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Measuring the Influence of Physiological Noise Corrections on ICA Derived Intrinsic Connectivity Brain Networks in Rest and Task fMRI

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Abstract

Physiological noise corrections using RETROICOR algorithm has been shown to increase signal sensitivity in resting state networks such as the default-mode network. However, independent component analysis (ICA)-based network approach may suffer from such corrections especially if there is any overlap between two sources in the decomposition domain. To address the extent the physiological noise corrections may impact ICA derived intrinsic connectivity brain networks, we measured network features including functional network connectivity (FNC), power spectra, and network spatial maps in the resting state and task functional magnetic resonance imaging (fMRI) data that were acquired in the same visit from a group of healthy volunteers. Statistical analysis showed functional connectivity between several networks were significantly changed after RETROICOR corrections in both rest and task fMRI. Significant FNC alterations were found in the subcortical, basal ganglia, salience, and default-mode networks. Power spectra analysis showed a trend toward lower power spectra in the subcortical and salience networks at [0.20 and 0.24] Hz after RETROICOR corrections in both rest and task fMRI. Furthermore, physiological noise corrections led to volumetric decrease in the resting state networks that included the subcortical, basal ganglia, salience, and default-mode networks, and volumetric enlargement in the sensorimotor and cerebellar networks. In task fMRI data, physiological noise corrections generally resulted in the expansion of networks except for task-activated networks including the anterior salience, central executive, dorsal attention, and cerebellar networks. If confirmed with larger sample sizes, these results suggest that physiological noise corrections alter some network features, and that such alterations are different between resting state and task fMRI data.

I. INTRODUCTION

Blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) detects neuronal activity indirectly via its assumed haemodynamic correlate. Physiological noise, including cardiac and respiratory cycles (which occur at relatively high frequency of $\approx 1\text{Hz}$ and $\approx 0.3\text{Hz}$, respectively) is always present in fMRI time courses and represents a confounding factor [1]. Several techniques have been proposed to reduce physiologically induced signal fluctuations and improve subtle BOLD signal detection [2]. Some noise reduction methods model quasiperiodic oscillations caused by cardiac and respiratory activity using peripheral measures of the subject's pulse and breathing (e.g., MR-compatible

pulse oximeter and pneumatic belt). A widely used physiological noise correction technique is RETROspective Image CORrection (RETROICOR) [3], which is based on fitting a low-order Fourier series defined by the phase relative to the cardiac and respiratory cycles at the time of image acquisition, and eliminating the corresponding components and their harmonics from voxel time series. Other artifact removal methods utilize the MRI data itself to estimate the noise. Blind source separation techniques, specifically Principal Component Analysis (PCA), and Independent Component Analysis (ICA), have been commonly used to detect noise components from the fMRI signals. For example, a Component based noise Correction method (CompCor) [4] applies PCA to the voxel time series exhibiting higher-than-average time course standard deviations – a feature typically seen in voxels contaminated with cardiac and respiratory noise. ICA has been shown to be a better method to remove structured noise such as respiration-induced susceptibility changes, while PCA was better at removing random noise (i.e., white noise) [5].

Both methods are shown to increase BOLD contrast sensitivity. A previous study, employing RETROICOR for physiological noise corrections showed a reduction in false positive resting-state activations attributed to the default-mode network [6]. It was thus hypothesized that such voxel-by-voxel corrections using the RETROICOR method might increase the sensitivity of detecting positively and negatively correlated regions in resting state fMRI. However, it has been shown that ICA decomposition may suffer from such corrections especially in resting state data [7] if there is any overlap between two sources in the decomposition domain [8]. In this study, we investigate the extent to which ICA derived intrinsic connectivity brain networks can be impacted by RETROICOR respiratory- and cardiac-related noise corrections. Using both resting state and task BOLD fMRI, we measure networks' spatial and temporal features including the spatial maps, BOLD power spectra, and functional network connectivity (FNC).

II. MATERIALS AND METHODS

A. Participants

Participants consisted of fifteen right-handed healthy volunteers (6 male, 9 females, mean age 40.87 years, range 27–62). Exclusion criteria included any major neurological disorder, a history of substance abuse, presence of metallic implants making MRI contraindicated, and any focal abnormalities found by MRI. All participants gave written, informed, IRB approved consent at Stanford School of Medicine and were compensated for their participation.

B. Data Acquisition and Experimental Paradigm

Scans were acquired on a 3T GE Discovery MR750 scanner (GE Healthcare, Waukesha, WI) with 8-channel head coil. The fMRI data were acquired using EFGRE3D pulse sequence (TR/TE = 2000/30 ms, FoV = 22 cm, acquisition matrix = 64×64, flip angle = 76°, slice thickness = 4 mm, gap = 1 mm, 31 slices, sequential ascending acquisition). Respiration data were collected by an MR-compatible chest plethysmograph and cardiac data were collected using an infrared pulse oximeter attached to the subject's left index finger. During the resting state scan, participants were asked to relax with their eyes closed.

Total resting state scan time was 12 minutes and 360 volumes were collected. During the task portion of the scan, participants were instructed to imagine a painful condition such as past back pain and then rate their pain. Total scan time for task fMRI was 12.5 minutes and 375 volumes were collected.

C. Data Analysis

Acquired images were transferred to off-line workstation, and two identical copies of the images were created. One copy was corrected for physiological noise prior to preprocessing using the RETROICOR algorithm [3] (DENOISED data), while the other copy was not corrected for physiological noise (RAW data). Both copies were preprocessed using SPM12. Preprocessing steps included motion and slice-time correction, spatial normalization to MNI space, spatial smoothing with an 8 mm FWHM Gaussian Kernel, and intensity normalization.

ICA was performed on preprocessed images using GIFT software package (Medical Image Analysis Lab, University of New Mexico). We selected 75-IC model order because recent ICA fMRI studies have shown that such high-order ICA models (e.g., above 70) yield more refined and particularly robust decomposition of components. Prior to group ICA, dimensionality of data was reduced at two levels using subject-specific data reduction PCA. Infomax algorithm was conducted to decompose the aggregated data into 75 components. To ensure stability of estimation, ICA algorithm was repeated 20 times in ICASSO followed by GICA3 back reconstruction method.

For FNC analysis, functional network connectivity toolbox (FNCTb) in GIFT was used. Correlation values were calculated following the methodology explained in [9], and saved for each data and separately for rest and task. To determine the significant differences in the connectivity between different conditions (i.e., RAW rest vs DENOISED rest, and RAW task vs DENOISED task), paired Student's *t*-test was performed at false discovery rate [FDR]-corrected threshold of 0.05. To compare BOLD power spectra, the power spectra were calculated using a fast Fourier transform (FFT) method, and compared at six equally spaced frequency bins of [0.00 – 0.24] Hz at 0.04 Hz intervals (paired *t*-test at $p < 0.0083 \approx 0.05/6$ Bonferroni-correction for 6 frequency bins). To evaluate spatial maps, network volumes and peak activations were computed for each condition. Components' spatial maps were thresholded at whole brain family-wise error (FWE)-corrected $p = 0.05$ and the number of voxels that survived this threshold were counted. To measure maximum activation, a voxel-wise one sample *t*-test were performed in SPM12 and the highest *t*-value and the locus of the peak activation (x, y, z) in MNI coordinates were saved.

III. RESULTS

We performed group ICA with 75-IC decomposition on RAW and DENOISED data containing resting state and task fMRI, and identified 16 components as intrinsic connectivity networks (Fig. 1). Based on their anatomical and functional properties, they were characterized as sensorimotor (SMN), cognitive / attention (CAN), salience (SN), basal ganglia (BG), subcortical (SCN), default-mode (DMN) and cerebellar (CN) networks. To

keep the number of calculations reasonable for this paper, we decided not to include the visual and auditory networks.

Figure 2 displays the FNC results for RAW (top), DENOISED (middle) and RAW - DENOISED (bottom) for resting state (2A) and task (2B). For each condition, mean maximal time-lagged Pearson's correlation differences as well as corresponding t -values from the paired t -test are shown. FNC pairs that survived FDR corrections, are marked with black asterisks (*). The results of the power comparisons between different conditions, and spatial feature calculations (i.e., volume and highest peak value) are shown in Figures 3 and 4, respectively. White asterisks in Fig. 3 denote results that survived $p < 0.05$.

IV. DISCUSSION

FNC results revealed significant changes in the connectivity of several networks in the DENOISED data in both rest and task conditions when compared with the RAW data. Significant FNC differences (FDR-corrected $p < 0.05$) was detected between the network pairs that included the subcortical (ICs 47 and 59), basal ganglia (IC 40) salience (ICs 10 and 29), and default-mode (IC 71) networks, especially in resting state condition. Generally, denoising led to slight decrease in connectivity values (i.e., lower Pearson's correlation r) with the exception of the sensorimotor networks. The greatest changes in connectivity were observed in the basal ganglia (IC 40) and the subcortical networks (ICs 47 and 59). IC 47 comprised of amygdala, hippocampus, and entorhinal cortices. IC 59 includes thalamus. Considering that these networks have subcortical structures that are particularly susceptible to the physiological rhythms due to, among others, proximity to ventricular CSF and the circle of Willis vasculature, denoising might have caused removal of some voxels that were identified as "artifactual" by RETROICOR correction algorithm and thus led to differences in FNC. Further, the FNC alterations pattern for task fMRI was slightly different compared to the resting state in that the FNC differences were more pronounced in the connectivity between the salience (ICs 10 and IC29), and default-mode networks with attention & cognitive control networks (ICs 61, 62, and 66).

The results of the power analysis were not significant at Bonferroni-corrected p -value of 0.05. However, at uncorrected p -value of 0.05, DENOISED rest and task data showed lower power spectra in a salience (IC 10) and a subcortical network (IC 47) at the frequency range of [0.20 – 0.24] Hz compared to the RAW data. Physiological noise corrections also resulted in the volumetric decrease in the resting state networks that included the salience (ICs 10, 49, 45), basal ganglia (IC 40), subcortical (ICs 47 & 59), and default-mode (IC 71) networks. Volumetric increase was found in the resting state sensorimotor (ICs 18, 30, 56), cognitive/attention (ICs 61 & 66), and cerebellar (IC 16) networks. In task data, physiological noise corrections generally resulted in the expansion of networks with the exception of salience (IC 10 and 29), two cognitive/attention (ICs 61 & 66) and cerebellar (IC 16) networks. Interestingly, networks that were activated during the task showed volumetric decrease after physiological noise corrections.

V. CONCLUSION

This study is a step toward better understanding how noise correction can impact fMRI outcome. Implicit in the results is the observation that the physiological “noise” might be part of functional signal, not real noise, which is an essential point that deserves to be further debated in the fMRI field.

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Fig. 1.
 Selected intrinsic connectivity brain networks (right = right).

Fig. 2. FNC results. Lower matrix: mean correlation difference; upper matrix: t -values. Black stars indicate pairs surviving the paired t -tests.

Fig. 3.

Power spectra comparison of RAW - DENOISED data for **A** REST and **B** TASK. Frequency bins 1: [0–0.04]Hz, 2: [0.04–0.08] Hz, 3: [0.08–0.12] Hz, 4: [0.12–0.16] Hz, 5: [0.16–0.20] Hz, 6: [0.20–0.24 Hz].

Fig. 4.

Network volumes and peak activations. For **A** REST, and **B** TASK, the top panel illustrates the network volumes averaged over subjects at FDR-corrected p-value of 0.05. The middle panel shows the network peak activation (i.e., highest *t*-value). The bottom panel lists the xyz coordinates of the maximum activation for each network in MNI space and their corresponding brain regions extracted using SPM Anatomy toolbox