Frequency characteristics of large scale resting state networks using 7T Spin Echo EPI

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Introduction: Resting state networks (RSN)s are generally believed to be driven by low frequency fluctuations below 0.1 Hz [1]. Recent work has called this belief into question. Niazy et al. showed that the low frequency dominance is not characteristic of RSNs, but of BOLD in general [2]. Our own previous work further investigated this, and showed that RSNs in GE FMRI data are better estimated using frequencies above 0.1 Hz [3]. An investigation into the linearity of SE-EPI at 4.7T has shown that it remains linear even at ISIs down to about 1s, whereas the GE-EPI response is attenuated [7]. This led us to hypothesise that the frequency response of SE-EPI in the resting state should be flatter than that of GE-EPI. The development of the PINS technique [8] made it possible to test this by utilising a TR-minimised SE-EPI PINS protocol at 7T [4].

Data and Methods: The 7T SE data used were acquired at 7T using PINS multiplexing a method that allows rapid, low SAR whole-brain SE-EPI at 7 Tesla, for RS-FMRI on a Siemens Magnetom system using a 32ch head coil [4]. Acquisition parameters for the SE-EPI were: TE 53 ms, sagittal orientation, phase encoding direction AP, matrix 160 × 160, voxel size 3x3x3.5mm3, flip angle 90°, PE-GRAPPA factor 3, bandwidth 1562 Hz/pixel, 40.3 ms readout train, PINS slice multiplex RF pulses. Non-selective fat suppression was applied. The reconstruction was performed offline using an implementation of the SENSE-GRAPPA algorithm [9] implemented in Matlab. Data for six right-handed subjects (5 male) were acquired, together with an MP2RAGE scan. For two subjects, an MPRAGE was already acquired on another system. TRs were chosen as low as possible, while staying within SAR limitations, and ranged between 1.05 and 1.22 seconds dependent upon coil loading, with 350 volumes being recorded for each subject. In addition, one subject was also scanned with a lower TR of 0.8s, and 525 total volumes scanned. Data were preprocessed using FSL's FEAT (http://fsl.fmrib.ox.ac.uk). This included motion correction, spatial smoothing with a 5mm FWHM Gaussian kernel, and temporal high pass filtering with a 100s cut off, to remove scanner drifts. A distortion correction coregistration algorithm was used to map the EPI to the MP(2)RAGE scan for each subject. Based on normalized mutual information of the average EPI volume and the T1 scan this routine simultaneously estimated both the rigid body transformation parameters and the non-linear transformation in the phase-encode direction of the EPI data [5]. After this distortion correction and coregistration, SPM5 (http://www.fil.ion.ucl.ac.uk/spm/) was used to transform the data to MNI space.

With the data in MNI space, the same methods and algorithms as used in [3] were applied. Briefly, Group ICA spatial maps from a previous paper were used to define eight RSNs [6]. Dual Regression was used to obtain subject specific versions of these networks in two steps. The first step is to perform a spatial regression using the group ICA spatial maps as regressors, resulting in a time course associated with each spatial map. The second step involves a second regression using these time courses, resulting in a spatial map of the subject specific version of this RSN. These maps were obtained both from the full dataset, and from band pass filtered versions of the data. The minimally filtered data (only high pass filtered during preprocessing) should contain all the information characterizing the RSN, and are used as reference maps. Spatial maps obtained from band pass filtered data were compared to these reference maps using the DICE overlap score, to give a value as to how good the estimation of this RSN is, based on the information in the frequency range of the band pass filter. When this is performed for multiple frequency ranges, it results in an estimation performance based on frequency. Network identifiability with increasing frequency was also estimated by comparing average z-scores of the network, with the average of the background. RSNs are more easily identified when this difference is greater.

Results: Data from all six subjects were successfully processed and analyzed. Cut off frequencies for 16 frequency bands were chosen to contain equal power in each frequency band. Spatial maps were obtained and DICE scores and z-score differences calculated for each subject, RSN and frequency band. Because of the difference in TR, data were resampled to one range of 32 centre frequencies using linear interpolation, in order to calculate averages over subjects and RSNs. Average z-score differences are shown in magenta in figure 1. DICE results are shown in magenta in figure 2. Both are plotted together with GE results from previous work. The other datasets are (all gradient echo EPI) one multi-echo protocol (DICoD-1), one regular GE-EPI protocol (Oxford data) and two multi-band protocols (NKI 1400ms and 645ms). One important result from the GE echo data is that each of the curves peak at frequencies well above 0.1Hz, and drop off again at higher frequencies. The SE data plateau at about 0.15 Hz and hardly show any drop off at higher frequencies.

Conclusion and Discussion: As is well known, SE EPI is more sensitive to signal from the microvasculature, in contrast to the sensitivity to the macrovasculature of GE EPI. Although this specificity comes at a price in signal sensitivity, it should make for a closer coupling between the neuronal activity, and the measured BOLD signal. Of greater importance is the reported more linear nature of neurovascular coupling in SE EPI by Zhang et al. [7]. The attenuation of the GE BOLD signal at short ISI corresponds to a reduced response at higher frequencies. The lower overall DICE and z-score difference of the SE results reflects both the reduced sensitivity of SE EPI, and the shorter measurement time of the SE data. In conclusion, this work shows further evidence for the relevance of frequencies above 0.1Hz in RS-FMRI, by demonstrating peak estimation and identifiability performance at frequencies above 0.1Hz. It also shows further evidence of the more linear nature of neurovascular coupling in SE BOLD. Most importantly it indicates that the underlying neuronal activity has a power spectrum that rises monotonically with frequency up until the plateau is reached, and is then nearly flat within the frequency range measured.

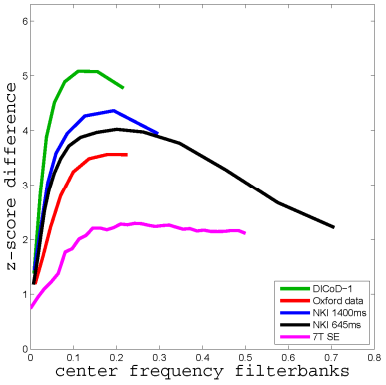

Figure 1, Z-score differences

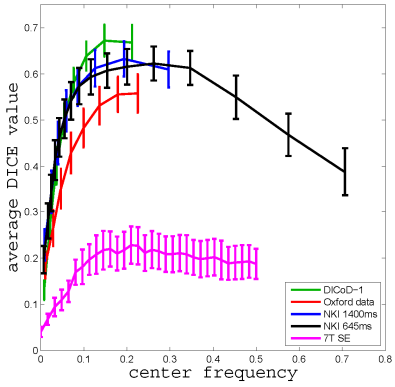

Figure 2, Average DICE scores

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