Depth-resolved laminar analysis of resting-state fluctuation amplitude in high-resolution 7T fMRI

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Introduction: The recent availability of highly parallel arrays of RF receive coils and increased magnetic field strength has enabled dramatic decreases in voxel sizes for fMRI studies. Together with new surface-based techniques for laminar analysis over large extents of cortex [1], this finer spatial sampling can potentially allow for the investigation of the amplitude of resting-state fluctuations as a function of cortical depth cortical layers. While voxels as small as 0.75 mm isotropic provide sufficient SNR, voxels falling within cortical gray matter are still influenced by partial volume contamination with white matter and CSF, which are known to contribute different levels of physiological noise [2,3]. Here we characterize the impact of partial volume effects as a function of cortical depth on the resting state fluctuation amplitudes at 7T. We demonstrate that even after partial volume effects are taken into account, the magnitude of resting state fluctuations increases steadily with proximity to the pial surface. This suggests that laminar differences in the resting state fluctuations exist and are not solely attributable to physiological noise contamination from white matter or CSF compartments but, rather, may reflect increasing dominance of extravascular BOLD signal changes surrounding large pial vessels.

Methods: Four healthy subjects were studied with a 7T Siemens scanner equipped with AC84 head gradients (80 mT/m, 400 T/m/s) and a custom-built 32-channel receive array. The BOLD acquisition consisted of 750 μm isotropic resolution GE single-shot EPI with 52 oblique-transverse slices parallel to the calcarine sulcus, 0.75-mm thick, no slice gap with TR/TE/flip=4000ms/27ms/90º, FOV=192mm×192mm, 256×256 matrix, 6/8 partial Fourier, bandwidth=1502 Hz/pixel, R=3 GRAPPA acceleration yielding an effective EPI echo-spacing of 0.27 ms. Four 5 min 20 sec scans were acquired each session with eyes-open fixation.

The resting-state data was corrected for slice timing, motion corrected, then temporally low-pass filtered with a cutoff of 0.08 Hz. Average signals from the whole brain, ventricals, and white matter along with the motion parameters were treated as nuisance regressors and removed from the data [5]. For each subject, surface reconstructions of the inner and outer boundaries of the cortical gray matter were generated by FREESURFER from 1 mm MPRAGE data collected in a separate 3T scan session, and a family of intermediate surfaces evenly spaced throughout the cortical depth was computed. The functional volumes were accurately aligned to the surfaces with a boundary-based registration method [6]. To reduce laminar position estimation errors, analysis was restricted to sulcal banks by mean curvature thresholding.

A partial volume map was generated for each subject by filling the pial surface and white matter surface reconstructions with a volume consisting of 0.25×0.25×0.25 mm labels, then deriving a volume consisting of three voxel components: white matter, gray matter, and cerebrospinal fluid (CSF). Each compartment was resampled to the geometry of the BOLD acquisitions.

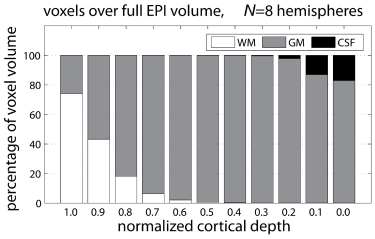

Fig. 1: Partial volume as a function of cortical depth. (Depth 1 = WM, Depth 0=pial surface.)

To extract the contribution of partial volume effects, a tissue class mixture model (based on the assumption of statistical independence of the fluctuations in each tissue compartment) was fit to the data at each depth via least squares. Under this model, the temporal variance of each EPI voxel is given by $\sigma^2_{EPI} = v_{GM}\,\sigma^2_{GM} + v_{WM}\,\sigma^2_{WM} + v_{CSF}\,\sigma^2_{CSF} + \sigma^2_{\varepsilon}$, where v_{GM}, v_{WM}, and v_{CSF} represent the partial volume percentages for gray matter, white matter, and CSF, respectively, and σ^2_{ε} represents the residual error.

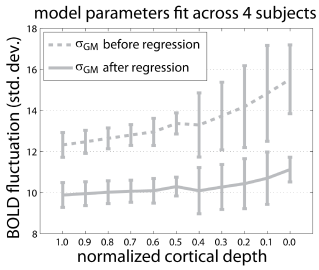

Fig. 2: Gray matter fluctuation computed from mixture model before and after regression of the nuisance effects. (Error bars indicate std. dev. across 4 subjects.)

Results: The calculated partial volume fractions across depths demonstrated a consistent dominance of CSF contribution close to the pial surface (see Fig.1). The model fit resulted in an increase of the gray matter fluctuations with proximity to the pial surface (Fig.2), with a substantial drop in noise in the case where the nuisance regressors were removed. However the residual error was not flat across depths but also increased with proximity to the surface (Fig.3), suggesting that the effectiveness of the model in explaining the variance was a function of cortical depth.

Discussion: A previous study of the relationship between physiological noise and cortical depth within a small patch of anesthetized rat olfactory bulb sampled with highly anisotropic 0.11×0.11×1.00mm voxels showed that physiological noise *decreased* with proximity to the pial surface [7], however the known effects of anaesthesia on the neurovascular coupling [8] make comparison to *in vivo* human data difficult. Furthermore in the current study the low pass filtering cutoff used in functional connectivity analysis was employed, which could affect the influence of respiratory and cardiac components (via, e.g., brain pulsatility) on the fluctuations. The spatial relationship between the gray matter fluctuations and cortical depth demonstrated here indicates that even the small 0.75 mm isotropic voxels employed in 7T laminar fMRI are not thermal noise dominated, but the noise distribution may be influenced in part by the coil sensitivity bias or the spatial pattern of GRAPPA noise enhancement [9]. The gray matter fluctuations increased uniformly with proximity to the large surface vessels, suggesting a strong influence of the extravascular BOLD signal changes, however no relative increase in fluctuations was observed in the central layers where the vascular density is known to peak [10]. This may be due to a spatial mismatch between the surfaces employed in this analysis with the positions of the vascular layers, causing a mixture of vascular layers at any given depth. The decrease in the residual error with depth could also stem from a statistical dependence between the tissue compartments.

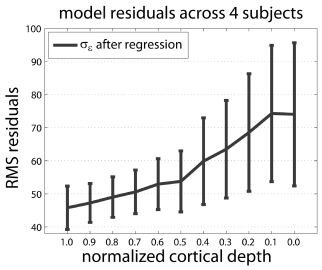

Fig. 3: Residual error from model fit, indicating that model explained less variance close to the pial surface. (Error bars indicate std. dev. across 4 subjects.)

References: [1] Polimeni *et al.* (2009) *Proc ISMRM* 1559. [2] Bodurka *et al.* (2007) *NeuroImage* 34:542-9. [3] Greve *et al.* (2008) *Proc OHBM* S787. [4] Wiggins *et al.* (2006) *Proc ISMRM* 415. [5] Van Dijk *et al.* (2008) *Soc Neurosci Abs* 885.24. [6] Greve & Fischl (2009) *NeuroImage* 48:63-72. [7] Pelled & Goelman (2004) *MRM* 52:913-6. [8] Martin *et al.* (2006) *NeuroImage* 32:33-48. [9] Triantafyllou *et al.* (2009) *Proc ISMRM* . [10] Lauwers *et al.* (2008) *NeuroImage* 39:936–48.

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