Temporal Resolution in Resting State Time-series Acquisitions for Functional Connectivity Mapping

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Introduction: The temporal correlation from low frequency (<0.1Hz) physiological fluctuations in the human resting brain have become an increasingly important tool for mapping functional connectivity (fcMRI) in brain networks. [1-3] Although many studies have utilized functional connectivity as a tool to uncover brain networks, limited effort has been devoted to characterizing the effect of image acquisition parameters such as temporal and spatial resolution on the quality of the connectivity maps. In a previous study [4] two spatial resolutions were examined (2mm and 3mm isotropic voxels) as well as the effect of modulating TR (2.5 and 5sec) with a constant total acquisition time. The aim of the present study is to examine the z-score statistics of the motor network as a function of altering TR with the total imaging time kept constant. In a separate experiment, TR was altered with the total number of time-points (N_{tp}) kept constant. Over the range of TR values used (2s to 6s), the z-scores in the motor network were increased when TR was shortened in the constant-time acquisition indicating that an increased number of samples at shorter TR afforded improved correlations. In contrast, the z-scores of the motor network correlations were approximately independent of TR for the acquisitions with a constant number of data-points. Additionally the z-scores in all cases were improved when image SNR was increased by using a 32 channel (32ch) receive array compared to a 12 channel (12ch) array.

Methods: Three healthy human subjects were imaged on a 3T Siemens system, (MAGNETOM Trio a Tim system, Siemens Healthcare, Erlangen, Germany), using the product 32ch and 12ch phased arrays head coils. Single-shot, gradient echo EPI measurements were obtained in the resting state with TE/flip=30ms/90°, FOV=192x192, Matrix=96x96, and slice thickness of 2mm. To investigate the effect of TR and acquisition time on functional connectivity mapping, two different experiments were performed. Firstly, the total acquisition time remained unchanged (6:24min), while the TR and number of measurements varied (TR=2s, 3s, 4s, 5s, and 6s with N_{tp}=188, 124, 92, 75 and 62 time-points respectively). During the second experiment, the number of time-points remained constant (124) while we modulated the TR from 2-6sec in 1s increments, resulting in acquisition times between 4:16 and 12:36min. Both experiments were repeated for the two different head coils for each subject. A 3D high resolution T1-weighted MP-RAGE structural scan was also collected; 1mm isotropic resolution, and TR/TI/TE/flip=2530ms/1100ms/3.48ms/7°. During the resting scans subjects were asked to fixate on a paper crosshair.

Data analysis was performed using combined analysis routines from SPM2 (Wellcome Trust for Neuroimaging, London, UK), and FSL (FMRIB, Oxford, UK). Initial fMRI pre-processing included slice timing correction, motion detection and correction, normalization to the atlas space (MNI), time-course drift correction and smoothing with a 6mm FWHM Gaussian kernel. Functional connectivity specific pre-processing routines were also applied, including low pass filtering with cut off frequency 0.08Hz and regression of nuisance variables (motion parameters, averaged signal from areas of white matter, global brain and ventricles and their first temporal derivative) [4]. Correlation maps for the various acquisition times, were generated using the seed-based approach (seeding the primary right motor cortex) and determining the correlation coefficient to every voxel in the brain. The resulting correlation coefficients were converted to z-scores using Fisher's r-to-z transformation [5] to ensure a more normal distribution of the correlations, indicating significant correlation to the seed region. Additional statistical corrections might be informative to take into account the reduced degrees of freedom in the low TR data where the time-points are expected to become temporally correlated. The acquisitions were evaluated based on the average z-score of the 5 most correlated voxels within a left motor cortex ROI.

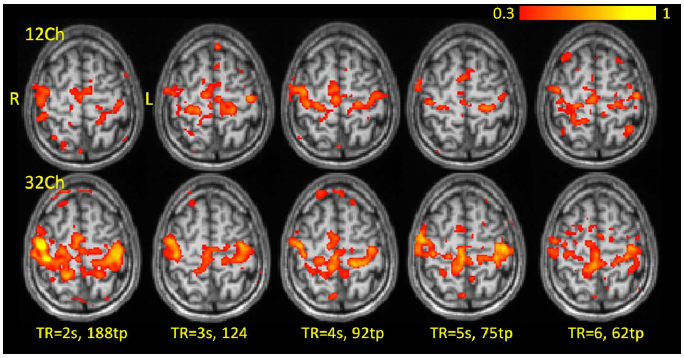

Figure 1: Single subject connectivity maps of the motor network for 12channel coil (top row) and 32channel array (bottom row). Numbers indicate the number of time points used for each acquisition with corresponding TR from left to right of 2,3,4,5,6 sec; total acquisition time was 6:24min for all runs.

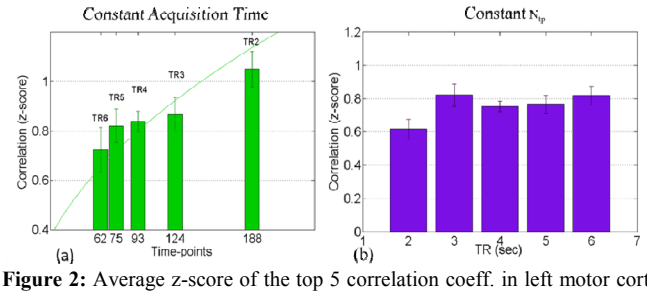

Figure 2: Average z-score of the top 5 correlation coeff. in left motor cortex, right motor cortex used as the seed region a) The constant-time experiment with 5 combinations of (TR, N_{tp}). Solid line is the fit to the equation $y=c\sqrt{N_{tp}}$, c is a constant). b) The constant N_{tp} experiment with 5 combinations of (TR, Acq. time).

Results and Discussion: Figure 1 shows single subject fcMRI maps for the constant scan-time acquisitions with variable number of measurements and TRs. The z-scores in the motor network were increased when TR was shortened in the constant-time acquisition. Furthermore, higher z-scores are observed with the 32ch coil. The average z-score in left motor cortex for the top 5 pixels are shown in Fig. 2 for both the constant-time measurements and the constant N_{tp} measurement. For the constant imaging time experiment, decreasing the TR and increasing the N_{tp} increased the z-score in a manner roughly proportional to $\sqrt{N_{tp}}$ suggesting that the measured correlation increases with N_{tp}. In contrast, the constant N_{tp} experiment showed approximately the same z-score regardless of TR. We report differences in z-score in individuals rather than statistics taken on group averages, which would likely show reduced temporal averaging effects. Both findings, as well as the 12 vs. 32ch comparison suggest that the 2mm isotropic resting-state time-series still contains significant thermal noise and an increased correlation score is seen with higher temporal resolution.

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) Lowe M, et al., NeuroImage 7, 119–132, 2001 4) Van Dijk KR, et al., J. Neurophysiology, *In print*, 2009 5) Zar JH. Biostatistical Analysis, 1996.