Resting-State fMRI Signal Anti-Correlation Exists in Absence of Global Signal Regression

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Target Audience Neuroscientists, fMRI Researchers

Purpose Studies of resting-state fMRI signals have reported anti-correlation between brain networks covering “task-negative” and “task-positive” regions [1]. Further investigations, however, indicated that negative correlations may be introduced by global signal regression (GSR), a commonly used pre-processing step [2-3]. On the other hand, in support of the original finding, the gamma band power of local field potentials (LFPs) recorded from the cat brain have been reported to show anti-correlation between the “task-positive” and ‘task-negative” regions, although only during brief time intervals [4]. Furthermore, the fMRI anti-correlation has also been observed within short time periods even without using GSR [5]. This apparent contradiction prompted us to reinvestigate the role of GSR in producing anti-correlation using a novel temporal decomposition technique [6].

Methods The resting-state data from 247 participants were selected from the “1000 functional connectomes project” (FCP) [7]. Typical preprocessing steps were applied, including motion correction, spatial (FWHM = 4 mm) and temporal (0.005 - 0.1 Hz) filtering, removal of linear and quadratic temporal trends, spatial co-registration to the MNI template, and nuisance regression of 6 motion parameters. Preprocessing was performed with and without GSR, which regresses out averaged signals from the white matter, cerebrospinal fluid (CSF), and whole brain. Additionally, in both cases, the fMRI voxel time series were demeaned and normalized by temporal standard deviation.

After pre-processing, a 15% subset of time points was selected from the data, based on when signal in the posterior cingulate cortex (PCC) was highest. The time points were classified into and then averaged within 8 groups, using *k*-means clustering based on their spatial similarity (Fig. 1) and resulting in 8 co-activation patterns (CAPs) [6]. A PCC based correlation map was also calculated. These analyses were performed for datasets with and without GSR.

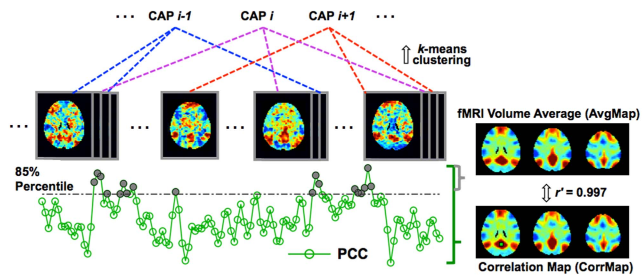

Fig. 1 Illustration of temporal decomposition procedure.

Results As shown in Fig. 2, simply averaging 15% of data selected according to the PCC signal (AvgMaps) almost perfectly replicates the default mode network (DMN) pattern obtained with seed-based correlation analysis based on the entire dataset (CorrMaps), both with incusion of GSR (r' = 0.997; spatial correlation r' was calculated without centering vectors to incorporate the effect of global correlation intercept) and without (r' = 0.998). The CAPs show various decompostions of the DMN that represent activity at distinct time points.

Other than DMN regions, the PCC-seeded correlation map using GSR shows strong negative values in a set of “task-positive” regions, and the CAPs decomposed from it, particularly those resembing the DMN pattern (CAP 1–4), also show negative values in these areas, suggesting that these regions tend to de-activate while the DMN co-activate (Fig. 2, left column). Skipping the GSR procedure made the correlation map statistics shift towards positive values and left almost no areas with strong negative correlation, confirming findings from previous studies [2-3]. This effect, however, is not uniform accross CAPs. CAPs 1–4 only show small shifts towards positive with CAP 2 showing almost no change at all; while CAPs 5, 6, and 8, which are related to visual and motor co-activations, demonstrate much larger shifts in their map statistics (Fig. 2, middle column).

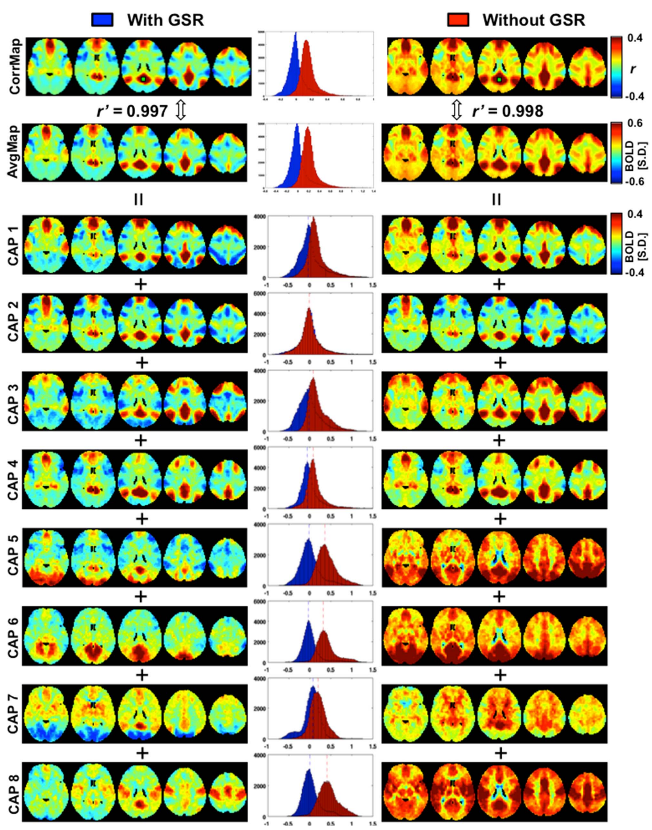

Fig. 2 Temporal decomposition of the DMN patterns obtained with (left) and without (right) using GSR, and a comparison of map statistics distributions (middle).

Discussion The result suggests that the “task-positive” and “task-negative” regions do show anti-phase activity at certain time points, even without the use of GSR. Moreover, the largest effects of GSR are seen for CAPs of sensory-related areas, suggesting global signal increases occur when sensory regions are active. This may indicate intermittent periods of arousal or other neuronal processes that modulate sensory activity. The contribution of global neuronal processes to the fMRI signal is consistent with a previous primate study [8].

Conclusion Temporal decomposition of activity patterns during rest suggests that anti-correlation between brain regions is not an artifact of global signal regression but may be caused by brief periods of negatively correlated neuronal activity.

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