Quantitative evaluation of RSN functional contrast in low-TR FMRI

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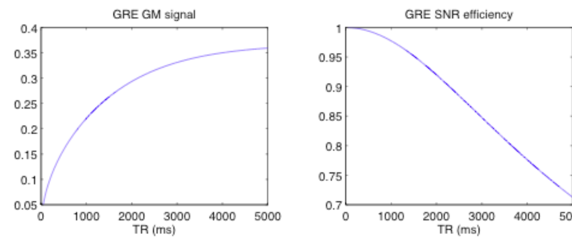
Introduction We have recently presented *[Feinberg in submission]* an approach for rapid, EPI-based FMRI through the combined use of two acceleration techniques that multiply together to give a significant reduction in TR. Although signal calculations predict a slight increase in SNR efficiency, the effective statistical properties of FMRI data are driven by several complex factors. Here, we investigate the BOLD CNR performance of accelerated acquisitions using resting state network (RSN) statistical significance as a quantitative measure.,



Signal Theory Signal was calculated over a range of TR at the Ernst angle assuming thermal noise and T_1=1.3s (grey matter at 3T). Reduction in TR has two counteracting effects on effective timeseries SNR: T_1 saturation reduces the signal level (left), while the increased number of timepoints reduces noise proportional to $1/\sqrt{TR}$. The net result is fairly constant efficiency ($SNR/\sqrt{TR}$, right), with 10-15% improvement at 0.4s compared to 3s. These calculations neglect g-factor losses associated with acceleration.

Data For 3 subjects, 10 minutes of resting data was acquired at 3 TRs (2.5, 0.8, 0.4s), 3x3x3mm, whole-brain, on a Siemens 3T (32-channel head coil). The 3 acquisitions had accelerations of 1x1, 2x2 and 3x3, respectively, where the first number refers to the SER (Simultaneous Echo Refocused) acceleration *[Feinberg MRM 2002]* and the second to the MB (Multiband) acceleration *[Larkman JMRI 2001, Moeller MRM 2010]*.

Identification of RSNs Independent component analysis (ICA) was used to identify RSNs and non-neural artefacts in the datasets using FSL's MELODIC *[Beckmann IEEE TMI 2004]*. ICA across all 3 TRs identified 100 components representing the effects present on average in all 3 datasets. Dual-regression (involving first a spatial, and then a temporal, multiple-regression) was applied to derive 100 corresponding TR-specific components for each TR *[Beckmann OHBM 2009]*. The 100 components were manually classified into RSNs vs. artefacts, resulting in ~62 RSNs.

Statistical Analysis The spatial map regression coefficients reflect RSN BOLD amplitude, which were converted into Z-stats. Autocorrelation in the residuals was corrected for by fitting a mixture model to the Z-stat histogram. The RSNs were then compared across the TRs: For each RSN and TR, the peak-Z was reported as a measure of statistical significance. At the peak-Z voxel, the BOLD effect size ("PE", as % signal change) and standard deviation of the residuals ("res") were also evaluated. Also, the sum of Z-stats of voxels that were considered above threshold (by the mixture modelling) was calculated (this gave similar results to the count of supra-threshold voxels, i.e. RSN spatial extent). Finally, we repeated this analysis with *single-regressions* (instead of multiple), extracting one RSN at a time from the datasets in a manner analogous to seed-based correlation analysis.

Results and Discussion Boxplot distributions are over ~62 RSNs and 3 subjects. The top row shows results for the 3 TRs, and the bottom shows the ratio of the 0.8 and 0.4s data to the 2.5s. We find: 1) Similar BOLD % signal change across all TRs. 2) Increased residuals at low TR and with single-regressions. 3) **Peak Z-stats are 60% higher at 0.4 vs. 2.5s, for multiple-regression**, and similar across TRs for single-regression. 4) Sum-of-Z, **significance×extent, is 100% higher at 0.4 vs. 2.5s, for multiple-regression**. The improvements at low-TR with multiple-regression are due to several factors: 1) Improved modelling of artefactual processes with multiple-regression and low-TR. 2) The large number of regressors is more detrimental to the temporal degrees-of-freedom with a smaller number of timepoints. 3) Because statistical significance in a multiple-regression is driven by each regressor's *unique variance* (compared with all other regressors), the low-TR data contains improved information with which to discriminate the different components temporally from each other. Both single-session ICA and dual-regression extraction of subject-specific components are effectively based around a multiple-regression, and hence benefit from the increase in temporal information available from low-TR data. However, methods related to single-regression, such as seed-based correlation, will not see this advantage, nor will model-based analysis in a task-FMRI experiment (although artefact removal would probably be improved in both scenarios when using lower-TR data). Nevertheless, even in the 'worst case' scenario, the Z-stats (effective CNR) of low-TR data are at least as good as higher-TR data (and, in other scenarios, are considerably better). Finally, given that the effective CNR is not compromised at low TR, the additional *richness* of temporal information for investigating biological processes may be very valuable.

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