Retrospective Estimation and Correction of Long-Term Physiological Effects in fMRI

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INTRODUCTION

Low-frequency fluctuations in the cardiac rate and the depth and the rate of breathing have been identified as a significant source of low-frequency (<0.1 Hz) fluctuations in the BOLD signal [1-3]. Removing these fluctuations is particularly beneficial in functional connectivity analysis based on temporal correlation. However, existing techniques [4, 5], focusing on instantaneous effects for quasi-periodic physiological processes, do not account for long term effects [3]. It has been suggested to include the respiration volume per unit time (RVT) and the cardiac rate as regressors of no interest in a general linear model (GLM) [2, 3], assuming that the physiological signal changes are proportional to an unknown time-shifted RVT or the cardiac rate. This assumption may be violated in some cases. The goal of this study is to estimate the physiological signal changes from BOLD timecourse by estimating their impulse response functions and to correct these signal changes, pixel-by-pixel.

THEORY and METHODS

The physiological signal change, x(t), of BOLD signal can be modeled as the physiological impulse train, in which each impulse represent the same relative cycle of physiological processes, e.g., R-peak in heart beat, convolved with an unknown impulse response h(t). In this point of view, techniques proposed in [4, 5] estimated unknown impulse responses for each physiological cycle using Fourier basis. We generalized this idea from one cycle to several cycles to account for long-term, low-frequency physiological effects. Assuming compact support (the 'p' physiological cycles) of h(t), x(t) can be expressed as $x(t) = \sum_{\{i|0<\theta_i(t)<p\}} c_i\, h(\theta_i(t))$ where θ_i is a relative cycle defined as eq.(1) in [4] and c_i is the respiration depth for respiration or 1 for heart beat. The N timepoint of ideal signal x(t) can be expressed in a matrix form after discretizing h(t) into M(≤N) bins, $\mathbf{x} = \mathbf{Ah}$ where **A** is an N x M matrix of {c_i}. With noise, the measured response becomes $\mathbf{y} = \mathbf{Ah} + \mathbf{n}$ where $\mathbf{n} \sim N(\mathbf{0}, \sigma^2 I)$. The impulse response, $\hat{\mathbf{h}}$ is estimated by penalized weighted least-squares estimator as follows, $\hat{\mathbf{h}} = [\mathbf{A'A} + \beta\sigma^2\mathbf{R}]\mathbf{A'y}$ where $\mathbf{R}$ is a matrix of $R(h) = \sum 1/2(h[n] - h[n-1])^2$ and β is a regularization parameter.

All MRI scan were performed on a Siemens 3T Trio (Siemens Medical Solutions, Malvern, PA) MR scanner. Five consecutive runs of resting-state BOLD were acquired from one subject (GE-EPI, TR/TE/FA/FOV =1.5s/35ms/50°/22cm, 19 axial slices with no gap, 3.44 x 3.44 x 5 mm^3, 120 volumes each run). Heart beat and respiration were recorded with a pulse-oximeter and a respiratory bellow, respectively. The proposed estimation and correction were performed by in-house MATLAB programs (p=7, β =0.5 σ =10). The datasets underwent slice-timing correction, motion correction, normalization with MNI152 template, and spatial smoothing with a 5mm using SPM5. RVT changes were created following the method described in [2] ([maximum - minimum] / inter-peak time). To test whether the proposed method can remove the respiratory effect, we compared the correlations between the BOLD signal and RVT changes. To derive t-map of correlation, the 7, 12 sec delayed RVT changes were used as contrast of interest in a GLM including 6 motion parameters and 8 physiological (up to 2^{nd} order terms) regressors [5] for both uncorrected and corrected datasets by AFNI software. The spatial distribution and the amount of estimated respiration-related signal fluctuations were assessed by maps of the fractional standard deviation (SD) in the original timecourse accounted for by respiratory SD in grey matter.

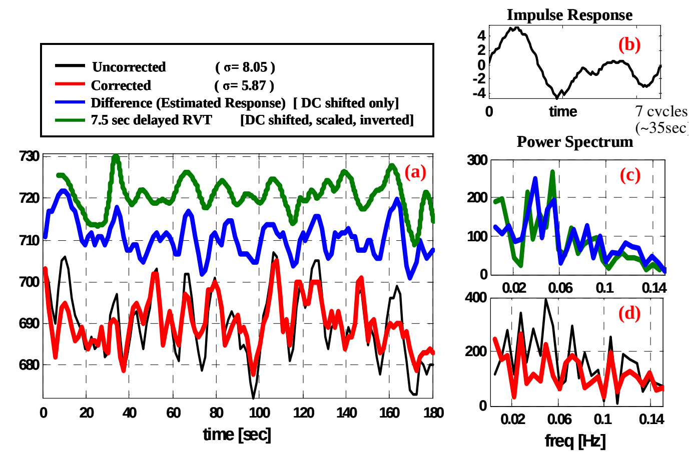

Figure 1. An example of the estimated respiration response in run 1; (a) time courses, (c, d) power spectrum, (b) the estimated respiration impulse response

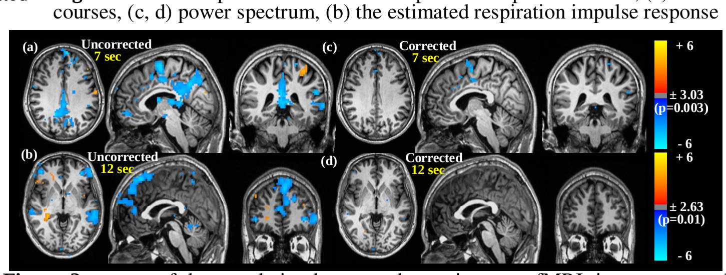

Figure 2. t-maps of the correlation between the resting-state fMRI timecourses and 7, 12 sec delayed RVT changes: (a,c) 7sec (b,d) 12sec for uncorrected (a,b) and corrected (c,d) timecouses in run 1.

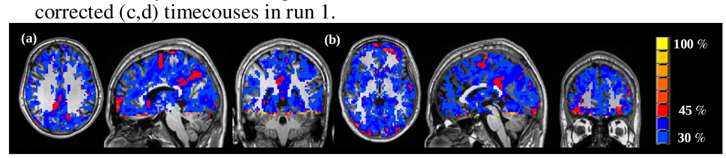

Figure 3. Maps of the fractional standard deviation (SD) in the original timecourse accounted for by respiratory SD in grey matter: these results (a,b) are for the same locations as shown in Figs. 2(a,b) respectively (thresholded with 30%).

Run	Respiration (mean ± SD)	Cardiac beat (mean ± SD)
1	26.71% ± 15.95	12.68 % ± 10.06
2	31.64 % ± 19.63	12.18 % ± 9.73
3	29.24 % ± 18.15	13.21 % ± 9.99
4	29.27 % ± 16.85	11.90 % ± 9.78
5	23.58 % ± 13.55	12.48 % ± 9.50
Average ± SD	**28.09 % ± 16.82**	**12.49 % ± 9.81**

Table 1. The mean of fractional SD in grey matter

Run	Mean of SD Uncorrected	Reduction in SD Corrected	Respiration	Cardiac beat
1	3.15	16.77%	11.72%	5.72%
2	3.04	15.16%	10.26%	5.46%
3	3.17	14.05%	10.93%	5.75%
4	3.16	15.68%	10.78%	5.50%
5	3.34	16.24%	11.78%	5.05%
Average ± SD	**3.17 ± 0.11**	**15.58 % ± 1.05**	**11.09 % ± 0.65**	**5.50 % ± 0.28**

Table 2. The mean of SD over the whole brain for uncorrected timecourse and the reduction in SD for corrected timecourses

RESULTS and DISCUSSION

The estimated respiration response was highly correlated with 7.5 sec delayed RVT change (see Fig. 1). This result agrees well with a previous study [2, 6] and demonstrates that the proposed method accurately estimated the respiration induced signal change. However, the impulse responses were different in different regions as expected. Unlike the "transfer function" in [6], averaged response of deep breaths across the whole brain from separate calibration scan, the impulse responses described here are estimated from the dataset itself, pixel-by-pixel. Several low-frequency components are present in the spectrum of the estimated response (<0.1Hz). The correlations between the resting-state fMRI timecourses and 7, and 12 sec delayed RVT changes are substantially reduced in the corrected dataset (see Fig. 2). The result demonstrates that the proposed method successfully reduced one of non-neuronal BOLD signal variations. Maps of the fractional SD are shown in Fig. 3. Most regions in grey matter were contaminated by respiratory effects. Several brain regions exhibited respiratory effects above 45% (red color). The mean of fractional SD in grey matter was 28.09% for the respiration and 12.49% for heart beat (see Table 1), respectively. The proposed correction reduced the mean SD over the whole brain by 15.58% (see Table 2)

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