Correction of Long-term Physiological Noise Effects Increases the Reproducibility of Resting-State Networks

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INTRODUCTION

Recently, increased attention has been directed at resting-state functional connectivity. However, physiological fluctuations arising from respiratory and cardiac processes are detrimental in resting-state functional connectivity analysis since their frequency range overlaps with the frequencies of fluctuations believed to reflect resting brain activity [1-3]. A technique, physiological impulse response function estimation and correction technique (PIRFECT) [3], was previously introduced to reduce voxel-specific long-term and short-term physiological effects. The present study aims to characterize the effects of physiological noise correction on the derived resting-state networks (RSNs). After correction, it is hypothesized that the reproducibility of RSNs will be increased by reducing the noise component of BOLD signal time series.

METHODS

Data Acquisition: Eleven healthy volunteers were scanned on a Siemens 3T Trio (Siemens Medical Solutions, Malvern, PA) MR scanner. Resting-state BOLD signal were acquired (GE-EPI, TR = 2.25 s, TE = 30ms, FA= 90°, FOV = 204 mm, 3×3×3 mm³, 37 interleaved axial slices with 0.5 mm gap, 148 volumes each run, GRAPPA with PE = 2). Heart beat and respiration were recorded with a pulse-oximeter and a respiratory bellow, respectively.

Preprocessing: After removing the first 4 volumes to account for the approach to steady-state, the datasets underwent motion correction, spatial smoothing (FWHM = 5mm), band-pass filtering (0.01 Hz - 0.08 Hz), linear detrending, and registration to MNI152. Nuisance signals were removed from the data via multiple regressions before connectivity analyses were performed. The common regressors include average signals from white matter, cerebrospinal fluid mask and 6 motion parameters. Physiological Noise Correction: Besides the common regressors, physiological fluctuations are modeled in 5 different ways to examine the effect of physiological noise correction on the derived RSNs. For each subject, 5 versions of time series were obtained, each with a different type of correction: (1) no correction, (2) shortterm only PIRFECT (equivalent to RETROICOR [4]: 8 regressors up to 2^{nd} orders of Fourier basis which account for short-term respiratory and cardiac fluctuations), (3) short-term & long-term PIRFECT (8 regressors for short-term effects and 12 regressors up to 3rd orders of Fourier basis which account for long-term respiratory and cardiac fluctuations), (4) RETROICOR regressors and global signal regressor, (5) RETROICOR and Birn's [5] & Chang's [2] long-term model (respiration volume per time (RVT) incorporated with respiration response function (RRF) and heart rate changes incorporated with cardiac response function (CRF)). Seed-based Correlation Analysis & Reproducibility: Each individual's 4D time series were split into two halves to evaluate the intra-session reproducibility of RSNs. Two halves were processed identically to derive RSNs. For deriving the default mode network, vision network and sensory/motor network, 3 seed regions of interest (ROIs) were identified according to the literature [5]: the posterior cingulate cortex (PCC; MNI Coordinate 0, -53, 26), the right primary visual cortex (V1; 30, -88, 0), and the right primary motor cortex (M1; 36, -25, 57). Connectivity maps corresponding to the 3 networks were derived by correlation with the time series of the

corresponding seed ROI. For each network, two maps were derived from the two halves of the data and the spatial correlations of the two maps were calculated to provide a measure of reproducibility.

RESULTS

The functional connectivity maps after the short-term & long-term PIRFECT correction are presented on the left of Fig. 1 with PCC, V1, and M1, respectively, as seed ROI. The reproducibility of the 3 networks obtained with the different correction techniques are shown on the right of Fig. 1. It is apparent that all 4 types of correction increased reproducibility. Furthermore, the short-term & long-term PIRFECT model led to RSNs with the highest reproducibility, demonstrating the utility of accounting both short-term and long-term effects in the correction.

DICUSSION and CONCLUSIONS

The reproducibility of RSNs was increased by removing short-term physiological fluctuations. More interestingly, accounting for long-term effects in addition to short-term effects resulted in the highest reproducibility. These results suggest that removing long-term physiological noise effects is important for resting-state functional connectivity analysis.

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Figure 1. Effects of physiological noise corrections on the reproducibility of functional connectivity maps using seed-based correlation analysis

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