Assessing functional connectivity measures at 3T and 7T

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Introduction: Functional connectivity, implied by inter-region correlation, has previously been reported in spontaneous resting state BOLD activity. Previous work has shown high correlation between BOLD fMRI signals from functionally related disparate brain regions [e.g. 1] implying that brain activity in these regions is connected even in the absence of external stimuli. It is well known that as magnetic field strength is increased, the BOLD contrast to noise ratio is improved, implying that a move to high field would increase the sensitivity and spatial specificity of functional connectivity measurements. However, fMRI signals are affected by non-neuronal artifacts arising from cardiac and respiratory fluctuations which increase with field strength, and can lead to spurious connectivity measurements [(2, 3)]. The advantage of ultra-high field (7T) to functional connectivity measurements is therefore currently unclear. RETROICOR[4] is a retrospective technique which can be applied to fMRI data to assess and correct non-neuronal physiological fluctuations using recordings of cardiac and respiratory modulations made during scanning. In this work, we investigate whether 7T fMRI can be used to accurately measure sensorimotor cortex connectivity with high spatial specificity. We employ RETROICOR to investigate the physiological noise contribution in resting state BOLD measurements at 3T and 7T and show that physiological noise has little effect on functional connectivity measurements in the motor cortex.

Methods: Five healthy, right-handed subjects took part in the study, which was approved by the local ethics committee. The task comprised two parts. First, a cued finger movement task (to localise sensorimotor cortex). Second, a 5 minute, eyes open, resting state scan. The experiment was performed at 3T at two spatial resolutions (1.5x1.5x3mm^3 and 3x3x3mm^3) and at 7T (1.5x1.5x3mm^3). Whole-head contiguous axial echo planar images (EPIs) were acquired on 3T and 7T Phillips Achieva systems (3T:- TR/TE=1500/40ms, FA 75^0, 3x3x3mm^3 resolution, 192x192x72mm^3 FOV, SENSE factor 2 and TR/TE=1500/40ms, FA 75^0, 1.5x1.5x3mm^3 resolution, 192x192x60mm^3 FOV, SENSE factor 3. 7T :- TR/TE 1500/25ms, FA 70^0, 1.5x1.5x3mm^3 resolution, 198x192x72mm^3 FOV, SENSE factor 3). A homogeneous B_0 field was achieved at 7T using parcellated shimming.

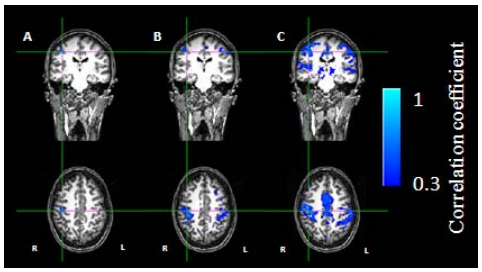

Figure 1. *Pearson correlation coefficient images. The seed is in right sensorimotor cortex. A) 3T 1.5x1.5x3mm^3 resolution B) 3T 3x3x3m^3 resolution C) 7T 1.5x1.5x3mm^3 resolution.*

Data Analysis: Images were corrected for motion using SPM5. RETROICOR was then applied to the data to correct for cardiac and respiratory artifacts. The corrected images were spatially smoothed using SPM5 (to maintain equivalence, the 7T 1.5x1.5x3mm^3 resolution data and 3T 1.5x1.5x3mm^3 data, were smoothed with a 3mm FWHM kernel; the 3T 3x3x3mm^3 resolution data were smoothed with a 4mm FWHM kernel). A seed based correlation technique [1] was applied to all data with an area in the sensorimotor cortex first identified by application of a GLM in SPM5 to the finger movement data. The right sensorimotor cortex was chosen as the seed region for subsequent analysis. The average resting state time course was extracted from the seed region (averaged over the seed peak voxel and its 8 nearest neighbours). The Pearson correlation coefficient was calculated between the resting state BOLD signal from the seed region and signals from all other voxels in the head to give a measure of functional connectivity. Connectivity maps were computed before and after RETROICOR and the correlation between maps calculated. In order to assess the contribution of physiological noise, the frequency spectrum was analysed at each field strength and resolution and the normalised sum of the square of the difference between the resting state frequency spectra before and after application of RETROICOR calculated on a voxel by voxel basis.

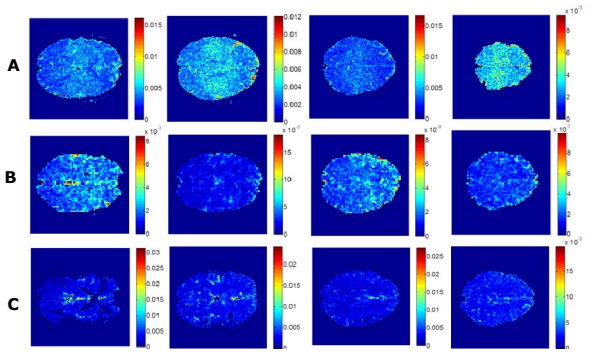

Figure 2. *Distribution of cardiac and respiratory noise across slices for a single representative subject at A) 3T 1.5x1.5x3mm^3 resolution B) 3T 3x3x3m^3 resolution C) 7T 1.5x1.5x3mm^3 resolution.*

Results: Figure 1 shows correlation coefficient images for a representative subject overlaid on their anatomical MRI for data collected at 3T and 7T. For the 7T 1.5x1.5x3mm^3 resolution and 3T 3x3x3mm^3 data, a high correlation was seen in left sensorimotor cortex with the seed region for all participants. The 3T 1.5x1.5x3mm^3 resolution data, however gave an unreliable pattern of functional connectivity across subjects due to low signal-to-noise. Figure 2 shows the maps of noise distribution for a single representative subject. It can be seen that at 7T the changes made by RETROICOR are structured and follow anatomy (i.e. the largest changes are around the large vessels) whilst at 3T, noise is distributed randomly. Figure 3 shows the frequency spectra before (red) and after (blue) RETROICOR. Spectra are averaged over voxels in right sensorimotor cortex for each field strength and resolution. At 3T and 7T there is little difference in the resting state spectra following RETROICOR, suggesting that the physiological fluctuations in sensorimotor cortex are small, even at 7T. This result is reflected by the correlation in connectivity maps obtained before and after RETROICOR which were 0.96±0.01, 0.992±0.005 and 0.989±0.003 for 3T 1.5x1.5x3mm^3, 3T 3x3x3mm^3 and 7T 1.5x1.5x3mm^3 respectively (average and standard deviation across subjects).

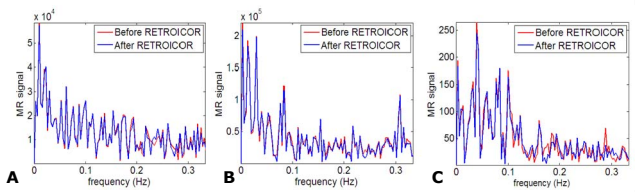

Figure 3. *Resting state frequency spectra before (red) and after (blue) application of RETROICOR for voxels in right sensorimotor cortex for a single subject. A) 3T 1.5x1.5x3mm^3 resolution B) 3T 3x3x3m^3 resolution C) 7T 1.5x1.5x3mm^3 resolution.*

Discussion and Conclusion: We have shown that correlation can be measured between right and left sensorimotor cortex in resting state data at both 3T and 7T. The spatial patterns of correlation measured at 3T 3x3x3mm^3 resolution and 7T 1.5x1.5x3mm^3 resolution agree with previous work [1]. Due to the decrease in the signal to noise ratio at 3T compared with 7T, the 3T 3x3x3mm^3 resolution images required more spatial smoothing meaning that connectivity images at 7T yield intrinsically higher resolution. It is thought that increased spatial smoothing on 1.5x1.5x3mm^3 resolution 3T data would result in a similar pattern of correlation. The 7T RETROICOR maps were dominated by localised cardiac changes in vessels and edge effects due to respiration. Despite the increase in physiological noise at higher field strength, the localised nature of the artifacts means that signals in the sensorimotor cortex are relatively unaffected. Our results therefore show that sensorimotor cortex connectivity can be measured accurately at 7T with little contribution from non-neuronal physiological artifact, and high spatial resolution.

References: [1] Biswal et al., (1995) MRM 34:537-541. [2] Birn et al., (2008) HBM 26:740-750. [3] Murphy et al., (2009) NeuroImage 44: 893-905. [4] Glover et al., (2000) MRM 44: 162-167.

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