Localization and Detrending of Physiological Noise in Resting State fMRI using Machine Learning

T. W. Ash[1], J. Suckling[2], M. Walter[3], C. Ooi[2], T. A. Carpenter[1], and G. B. Williams[1]
[1]Wolfson Brain Imaging Centre, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, [2]Brain Mapping Unit, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom, [3]Department of Psychiatry, University of Magdeburg

Introduction:
BOLD signal contrast fMRI is subject to a wide variety of noise inputs. Amongst these are the effects of physiological based noise caused by the respiratory and cardiac cycles. The trend towards higher magnetic field strength and the linked increase in sensitivity to this noise, coupled with the interest in resting state fMRI, has motivated investigation into the estimation and correction of these signal sources.
We used a multivariate machine learning regression tool, Support Vector Machines (1,2) to characterize physiological noise in a series of resting state fMRI data sets, and used the mean weight vector to localize the voxels most predictive of this physiological noise. Using this information we developed a noise removal tool, SPAR (Simple Physiological Artifact Removal) which we compared with RETROICOR (3) via the independent metric of the Hurst exponent.

Methods:
Acquisition
27 healthy volunteers were scanned whilst resting with their eyes closed. At each acquisition echo-planar imaging (EPI) was used to collect 488 volumes with the following parameters: Repetition time, TR = 1.25 seconds, field of view 220mm x 220mm x 120mm, 26 slices, giving 5mm isotropic resolution. Total scan time was 10 minutes and 10 seconds. Concurrent with fMRI scanning, a respiratory bellows and pulse oximeter measured respiratory and cardiac cycles respectively. The physiological monitoring device sampled each cycle at a frequency of 49.82Hz with a time stamp on the output allowing temporal registration to the fMRI time series. T1-weighted, MPRAGE structural scans (with 1mm isotropic resolution) were also acquired for registration to standard coordinate space.

Quantification and localization
A support vector machine multivariate regressor was trained on the first half of fMRI raw imaging data to regress to the outputs of the pulse oximeter and respiratory bellows. Accuracy of this classifier was then determined by error of predictions as compared to recorded values on the second half of the data. Identification of predictive voxels was accomplished by considering the elements of the weight vector from the linear classifier.

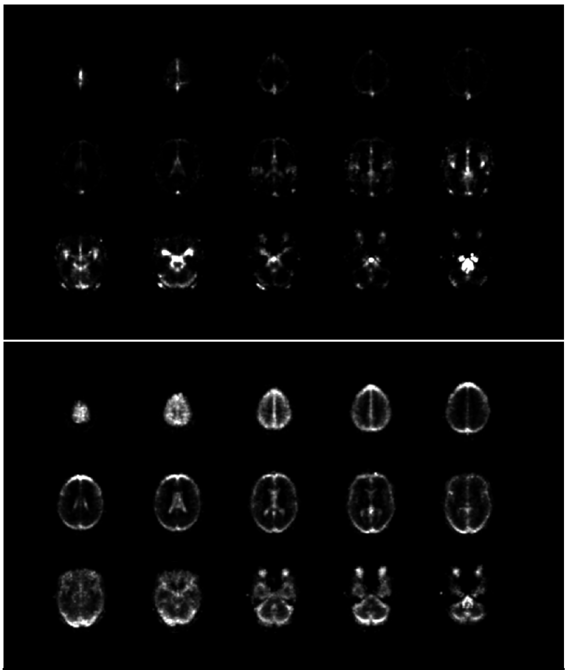

Fig. 1. Mean weight vector showing regions most predictive of the cardiac (top) and respiratory cycles in resting state fMRI.

Removal of Physiological Noise
SPAR is a simple tool designed to remove the trend that the classifier was trained on. This is the relationship between voxel intensity and output from physiological monitoring devices. This relationship was detrended by a third order polynomial on a voxelwise basis, which left a dataset from which the classifier could no longer make predictions better than random chance.
We tested the effects of this on the Hurst exponent (4), and compared to the effects of RETROICO (3), a commonly used retrospective physiological artifact correction tool. The Hurst exponent lies in the range $0 < H < 1$. If $0 \leq H < 0.5$, the auto-covariance is negative and the signal is anti-correlated; whereas, if $0.5 < H \leq 1$, then the auto-covariance is positive and the signal has long-memory or positive autocorrelations over long time lags.

Results and discussion:
In all of our datasets the classifier gave predictions significantly better than chance ($p<1x10^{-16}$ in a paired 2-tail t-test). The accuracy of such predictions has potential as a metric for evaluation of physiological noise in data sets, with more accurate predictions showing more predictable physiological noise in a data set. These effects were localized via the weight vector (Fig. 1) to the CSF in both cycles, and also to major neurovascular regions in the cardiac cycle and the brain edges in the respiratory cycle. These regions are in agreement with previous work on physiological noise in fMRI. After applying SPAR to our datasets, the Hurst exponent significantly decreased in most of the grey matter of the brain (compared with a paired t-test, FDR 0.01), Fig 2. This indicates that the tool is removing some autocorrelation in the time series caused by physiological noise, autocorrelation that may otherwise have been attributed to neuronal activation. We found no voxels with significantly changed Hurst exponent after application of RETROICOR, showing that RETROICOR (a phase driven detrending tool) and SPAR (an amplitude driven detrending tool) are not modeling physiological noise in comparable ways.

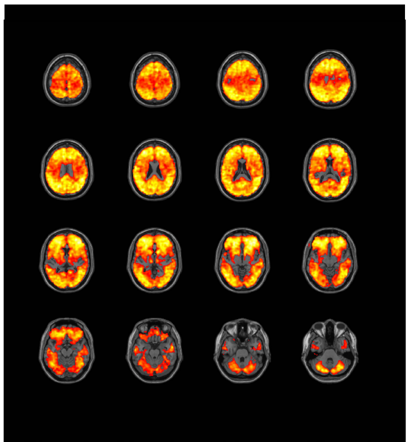

Fig. 2. Voxels with significantly decreased Hurst exponent after SPAR.

Conclusions:
A machine learning regressor has been used to identify regions sensitive to physiological noise in resting state fMRI datasets. The weight vector displaying voxels used in these predictions shows high sensitivity to the cardiac cycle in voxels with a large vascular or CSF components, and respiratory-related sensitivity in CSF and near the brain edge, in accordance with existing reports. However after detrending the voxel intensity using the physiological regressor output ('SPAR'), autocorrelation of intensity was reduced in the majority of grey matter, whilst the existing physiological detrending algorithm RETROICOR was not found to significantly affect measures of autocorrelation.

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