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Improving the use of principal component analysis to reduce physiological noise and motion artifacts to increase the sensitivity of task-based fMRI

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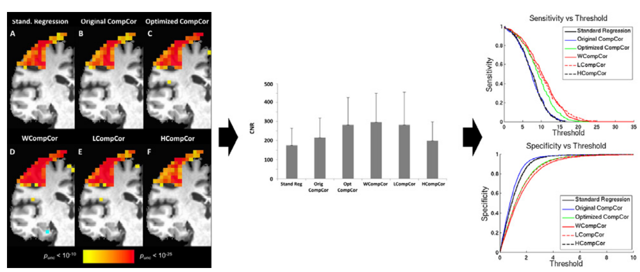
HIGHLIGHTS

- We developed four new PCA methods to identify nuisance regressors in fMRI analysis.
- We compared these PCA methods with CompCor, an established PCA method.
- The best improvement in CNR and sensitivity resulted from the whole brain component correction (WCompCor) method.
- However, regressing noise signals showed a paradoxical consequence of reducing specificity for all noise reduction methods attempted.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Functional magnetic resonance imaging (fMRI) time series are subject to corruption by many noise sources, especially physiological noise and motion. Researchers have developed many methods to reduce physiological noise, including RETROICOR, which retroactively removes cardiac and respiratory waveforms collected during the scan, and CompCor, which applies principal components analysis (PCA) to remove physiological noise components without any physiological monitoring during the scan.
New method: We developed four variants of the CompCor method. The optimized CompCor method applies PCA to time series in a noise mask, but orthogonalizes each component to the BOLD response waveform and uses an algorithm to determine a favorable number of components to use as "nuisance regressors." Whole brain component correction (WCompCor) is similar, except that it applies PCA to time-series throughout the whole brain. Low-pass component correction (LCompCor) identifies low-pass filtered components throughout the brain, while high-pass component correction (HCompCor) identifies high-pass filtered components.
Comparison with existing method: We compared the new methods with the original CompCor method by examining the resulting functional contrast-to-noise ratio (CNR), sensitivity, and specificity.

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Results: (1) The optimized CompCor method increased the CNR and sensitivity compared to the original CompCor method and (2) the application of WCompCor yielded the best improvement in the CNR and sensitivity.
Conclusions: The sensitivity of the optimized CompCor, WCompCor, and LCompCor methods exceeded that of the original CompCor method. However, regressing noise signals showed a paradoxical consequence of reducing specificity for all noise reduction methods attempted.

1. Introduction

Blood oxygenation-level dependent (BOLD) functional magnetic resonance imaging (fMRI) is plagued by raw intrinsic noise, subject motion, and physiological noise. The presence of noise reduces the sensitivity of BOLD fMRI studies and reduces the efficacy of fMRI as a biomarker. If BOLD fMRI were to be used as an endpoint in device trials or for diagnostics, it is essential to understand the value of computational methods for noise reduction upon the sensitivity and specificity of the BOLD signal.

Raw noise, which is independent of the MR signal (Edelstein et al., 1986), is composed of both thermal noise and system noise. Thermal noise derives from the random motion of electrons in the radiofrequency (RF) coil and the tissue being imaged (Haacke et al., 1999). A rise in temperature increases the motion of electrons, increasing thermal noise. Imperfection of the hardware leads to system noise, including low frequency drift (Smith et al., 1999), static field inhomogeneities due to imperfect shimming, nonlinearities in the gradient fields, and irregularities in the performance of the RF coil (Huettel et al., 2004).

Subject motion constitutes a major source of noise in fMRI (Friston et al., 1996). Even head motion of a few millimeters increases the variability of voxel signal intensity as the relative proportion of different tissue types changes inside each voxel. Rigid-body registration methods have been developed to correct for intrascan motion (Cox and Jesmanowicz, 1999). Stimulus- and task-correlated motion can increase the presence of false positives or false negatives in fMRI activation maps (Yetkin et al., 1996). To overcome correlated motion effects, one can use event-related designs (Birn et al., 1999), optimized block durations (Birn et al., 2004), or post-processing methods (Bullmore et al., 1999; Soltysik and Hyde, 2006) to separate true BOLD responses from motion artifact responses.

Physiological noise consists of signal variation in images caused by various processes of the human body. Weisskoff et al. (1993) first reported the presence of cardiac and respiratory waveforms in the power spectra of cortical voxel time series. Cardiac-driven signal changes are mostly due to motion from vascular pulsations in voxels near arterial and venous structures (Dagli et al., 1999). Bulk susceptibility variations in the lungs during respiration leads to systematic variations in the static magnetic field within brain tissue (Raj et al., 2001). These field strength variations lead to image shift, signal changes in the phase encoding direction, and signal variation due to intravoxel dephasing. Mitra et al. (1997) found vasomotor oscillations (0.1 Hz). Furthermore, researchers have discovered low-frequency fluctuations (0.03 Hz) in fMRI data that result from small fluctuations in end-tidal CO_2 that occur naturally during normal breathing (Wise et al., 2004). Fluctuations in both the respiratory volume per time (RVT) (Birn et al., 2006) and the cardiac rate (Shmueli et al., 2007) are also present in fMRI data. Spontaneous BOLD fluctuations that occur without a designated stimulus or task also represent a source of structured noise in fMRI data (Biswal et al., 1995). Because physiological noise results from physiological-dependent fluctuations in the baseline signal, it is proportional to the MR signal, S (Krueger et al., 2001):

$$\sigma_P = \lambda S$$

where λ is a tissue-dependent parameter. Physiological noise will increase with the MR signal, which, in turn, will increase with flip angle (up to the Ernst angle) (Haacke et al., 1999), magnetic field strength, or voxel volume (Edelstein et al., 1986). With increasing field strength, physiological noise limits the achievable image signal-to-noise ratio (SNR) (Krueger et al., 2001), but not the BOLD contrast (Gati et al., 1997). However, other factors may limit BOLD contrast above 7 T (Seehafer et al., 2010).

Many retrospective methods have been developed to reduce the cardiac and respiratory aspects of physiological noise. Biswal et al. (1996) used digital notch filters to remove the frequency components of cardiac and respiration noise. This technique fails, however, when the noise is aliased into the frequency spectrum of the task, as fMRI data is generally acquired with a temporal resolution of 2–4 s. Hu et al. (1995) developed a method called RETROKCOR that fits a low-order Fourier series to the *k*-space time-series data using phase information from the respiratory or cardiac cycles. However, only low-order corrections are possible, and the method introduces unwanted correlations between voxels. Glover et al. (2000) developed a method called RETROICOR that was similar to the method of Hu et al. (1995) but operates in image space. Cardiac and respiratory signals are monitored and recorded during the scan. Physiological noise is modeled as a low-order Fourier series, which can then be subtracted from voxel time series.

Thomas et al. (2002) used principal component analysis (PCA) and independent component analysis (ICA) methods to isolate and remove structured noise (cardiac and respiration) and random noise (white noise) from fMRI time series. After component decomposition, the method involved spectral analysis, component identification and deletion, and signal reconstruction. Thomas et al. found that ICA was a better method to remove structured noise, while PCA was better at removing random noise. Both methods resulted in increased BOLD contrast sensitivity.

Behzadi et al. (2007) developed a method called CompCor, which applied PCA only to voxel time series exhibiting the highest temporal standard deviations. These voxels were believed to be contaminated with cardiac and respiratory noise. The top six components resulting from this PCA analysis, believed to represent cardiac and respiratory noise, were regressed from the entire data set. The reduction in noise achieved with CompCor was found to be greater than that achieved with RETROICOR with the extra advantage in that physiological monitoring was not required. However, for subjects with especially severe motion artifacts, CompCor identified signal components associated mostly with motion.

Early papers suggested that respiration accounted for 10–20% of the temporal variance at 1.5 T (Raj et al., 2001) or that cardiac and respiration accounted for as much as 30–36% of the noise at 4 T (Thomas and Menon, 1988). Therefore, existing methods to remove physiological noise have focused predominantly on removing cardiac and respiratory noise. However, recent evidence suggests