Subject-specific modeling of physiological noise in resting-state fMRI at 7T

Sandro Nunes[1], Marta Bianciardi[2], Afonso Dias[1], Rodolfo Abreu[1], Juliana Rodrigues[1], L. Miguel Silveira[3], Lawrence L. Wald[2], and Patricia Figueiredo[1]

[1]Institute for Systems and Robotics and Department of Bioengineering, Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Lisbon, Portugal, [2]Department of Radiology, A.A. Martinos Center for Biomedical Imaging, MGH and Harvard Medical School, Boston, MA, United States, [3]INESC-ID and Department of Electrical and Computer Engineering, Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Lisbon, Portugal

Target audience: Neuroscientists, engineers and clinicians interested in physiological noise and resting-state fMRI at ultra-high field.

Purpose: Functional connectivity measurements underlying the study of resting-state networks using fMRI (rs-fMRI) may be seriously compromised by non-neuronal mechanisms producing correlated signal fluctuations across the brain, most commonly referred to as physiological noise[1], and this problem becomes even more prominent at ultra-high-field (7T)[2]. A number of strategies have been proposed for modeling physiological noise in rs-fMRI, including different models of the respiratory volume per time (RVT) and heart rate (HR) contributions[3,4,5,6]. however, a systematic comparison of these models is still missing. Here, we aim to compare previously proposed as well as new models of both RVT and HR contributions to physiological noise in rs-fMRI at 7T, and test subject-specific vs group-level optimization of RVT and HR response lags.

Methods: 9 healthy subjects were studied on a 7T whole-body scanner with a 32-channel receive RF coil. About 10min of rs-fMRI EPI data were collected using simultaneous-multi-slice factor = 3, TE=32ms, TR=2.5s, FA=75º, GRAPPA factor = 3, nominal echo spacing = 0.82ms, whole-brain coverage by 123 sagittal slices and 1.1mm isotropic resolution. Cardiac and respiratory data were simultaneously recorded using a pulse transducer (ADInstruments) placed on the left index finger and a pneumatic belt (UFI) strapped around the chest. A T1-weighted structural image was also acquired using multi-echo MPRAGE, with 1mm isotropic resolution[7]. Data analysis was carried out using Matlab, FSL and SPM tools. Data pre-processing included: low-pass filtering of cardiac and respiratory data; slice timing correction, motion correction and spatial smoothing (1.5mm Gaussian kernel) of rs-fMRI data; tissue segmentation of MPRAGE images; and co-registration of rs-fMRI with MPRAGE and MNI standard brain. A nested-model general linear modeling (GLM) approach was employed for the optimization of the physiological noise model[3,4]. The following sets of explanatory variables were included if the associated variance explained (VE), computed in relation to the preceding model based on the adjusted coefficients of determination (R^2_{adj}) of the two models, was significantly different from zero ($p<0.05$) on average on a gray matter region: 1) slow-drifts described by 3rd order polynomials; 2) extended RETROICOR including respiratory/cardiac phase regressors up to 2nd/3rd order, respectively; 3) RVT and HR optimal models; 4) average CSF and WM fluctuations; and 5) subtle and large motion parameters. The following models of RVT and HR contributions to physiological noise were compared, where temporal lagging and convolution with previously proposed impulsive response functions are considered, and the one yielding maximum VE was added to the GLM: a) single-lag; b) single-lag convolution (with respiratory response function, RRF[1] / cardiac response function, CRF[6]; and c) dual-lag[4]. In each case, lags were optimized in 1s steps in the range [-20; +20]s, on both group and subject levels.

Results: A significant main effect on VE in gray matter was found for subject vs group lag optimization and also for dual-lag relative to single-lag and convolution models, for both RVT and HR (repeated measures ANOVA, $p<0.05$), with the dual-lag model with subject-specific lag optimization providing maximum VE (Fig.1). The dual-lag behavior and inter-subject variability of the optimal lags underlying this result are illustrated in Fig.2. The spatial distribution of VE for RVT/HR in one subject is illustrated in Fig.3, showing substantial differences. The optimal model explained 33.8±5.9% of variance of rs-fMRI data in gray matter: slow drifts (19.6±3.3%) were followed by motion (5.9±1.2%), RVT/HR (3.31±0.32%), RETROICOR (3.27±0.30%) and CSF/WM fluctuations (1.35±0.08%).

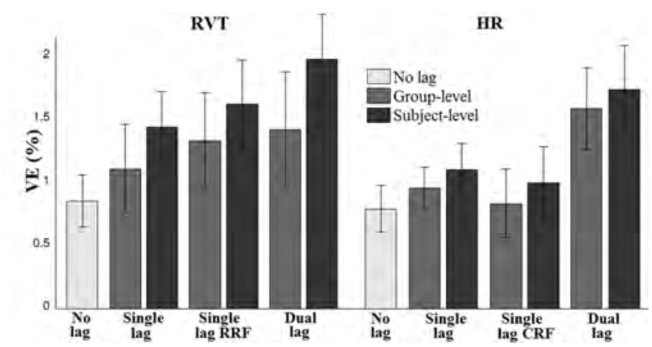

Fig. 1 Group average VE in gray matter for all RVT and HR models tested.

Conclusion: In a systematic comparison of physiological noise models of RVT and HR sources in rs-fMRI at 7T, we found that a dual-lag model with subject-specific lag optimization explained significantly more variance than single-lag or convolutions models, or group optimization. These findings are consistent with a recent report that physiological noise variability in rs-fMRI is lower within-subjects compared with between-subjects[3]. Future work should examine whether subject-specific optimization reduces inter-subject variability of rs-fMRI connectivity measurements, and also whether a region-based optimization would further improve the results.

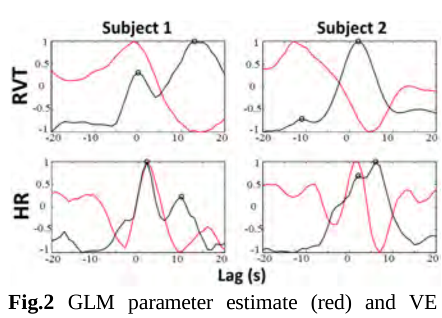

Fig.2 GLM parameter estimate (red) and VE (black) as a function of lag, in two subjects. Note the optimal lags inter-subject variability.

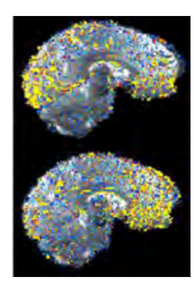

Fig.3 VE maps for RVT (top) and HR (bottom) in one subject.

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References: **1.** Birn et al., NeuroImage 2006, 31(4):1536-48. **2.** Kruger et al. Magn Reson Med 2001, 46(4):631-7. **3.** Birn et al., Brain Connectivity 2014, 4(7):511-22. **4.** Bianciardi et al., Magn Reson Imag 2009, 27(8):1019-29. **5.** Jorge et al., Magn Reson Imag 2013, 31(2):212-20. **6.** Chang et al., NeuroImage 2009, 44(3):857-69. **7.** van der Kouwe et al., Neuroimage 2008, 40(2):559-69.