

Syllabus Outline

Specialty area: An Update on fMRI

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Date/Time: 10th May 2014/Morning session

Highlights

- Recent scanner hardware improvements that assist spatial resolution
- Biophysics of neurovascular coupling
- Layer-dependent fMRI: difficulties and potential

TALK TITLE : High-resolution fMRI in Humans: What is the Limit?

TARGET AUDIENCE – Grad students, post-docs and staff scientists involved in brain research.

OUTCOME/OBJECTIVES – Enabling more widespread and better-informed high resolution MR imaging of human brain function, with a good understanding of practical and theoretical limitations.

PURPOSE – Recent studies have shown that fMRI can depict brain activity at spatial scales much finer than those commonly considered in experimental cognitive neuroscience. This clearly allows much more direct correlation of brain activity with its neural substrate (Turner 2013), and may enable discrimination of cortical columnar structure, and assignment of layer-specific functional roles across the cortical thickness. It may also improve our understanding of the spatial correlations observed in task-independent spontaneous fluctuations of brain activity. Robust findings from such studies, and the quality of ensuing theories of brain mechanisms, require optimal data. Attainable fMRI spatial resolution is limited both by neurophysiology and by MRI physics. The lecture will explain each of these limitations and suggest optimal approaches to data collection and interpretation.

METHODS – The recommendations to be presented are built on a large neuroscience literature on animal models using a variety of methodologies, and on recent improvements in MRI hardware data acquisition. These comprise: increased B₀ field strength, improved gradient coil performance, multichannel RF coils, parallel imaging, simultaneous multi-slice acquisition, and inner-volume imaging. Functional brain imaging is normally performed using BOLD contrast, but new methods to using measure cerebral blood volume changes have been shown to compete with BOLD at ultra-high field strength, and are expected to provide far better spatial specificity. Better methods of dealing with head motion, such as prospective motion correction, open the door to many more potentially high resolution, high sensitivity fMRI acquisition techniques. Improved image analysis methods are also required to reap the harvest of insights available from the much better data.

RESULTS – Results to be discussed will include Harel (2006), describing an early ultra-high resolution animal study of BOLD cortical layer dependence; Zhao (2006) and Jin (2008), comparing layer-dependency of animal CBV and BOLD signals; Polimeni (2010), Koopmans (2010, 2011), Olman (2012) and Chen (2013), showing layer-dependent BOLD sensitivity; Satpute (2013), showing discrimination of functional areas within periaqueductal grey matter; Sanchez-Panchuelo (2013) and Kuehn (2013), describing discrimination of Brodmann areas within somatosensory cortex; Siero (2013), discussing relative spatial specificity of gradient echo and spin echo BOLD; Goense (2012) and Moon (2013), discussing intracortical variations in neurovascular coupling; Heidemann (2012), describing zoomed and accelerated EPI to obtain very high spatial resolution BOLD signal; Petridou (2013) showing the benefits for spatial resolution of high-density multi-element small RF receive coils; Olman (2011) describing strategies for obtaining high spatial resolution BOLD; Yu (2013), showing that laminar-specific neural inputs can be deciphered with line-scanning fMRI; van der Zwaag (2013) demonstrating digit-specific BOLD activation in cerebellum; Huber (2013), showing excellent sensitivity at 7T for VASO CBV functional MRI; de Martino (2013), showing tonotopic gradients within human inferior colliculus; Moerel (2012), analysing auditory cortex tonotopy in detail; Schulz (2013) showing that prospective motion correction can dramatically reduce false positive activations in fMRI; and Waehnert (2013), describing a cortical contouring model that respects the anatomical layer structure suitable for analysing high resolution fMRI data by cortical layer.

DISCUSSION – The correlation between the vascular changes observed with MRI techniques and the underlying neural activity requires very careful understanding before ultra-high resolution fMRI data can be properly interpreted. Analysis of such data needs improved tools and better conceptualization of typical

patterns of neural activity, together with systematic mapping of cortical areas, guided by the myeloarchitecture visible in good quality structural images of human brain.

CONCLUSION – Considerable progress has been made recently in obtaining human ultra-high resolution fMRI, largely due to the much greater sensitivity available at MRI field strengths of 7T and greater. Parallel imaging, especially simultaneous multislice (SMS) imaging, will further increase the signal-to-noise per unit time available, and hence the feasible spatial resolution. This enables structure, function and connectivity to be correlated at submillimeter spatial scales, thinner than the cerebral cortex. For neuroscience and clinical neurology to benefit from this progress will require further well-controlled comparisons between systems-level neuroscience in human and animal brains.

REFERENCES

- Chen G, Wang F, Gore JC, Roe AW. Layer-specific BOLD activation in awake monkey V1 revealed by ultra-high spatial resolution functional magnetic resonance imaging. *Neuroimage*. 2013 Jan 1;64:147-55.
- De Martino F, Moerel M, van de Moortele PF, Ugurbil K, Goebel R, Yacoub E, Formisano E. Spatial organization of frequency preference and selectivity in the human inferior colliculus. *Nat Commun*. 2013;4:1386.
- Goense J, Merkle H, Logothetis NK. High-resolution fMRI reveals laminar differences in neurovascular coupling between positive and negative BOLD responses. *Neuron*. 2012 Nov 8;76(3):629-39
- Harel N, Lin J, Moeller S, Ugurbil K, Yacoub E. Combined imaging-histological study of cortical laminar specificity of fMRI signals. *Neuroimage*. 2006 Feb 1;29(3):879-87.
- Heidemann RM, Ivanov D, Trampel R, Fasano F, Meyer H, Pfeuffer J, Turner R. Isotropic submillimeter fMRI in the human brain at 7 T: combining reduced field-of-view imaging and partially parallel acquisitions. *Magn Reson Med*. 2012 Nov;68(5):1506-16.
- Huber L, Ivanov D, Krieger SN, Streicher MN, Mildner T, Poser BA, Möller HE, Turner R. Slab-selective, BOLD-corrected VASO at 7 tesla provides measures of cerebral blood volume reactivity with high signal-to-noise ratio. *Magn Reson Med*. 2013 Aug 20
- Jin T, Kim SG. Cortical layer-dependent dynamic blood oxygenation, cerebral blood flow and cerebral blood volume responses during visual stimulation. *Neuroimage*. 2008 Oct 15;43(1):1-9.
- Koopmans PJ, Barth M, Norris DG. Layer-specific BOLD activation in human V1. *Hum Brain Mapp*. 2010 Sep;31(9):1297-304
- Koopmans PJ, Barth M, Orzada S, Norris DG. Multi-echo fMRI of the cortical laminae in humans at 7 T. *Neuroimage*. 2011 Jun 1;56(3):1276-85
- Kuehn E, Trampel R, Mueller K, Turner R, Schütz-Bosbach S. Judging roughness by sight--a 7-Tesla fMRI study on responsivity of the primary somatosensory cortex during observed touch of self and others. *Hum Brain Mapp*. 2013 Aug;34(8):1882-95.
- Moerel M, De Martino F, Formisano E. Processing of natural sounds in human auditory cortex: tonotopy, spectral tuning, and relation to voice sensitivity. *J Neurosci*. 2012 Oct 10;32(41):14205-16.
- Moon CH, Fukuda M, Kim SG. Spatiotemporal characteristics and vascular sources of neural-specific and -nonspecific fMRI signals at submillimeter columnar resolution. *Neuroimage*. 2013 Jan 1;64:91-103.
- Olman CA, Yacoub E. High-field FMRI for human applications: an overview of spatial resolution and signal specificity. *Open Neuroimag J*. 2011;5:74-89.

- Olman CA, Harel N, Feinberg DA, He S, Zhang P, Ugurbil K, Yacoub E. Layer-specific fMRI reflects different neuronal computations at different depths in human V1. *PLoS One*. 2012;7(3):e32536.
- Petridou N, Italiaander M, van de Bank BL, Siero JC, Luijten PR, Klomp DW Pushing the limits of high-resolution functional MRI using a simple high-density multi-element coil design. *NMR Biomed*. 2013 Jan;26(1):65-73.
- Polimeni JR, Fischl B, Greve DN, Wald LL. Laminar analysis of 7T BOLD using an imposed spatial activation pattern in human V1. *Neuroimage*. 2010 Oct 1;52(4):1334-46.
- Sánchez-Panchuelo RM, Besle J, Mougín O, Gowland P, Bowtell R, Schluppeck D, Francis S. Regional structural differences across functionally parcellated Brodmann areas of human primary somatosensory cortex. *Neuroimage*. 2013 Apr 1. pii: S1053-8119(13)00294-2.
- Satpute AB, Wager TD, Cohen-Adad J, Bianciardi M, Choi JK, Buhle JT, Wald LL, Barrett LF. Identification of discrete functional subregions of the human periaqueductal gray. *Proc Natl Acad Sci U S A*. 2013 Oct 15;110(42):17101-6.
- Schulz J, Siegert T, Bazin PL, Maclaren J, Herbst M, Zaitsev M, Turner R. Prospective slice-by-slice motion correction reduces false positive activations in fMRI with task-correlated motion. *Neuroimage*. 2014 Jan;84:124-32.
- Siero JC, Ramsey NF, Hoogduin H, Klomp DW, Luijten PR, Petridou N. BOLD specificity and dynamics evaluated in humans at 7 T: comparing gradient-echo and spin-echo hemodynamic responses. *PLoS One*. 2013;8(1):e54560
- Turner R. Where Matters: New Approaches to Brain Analysis (2013). In S. Geyer and R Turner (eds), *Microstructural Parcellation of the Human Cerebral Cortex*, Springer, Heidelberg.
- van der Zwaag W, Kusters R, Magill A, Gruetter R, Martuzzi R, Blanke O, Marques JP. Digit somatotopy in the human cerebellum: a 7T fMRI study. *Neuroimage*. 2013 Feb 15;67:354-62
- Waehnert MD, Dinse J, Weiss M, Streicher MN, Waehnert P, Geyer S, Turner R, Bazin PL. Anatomically motivated modeling of cortical laminae. *Neuroimage*. 2013 Apr 16. pii: S1053-8119(13)00348-0.
- Yu X, Qian C, Chen DY, Dodd SJ, Koretsky AP. Deciphering laminar-specific neural inputs with line-scanning fMRI. *Nat Methods*. 2013 Nov 17
- Zhao F, Wang P, Hendrich K, Ugurbil K, Kim SG. Cortical layer-dependent BOLD and CBV responses measured by spin-echo and gradient-echo fMRI: insights into hemodynamic regulation. *Neuroimage*. 2006 May 1;30(4):1149-60