Resting-state correlations between depths within columns of voxels radial to the cortical surface

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Introduction: Increasingly smaller fMRI voxel sizes, afforded by higher field strengths and highly-parallel receive coil arrays, enable anatomically-informed, targeted sampling of the cortical gray matter at various depths over large extents of the cortex [1]. In a previous study [2], we employed this methodology to demonstrate laminar-specific functional connectivity from high-resolution resting state fMRI (rs-fMRI) data at 7T, suggesting that BOLD can be used to detect differential activations from neighboring cortical layers. Here we provide further characterization of the radial independence of the fluctuations at each depth below a given cortical location. This radial correlation length of resting state fluctuations was measured using gradient echo (GE) and spin echo (SE) EPI. The radial correlation length is strongly affected by the removal of confounding physiological signals in a counter-intuitive way—namely the global signals regressed out do not seem to produce an artifactual high-correlation between layers, but rather mask the presence of correlations between different depths. Similarly, the SE acquisition, which is also expected to remove relatively global fluctuations [3], uncovers additional underlying radial correlations.

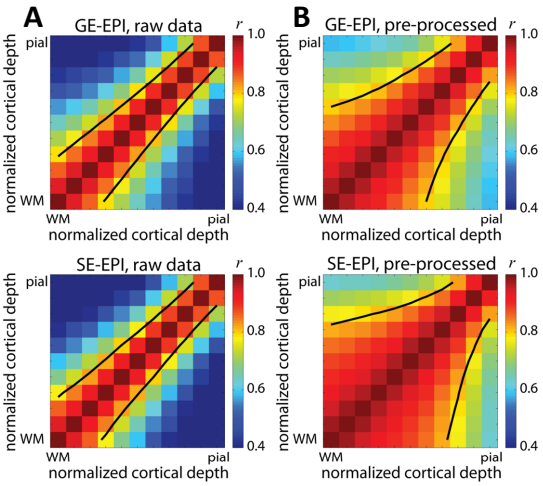

Fig. 1: Correlation coefficient matrix of resting state data across cortical depths for GE-EPI (*top row*) and SE-EPI (*bottom row*) averaged over populations. Matrices are presented for (A) raw image data and (B) data after preprocessing including regression of ventricle, white matter, whole-brain nuisance physiological signals. Contour lines indicate position of r=0.8.

Methods: Twelve healthy volunteers 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 [4]. Both the GE and SE BOLD acquisitions consisted of 750μm isotropic resolution single-shot EPI with 52 oblique-transverse slices parallel to the calcarine sulcus, 0.75-mm thick, no slice gap, 90° flip, FOV=192mm×192mm, 256×256 matrix, 6/8 partial Fourier, 75 timepoints per scan, and R=3 GRAPPA acceleration yielding an effective EPI echo-spacing of 0.27 ms. For the GE protocol, TR/TE/BW=4000ms/27ms/1502 Hz/pixel; for the SE protocol, TR/TE/BW = 5100ms/47ms/1396Hz/pixel. Eight 5 min GE (or 6 min SE) scans were acquired each session. The room lights were off and the subjects were asked to close their eyes. Seven subjects were scanned with the GE protocol and five with the SE protocol.

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, ventricles, and white matter together with the motion parameters were regressed out of the time series data [5]. A family of 11 intermediate surfaces, evenly spaced throughout the cortical depth, was generated by FREESURFER from 1 mm MEMPRAGE data collected in a separate 3T scan session. The functional volumes were aligned to the surfaces using boundary-based registration [6], and the cortical depths intersecting each functional voxels were identified.

For each vertex on the cortical surface, the Pearson correlation coefficient, r, was computed between all pairs of cortical depths to generate an 11×11 laminar coupling matrix for that location on the cortex. These matrices were then averaged across all cortical locations within the acquisition volume. This differs from our previous analysis [2] in that it considers temporal correlations only between the radial set of voxels locally perpendicular to the surface at a particular cortical location, analogous to a single cortical column (rather than the pooled correlations between all voxels within two cortical areas, aggregated by cortical depth). Thus the values along the matrix diagonal are equal to unity by definition (not by normalization). The approach is thus similar to that used in a recent study exploring laminar correlations in local field potential signals from a depth electrode array [7].

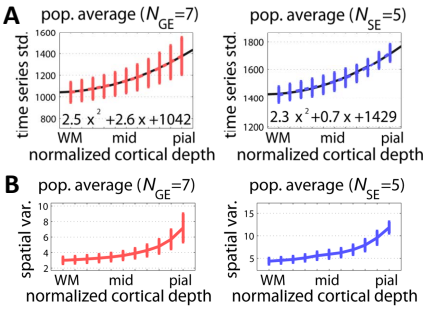

Fig. 2: Fluctuation amplitude over cortical depth for GE-EPI and SE-EPI. (A) BOLD fluctuations as a function of cortical depth. Best-fitting quadratic is super-imposed. (B) Spatial variability of fluctuation amplitude. (Error bars indicate s.e.m. over the populations.)

Results: The depth correlation coefficient matrices for GE and SE are shown in Fig. 1, calculated before and after the standard nuisance regressors are removed. While the raw data exhibits low correlations between non-adjacent depths, after physiological nuisance removal the correlation coefficient increases between non-adjacent cortical depths and broadens the distribution of correlations about the diagonal. This suggests that the non-local nuisance regressors successfully removed confounding fluctuations which mask the correlations between different depths along the cortical column. The correlation matrix structure is similar between the SE- and GE-EPI, with the SE-EPI exhibiting a longer radial correlation length—especially for deeper layers—suggesting less influence of non-local physiological signals in the SE-EPI data. However, near the pial surface the SE-EPI correlations also decrease rapidly. Fig. 2A shows fluctuation amplitudes vs. depth for the two acquisitions. Both GE and SE exhibit a quadratic increase in fluctuation amplitude near the pial surface. The tangential spatial heterogeneity of the fluctuations at a particular depth also increases near the pial surface (Fig. 2B), likely due to the heterogeneity of surface vessel sizes [8]. These three observations suggest that while the SE-EPI eliminates some non-local physiological signals an influence of surface vessels remains.

Discussion: Preprocessing of the resting-state data removes non-local physiological signals and increases the local correlations between layers in both GE and SE data. The steep increase of the radial correlation length with depth suggests that the surface vasculature may be a source of a spatially varying physiological noise over the cortical depths. Our results do not reveal the segregated correlations confined to either the upper or lower layers demonstrated in a recent microelectrode study of local field potentials across multiple time scales (but confined to a small region within V1) [7].

References: [1] Polimeni *et al.* (2010) *NeuroImage* 52:1334-46. [2] Polimeni *et al.* (2010) *ISMRM* 18:353. [3] Yacoub *et al.* (2005) *NeuroImage* 24:738-50. [4] Keil *et al.* (2010) *ISMRM* 18:1493. [5] Van Dijk *et al.* (2010) *J Neurophysiol* 103:297-321. [6] Greve & Fischl (2009) *NeuroImage* 48:63-72. [7] Maier *et al.* (2010) *Front Syst Neurosci* 4:31. [8] Duvernoy *et al.* (1981) *Brain Res Bull* 7:519–9.

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