Structured networks observed in resting fMRI "noise"

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Target Audience: Researchers interested in quantifying resting-state signals and functional connectivity networks using BOLD fMRI.

Purpose: The purpose of this study is to determine whether structure similar to functional connectivity networks is present within the noise data typically removed from fMRI time series. We quantify these effects with physiological and head motion noise regressors and explore the implications for resting state analyses and our understanding of intrinsic network oscillations.

Methods: Resting fMRI data were collected in 12 healthy subjects (aged 32 ± 6 years, 5 female) using a 3 T GE HDx scanner and a BOLD-weighted gradient-echo EPI sequence (TR/TE = 2000/35ms; FOV=22.4 cm; 35 slices, resolution = 3.5x3.5x4mm^3, 165 volumes, 5.5 minutes). Cardiac pulsations (via finger plethysmograph) and expired gas content (via nasal cannula) were continuously monitored; heart rate (HR) and end-tidal CO_2 regressors were extracted. Data were motion corrected (AFNI); the 3 translation and 3 rotation regressors were recorded and their derivatives calculated.

Random noise regressors were also generated: the HR, CO_2 and 12 motion regressors were phase-randomised and then orthogonalised to the original noise regressors, ensuring new regressors with similar frequency characteristics to the true noise sources but with minimal relationship. This process was repeated 10 times. Using a general linear model, noise regressors were removed from the resting BOLD data in the following groups: 2 physiological regressors and 3 (translation), 6 (and rotation), or 12 (and derivatives) motion regressors. The signal variance removed by this noise correction was used as an input to an independent component analysis (data concatenated across subjects, 20 dimensions, MELODIC, FSL). Spatial correlation was used to identify network-related components in the original data and noise data[1]. Finally, four nodes of the default mode network were identified by clustering the ICA results from the original data; the mean time series in these nodes were extracted for the noise and cleaned datasets, and correlations calculated for each node pair.

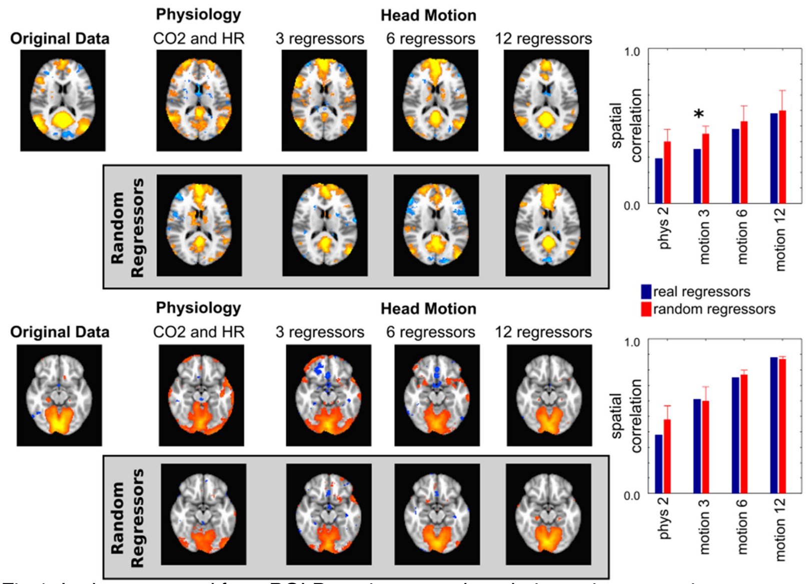

Fig.1. In data removed from BOLD resting state data during noise correction, we observe the default mode and visual networks. This structure remained visible when random noise regressors were used. As more noise regressors were considered, ICA maps of these networks looked increasingly similar to the original network maps.

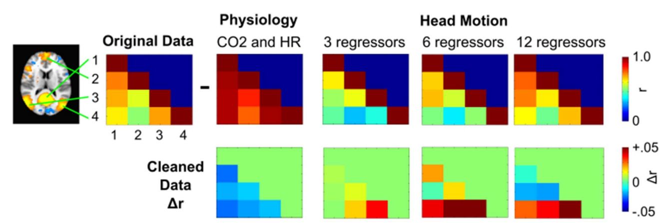

Fig. 2. Correlation between nodes (default mode network) in original and noise data, and changes in correlation after noise correction.

Results: We observed functional connectivity networks in the data variance associated with both the physiological and motion-related noise regressors and their randomized counterparts. As the number of noise regressors increases, the spatial correlation between noise networks and the original data network increases (Fig. 1), as is expected with greater degrees of freedom in the GLM fit. In the physiological noise dataset, the correlations between all pairs of nodes in the default mode network were strongly positive, and physiological noise correction caused decreases in all correlations (Fig. 2). The motion regressors affected nodal correlations in a more varied way.

Discussion: The data variance removed during noise correction is structured into familiar connectivity networks. As we observe this phenomenon using random regressors uncoupled to physiology or motion, this appears to be inherent to the regression of any regressors of similar frequencies. Additionally, the network structure becomes more robust as more regressors are used. This has critical implications for the use of up to 36 noise regressors currently proposed to address the effects of head motion on mapping functional connectivity[2], suggesting these methods remove significant "signal" in addition to the intended "noise." In contrast, the physiological and motion regressors have differing effects on correlations between nodes of the default mode network, supporting the existing literature on the measurement and modeling of physiological and other noise sources.

Conclusion: Noise correction is an important aspect of quantifying resting-state correlations, but it has inherent confounds: any noise regressors extract data variance associated with the network structure of interest. New methods must be developed, perhaps involving ICA of the fitted noise dataset during preprocessing, to prevent the removal of interesting signal structure at the same time as unwanted physiological or motion-related variance.

References [1] Smith et al. (2009) Proc Natl Acad Sci USA 106(31):13040-5, [2] Satterthwaite et al. (2013) Neuroimage 64(1):240-256.