RELATIONSHIP BETWEEN RESPIRATORY VARIATIONS AND END-TIDAL CO$_2$ IN BOLD FMRI PHYSIOLOGICAL NOISE

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Introduction

Physiological processes introduce noise into the BOLD fMRI time series, thereby interfering with studies of neural activation and connectivity. One major source of physiological noise can be traced to subtle variations in respiration depth and rate[1]. It has been shown that one can model and reduce such effects by (1) computing a breath-to-breath measure of respiratory variation ("RVT") based on data from a pneumatic belt placed around a subject's abdomen, (2) convolving RVT with an impulse response function (the "RRF"), which has been shown to be an optimal linear mapping between RVT and fMRI time series[2,3] and (3) projecting out the resulting waveform from the fMRI time series of each voxel.

RVT is believed to modulate the BOLD signal primarily by varying the level of arterial CO$_2$, a potent vasodilator[1]; indeed, a separate study found that spontaneous fluctuations in end-tidal CO$_2$ (PETCO$_2$) have a significant correlation with resting-state fMRI time series[4]. However, the degree to which RVT and PET-CO$_2$ relate to one another, or explain common components of the BOLD signal – and across common brain regions – is unknown. It is furthermore unknown whether PETCO$_2$ is better or worse at removing physiological noise from time series than RVT, which is a seemingly more indirect measurement of quantities relating to BOLD signal change (but which may account for factors other than CO$_2$).

In the current study, we directly compare measurements of RVT, PETCO$_2$, and the resting state BOLD signal. We aim to (1) quantify the relationship between RVT and PETCO$_2$, thereby probing the mechanism by which RVT explains BOLD signal changes, and (2) examine the relative efficacy of each signal (and linear transformations thereof) in removing physiological noise across the brain.

Methods

Data Acquisition and Pre-processing: Three healthy volunteers were scanned while resting with their eyes closed for 10 min (3T GE 750, spiral in-out sequence[5], TR=2s). fMRI data were pre-processed with slice-timing correction, spatial smoothing (5mm Gaussian), and removal of linear and quadratic trends. Subjects wore a nasal cannula through which CO$_2$ was continuously monitored using capnography (Capnomac, Datex Corp.). Respiration was monitored using a pneumatic belt placed around the upper abdomen. The cardiac cycle was recorded with a photoplethysmograph placed on the finger, but cardiac data were not used in the present study.

Analysis: RVT was computed using methods described in [1]. RVT was convolved with the RRF, forming a separate waveform ("RVT-RRF"). PETCO$_2$, defined as the peak value at each expired breath) was computed from the raw CO$_2$ waveform and was subsequently interpolated and time-shifted to account for the gas transport delay. To examine the relationship among the physiological waveforms and the brain, physiological waveforms were cross-correlated with one another and with the time series of each brain voxel. A maximum time lag of 16s was permitted for the cross-correlation. To examine linear mappings between PETCO$_2$ and RVT, and between PETCO$_2$ and the fMRI time series, impulse responses were obtained using constrained Bayesian deconvolution with smoothness priors [3].

Results/Discussion

1. RVT-RRF was highly correlated with PETCO$_2$ (r=0.77, SD=0.03; Fig. 1), with an average lag of 10s. This suggests a deterministic mapping between chest expansion (RVT) and PETCO$_2$ that resembles the RRF.

2. PETCO$_2$ and RVT-RRF both accounted for significant BOLD signal variance across gray matter, and greatly overlapped in spatial extent (Fig. 2, Table 1). In some voxels, RVT-RRF explained significantly greater variance than PETCO$_2$, as apparent in Fig. 2B. This suggests that while RVT-RRF is largely accounted for by CO$_2$, there may be additional physiological processes embedded in the RVT measure that affect BOLD signal change, such as those related to the cardiac cycle.

3. For all subjects, the impulse response relating PETCO$_2$ to the whole-brain average fMRI signal was positive and unimodal, peaking at around 8-10s. However, it was observed that convolving PETCO$_2$ with this inpulse response did not explain significantly more variance across the brain than a simple cross-correlation (i.e. using a shifted delta-function as the impulse response).

Conclusions

Our data suggest that RVT and CO$_2$ have a strong linear relationship, supporting the notion that RVT acts to modulate the BOLD signal primarily via CO$_2$ changes. The remarkable spatial and temporal overlap between the BOLD signal variance explained by RVT-RRF and CO$_2$ suggests that removing the effects of CO$_2$ can be accomplished using RVT-RRF, thereby avoiding the need for separate end-tidal CO$_2$ monitoring.

Subj.	PETCO$_2$ $R^2 \pm$ SD (%brain)	RVT-RRF $R^2 \pm$ SD (%brain)
1	0.18±0.09 (37.0%)	0.19±0.09 (39.4%)
2	0.13±0.09 (93.0%)	0.18±0.11 (94.3%)
3	0.23±0.11 (73.2%)	0.14±0.07 (77.9%)

Table 1. R^2 values between PETCO$_2$ and the brain, and between RV-RRF and the brain, across all significant (p<0.001) voxels. Percentage of the brain where significant variance was explained appears in parentheses.
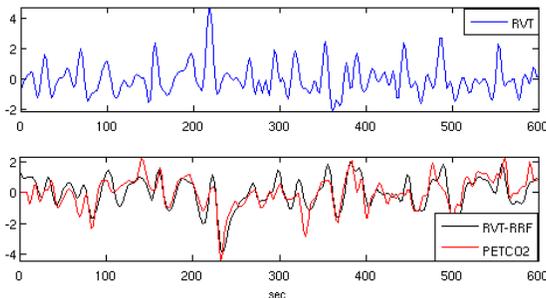

Figure 1. Normalized RVT (above), RVT-RRF, and PETCO$_2$ (below), for 1 subject. PETCO$_2$ has been time-shifted by 10s.
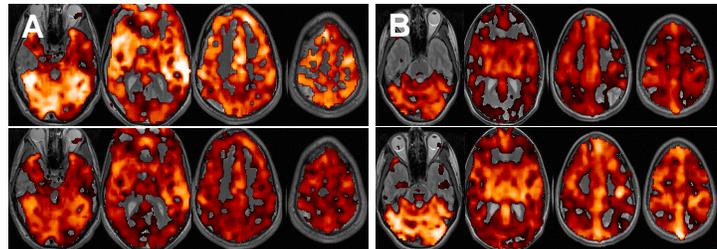

Figure 2. Significant (p<0.001) cross-correlation between fMRI and PETCO$_2$ (top) and RVT-RRF (bottom), shown for 2 subjects (A and B). In Subject A, PETCO$_2$ tended to correlate more strongly with the brain than RVT-RRF, while in Subject B the opposite was true.

References: [1] Birn et al, 2006, Neuroimage 31,1536-1548. [2] Birn et al, 2008, Neuroimage 40:644-654. [3] Chang et al, 2008, Neuroimage (in press). [4] Wise et al, 2004, Neuroimage 21:1656-1664. [5] Glover & Law, 2001, MRM 39:361-368.