enhance external field)



Oxyhemoglobin (Hb)

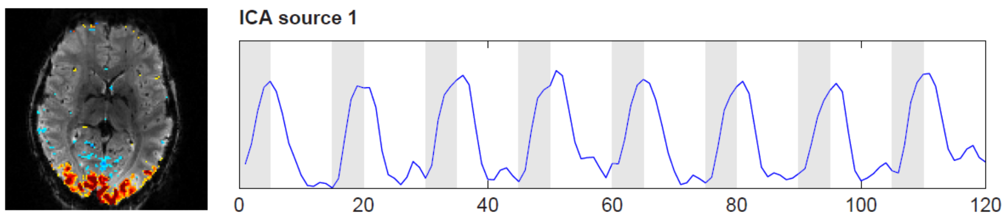
Deoxyhemoglobin (dHb)

$$S_{BOLD} \propto exp(-TE/T_2^*)$$

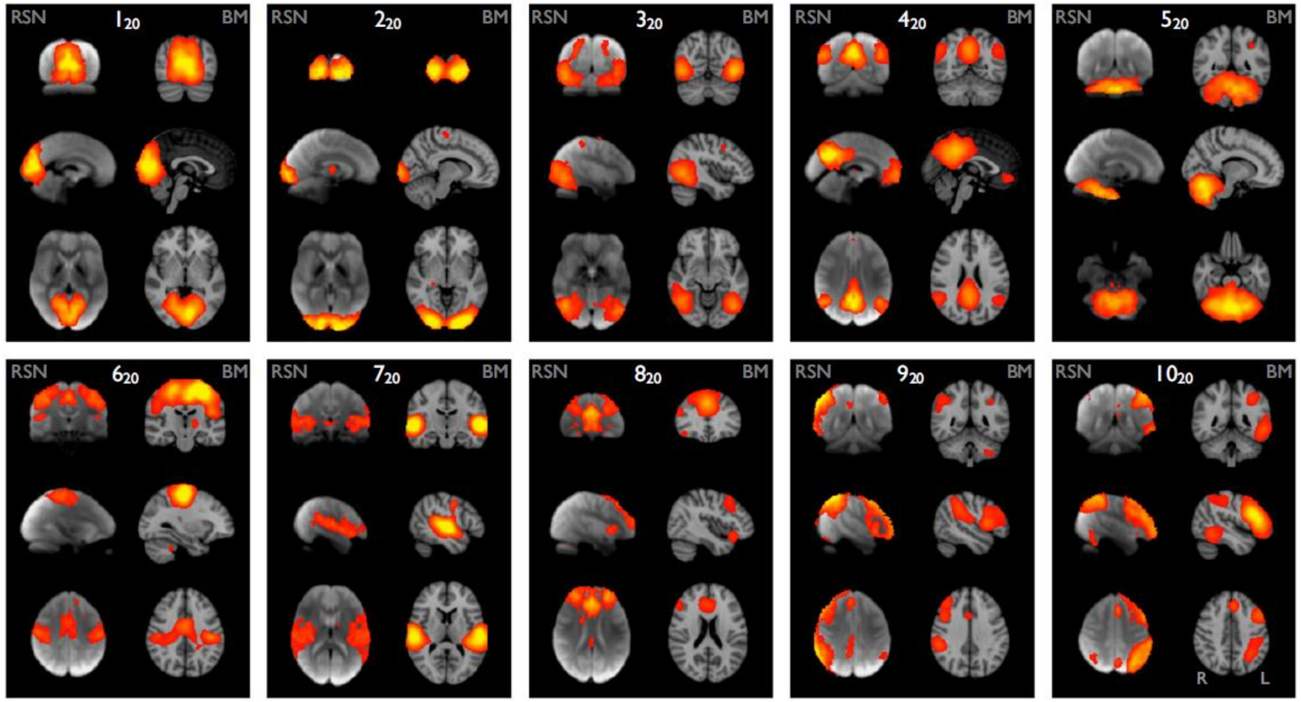
- **BOLD functional MRI**
  - local ↑neuronal activity ⇨ ↑O_2 consumption ⇨ ↓BOLD
    ⇨ ↑↑ cerebral blood flow (CBF) ⇨ ↑BOLD
    ⇨ ↑ cerebral blood volume (CBV) ⇨ ↓BOLD

0. Task vs. Resting-state fMRI

Task fMRI



Resting-state fMRI

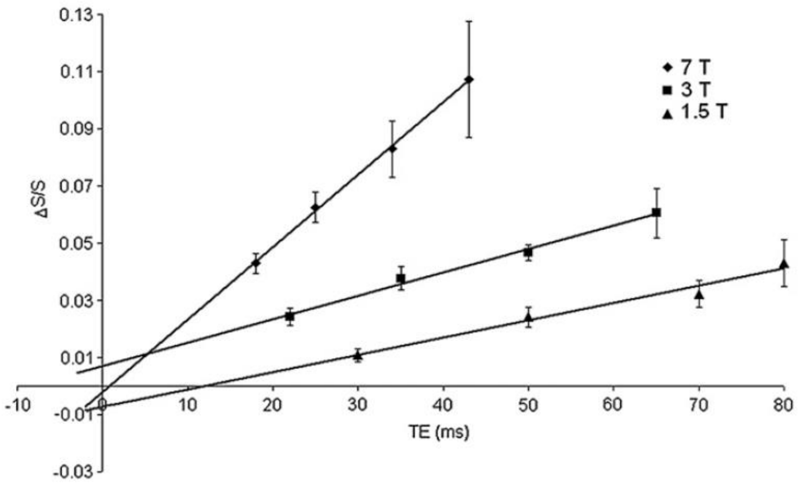


Smith et al, 2009, PNAS

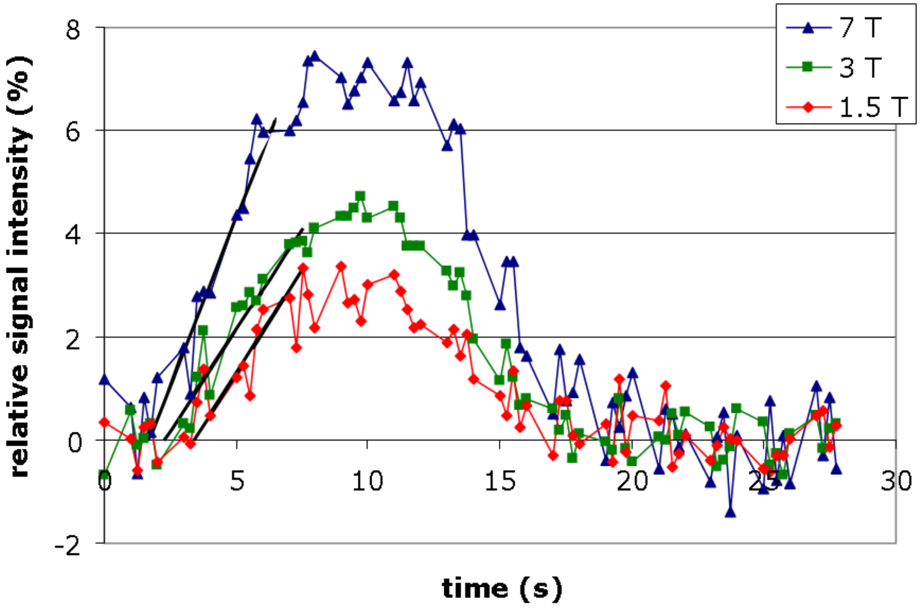
1. Why fMRI at 7 Tesla?

- **BOLD sensitivity**
  - ⬆B_0 ⇨ ⬆MR signal — $SNR_{image} \propto B_0^{\ 1.65}$ (Pohmann et al, 2016)
  - ⬆B_0 ⇨ ⬆field inhomogeneities ⇨ ⬆BOLD contrast — $\Delta B_{dHb} \propto \chi_{dHb} B_0$

Response in the motor cortex at 1.5, 3 and 7 T



van der Zwaag et al, 2009, Neuroimage



1. Why fMRI at 7 Tesla?

- **BOLD sensitivity**
  - ⬆B_0 ⇨ ⬆MR signal
  - ⬆B_0 ⇨ ⬆field inhomogeneities ⇨ ⬆BOLD contrast

$SNR_{image} \propto B_0{}^{1.65}$ (Pohmann et al, 2016)

$\Delta B_{dHb} \propto \chi_{dHb} B_0$

- **Also important with ⬆B_0**
  - **Specificity:** ⬇T_2 of venous signal ⇨ smaller venous contributions
  - ⬇**Optimal TE for BOLD** ⇨ less time for k-space readout, but faster volume sampling
  - ⬇**B_0 homogeneity** ⇨ ⬆spatial distortions, ⬆signal loss in certain regions
  - ⬇**B_1 homogeneity** ⇨ ⬆heterogeneity in SNR across regions
  - ⬆**Rel. sensitivity to non-white noise sources** (physiological noise, etc.)

1. Why fMRI at 7 Tesla?

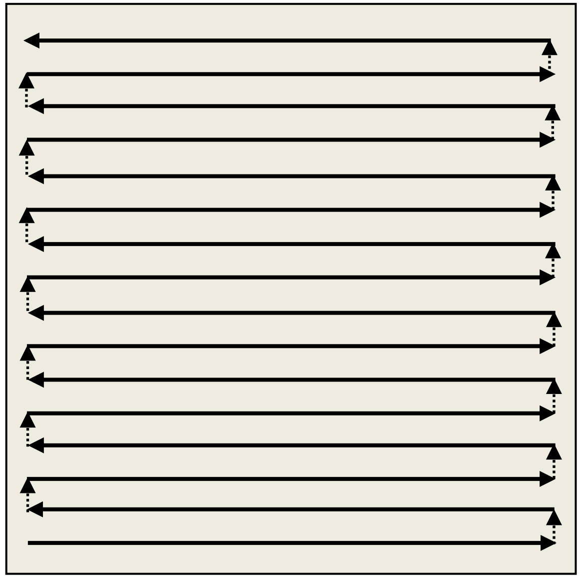
The greater signal, bold contrast and spatial specificity at ultra-high filed can be exploited to:

a. Improve the spatial resolution (i.e., smaller voxel size).
b. Reduce the number of trials to demonstrate robust activation.
c. Facilitate the study of the response to *rare events*
d. Investigate *subtle cognitive effects* (e.g., single subject differences).
e. Improve the temporal resolution (ie TR^{-1}, sampling rate)

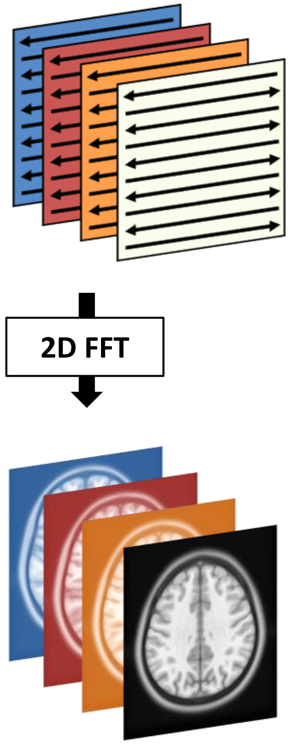
2. 2D-EPI vs. 3D-EPI

BOLD fMRI needs fast sampling rate & high SNR → **Echo Planar Imaging (EPI)**

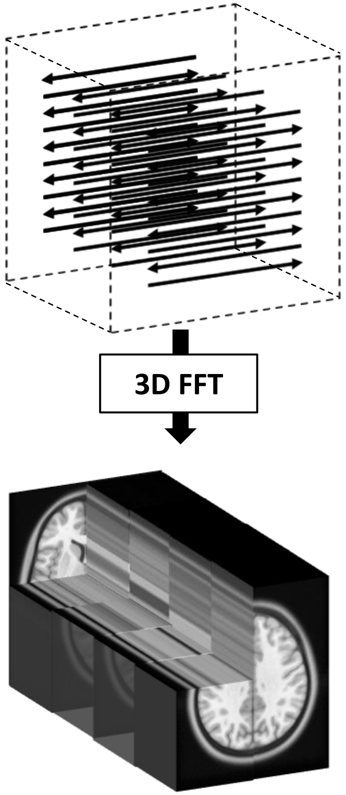
EPI sampling



2D EPI



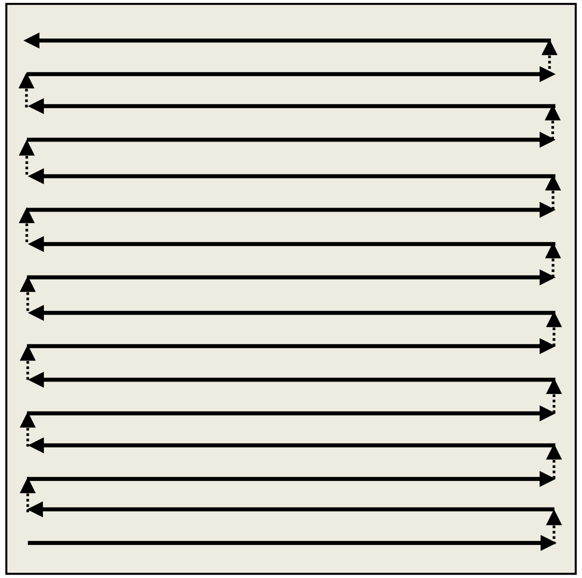
3D EPI



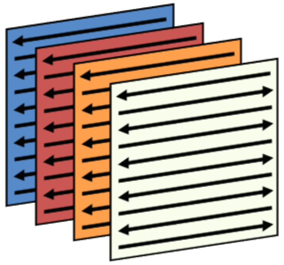
2. 2D-EPI vs. 3D-EPI

BOLD fMRI needs fast sampling rate & high SNR ➔ **Echo Planar Imaging (EPI)**

EPI sampling

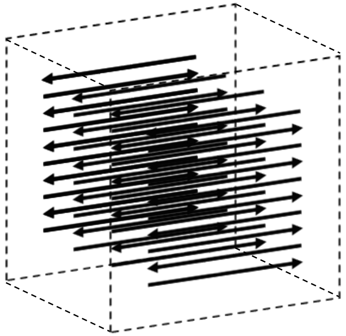


2D EPI



- Fast sampling rate
- Gold standard

3D EPI

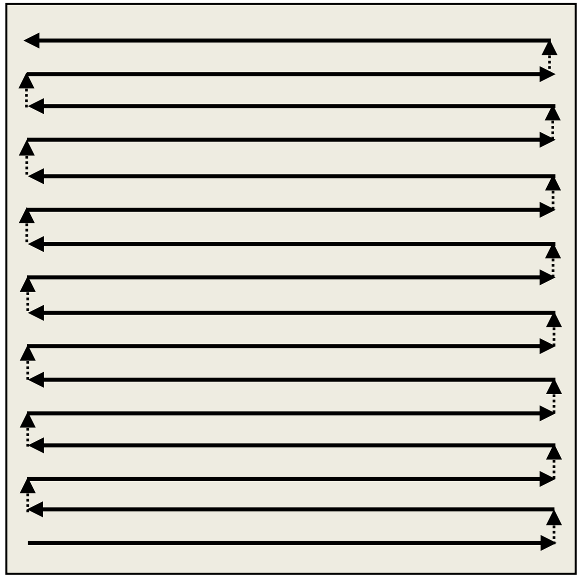


- Higher signal
- Long Read-out train
- Increased distortions
- TE too long for fMRI

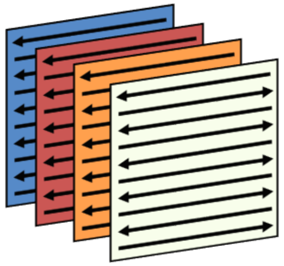
2. 2D-EPI vs. 3D-EPI

BOLD fMRI needs fast sampling rate & high SNR ➔ **Echo Planar Imaging (EPI)**

EPI sampling

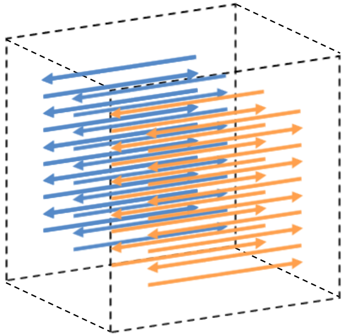


2D EPI



- Fast sampling rate
- Gold standard

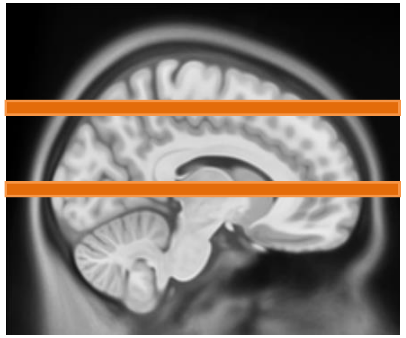
3D EPI

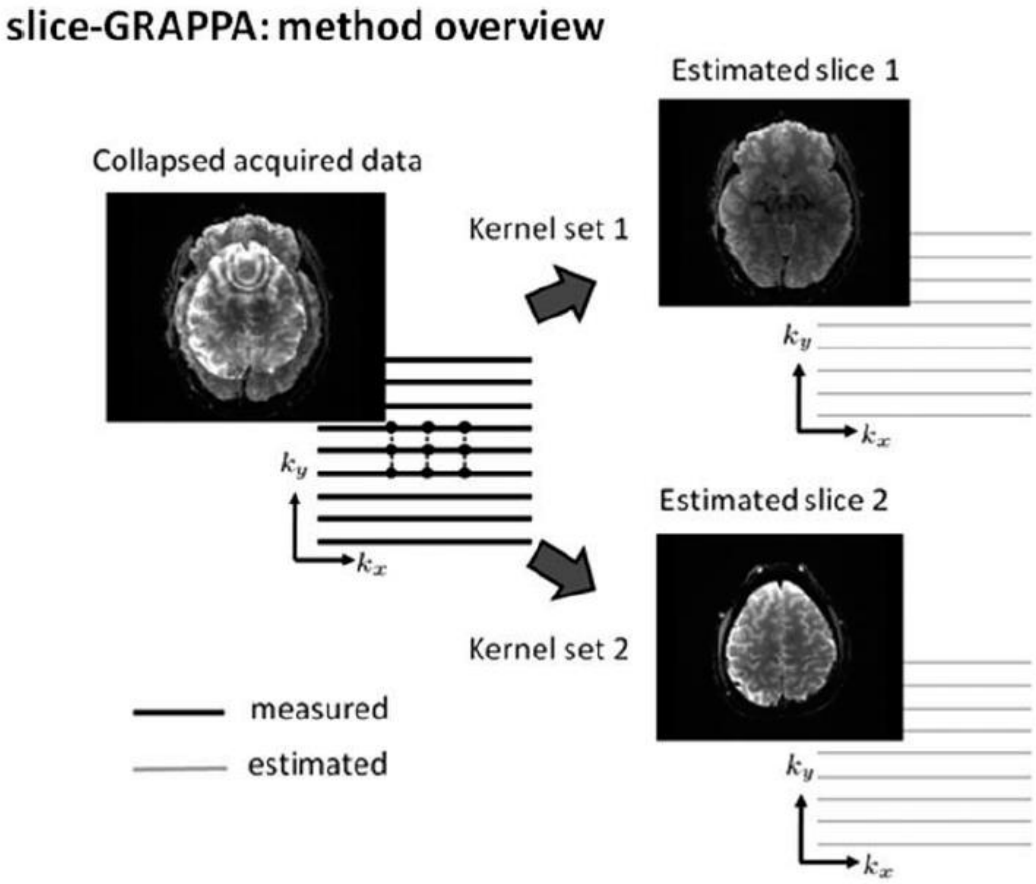


- Higher signal
- Short TE
- Less distortions
- Sensitivity to motion

Gold standard for 2D-EPI:
Simultaneous Multi-Slice (SMS) / Multi-Band excitation

RF Excitation

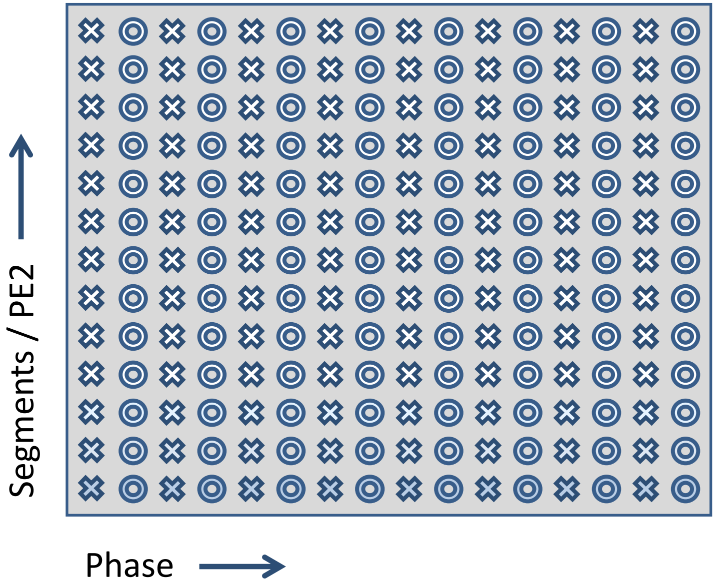




Setsompop et al, MRM 2012

Accelerating 3D-EPI data using undersampling

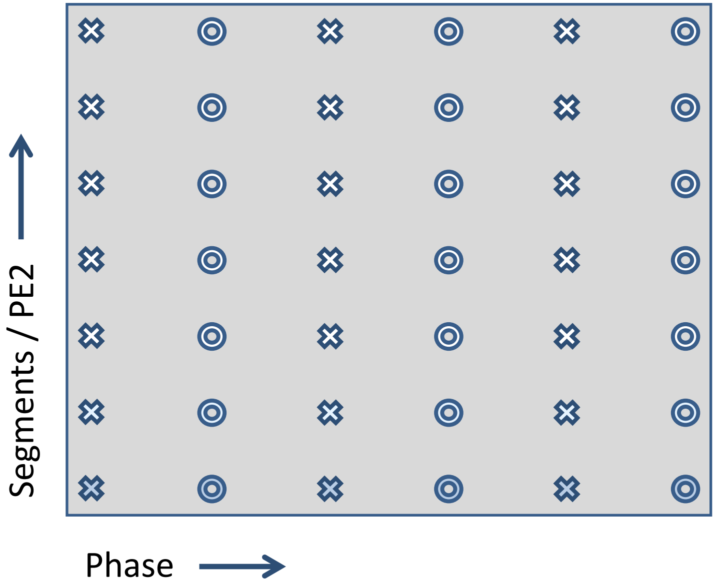
Fully sampled 3D-EPI



Accelerating 3D-EPI data using undersampling

GRAPPA along PE & PE2

GRAPPA R=3x2



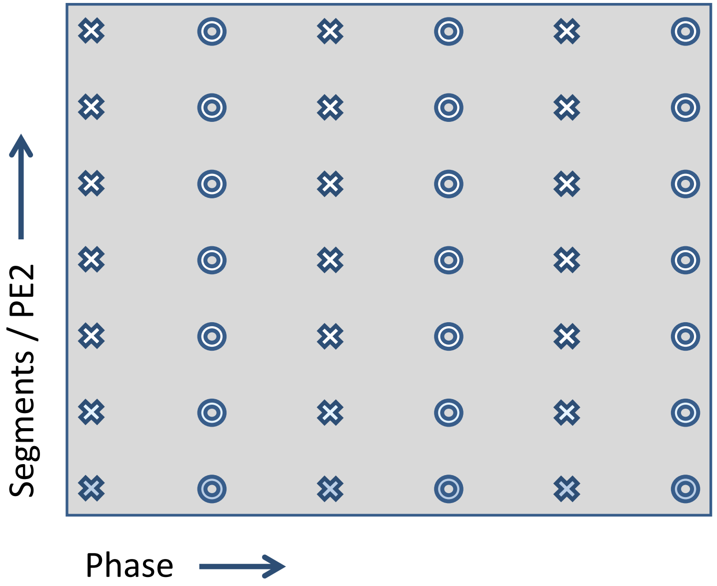
Poser et al, Neuroimage 2009

Accelerating 3D-EPI data using undersampling

GRAPPA along PE & PE2

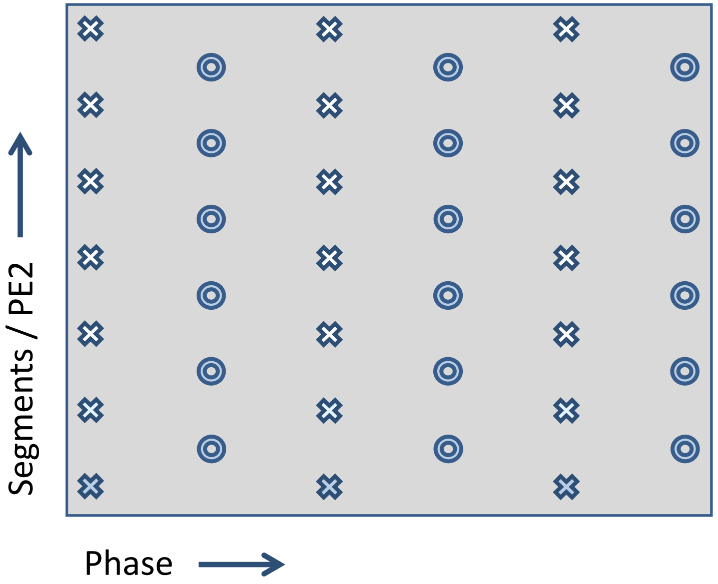
Controlled aliasing (**CAIPIRINHA**)

GRAPPA R=3x2



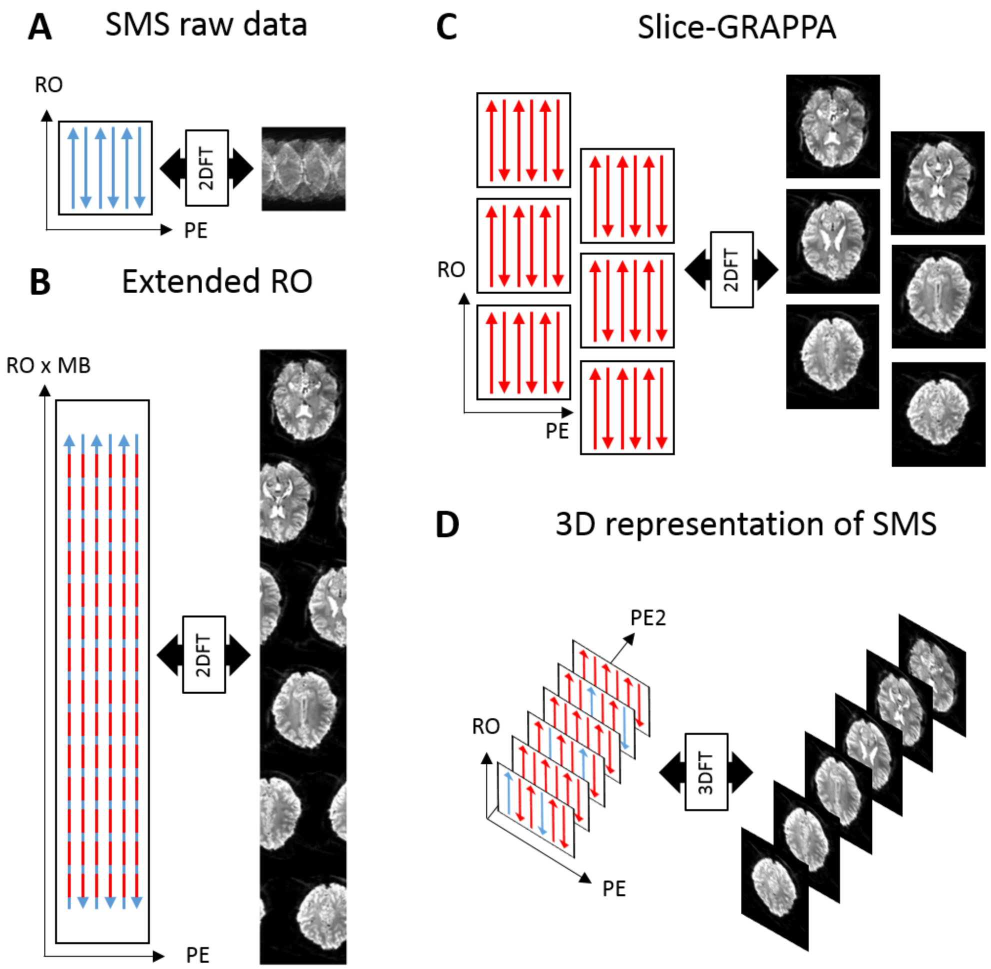
Poser et al, Neuroimage 2009

GRAPPA 3x2 + CAIPIRINHA (Δ=1)



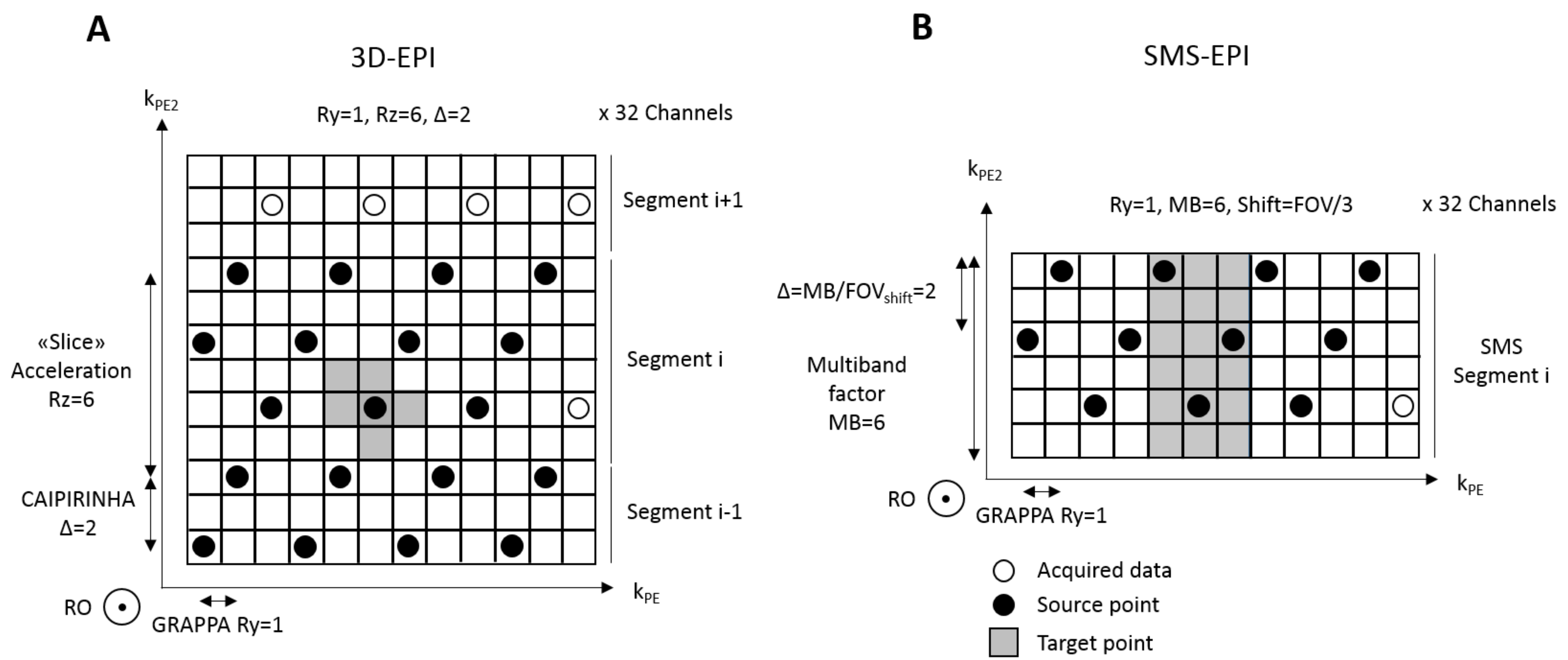
Narsude et al, MRM 2013
Narsude et al, MRM 2015

Equivalence 2D / 3D-EPI



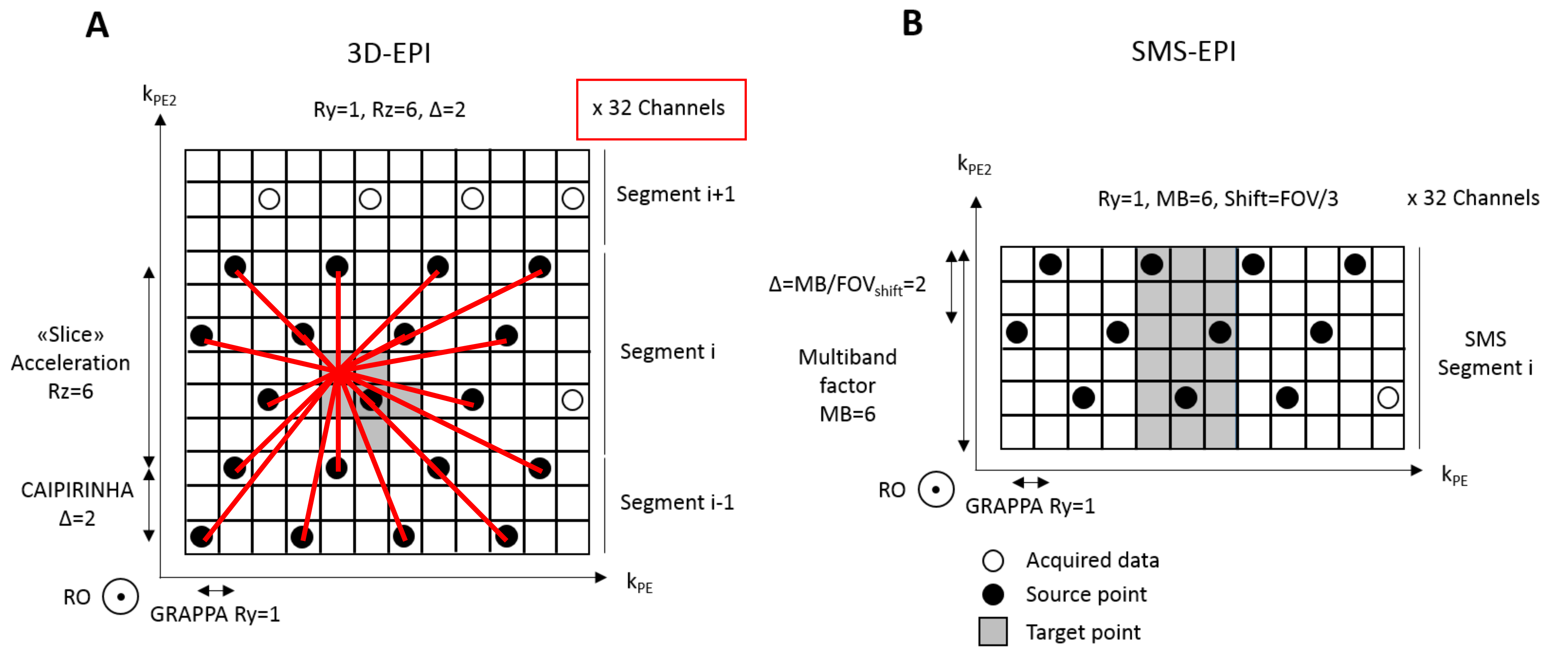
Reynaud et al, MRM 2017

Equivalence 2D / 3D-EPI



Reynaud et al, MRM 2017

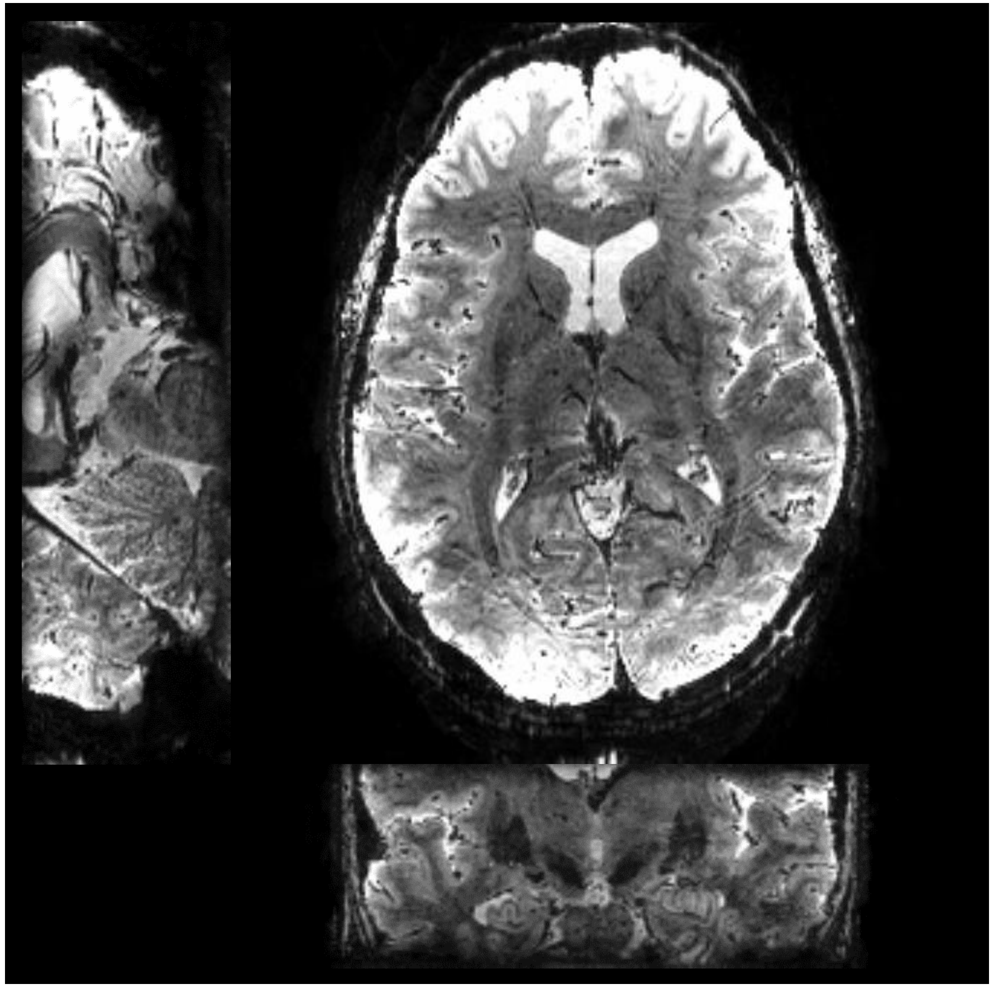
Equivalence 2D / 3D-EPI



Reynaud et al, MRM 2017

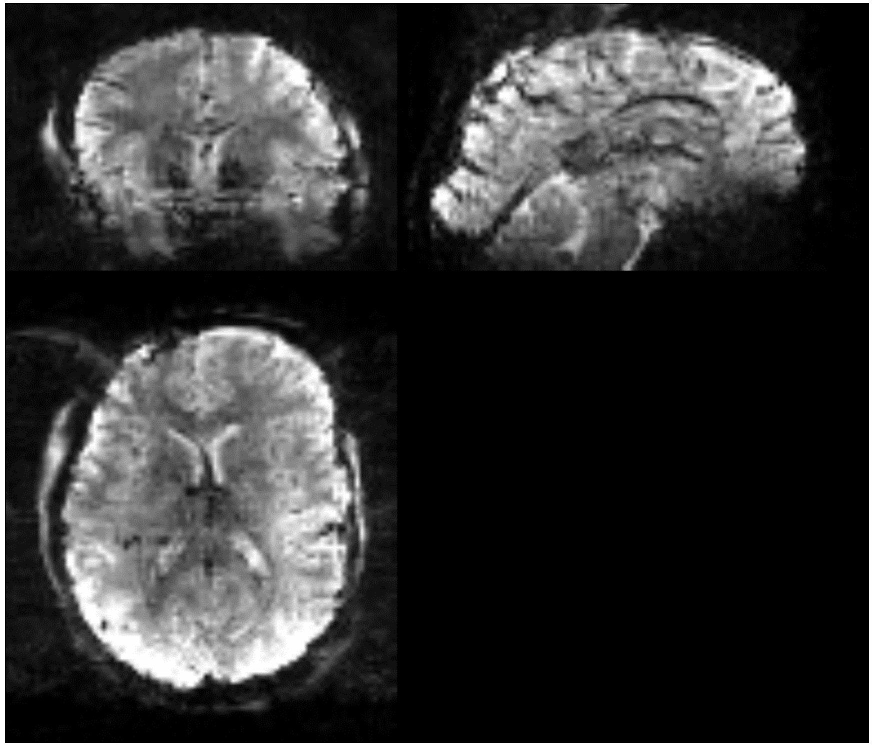
High spatial resolution 3D-EPI-CAIPI data

Matrix 256*256*72
res. 0.8mm isotropic
TR=2880ms (min 2s)
TE=27ms
$GRAPPA_{PE}$ =4
$GRAPPA_{PA}$ =2
CAIPI shift Δ=1

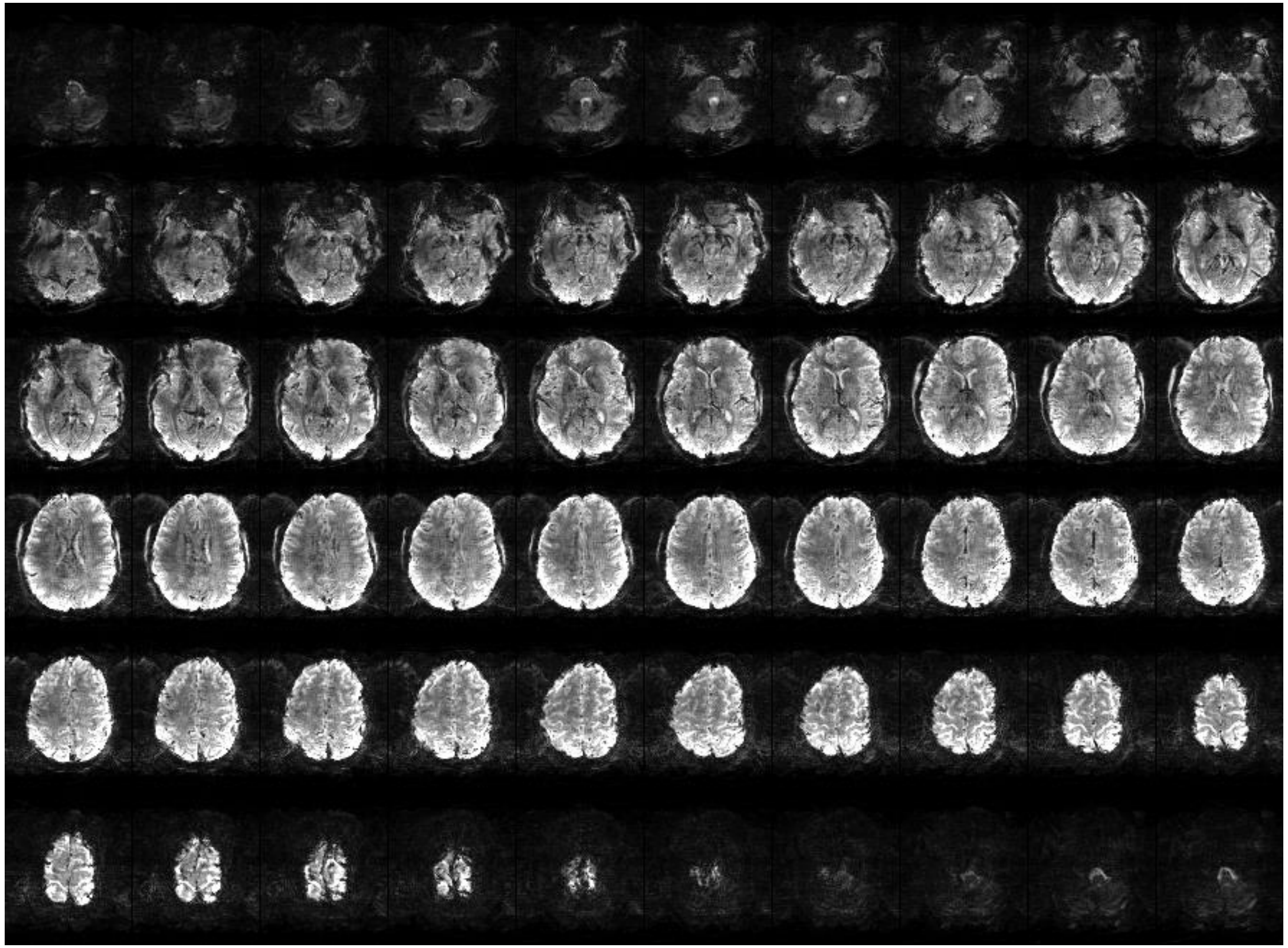


High temporal resolution 3D-EPI-CAIPI data

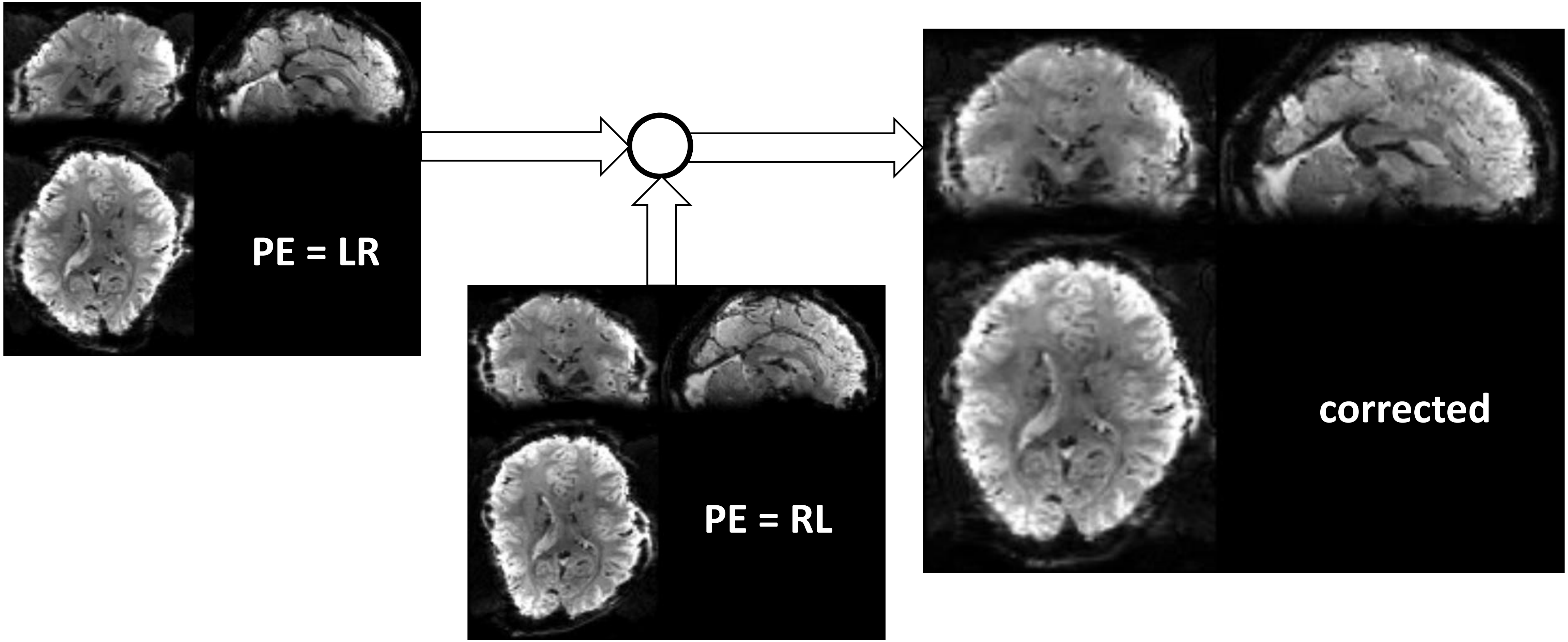
TR=399ms
(7 segments,
$TR_{segment}$=57ms)
TE=26ms
Res. 2×2×2 mm^3
matrix size 106x106x60
PPA = 1x6, Δ =2, PF_z=6/8



High temporal resolution 3D-EPI-CAIPI data



Distortion correction



3. 7T fMRI applications

RF Coil comparison

Physiological noise Characterization

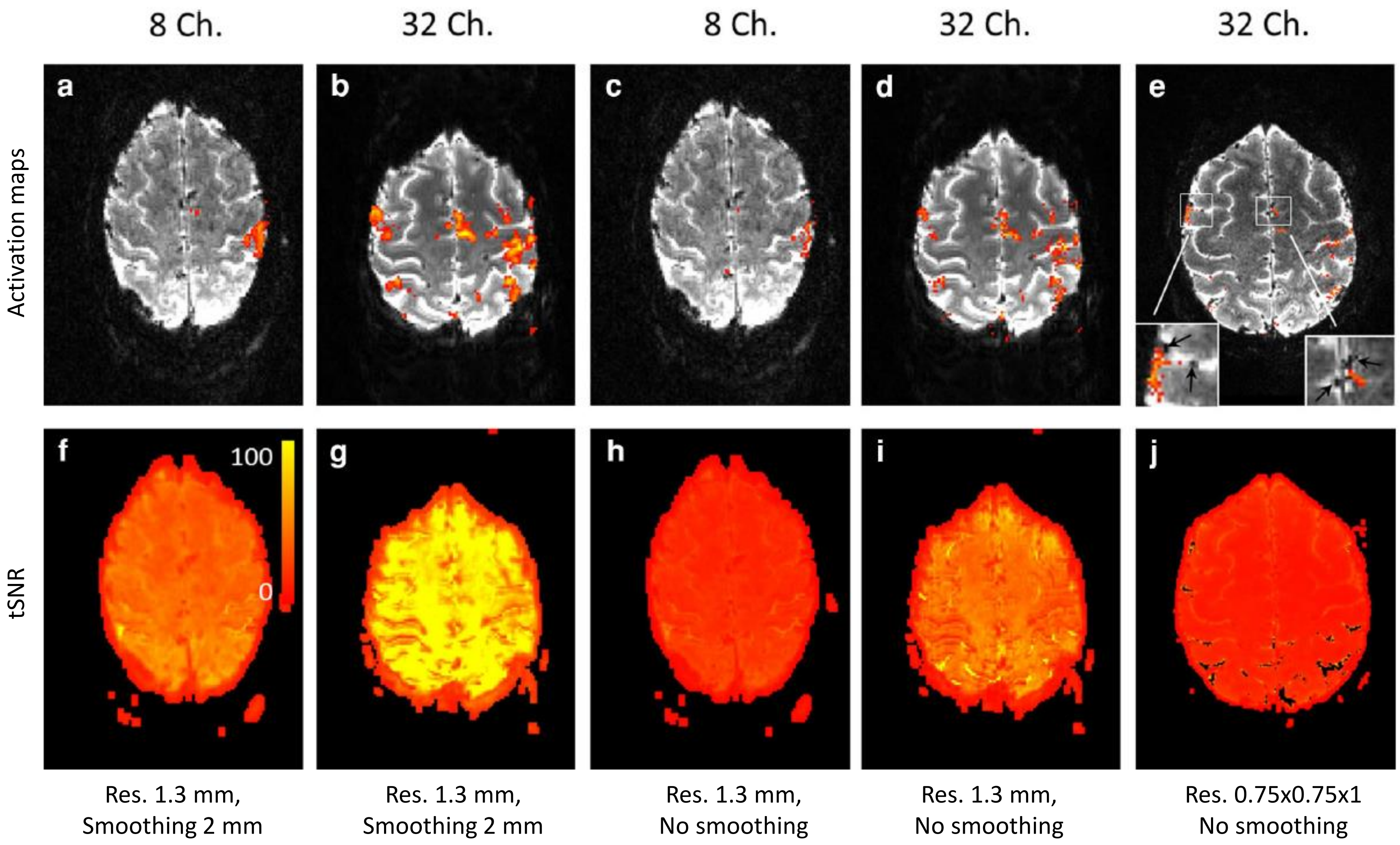
Localized fMRI

Probing the Hemodynamic Response Function (HRF)

Human Brain Mapping

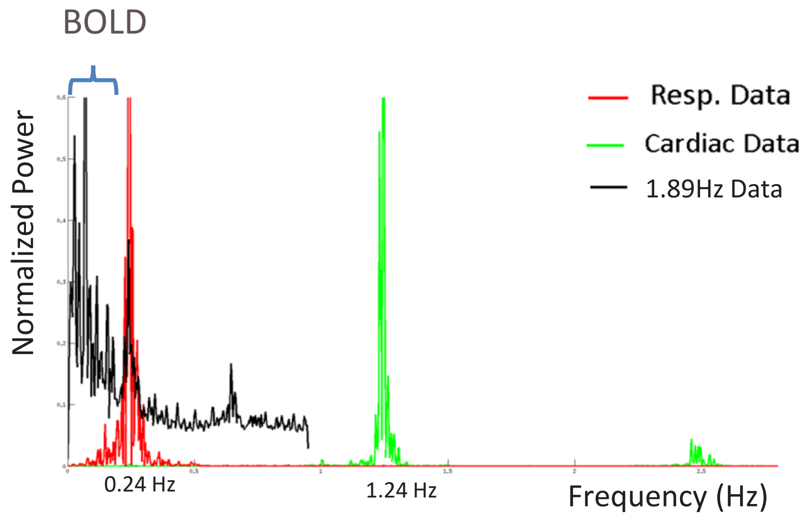
Simultaneous EEG-fMRI

8-Channel vs. 32-Channel Coil for High-Resolution fMRI at 7 T

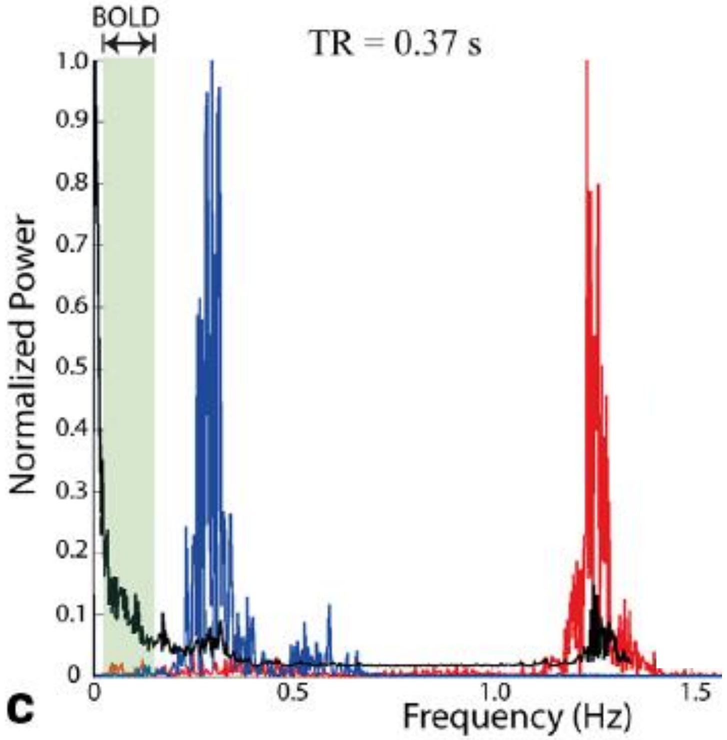


Salomon et al. Brain Topogr (2014)

Characterization of physiological noise in BOLD fMRI data

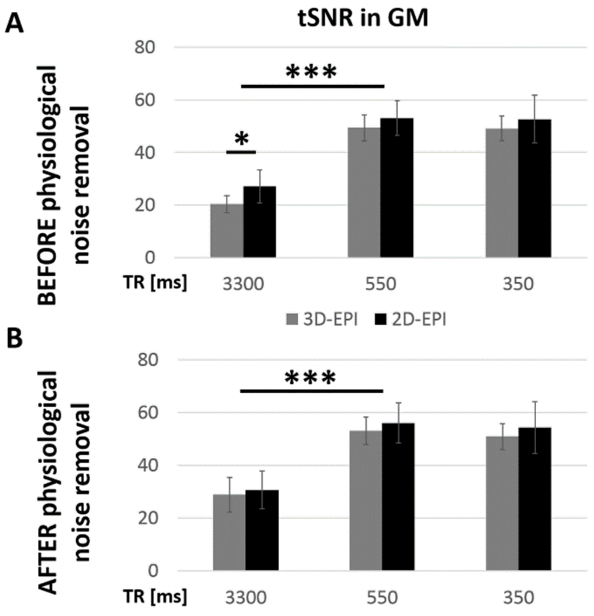


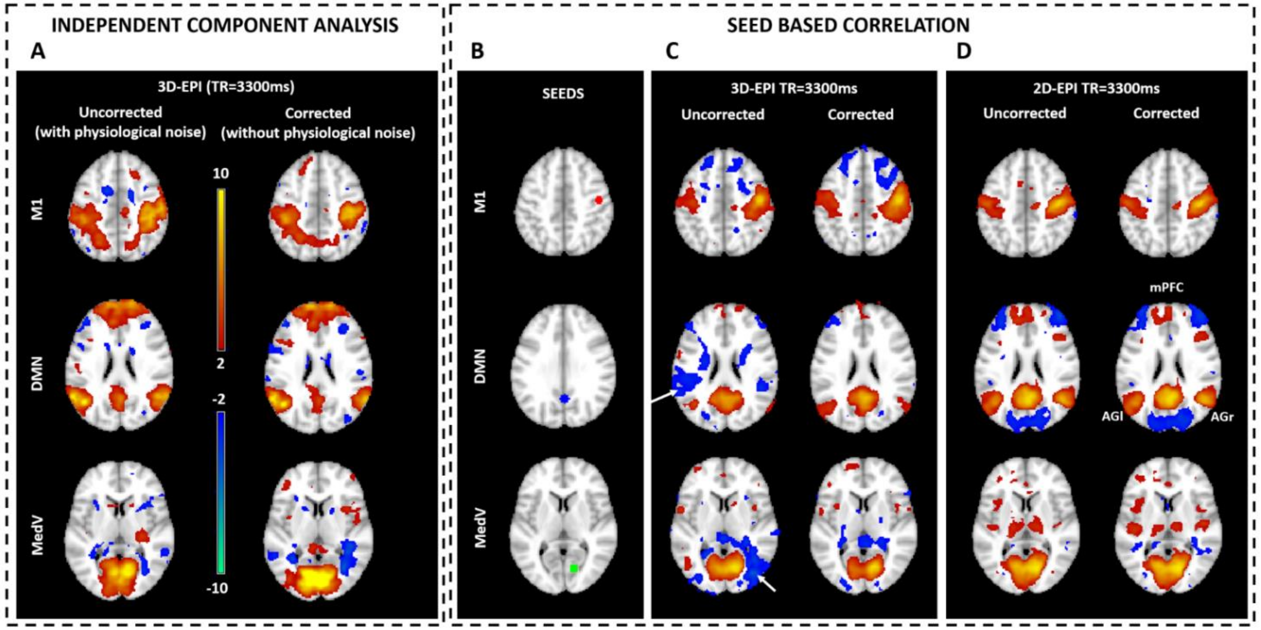
Narsude et al, MRM 2015



- Cardiac and respiratory processes have main frequencies of ~1 and ~0.3 Hz
- TR<500ms for automatic filtering of noise (including cardiac peaks)

Impact of physiological noise correction on accelerated 2D and 3D-rsfMRI data



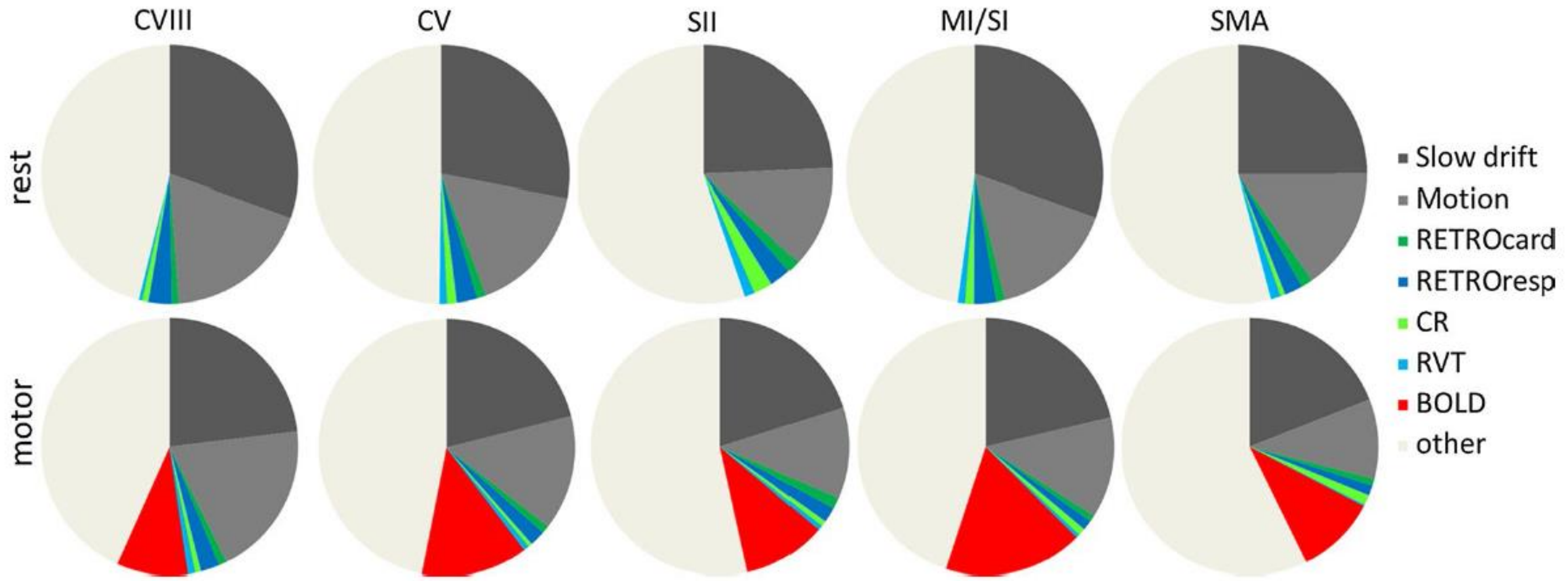


Reynaud et al, MRM 2017

- Clear interest in accelerating EPI data with similar 2D/3D performances (x6-8)
- Physiological noise affects mostly 3D-EPI (TR>3s)
- ICA more robust than SBC (or task) regarding physiological noise

Physiological noise in human cerebellum

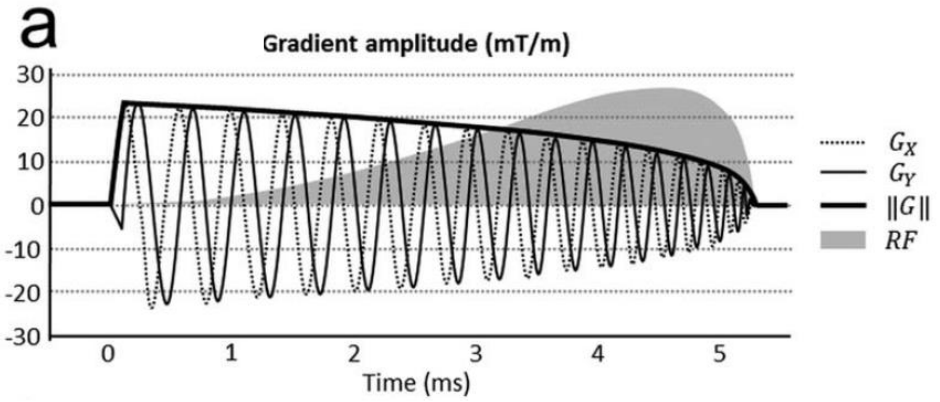
Variance per ROI

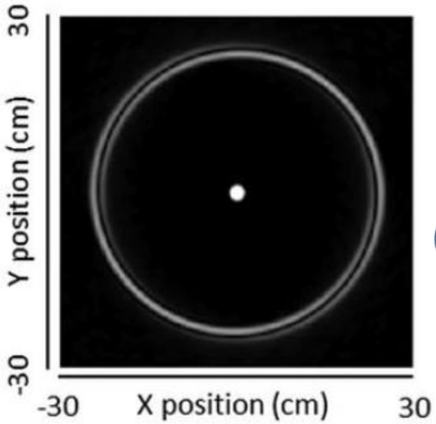


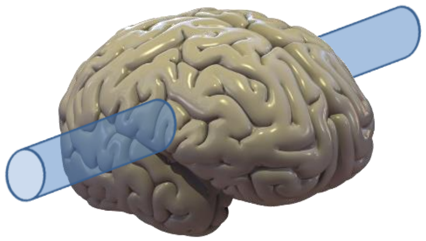
Van der Zwaag, MAGMA 2015

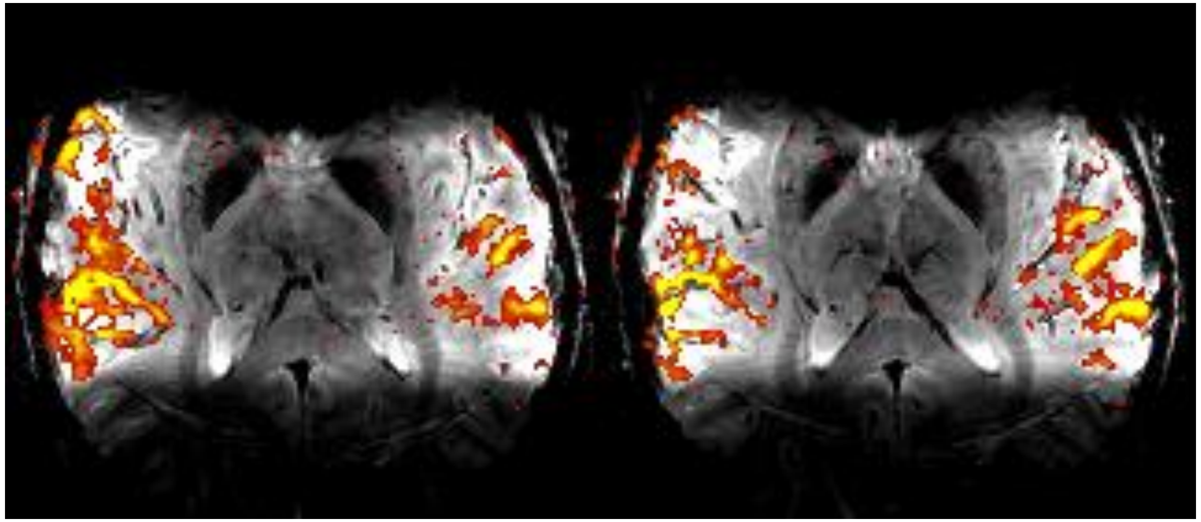
- Higher respiratory influence in cerebellum (+80% vs. motor cortex)
- Cardiac fluctuations predominant in SII

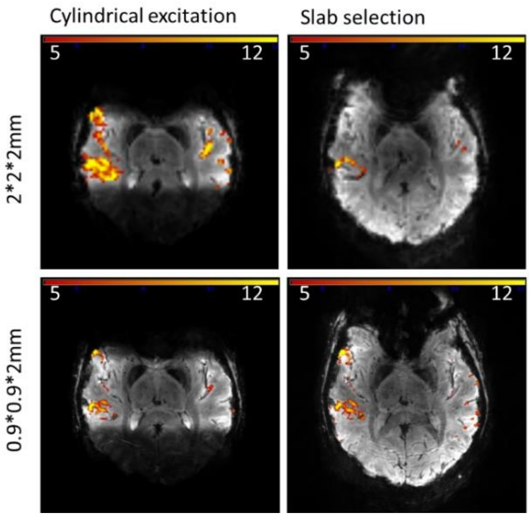
Reduced Field-of-View fMRI









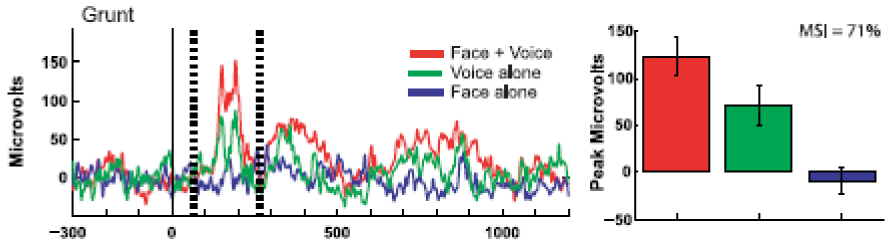


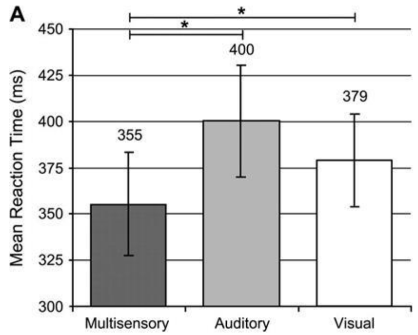
Van der Zwaag, MRM, 2017

Multisensory facilitation using fast fMRI

MRI + jittering: Martuzzi et al., 2007, Cereb Cortex

EEG: Ghazanfar et al., 2005, J. NeuroSci



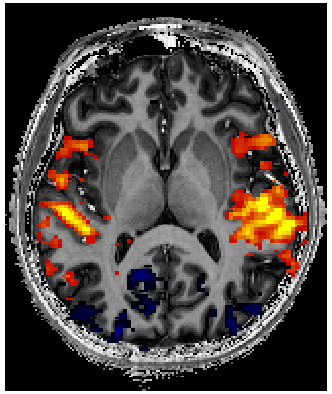


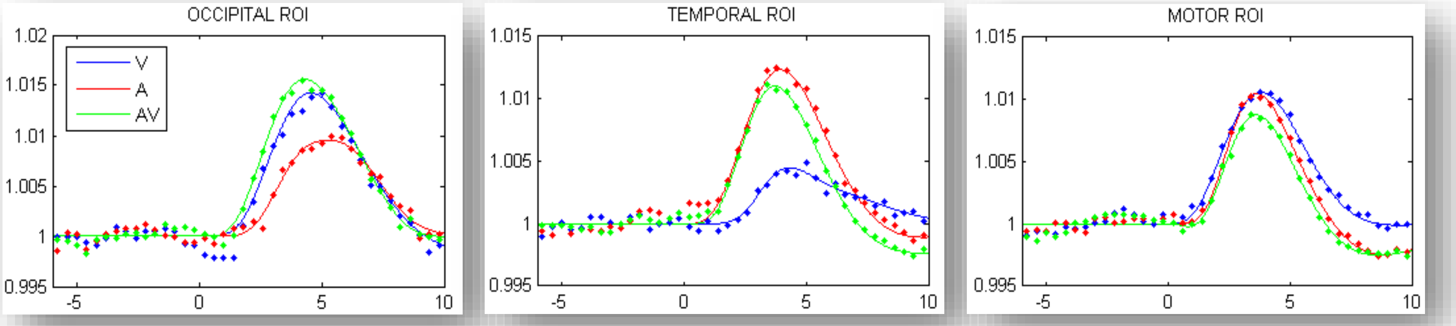
3D-EPI-CAIPI

2 mm isotropic

0.4 s volume TR

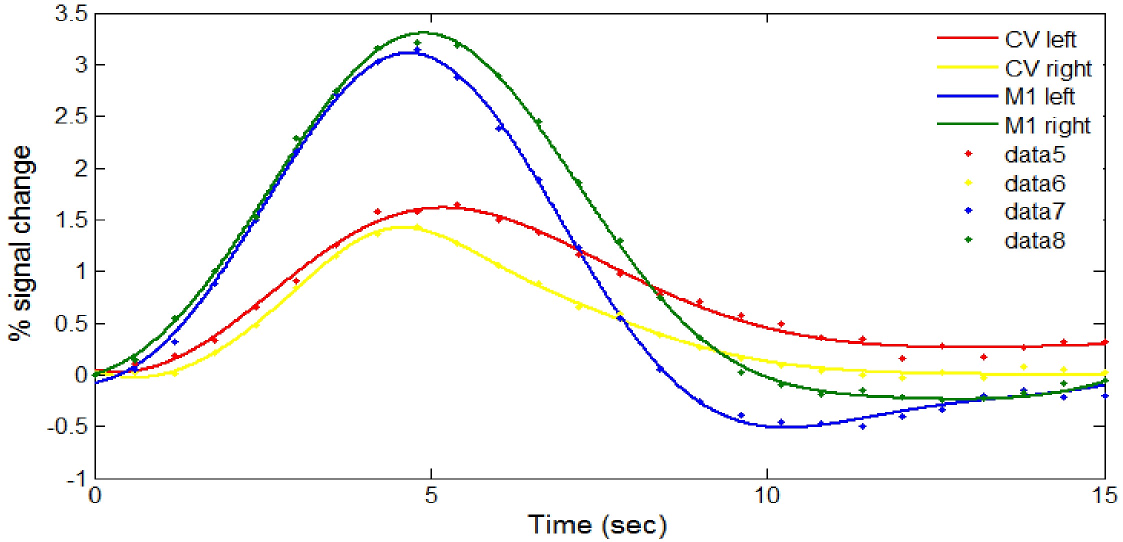
3D-EPI-CAIPI timecourses reordered relative to stimulus onset and fitted double gamma function in 3 ROIs following delivery of Visual, Auditory and Audio-Visual stimuli. (single subject data).





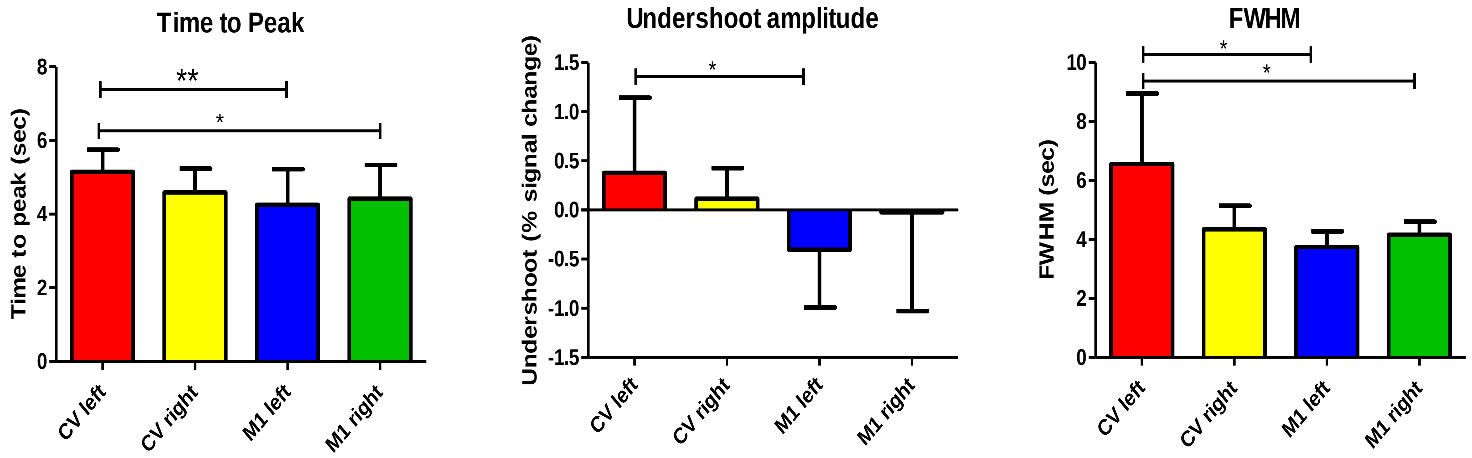
Narsude et al., 2015, HBM

HRF estimation using fast fMRI

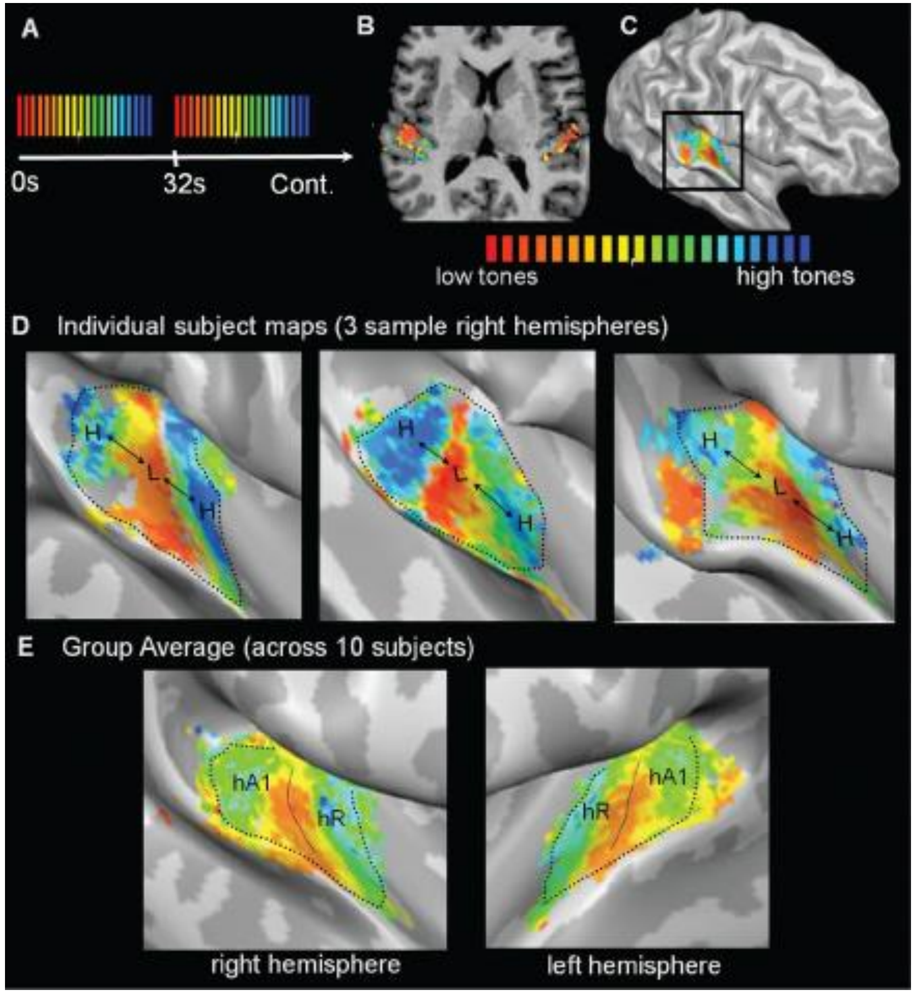


- High spatial resolution allows the comparison of different HRFs
- Increased sensibility in a GLM might be increased through the use of an optimal model function
- The physiological basis of cerebellar BOLD responses might be better understood via comparisons to the cerebral HRF.

Narsude et al., 2015, HBM



Tonotopic mapping in individual subjects



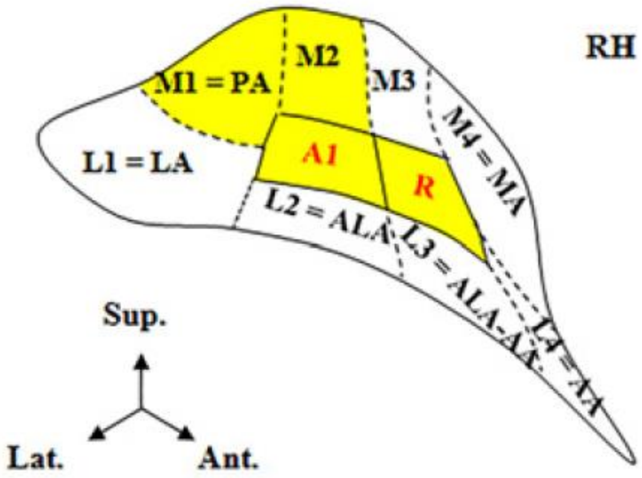
Da Costa et al., 2011, J Neuroscience

- **GRE-EPI**, 1.5 mm^3 voxel size, TR=2s
- 28 s low-to-high pitch progression
- 10 subjects

➔ **Human primary auditory cortex follows the shape of Heschl's gyrus.**

Tonotopic mapping in individual subjects

Impact of repetition on early-stage auditory areas

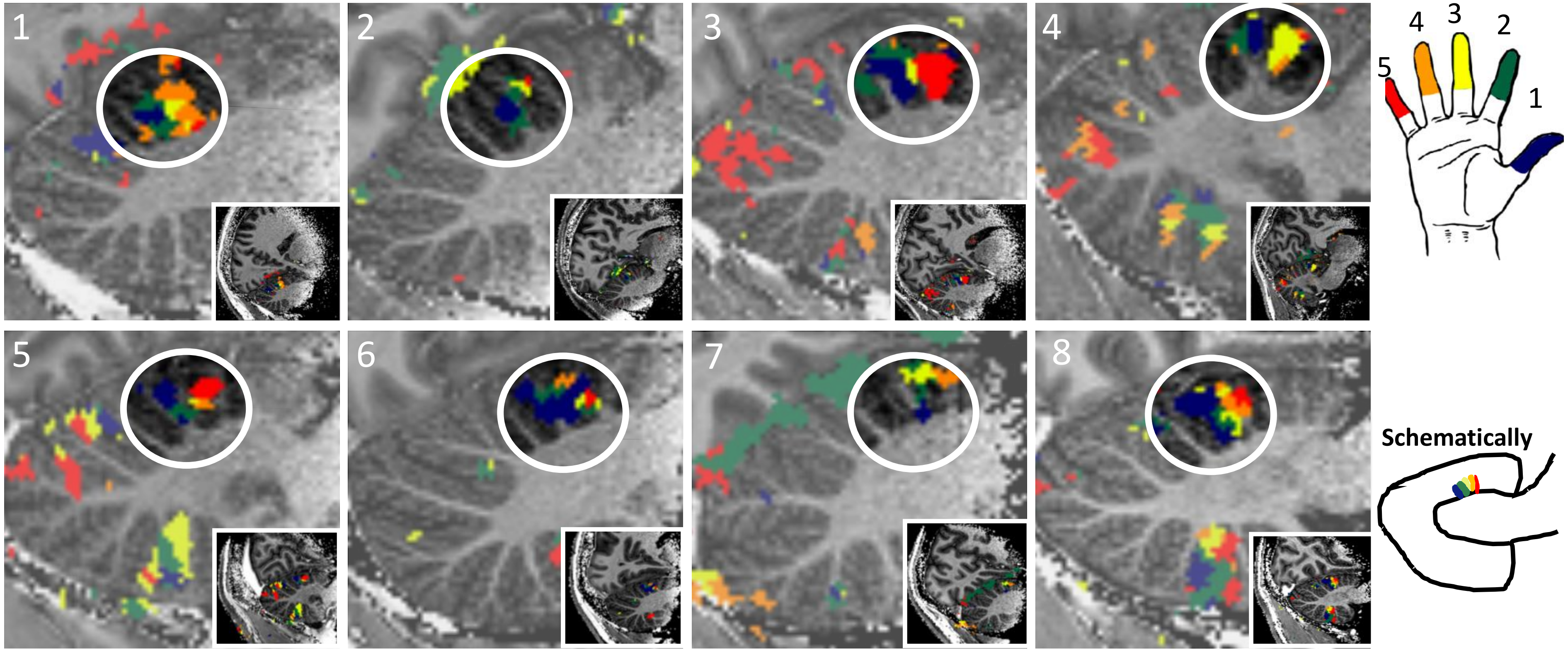


Da Costa et al., 2015, POne

- Significant repetition suppression effects within a subset of early-stage areas.
- This effect was found within the right hemisphere in primary areas A1 and R as well as two non-primary areas on the antero-medial part of the planum temporale.
- Within the left hemisphere, A1 and a non-primary area on the medial part of Heschl's gyrus are
- Thus, several, but not all early-stage auditory areas encode the meaning of environmental sounds.

Somatotopic mapping in individual subjects

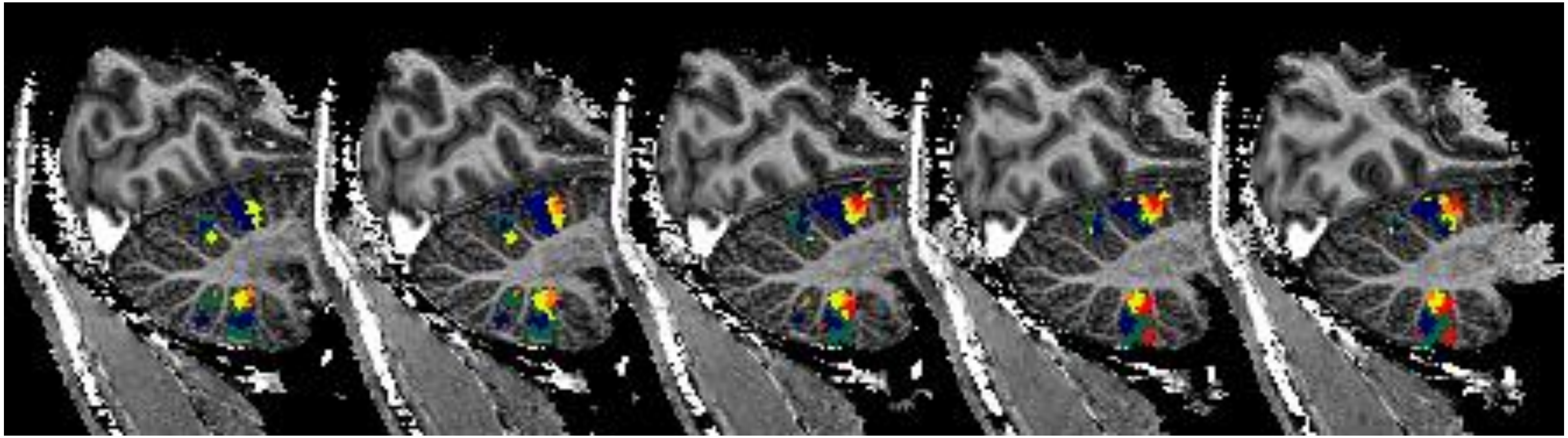
- Somatotopic patterns were consistent across slices
- **And across subjects in lobule V**



van der Zwaag et al., Neuroimage 2013.

Somatotopic mapping in individual subjects

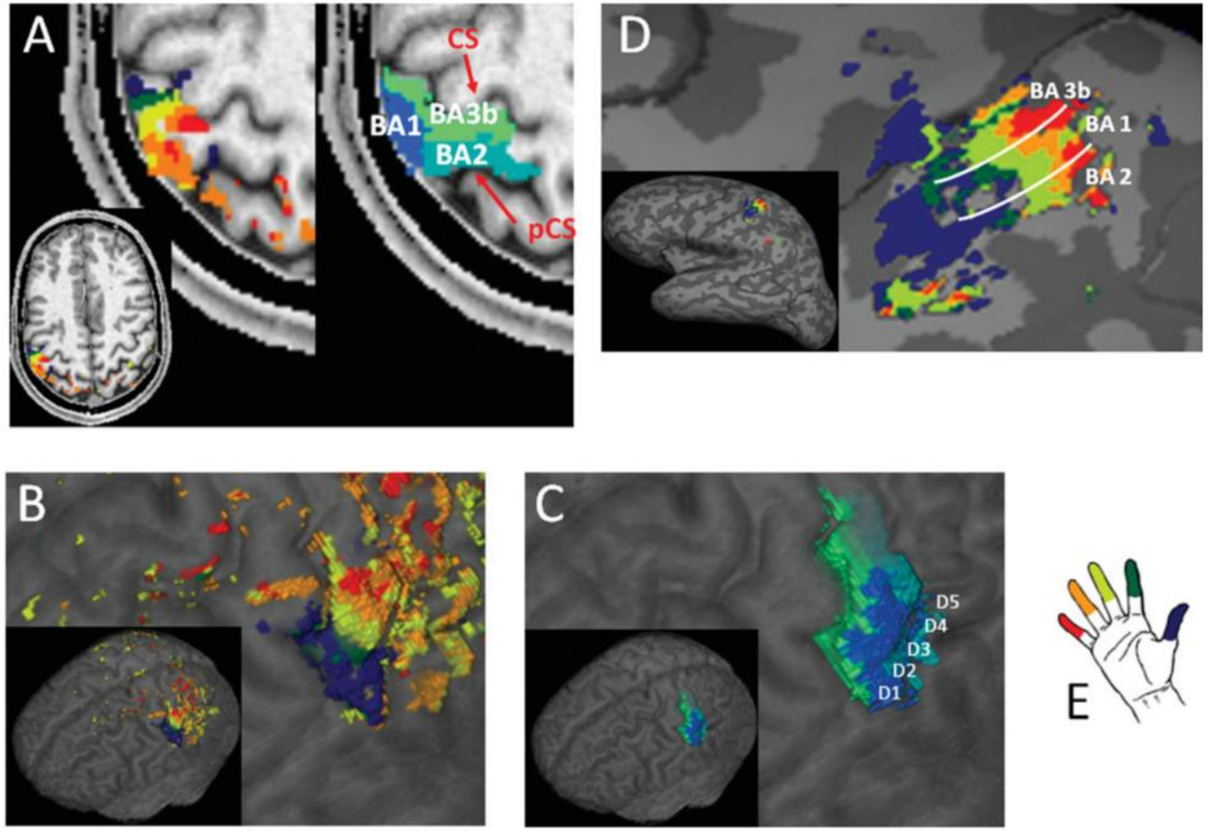
- Somatotopic patterns were consistent across slices
- **And across subjects in lobule V**



Digit labelling maps in **cerebellum** (1.2 mm^3 voxel size, TR= 2.5).

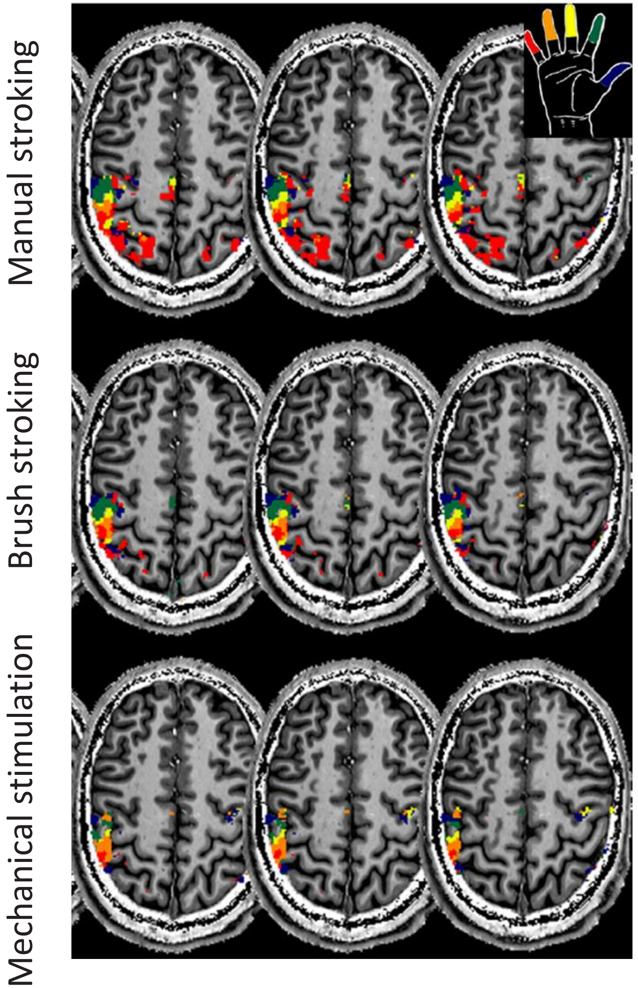
Somatotopic mapping in individual subjects

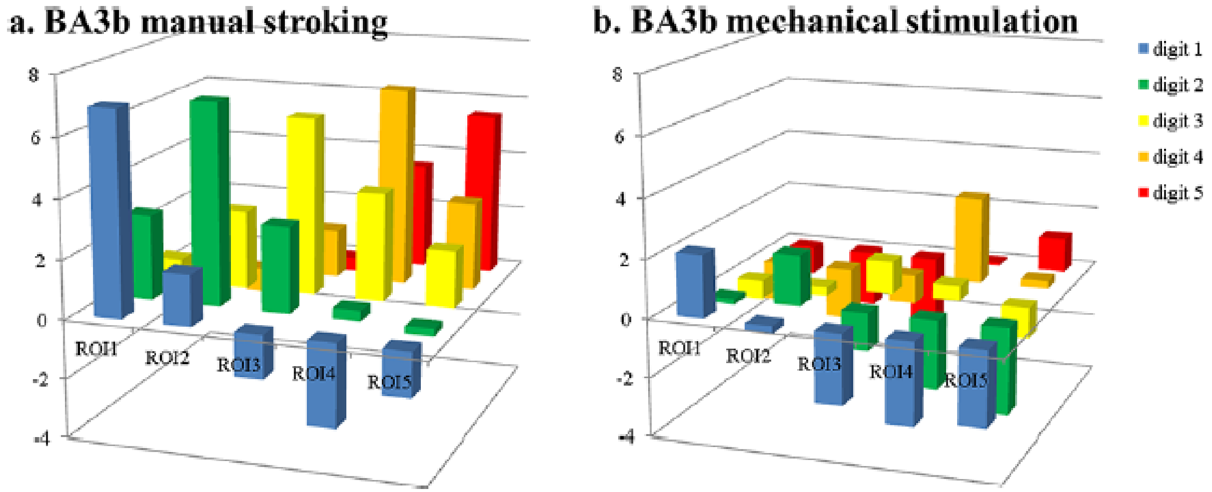
Martuzzi et al., 2014, HBM



- *Digit labelling maps* in **somatosensory cortex**
- 1.3 mm^3 voxel size, TR=2.5 s

Comparison of Somatosensory Touch Stimuli Using 7 Tesla fMRI

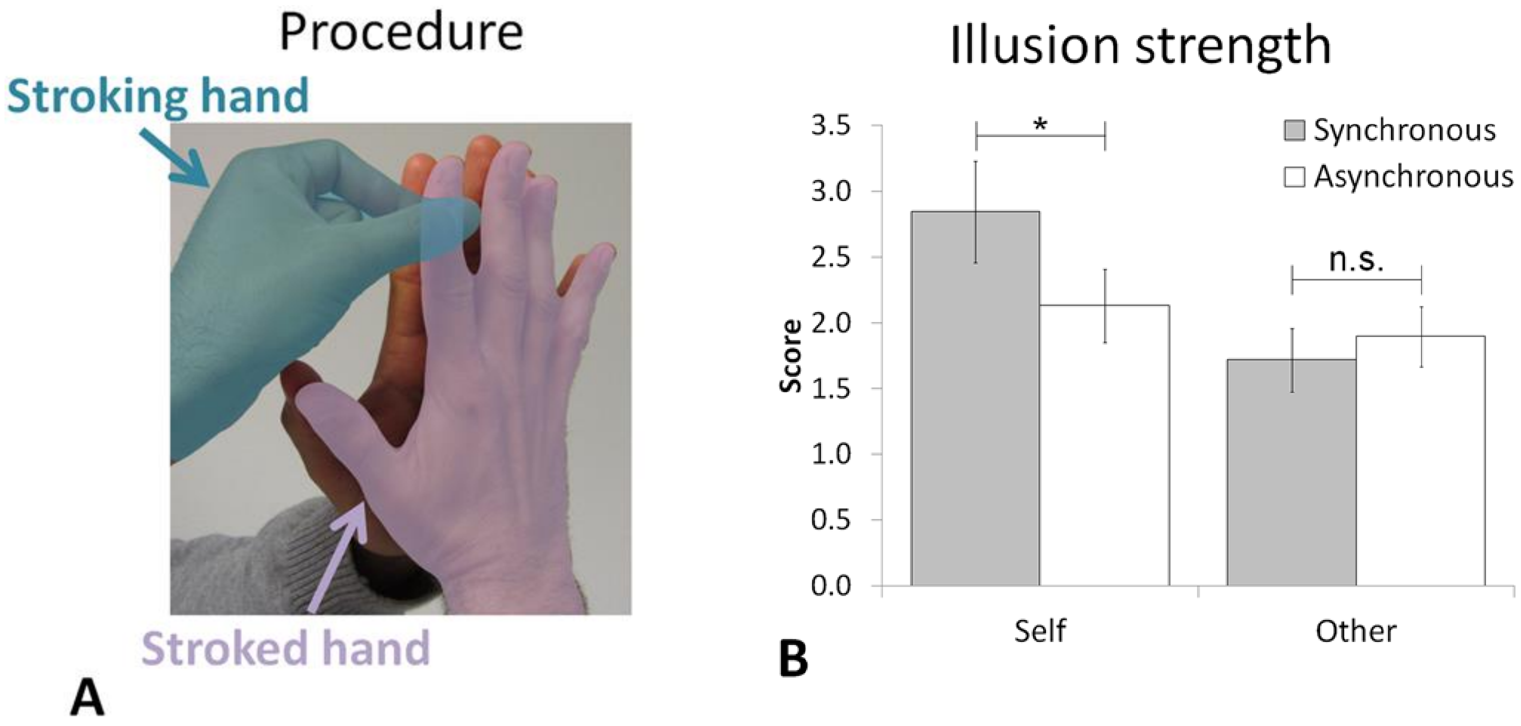




van der Zwaag et al., 2015, POne.

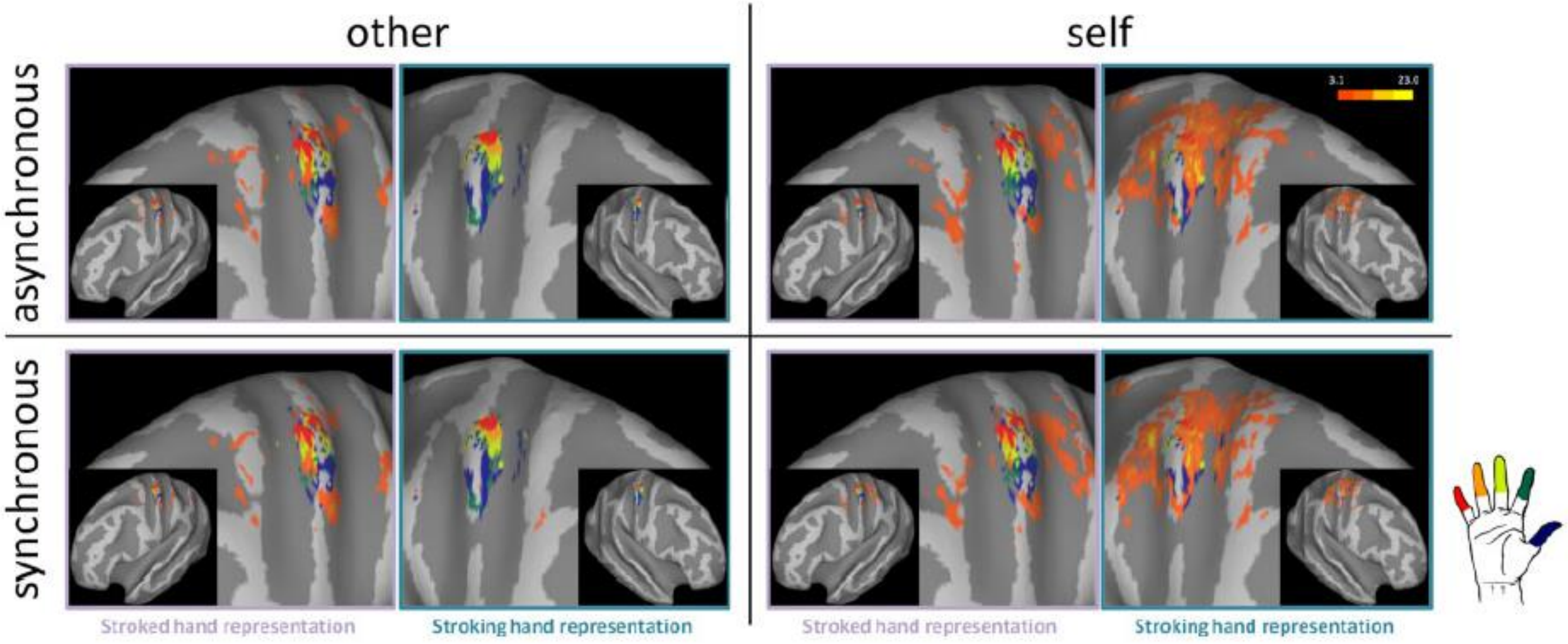
Investigation of Broadmann areas vs. body ownership

- Simple tactile stimulations can create a mismatch between where the touch is applied and where it is predicted (e.g. by crossing the hands or by interposing another person's finger) and induce ownership for a fake hand: *Numbness illusion (NI).*



Martuzzi et al, Soc Cogn Affect Neurosci (2015)

Investigation of Broadmann areas vs. body ownership



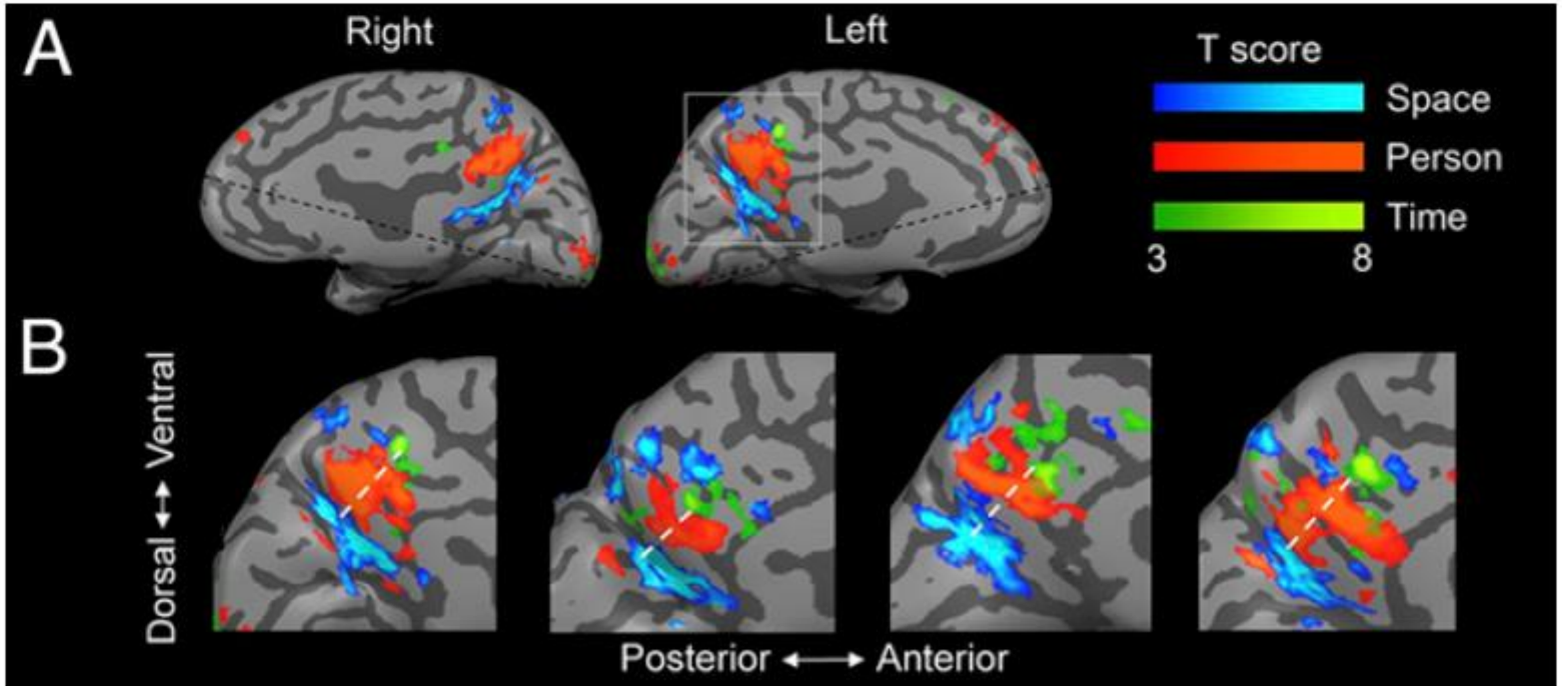
Martuzzi et al, Soc Cogn Affect Neurosci (2015)

- ➔ Modulation of the activity of the BA 2 representation of the stroked hand and of the BA 1 representation of the stroking hand.
- ➔ The high degree of somatosensory specialization in S1 extends to bodily self-consciousness.

Brain system for mental orientation in space, time, and person

1.7 mm^3 voxel size, TR=2.5 s

Peer M, Salomon R et al, PNAS, 2015



Cortical activation related to orientation in space, time, and person in a precisely localized set of structures in the precuneus, inferior parietal, and medial frontal cortex.

Brain system for mental orientation in space, time, and person

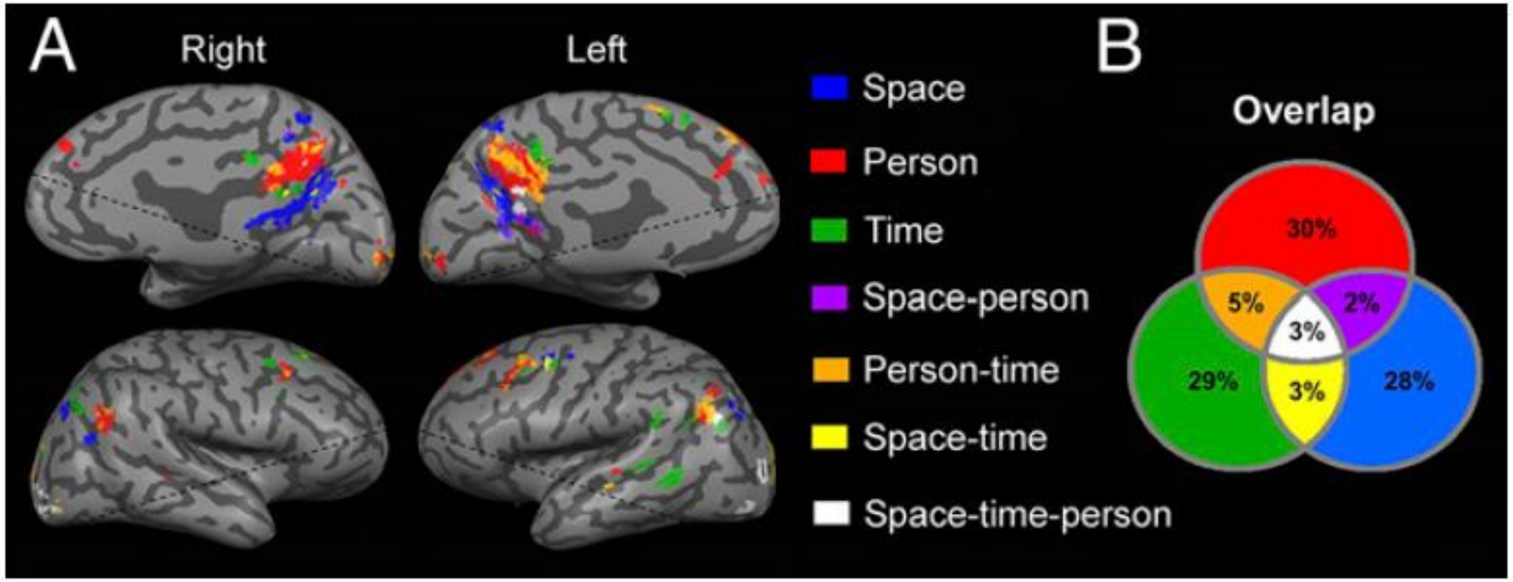
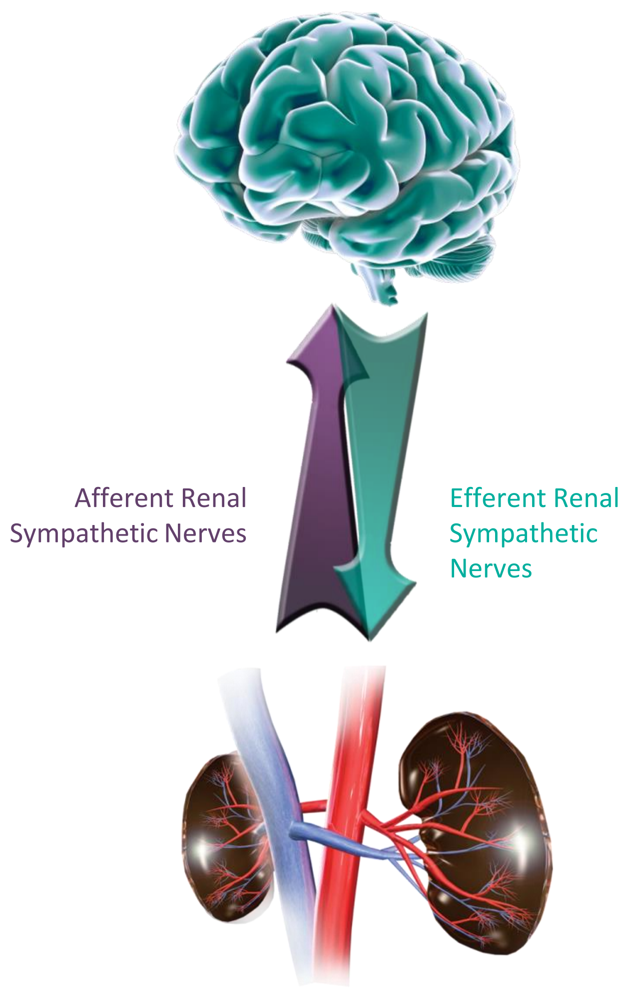


Fig. 3. Overlap between activations in the space, time, and person domains. (*A*) Overall orientation-related activity in a representative subject, identified by contrasting activity between each orientation domain and the lexical control task, showing overlap between regions ($P < 0.05$, FDR-corrected, cluster size >20 voxels). (*B*) Group average of the percent of overlap between active voxels in each orientation domain, demonstrating a partial overlap between domains (for group-level results, see Figs. S3*B* and S4*B*).

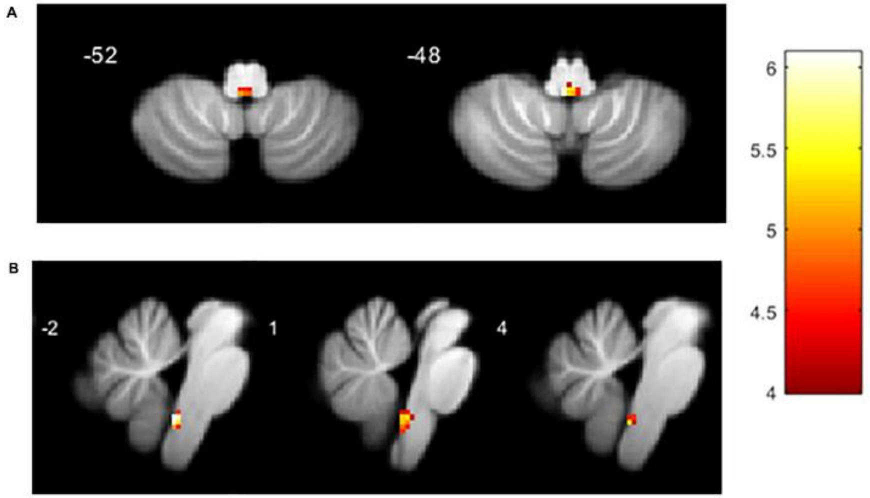
Sympathetic Nerve Impact on Blood Pressure



Hypothesis:

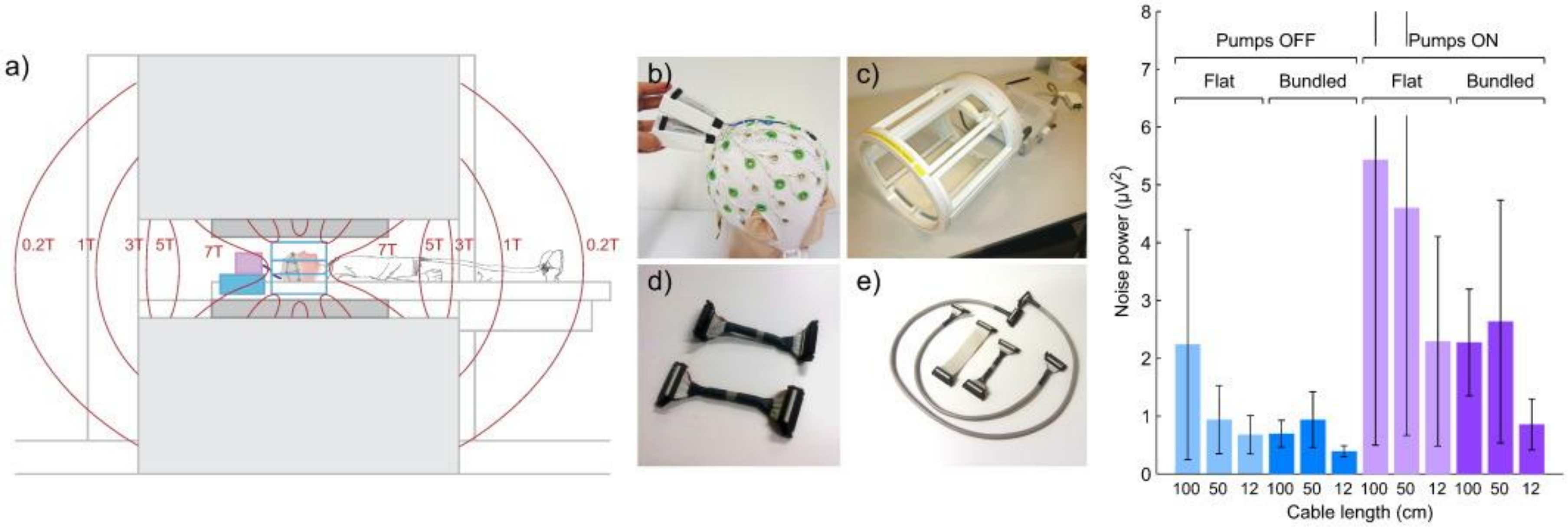
A stress test which increases BP should change the activity of the medulla region of the brainstem

Brainstem analysis:



Hendricks-Balk et al, Frontiers in Neuroscience 2020

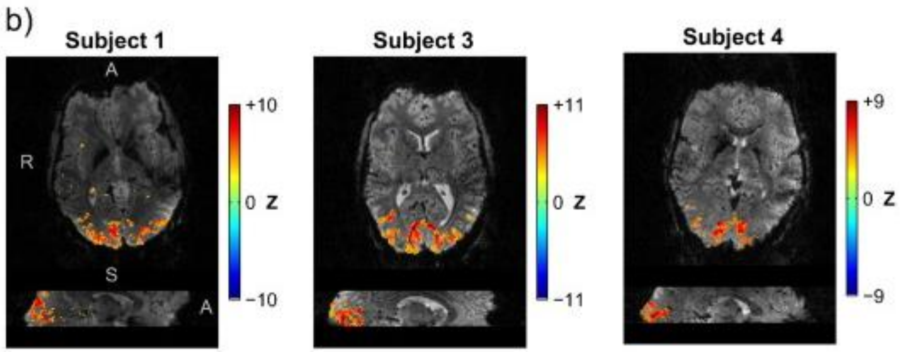
Simultaneous EEG-fMRI at 7 T: Artifact prevention and safety assessment

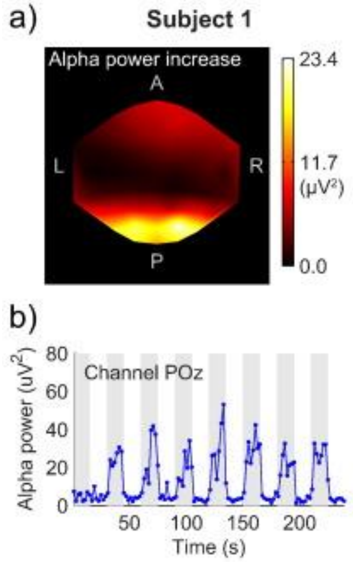


- EEG setup optimization can result in significant noise reductions for EEG recordings.
- Optimized EEG–fMRI recordings can be safely performed in humans at ultra-high field.

Jorge et al, Neuroimage 2015

Simultaneous EEG-fMRI at 7 T: Artifact prevention and safety assessment



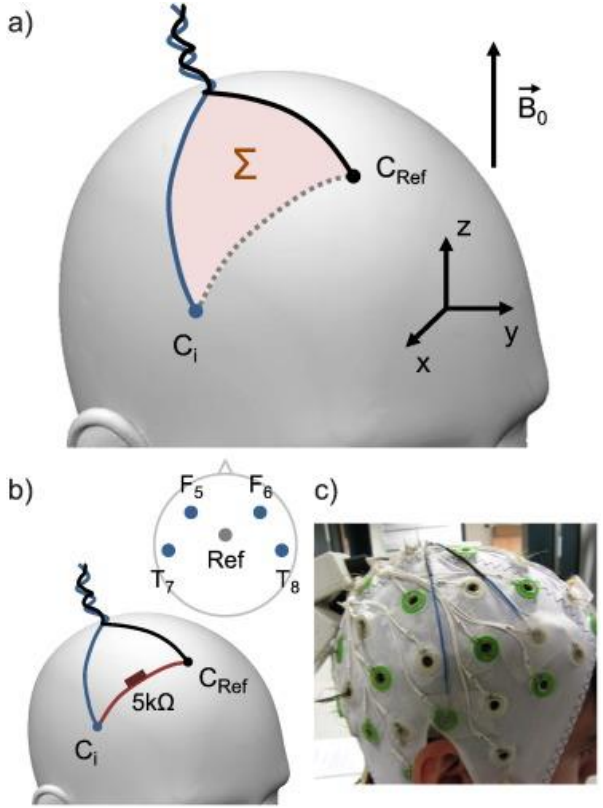


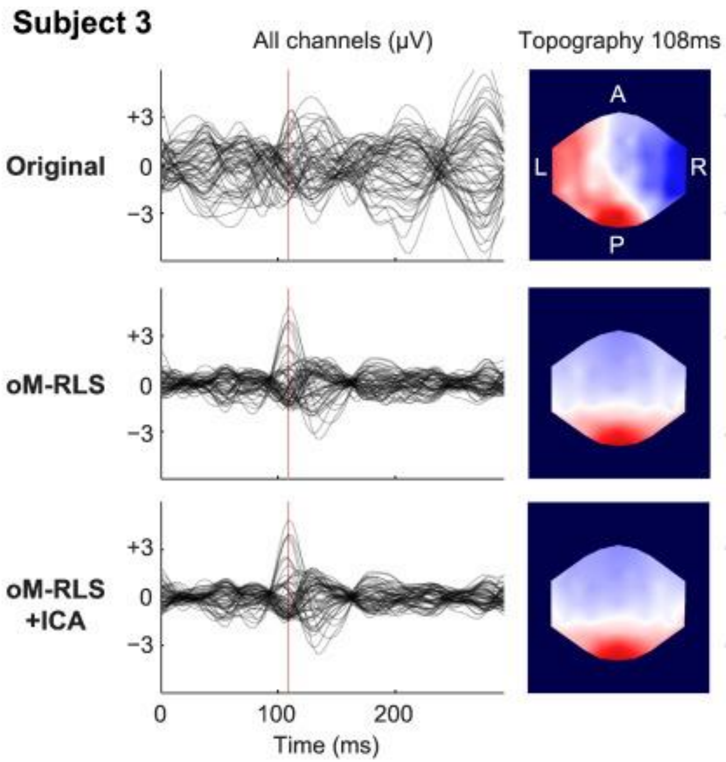
- Alpha-wave modulations and VEPs can be measured with adequate sensitivity.
- High quality BOLD-sensitive MR images can be obtained from the visual cortex.

Jorge et al, Neuroimage 2015

Simultaneous EEG-fMRI at 7 T: Detection and reduction of EEG artifacts due to head motion

Jorge et al, Neuroimage 2015 (2)



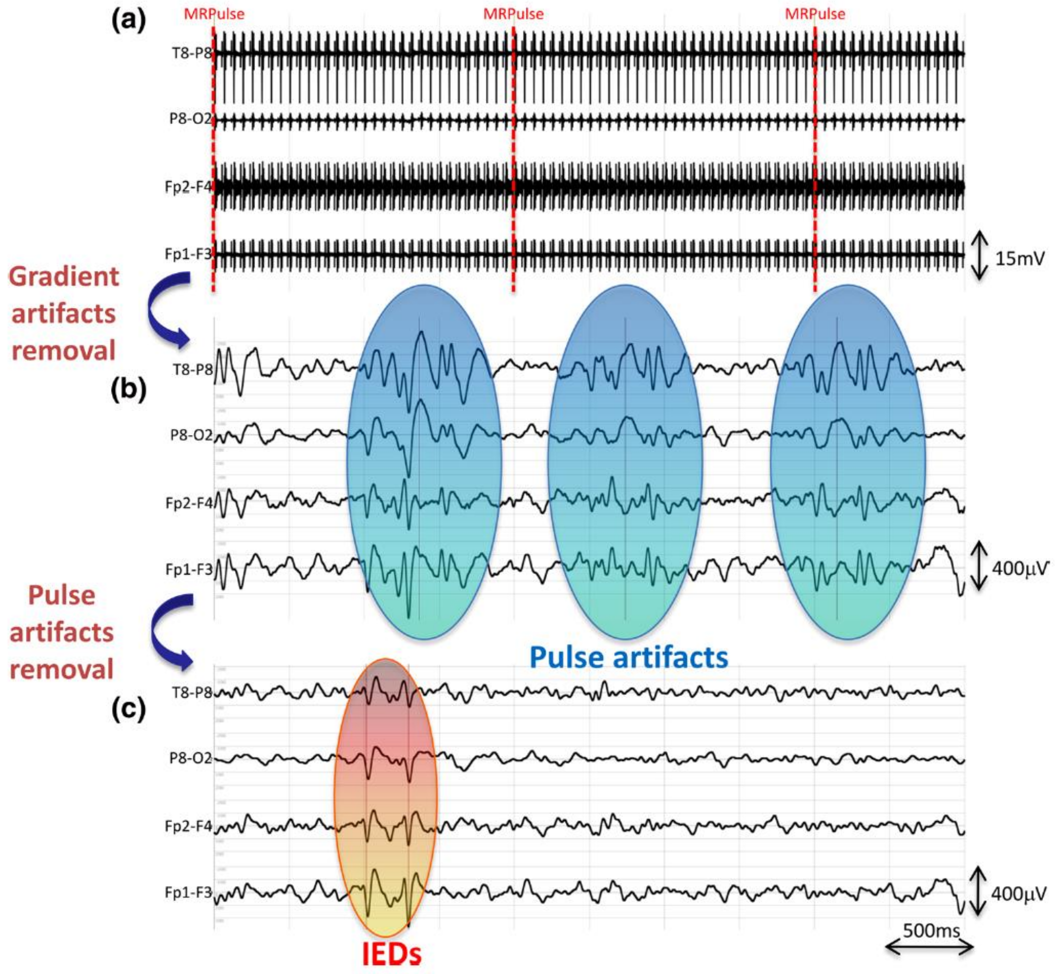


Four electrodes are non-permanently adapted to record only magnetic induction effects.

Combined with ICA, 74% power reduction and an 86% increase in trial consistency.

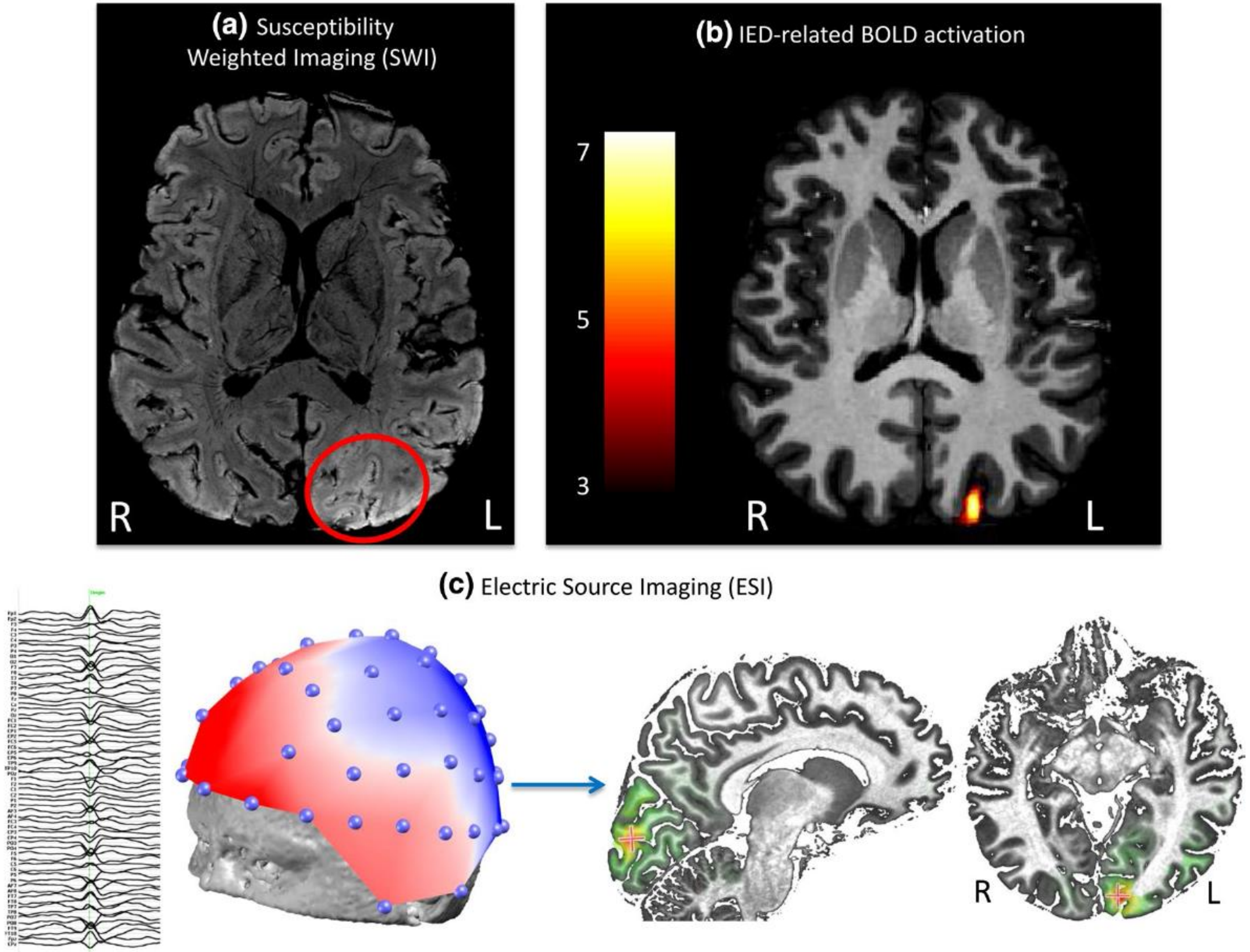
Pre-surgical mapping on epileptic patients

Grouiller et al, MAGMA 2016

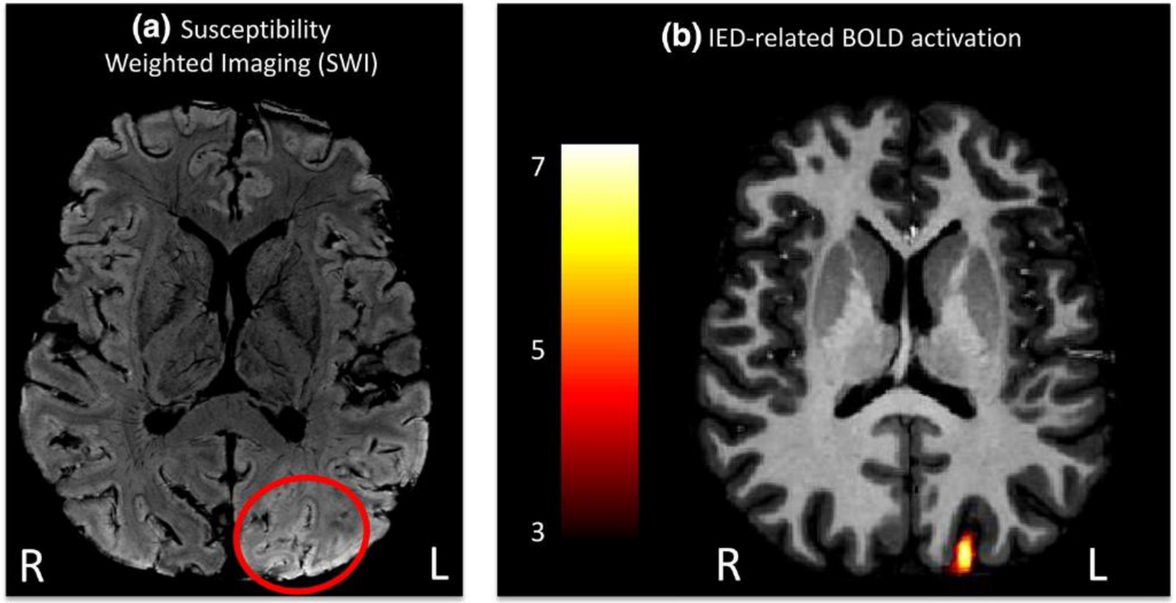


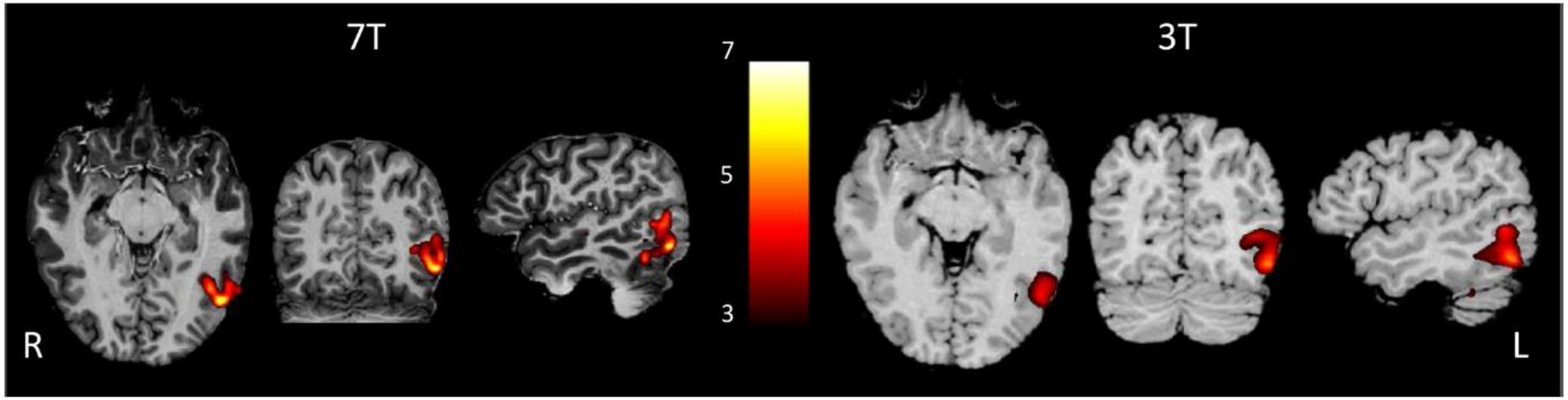
Pre-surgical mapping on epileptic patients

Grouiller et al, MAGMA 2016



Pre-surgical mapping on epileptic patients



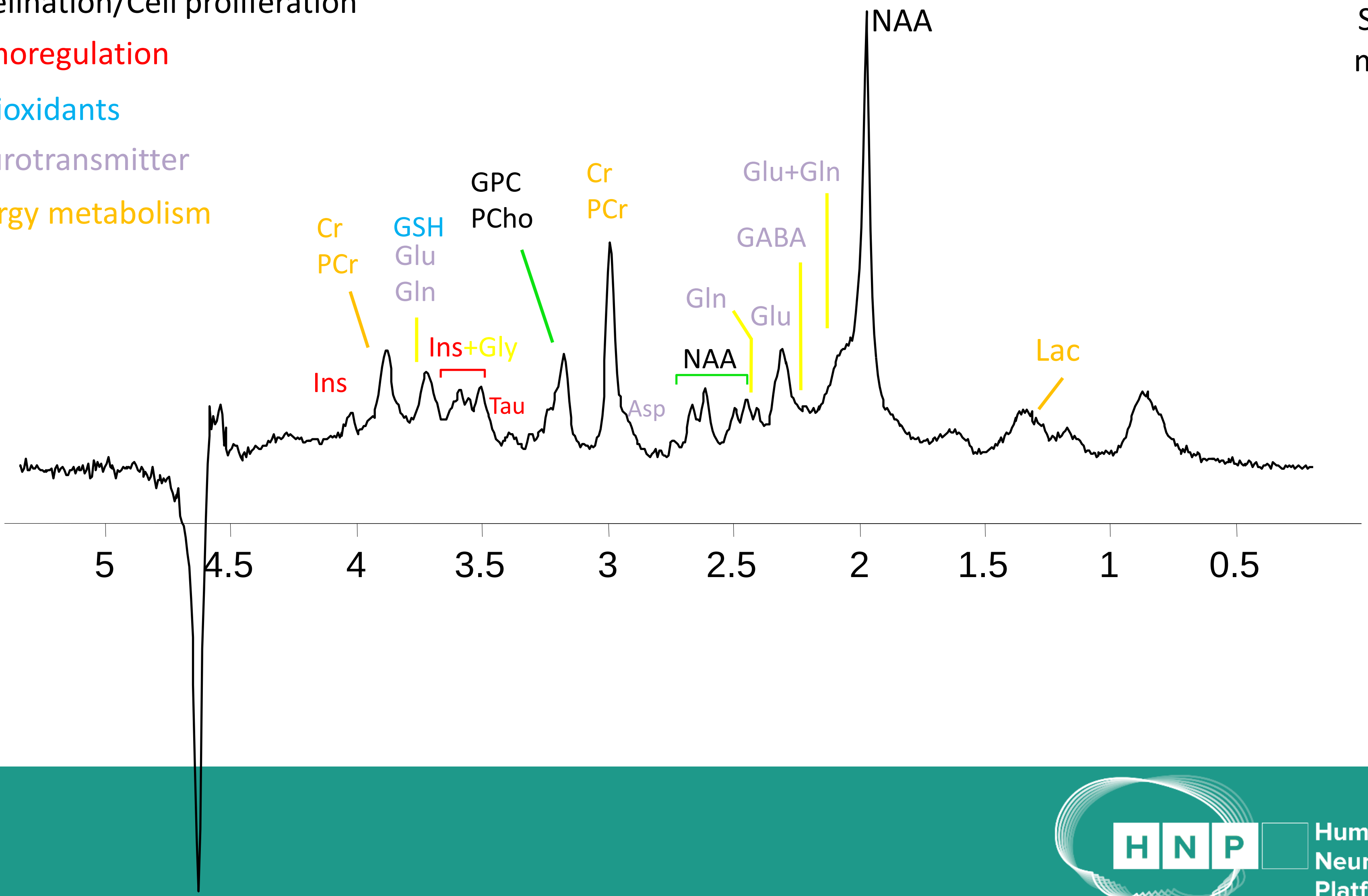


Grouiller et al, MAGMA 2016

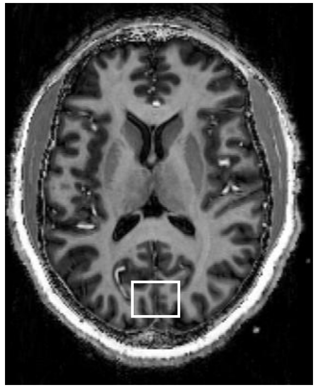
Human Neuroscience Platform
campus biotech
Fondation Campus Biotech Geneva

4. fMRS - Single voxel ^{1}H MRS at 7T

Myelination/Cell proliferation
Osmoregulation
Antioxidants
Neurotransmitter
Energy metabolism

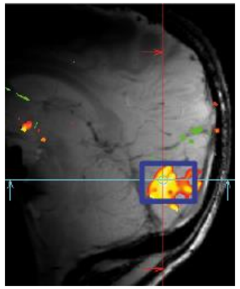


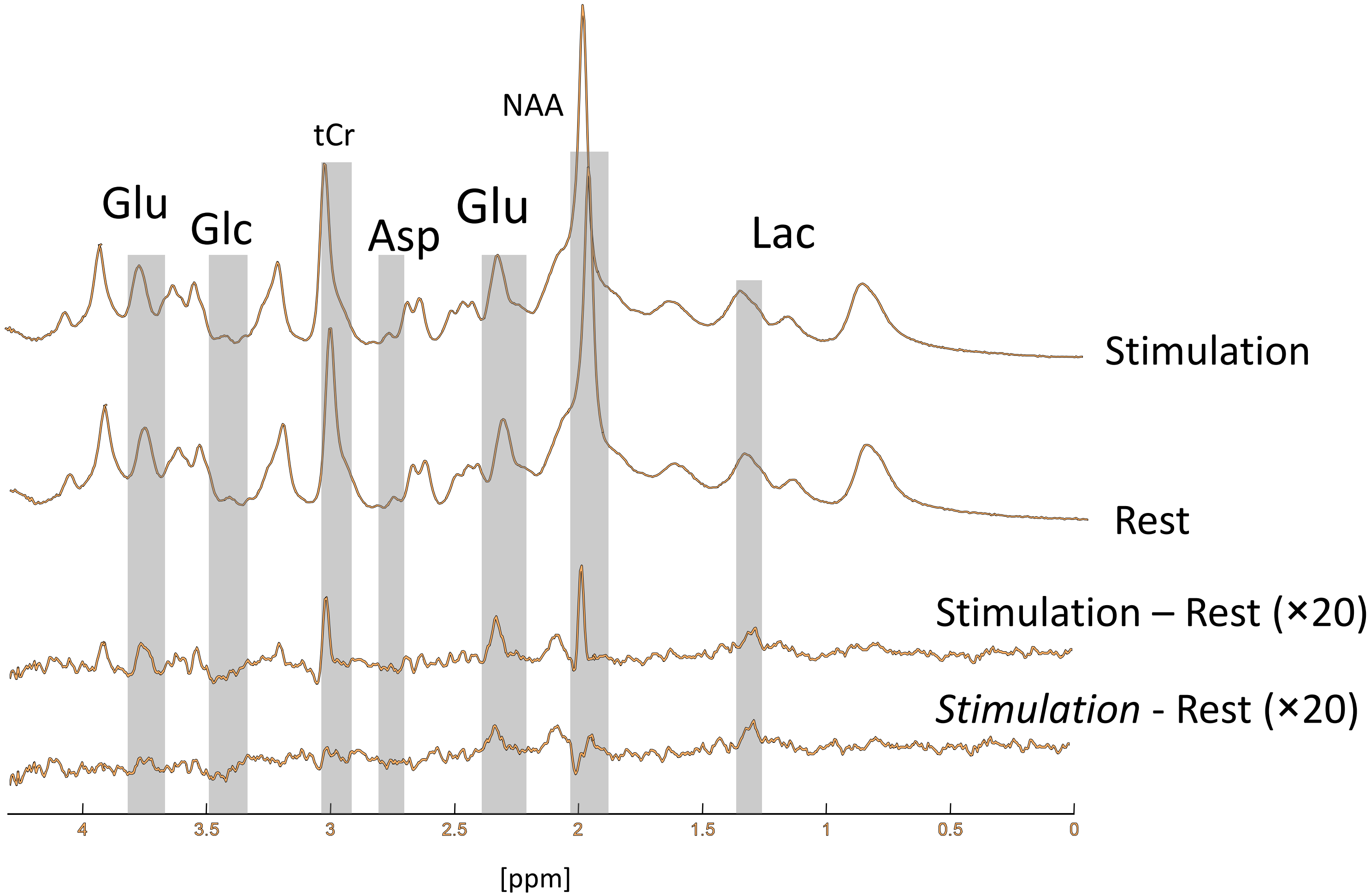
Human occipital lobe (VOI 20×15×20 mm^3) at 7T SPECIAL sequence , TE = 6 ms, NA=32, 3min scanning time.



Functional MRS during visual stimulation

- 6 Subjects
- 480 (6×80) scans
- *line broadening* = 0.4Hz





<u>Changes:</u>

[Glu]= 0.28 ± 0.01µmol/g

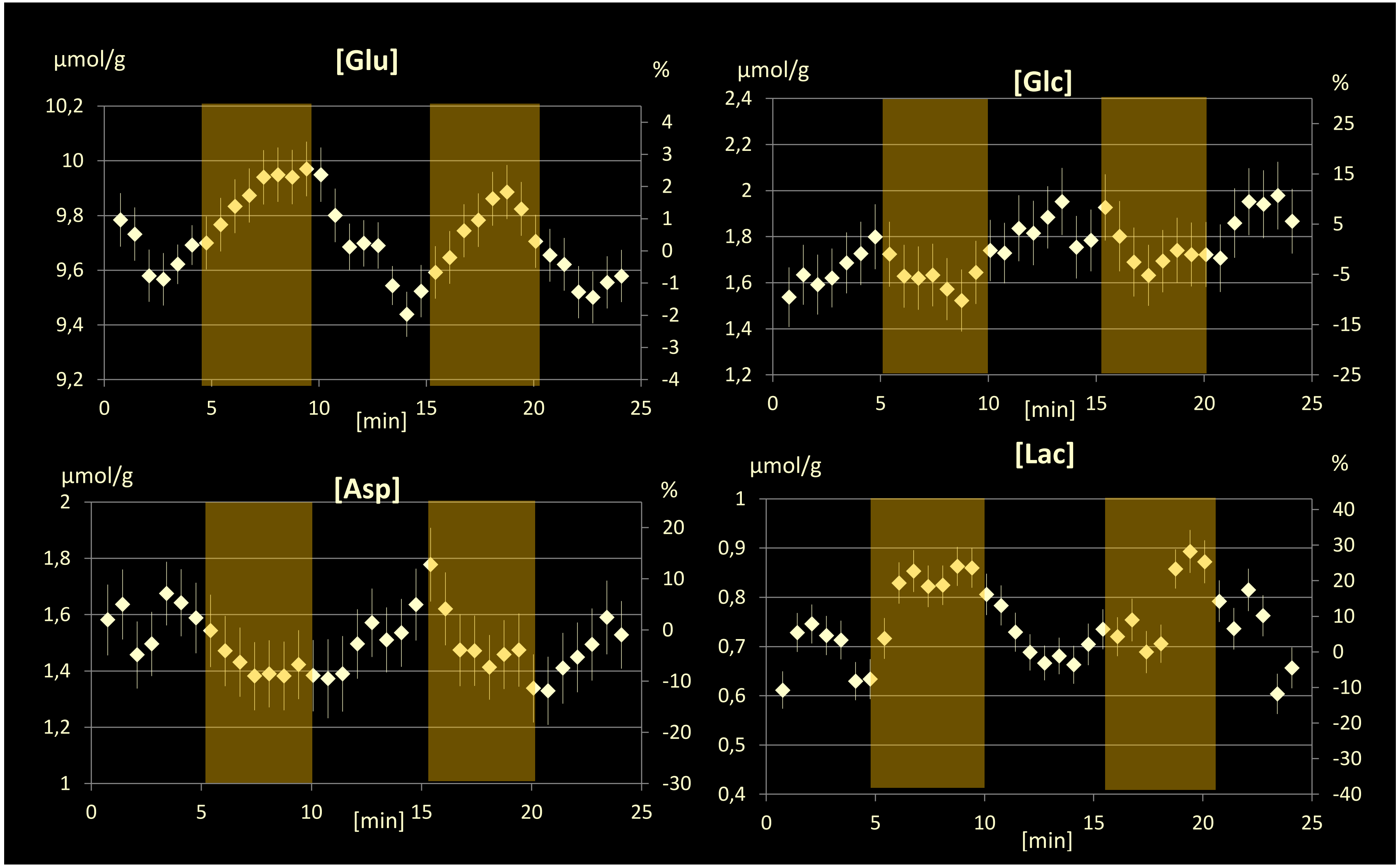
[Lac]= 0.18 ± 0.01µmol/g

[Glc]= -0.17 ± 0.01µmol/g

[Asp]= -0.11 ± 0.02µmol/g

Schaller et al. 2013, J Neurosci Res

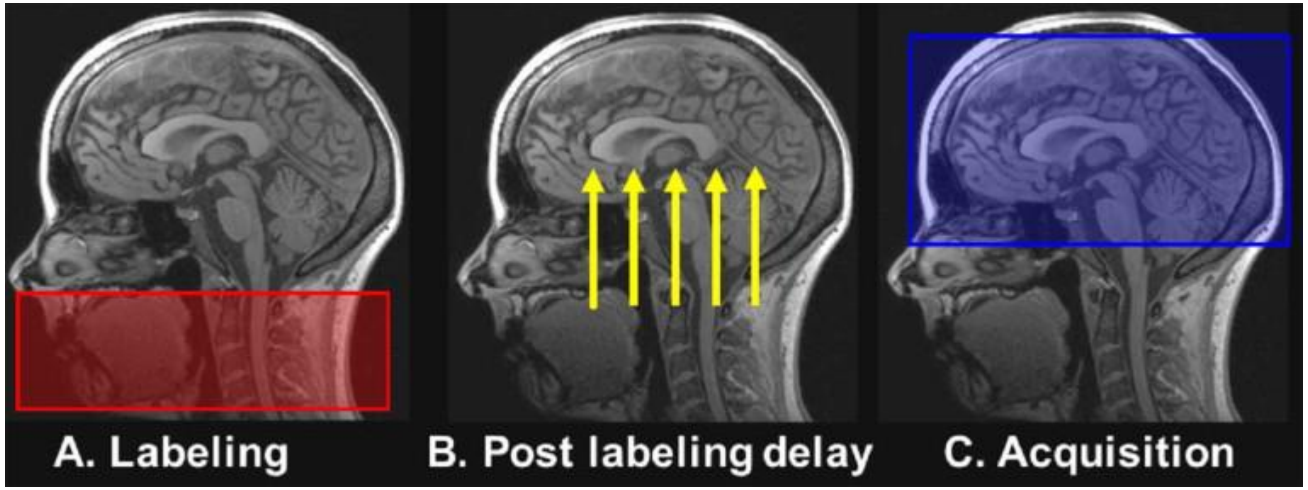
Time courses of metabolic changes during stimulation



- 6 subjects
- 24 scans (4 scans/subject) averaging

- CRLB<25% for Glu, Lac, Asp and Glc
- Time resolution of 20s

5. Perfusion fMRI



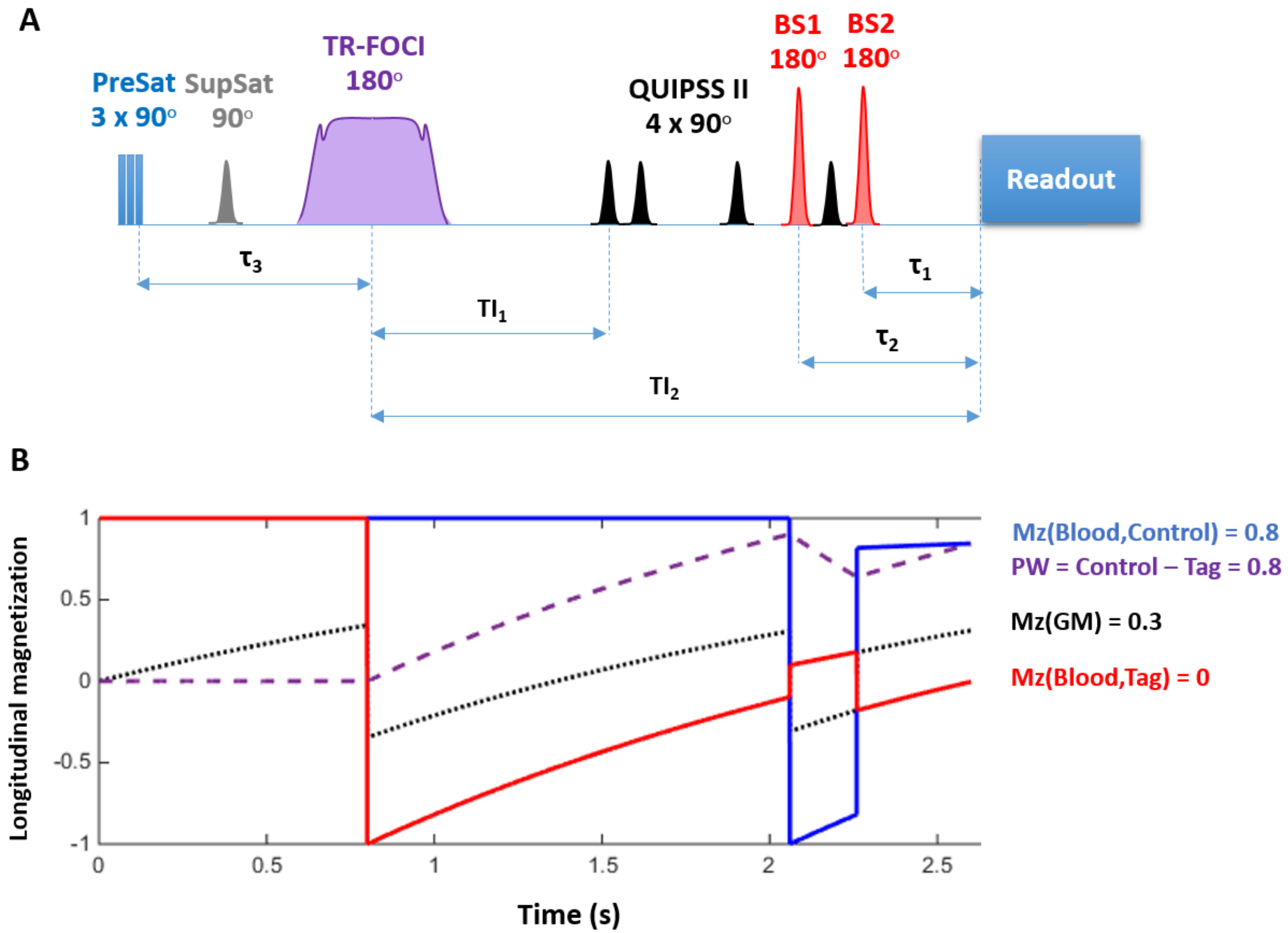
B0+B1 inhomogeneities

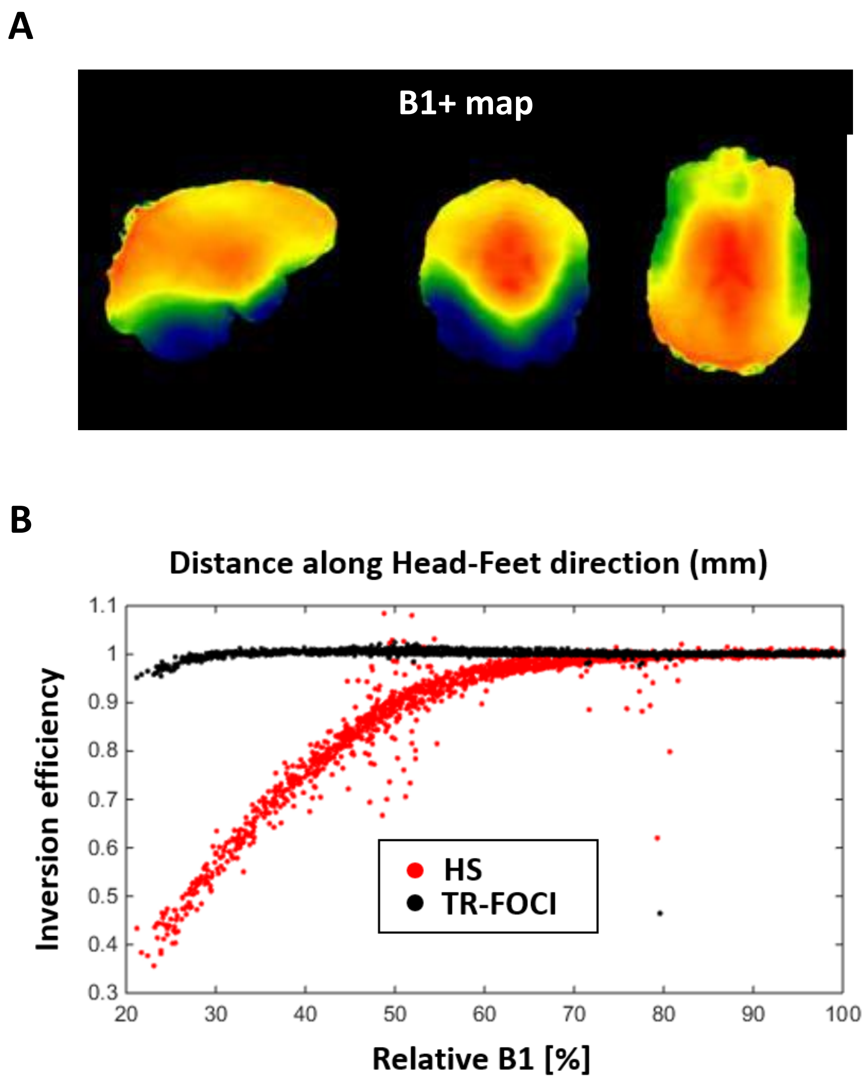
RF coverage

High SAR deposition

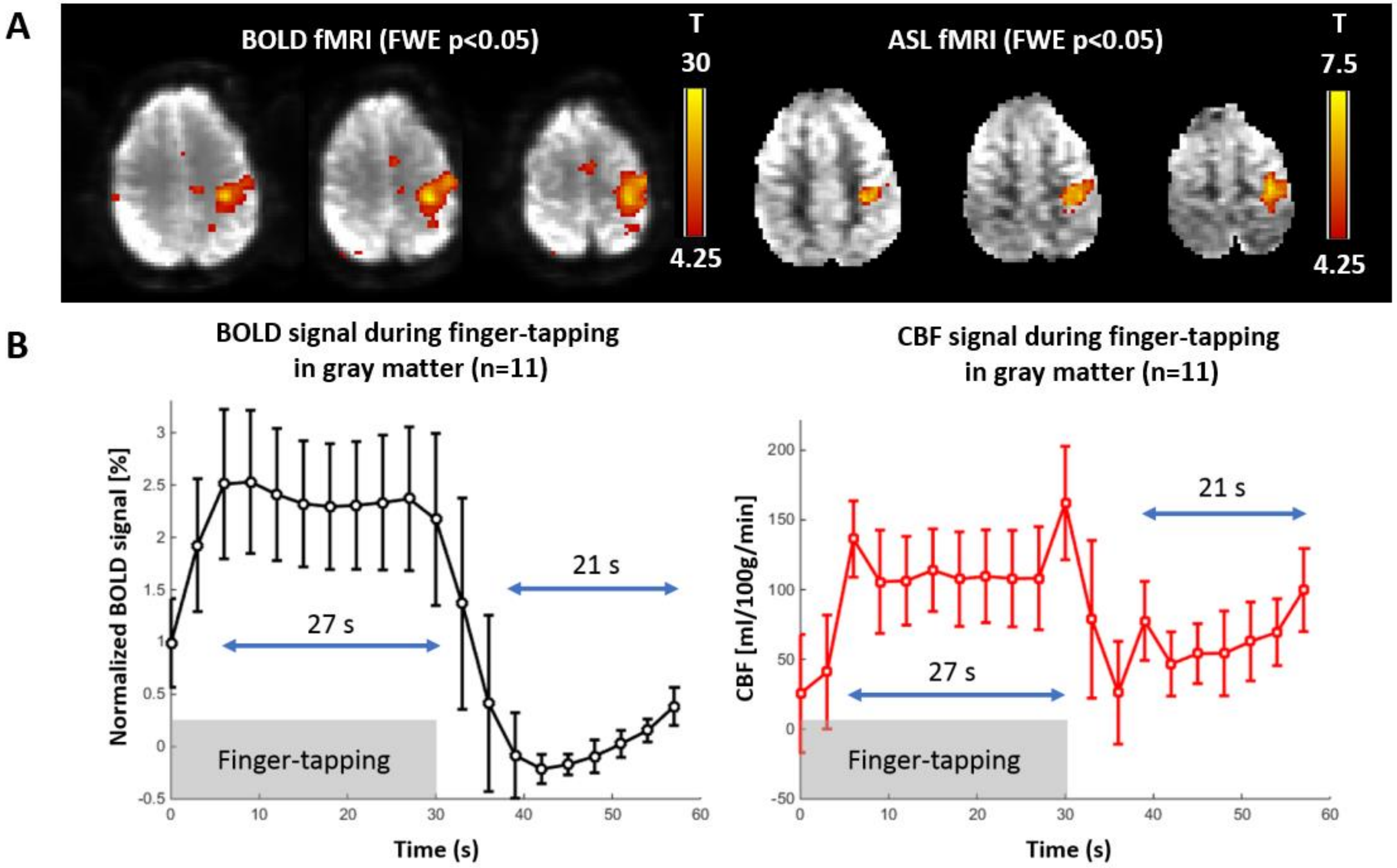
Importance of timing and inversion efficiency

Greco & Reynaud, ISMRM 2017





Single subject ASL fMRI at 7 Tesla



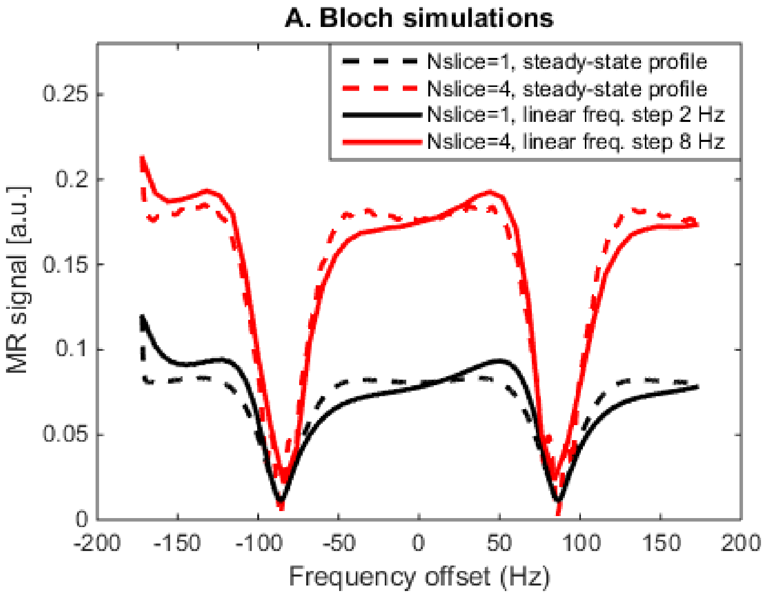
bSSFP fMRI at 7 Tesla

Why bSSFP ?

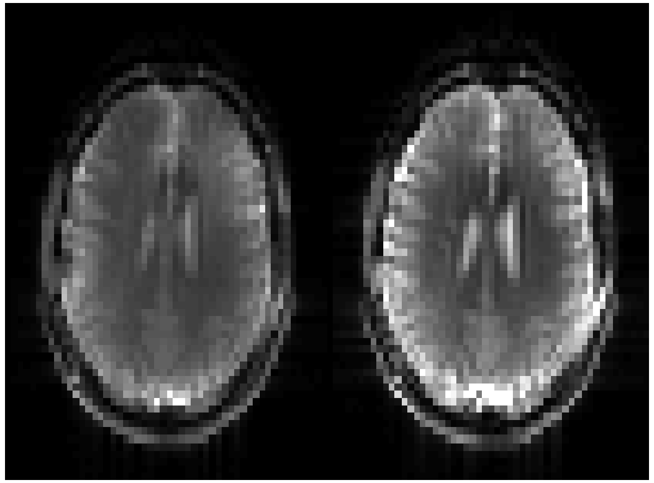
No distortions but signal drop-outs (transition bands)

Highest SNR / unit time (in 3D mode)

Proof of concept of 2D bSSFP for localized fMRI

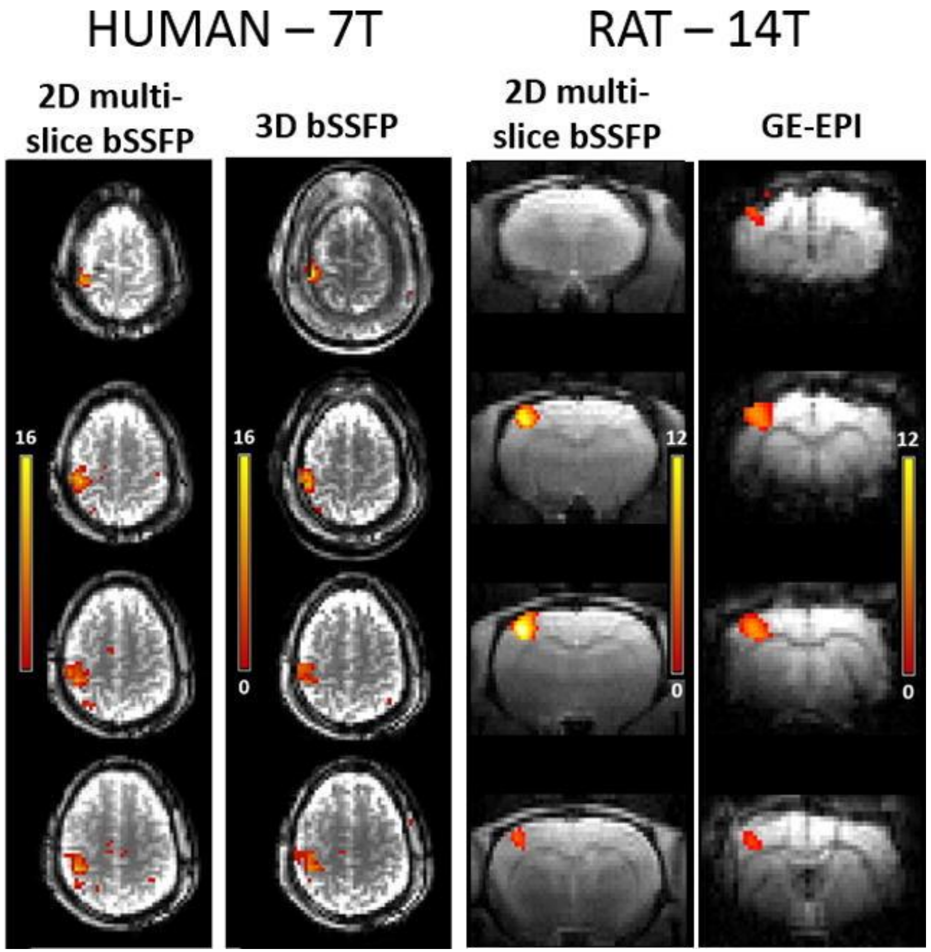


B. Single-slice/2D bSSFP experimental profile



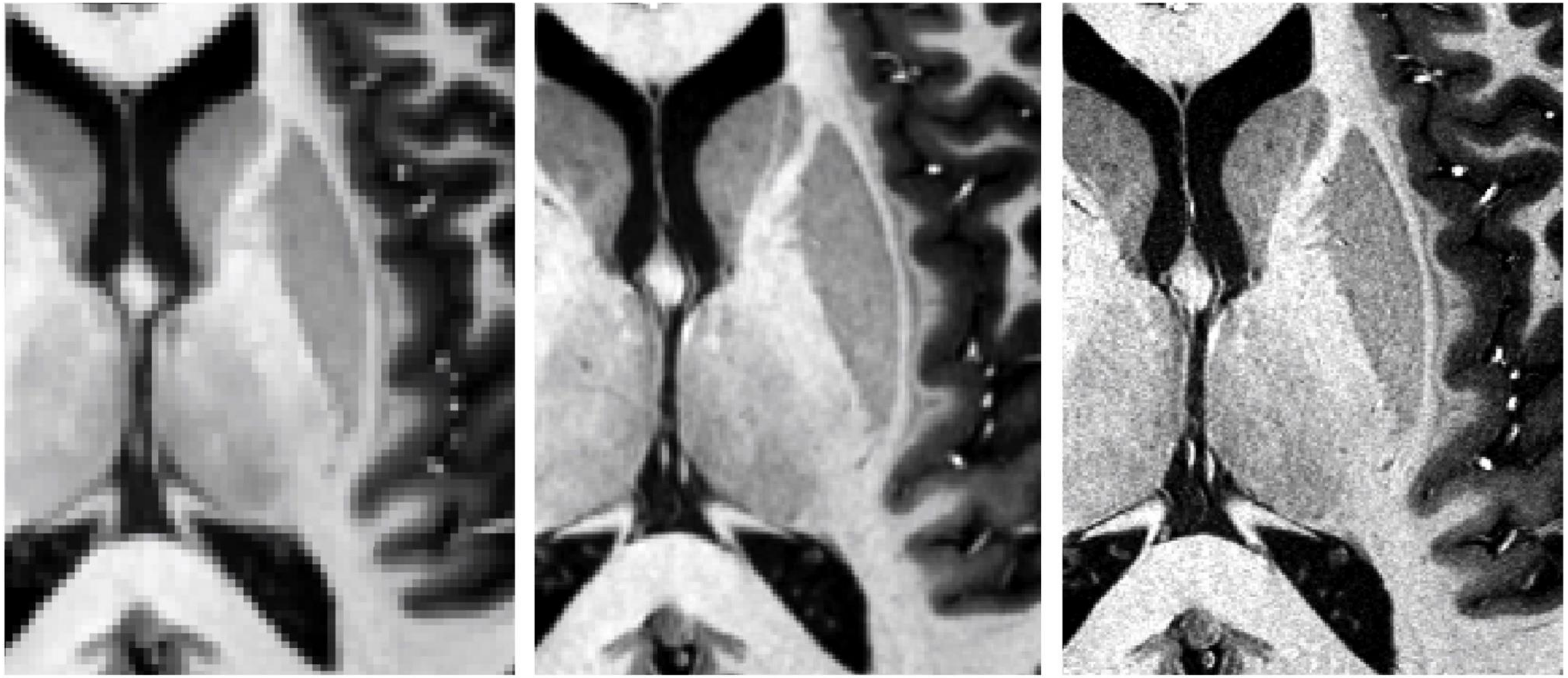
Reynaud et al, JMR 2019

bSSFP fMRI at 7 Tesla



Reynaud et al, JMR 2019

More than just fMRI



1 mm resolution (1000 nl) | 500 µm resolution (125 nl) | 350 µm resolution (43 nl)

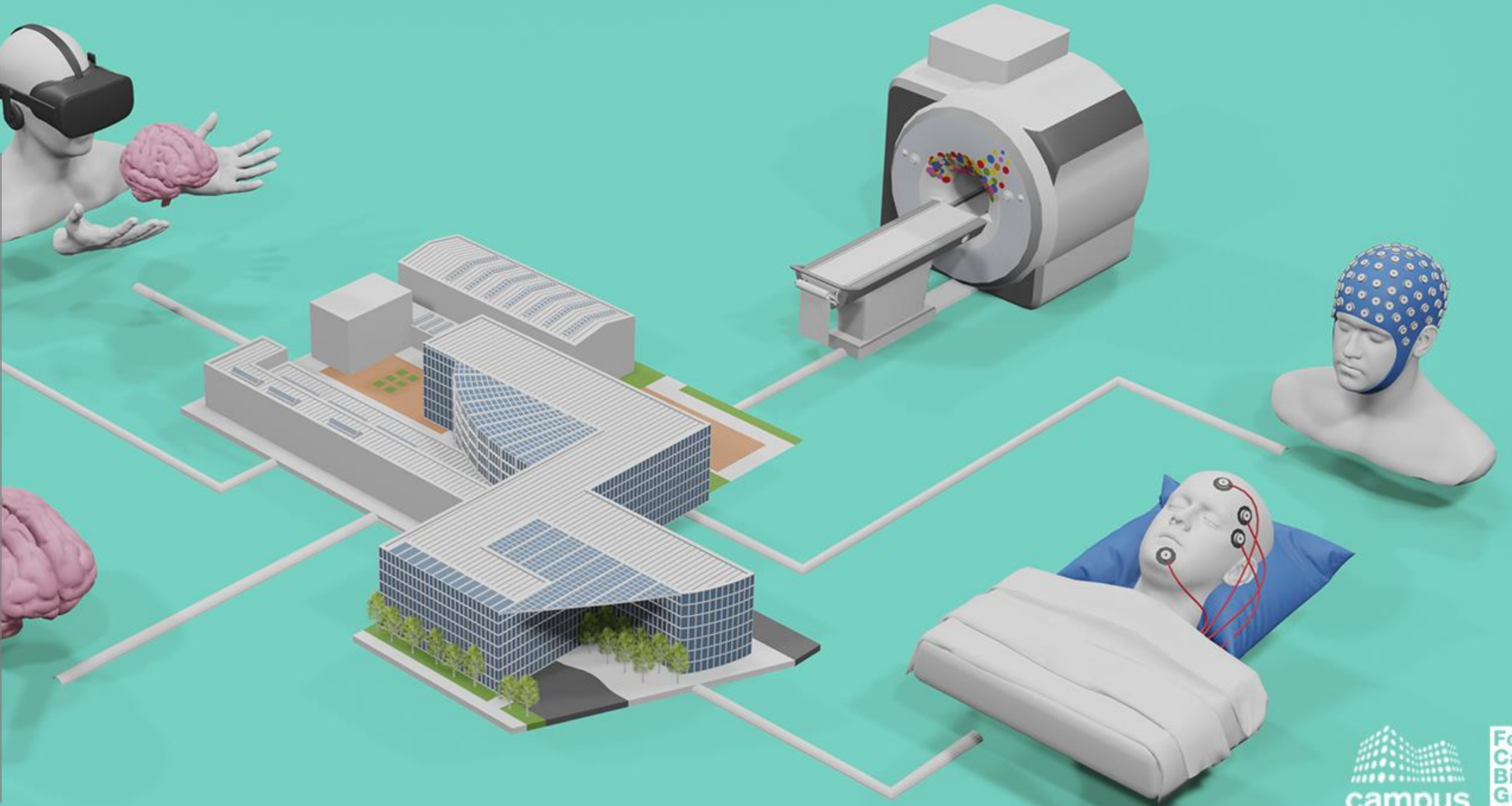
Gallichan et al. 2015, MRM

HUMAN NEUROSCIENCE PLATFORM

humanneuroscience@fcbg.ch

HNP
Human Neuroscience Platform

Acknowledgements:
Rolf Gruetter
Wietske van der Zwaag
Domenica Bueti
Sandra DaCosta
José Marques
João Jorge
Yohan Boillat
Daniel Gallichan
Lijing Xin
Ileana Jelescu



campus biotech

Fondation Campus Biotech Geneva