Respiratory Volume Over Time Effects in Resting-State Gradient-Echo and Spin-Echo EPI BOLD

Yasha Khatamian[1] and J. Jean Chen[1]

[1]*Rotman Research Institute, Toronto, ON, Canada*

Target audience: Researchers in fMRI-based resting-state functional connectivity and fMRI contrast mechanisms

Purpose: Resting-state functional MRI (fMRI) [1] reveals consistent brain networks [2] and has potential for wide application in the study of functional connectivity and detection of neurological abnormalities. Unfortunately, fMRI is contaminated by physiological noise [3], including respiratory noise induced by variations in lung volume and blood CO_2 [4,5]. In fact, a slow change in respiration volume over time (RVT) [4] has strong global correlations with the resting-state blood oxygen level dependent (BOLD) signal [5]. The vast majority of resting-state fMRI scans use gradient-echo EPI (GE-EPI) sequences, due to their sensitivity to fluctuations in the BOLD signal, though they can include strong intravascular effects from large veins. Spin echo EPI (SE-EPI) sequences are relatively more sensitive to the extravascular effects surrounding microvasculature, and hence may provide better spatial specificity for detecting neuronal activity [6], while also minimizing signal loss/artifacts caused by susceptibility gradients. In our previous work [7], we showed that SE-EPI was better at capturing resting-state functional connectivity in high-susceptibility regions. We continue this theme in this study by looking at the vulnerability of both GE- and SE-EPI resting-state fMRI data to respiratory effects, specifically the RVT.

Methods: 5 subjects were scanned on a 3T Tim Trio scanner (Siemens, Erlangen, Germany) with a 32-channel head coil. Two 8 min resting-state scans, one a GE-EPI scan (TE = 30ms, 26 slices, 4.6mm slice thickness, echo spacing = 0.55ms, readout train = 35.2ms) and the other a SE-EPI scan (for four subjects: TE = 45ms, 26 slices, 4.6mm slice thickness, echo spacing = 0.55ms, readout train = 35.2ms; for one subject: TE = 40ms, 24 slices, 5.75mm slice thickness, echo spacing = 0.47ms, readout train = 30.1ms) were acquired for each subject (all with TR = 2000ms, 64x64 matrix, 3.44mm in-plane resolution, flip angle = 90^o) as well as a T1 weighted anatomical scan (3D-MPRAGE, TR/TE/TI = 2400/2.43/1000ms, 256x256x192 matrix, 1x1x1mm^3 resolution, flip angle = 8^o). Respiratory volume was recorded during resting-state scans using a BioPac (BioPac, Goleta, USA) respiratory belt placed around the abdomen. We performed physiological noise removal on the functional data using RETROICOR [8], as well as slice timing and motion corrections, co-registration, spatial smoothing (5mm FWHM) and removal of linear and cubic temporal trends. RVT time-courses were calculated from the respiratory belt recordings and convolved with a respiratory response function (RRF [5]). We assessed the influence of the RVT and RRF convolved RVT (RRF-RVT) on both the GE- and SE-EPI data through cross-correlations between the functional data and corresponding RVT/RRF-RVT (shifted from -20 to 30 s in increments of 1 s; positive shifts indicate a lag in the fMRI data) to find the max correlation of each voxel to both signals. Resulting correlation maps were spatially normalized to MNI305 space and averaged across all subjects.

Results: The statistically significant group-average max correlations between the GE-/SE-EPI scans and RRF-RVT are shown in Fig. 1, while Fig. 2 plots the mean/standard deviation of those correlations found in the gray matter of each subject. Fig. 3 and 4 show the same information for correlations to RVT. GE- showed stronger (with the exception of subject 1 in Fig. 2) and more spatially structured correlations to RRF-RVT than SE-EPI (Fig. 1). GE- also showed stronger correlations to RVT (Fig. 4) than SE-EPI, though not as spatially structured (Fig. 3-A) as to RRF-RVT (Fig. 1-A). Similarly, in white matter, GE- consistently showed stronger correlations than SE-EPI to both RRF-RVT and RVT.

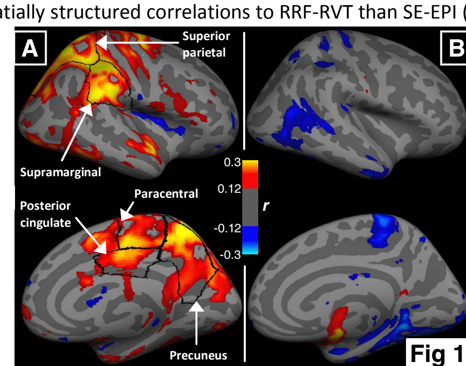

Fig 1: Max correlations (average of all subjects) to RRF-RVT across all lags for A) GE- and B) SE-EPI (displayed on inflated surface)

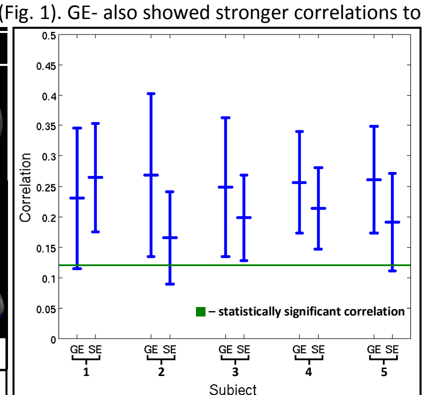

Fig 2: Absolute max correlation values (across all lags) to RRF-RVT in gray matter voxels for each subject and scan type

Discussion: The strong spatial structure of the correlations between GE-EPI and RRF-RVT gives credence to the idea that RVT effects are not due solely to breathing-related magnetic susceptibility effects, but likely have a macrovascular origin. Such an observation would be consistent with the proposed link between RVT and end-tidal carbon dioxide [4,9]. Our primary finding is that in resting-state, RVT effects are lower in SE- than GE-EPI. The SE-EPI associated RRF may actually be different than that associated with GE-EPI, and therefore the weaker correlations of SE-EPI to RRF-RVT, when compared to those of GE-EPI to RRF-RVT, may be a result of the RRF having been developed using GE-EPI data [5]; however, the fact that SE- showed weaker correlations to RVT than GE-EPI sheds doubt on this hypothesis. In short, SE- is less explained by RVT than GE-EPI is. This may have contributed to our previous observation of more consistent SE-EPI based BOLD functional connectivity in a number of networks [7]. In future work, we aim to better quantify this effect.

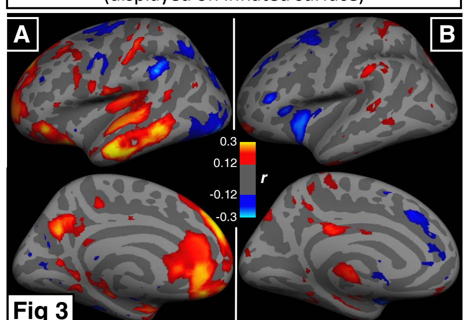

Fig 3: Max correlations (average of all subjects) to RVT across all lags for A) GE- and B) SE-EPI (displayed on inflated surface)

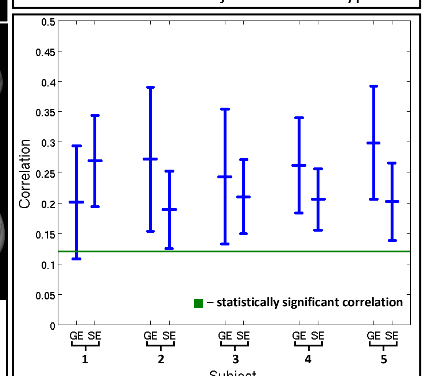

Fig 4: Absolute max correlation values (across all lags) to RVT in gray matter voxels for each subject and scan type

Conclusion: Compared to GE-, SE-EPI showed less vulnerability to being contaminated by RVT effects, highlighting that SE-EPI is less sensitive to respiratory noise. Considering that SE-EPI has been shown to accurately generate functional connectivity maps in humans [7], the findings presented here only further support the use of SE-EPI for resting-state functional MRI.

References: **[1]** Biswal, B et al. Magn Res Med 1995; 34:537-41 **[2]** Damoiseaux, J et al. Proc Natl Acad Sci USA 2006; 103:13848-53 **[3]** Dagli, M.S. et al. Neuroimage 1999; 9:407-15 **[4]** Birn, R.M., et al. Neuroimage 2006; 31:1536-48 **[5]** Birn, R.M., et al. Neuroimage 2008; 40:644-54 **[6]** Yacoub, E et al. Magn Res Med 2003; 49:655-64 **[7]** Khatamian, Y et al. Proc Intl Soc Mag Res Med 2013; 21:2234 **[8]** Glover, G.H. et al. Magn Reson Med 2000; 44:162-7 **[9]** Chang, C. et al. Neuroimage 2009; 47:1381-1393