Improved physiological noise modelling for brainstem functional imaging

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Abstract

Respiratory and cardiac effects contribute towards signal variability found in functional magnetic resonance imaging (FMRI) signals. A modified version of the retrospective image correction (RETROICOR) method for physiological noise correction was implemented on resting brainstem echo-planar imaging (EPI) data. Pulse oximetry, respiratory volumes and EPI data were acquired to extract the physiological effects from the FMRI signal. Low-order Fourier series were fitted to the image data based on the phase information and the RETROICOR model. F-test statistical analysis tested the regression analysis residuals, calculated from combinations of respiratory, cardiac and multiplicative harmonics. The optimal model contained 3 cardiac (C) and 4 respiratory (R) harmonics, and 1 multiplicative (X) term: "3C4R1X". Interactions between cardiac and respiratory fluctuations are significant sources of physiological noise in brainstem EPI data. The utility of this approach is demonstrated for a single subject during painful thermal stimulation of the left arm, and revealed increased significance of activated brainstem nuclei when compared to a basic model, which did not account for physiological noise.

Introduction

The brainstem is a challenging part of the central nervous system to acquire FMRI data from - largely because of its small size, proximity to tissues producing magnetic susceptibility effects leading to image distortion and the greater degree of noise observed there in the blood oxygenation level dependent (BOLD) MRI signal. Various strategies have been used to reduce the effects of physiological noise, such as the image- and k-space correction schemes proposed by Glover et al (2000) and Hu et al (1999), respectively. These techniques rely on independent measurement of cardiac and respiratory waveforms using e.g. pulse oximeter and respiratory bellows, which are then used to model sources of noise within recorded FMRI data. Recently a modification to the RETROICOR approach has been proposed (Brooks et al, NeuroImage, In Press) which, in addition to "simple" cardiac and respiratory effects, also models the interaction between these processes, which is thought to driven by the intrathoracic pump (the effect of lung pressure on cardiac stroke volume). The aim of this study was to implement a modified RETROICOR and find a statistically optimal set of regressors for brainstem imaging. Models with different combinations of cardiac and respiratory sine and cosine harmonics were tested to find the combination that most effectively reduces FMRI signal variability, without over-fitting. Lastly, the improvement obtained in an activation study using painful stimulation was assessed.

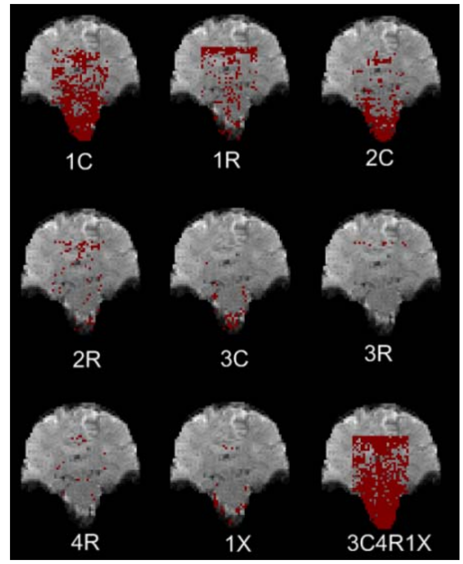
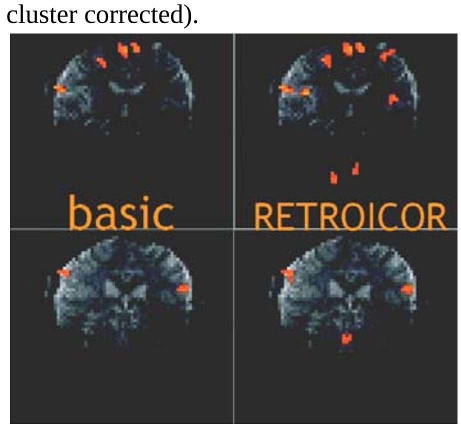


Figure 1 (above): F-test results for a single slice of a single subject, showing the significant Fstat voxels in the ROI (thresholded at F>3.5, p<0.01 uncorrected).

Figure 2 (below): Pain-related activation revealed in the brainstem and periaqueductal grey matter when using a modified RETROICOR (Z>2.3, p<0.05 cluster corrected).



Materials and Methods

Twelve healthy subjects (mean(SD) age 32(5) years, 3 females) were recruited and, for each subject, 1130 T_2*-weighted echo planar image volumes were acquired on a Siemens Trio 3T scanner using an eight-channel head coil. The acquisition comprised 16 coronal oblique slices of the brainstem (sequence parameters: TE/TR=30/1000ms, voxel size 2.5 x 2.5 x 3 mm, flip 70^o). Respiratory volume and pulse oximetry recordings were taken during the experiment. In a single subject a coronal oblique EPI dataset was acquired during an event-related FMRI paradigm, consisting of moderately painful thermal stimuli applied to the left forearm. Physiological data was recorded using pulse oximeter and respiratory bellows (401 volumes, TE/TR=34/3000ms, 24 slices, voxel size 3 x 3 x 2mm, flip 87^o). Resting data were analysed in Matlab, and the modified RETROICOR model (which included sine and cosine terms for 5 cardiac (C), 5 respiratory (R), and 2 interaction (X) harmonics) implemented in a general linear model (GLM). Assessment of the significance of each component was based on hierarchical F-tests. The chosen model was then applied to activation data within FEAT 5.92 (part of FSL 4.0), and improvement assessed on the basis of difference in Z-scores (and size of clusters) of pain-related activation.

Results and Discussion

The spatial pattern of signal components which significantly explained structured noise within the resting data are shown in Figure 1. Based on hierarchical F-tests, the model which explained the recorded physiological signals without over-fitting to the noise contained 3 cardiac and 4 respiratory harmonics, plus first order interaction terms. Using this model it was possible to detect activation in the brainstem following painful stimulation (that was absent with basic modelling), see Figure 2. Across the brain, Z-scores were higher following modelling with a GLM including a modified RETROICOR. Reducing physiological noise in the brainstem may help to interpret FMRI data from studies investigating the control of breathing, cardiovascular control and reception and modulation of pain. Improvements in activation was observed in widespread cortical regions, indicating that this technique may be usefully applied to conventional whole-brain FMRI studies in addition to those examining the brainstem and spinal cord.