Effect of Voxel Size and Spatial Smoothing in Functional Connectivity

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Introduction: Functional Connectivity MRI (fcMRI) has become a useful tool for delineating brain networks that show functional connectivity based on resting-state correlations [1,2]. The improved sensitivity and resolution of functional MRI from advances in array coils and higher field strength allows resting state networks to be probed at higher spatial resolution, providing a tradeoff between spatial resolution with reduced partial volume dilution of the cortical source and thermal noise components which dominate at higher resolutions. In this study we investigate the effect of voxel size, across a range of isotropic resolutions. Furthermore, we determine whether acquisition at high spatial resolution and smoothing in post-processing is a favorable strategy compared to direct acquisition at the larger voxel size, as was found for acquisitions expected to be dominated by physiological nuisance fluctuations in fMRI.[3] The comparisons indicate that at least 3x3x3mm^3 voxels are needed to see robust correlations in the unsmoothed maps, but smoothing to 6mm reveals the correlations with approximately equal z-scores regardless of the original acquisition resolution. As in fMRI time-series metrics, acquiring at high spatial resolution and smoothing to low resolution was found to be a favorable strategy compared to direct acquisition at the lower resolution; a feature of physiological noise dominated acquisitions which contradicts the standard "smoothing penalty" associated with Fourier encoding.

Methods: Data from three subjects were acquired using a 3T Siemens scanner (MAGNETOM Trio a Tim system, Siemens Healthcare, Erlangen, Germany) and a 32channel phased array receive-only head coil. The motor cortex was chosen as a well studied network [1,4]. Resting-state time-series were obtained using a single-shot GrE-EPI sequence with TR/TE/flip=5000ms/30ms/90^o and 70 measurements. The time-series were collected at five isotropic spatial resolutions: 1mm (33 slices), 2mm (64 slices), 3mm (45 slices), 4mm (35 slices) and 5mm (30 slices), with slice prescription parallel to the AC-PC plane. During the resting scans, no stimulus was applied, subjects were asked to relax and fixate on a paper crosshair. A 3D high resolution T1-weighted MP-RAGE was collected with voxel size of 1x1x1 mm^3, TR/TI/TE/flip=2530ms/1100ms/3.48ms/7°. Data were first pre-processed using typical fMRI analysis routines (SPM2 (Wellcome Trust for Neuroimaging, London, UK), and FSL (FMRIB, Oxford, UK), including time slice correction and motion correction. No spatial smoothing was applied; the data were kept in their original nominal voxel size for comparison purposes. Anatomical and functional data were transformed to atlas space (MNI). Commonly used functional connectivity preprocessing procedures, involving temporal filtering, estimation and regression of nuisance signals (motion parameters, white matter, whole brain, and ventricles) were applied prior to the correlation analysis. The connectivity analysis was performed on the residual volumes after the regression procedures. Functional connectivity maps were then generated by computing the Pearson's product moment correlation between the average seed region of the right motor cortex and the time courses of all other voxels in the brain. Correlation maps were converted to z-maps using Fisher's r-to-z transformation [5], values were then overlaid on the structural scan. To investigate the effect of spatial smoothing, post processing analysis was employed to generate additional low resolution images by convolving the high resolution 2x2x2 mm^3 resting data with different sized Gaussian smoothing kernels chosen to match the voxel size of the lower resolution acquisitions (FWHM=3, 4, 5mm). The results were evaluated based on the average z-score of the 5 most correlated voxels within a left motor cortex ROI, on both the original scans and the smoothed images.

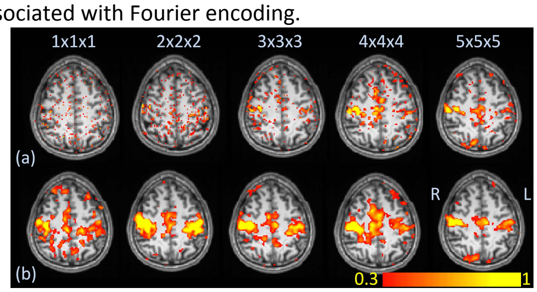

Figure 1: (a) Connectivity maps derived from the original unsmoothed data.The stated resolution indicates resolution of acquisition. (b) Corresponding maps generated when the data were smoothed with Gaussian kernel of 6mm, all resol.

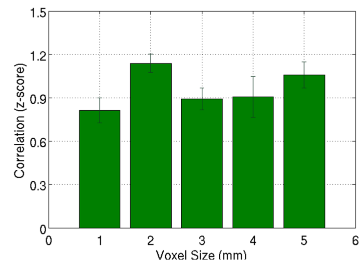

Figure 2: Estimated z-score when data from all resolutions smoothed with a 6mm Gaussian kernel corresponding to connectivity maps in Figure 1(b).

Results and Discussion: Fig. 1a shows the dependence of the correlation maps on different spatial resolutions when data analyzed at the resolution it was acquired (no smoothing was applied). Higher spatial resolution shows better gray matter localization, however the strength of the correlation between seed (right motor cortex) and target (left motor cortex) regions is weak, presumably from thermal noise dominance at high spatial resolution. In contrast, when a typical fcMRI smoothing kernel was used (6mm) the corresponding connectivity maps show more robust correlations (Fig. 1b). Fig. 2 illustrates the respective z-statistics estimated on the left motor area, when the 6mm smoothed data were examined, showing approximately the same z-score regardless of original resolution. Fig. 3 shows single subject fcMRI maps generated from the 2mm isotropic data when they smoothed to match the acquired resolutions. The z-score obtained for the smoothed 2mm isotropic data are always higher than that obtained when from direct acquisition at the larger voxel size (Fig. 4), similar to previous studies of time-series SNR in fMRI [3].

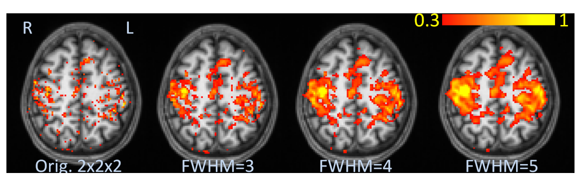

Figure 3: fcMRI maps at different degrees of spatial smoothing of the 2mm isotropic data.

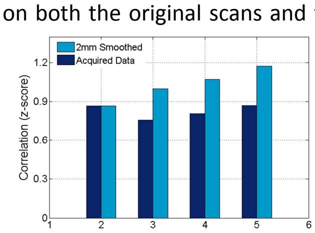

Figure 4: Light bars indicate z-score estimated from 2mm acquired data when smoothed to 3,4, and 5mm. Dark bars correspond to the unsmoothed data acquired at these resolutions.

References: 1) Biswal B, et al., Magn Reson Med 1306 34(4):537-41, 1995 2) Fox MD and Raichle ME, Nat Rev Neurosci 8(9):700-11, 2007 3) Triantafyllou et al., NeuroImage, 32, 551-557, 2006 4) Lowe M, et al., NeuroImage 7, 119–132, 2001 5) Zar JH. Biostatistical Analysis, 1996 6) Van Dijk KR, et al., J. Neurophysiology, *In print*, 2009.