The possibility to image functional changes in cortical laminae using fMRI

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Probing laminar circuitry

- The laminar level is a relevant level to address important neuroscience questions (next talks and references below)
- This scale of spatial resolution is difficult to obtain in humans but was reliably obtained in animal experiments
- First studies show that non-invasive experiments can be performed in vivo using BOLD fMRI in the human brain

Self, M. W., van Kerkoerle, T., Supèr, H., & Roelfsema, P. R. (2013). Distinct Roles of the Cortical Layers of Area V1 in Figure-Ground Segregation. *Current Biology*

Animal Studies

Laminar fMRI has been successfully performed in animal studies using various methods, such as blood volume (CBV), perfusion, SE and GE BOLD fMRI:

Human studies

Proof of principle: High resolution "functional MR venography"

- Large veins cause degradation of the spatial localisation of activation in fMRI
- We aimed to identify the veins directly in the functional scans and remove them from analysis (manually or automatically) to increase specificity of BOLD signal
- We used parallel imaging to obtain a temporal resolution compatible with a functional block design

Single slice @ 1 mm resolution (left) and 0.75 mm resolution (right); white arrows depict veins

Barth & Norris, NBM 2007
Before elimination of veins

Subject 1: 1 mm
Subject 2: 1 mm
Subject 2: 0.75 mm

Barth & Norris, NMR in Biomedicine 2007
After elimination of veins

Subject 1: 1 mm

Subject 2: 1 mm

Subject 2: 0.75 mm

Barth & Norris, NMR in Biomedicine 2007
Signal change versus cortical depth. The gray shading depicts the approximate cortical thickness. The red shading depicts standard error of the mean.

Koopmans et al, HBM 2010
Koopmans et al, NI 2011
Why should laminar BOLD fMRI be possible?

Due to venous architecture: Blood drains within a layer first

Laminar BOLD model

Origin of BOLD signal across the cortex from a vascular layer for GE

Markuerkiaga et al, ISMRM 2014
Limitations of 2D EPI

- 2D EPI has been the workhorse of BOLD fMRI since twenty years using a ‘typical’ resolution \( \sim 3.5 \text{ mm}^3 \) and typical \( B_0 \)
- Standard 2D EPI was slow for high resolution with many slices, this is now solved by Multiband (MB) EPI

Issues that remain even with MB 2D EPI:
- Thin slices result in low SNR
- Imperfect slice profile
- Increased motion-sensitivity (spin-history effects)
- High power deposition with MB EPI
3D sequence vs. 2D sequence

3D excites the whole volume
→ $M_z$ is lower
→ sample signal from factor $N_{slices}$ larger volume
→ $\sqrt{N_{slices}}$ efficiency and SNR increase

more slices → larger gain

Poser et al, NI 2010
MR acquisition with 3D EPI:

- 3 T or 7 Tesla MR scanner (Magnetom, Siemens Healthcare)
- 32 channel head coil

Typical sequence parameters for 3D EPI:

- 1 mm isotropic resolution, TR/TE/alpha = 45ms/17ms/15deg, \( \text{TR(volume)} = 2.3 – 3.2 \text{ s} \), MA = up to 200x200, up to 112 slices, 2D acceleration = 4x2 or 3x3
Example of a single 3D EPI volume with 96 slices acquired in 2.3 seconds at a resolution of 1 mm (left) and several enlarged slices (right)

Poser et al, NI 2010
Co-registration of EPI and structural MRI data

Phase encoding direction

After Boundary Based Registration

van Mourik et al, ISMRM 2014
7T MP2RAGE at different resolutions
Resolution: 1 mm isotropic
TA: 6min
7T MP2RAGE at different resolutions
Resolution: 0.75 mm isotropic
TA: 7.5 minutes
7T MP2RAGE at different resolutions
Resolution: 0.5 mm isotropic
TA: 9.5 minutes
Image processing: A. Jancke
Layer specific fMRI using 3D EPI at 3 Tesla using chromatic vs. achromatic stimuli

Koopmans et al, abstract HBM 2010

Normalised signal change versus cortical depth

Normalised signal change vs. depth

Normalised signal change versus cortical depth

Koopmans et al, abstract HBM 2010
Replication of the BOLD increase around the middle layers

Laminar profiles exhibit strong or weak linear trends

Fracasso et al, ISMRM 2014
Single line-scanning BOLD fMRI in rat somatosensory and motor cortex: 50 um resolution with 50ms temporal resolution

Yu et al, Nature Methods, 2014
Inverse Imaging (InI) or MR-encephalography (MREG)

- Extreme case of parallel imaging where one dimension of gradient encoding is completely replaced by using only coil sensitivities, i.e. a 3D volume is collapsed into only one thick 2D slice
- Regularization using prior knowledge (e.g. reference data, pre-scan) is needed
- Ultra-fast acquisition times are achievable (TR~100ms)
- But this results in reduced spatial resolution in the aliased dimension

Lin et al, MRM 2005
Hennig et al, NI 2007
Addition of the confound regressors into the GLM improves localization (yellow circles) and increases z-statistics.

Boyacioglu and Barth, MRM 2013
3D EPI with CAIPIRINHA
7T examples @16x acceleration

3.0mm, 64x64x64
TE=19ms

TR=148ms

0.8mm, 240x240x208
multi-TE=9/22/35ms

TR=7.3s

0.8mm, 240x240x208
TE=19ms

TR=1.99s
Discussion and Conclusions

- fMRI on a laminar scale is possible in humans, but is challenging regarding acquisition and analysis
- potentially useful to investigate brain function on a mesoscopic scale

Open questions:
- How does BOLD relate to neural activity?
- Will it possible to distinguish timing/onset differences in humans on a laminar scale?
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