Weaker Brain Dynamics during Sustained Working Memory Task: Perspectives from Co-activation Patterns

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Target Audience: Neuroscientists interested in brain resting-state dynamics

Introduction: Brain resting-state (RS) is believed to be a varying mixture of arousal, levels of attention, mind wandering, etc., various on-going conscious processes may cause considerable fluctuations in the observed network patterns. We therefore have hypothesized that weaker connectivity dynamics should be observed when subjects are under less variable conscious states, for example, when their attentions are primarily engaged by sustained external tasks. Using sliding-window approach, we have demonstrated less variability of Pearson correlations with respect to the default-mode network (DMN) during working memory (WM) state compared to rest (Figure 1 (a))[1]. Very recently, it was found that conventional correlation analysis may indeed be driven by activity at only a few critical points, and that multiple spatial patterns (referred to as co-activation patterns (CAPs)) could be further obtained via temporal decomposition of these critical frames[2]. These reproducible CAPs reflect a repertoire of brain patterns, and the corresponding temporal information allows us to track state alternations at each individual frame, thus offering a more direct way to unveil neural information carried by the source signals. Here, we attempt to employ CAPs analysis to examine the fundamental changes in brain repertoires that underlie the macroscopic decrease in correlation variations during WM task, as shown by sliding-window analysis.

Methods: fMRI Images from 17 healthy subjects were acquired at 3T (GE Signa 750, spiral-in/out sequence[3], TR=2s). Respiration and cardiac (pulse oximetry) data were recorded using the scanner's built-in physiological monitoring system. ***Experiments:*** Each subject underwent (1) a resting-state scan (8 min, relaxed & closed eyes); (2) a continuous 2-back WM task (8min, inter stimulus interval = 3s). ***Preprocessing***: Physiological noise correction[4,5], slice time correction, detrending, spatial smoothing (Gaussian FWHM = 4mm), nuisance regression (six head motion parameters, signals from the white matter and the CSF, subjects' behavioral data[1]) and < 0.1 Hz low-pass filtering were applied. Datasets were further transformed to z scores and normalized to the MNI template. Brain dynamics with respect to the DMN and executive control network (ECN) were examined here. ***Sliding-window Correlation Analysis***: standard deviations of the sliding-window Pearson correlation (window size = 1min, window step = 4s) sequences with respect to two network ROIs [DMN, MNI(-6, -58, 28), ECN, MNI(34, -54, 46)] were computed and utilized to reflect the macroscopic variability of functional connectivity with DMN/ECN across a single scan; ***CAPs analysis**:* (1) frames with ROI signal intensity amongst the top 30% were selected and temporally concatenated; (2) the extracted time frames were further temporally decomposed into multiple CAPs based on their spatial similarity using the k-means clustering method (cluster number ranges from 2 to 16). To account for the instability of single trial clustering result, for each cluster number, we repeated k-means clustering 1000 times, then synthesized the 1000 classification results into one via Normalized-cut method[6] (the weighting between two time points *i, j* were defined as $w_{i,j}=\sum_1^{1000}\mathbb{1}\{\text{frame } i \text{ and } j \text{ are within the same cluster}\}$); (3) For each cluster number n, only those 'dominant CAPs' were preserved for later comparisons (*see Figure 2*).

Results & Discussions:

(1) ***Sliding-window correlations***: Standard deviations of the time-varying correlations with respect to ECN were also decreased during WM (*Figure 1 (b)*), suggesting weaker dynamics in broader brain networks.

(2) ***CAPs***: As shown by Liu's paper, DMN and ECN patterns could be perfectly replicated by averaging the selected temporal frames (*Figure 3 (a)(b)*, *top rows*). Dominant CAPs corresponding to n clusters (n=8 for DMN-CAPs, n=6 for ECN-CAPs) are reported here (identical dominant CAPs were observed in neighboring numbers of n, we therefore believed that the selected n values were representative to present the intrinsic structure of the data). As shown in Figure 3, WM state was dominated by fewer CAPs compared to rest (3 vs. 4 for DMN, 4 vs. 5 for ECN), indicating more monotonic repertoires of brain patterns associated with both networks. In further comparisons of temporal fractions (Table 1), the 1st dominant WM-DMN-CAP exhibited a significant increase compared to the 1st dominant REST-DMN-CAP, implying less frequent state alternations in WM state; CAPs associated with ECN didn't show the same trend, however, given the 1st and 2nd dominant WM-ECN-CAPs had a high spatial similarity (r = 0.61 compared to r = 0.43 in the DMN case), pattern alternations between the two were less likely to incur wild dynamics in the macroscopic correlations. If we extended similar analysis to cases when the two CAPs were grouped in the same cluster (n=2 in table 1), significantly higher temporal fractions of the 1st dominant CAP were observed in WM cases. Collectively, the results were in line with the findings from sliding-window analysis and further supported reduced brain dynamics under WM.

(3) Notably, in both the DMN and ECN cases, the dominant WM-CAPs showed salient similarity with the dominant REST-CAPs, which provided novel insights into the interaction changes revealed by conventional correlation analysis: the higher level correlation differences (*Figure 3 (a)(b, top rows)*) may not source from distinct repertoires of state patterns, but changes in their associated temporal fractions.

Conclusions:

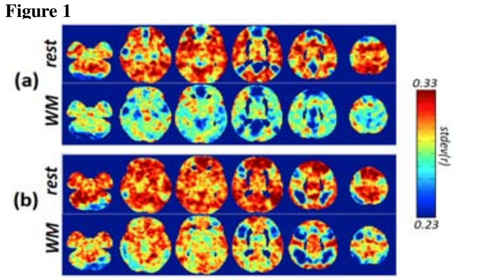
(1) Both sliding window analysis and CAPs analysis reflected weaker brain dynamics during sustained WM task compared to rest, indicating considerable contributions from on-going conscious processes to the widely observed RS brain dynamics.

(2) By elaborately examining the repertoire of brain patterns, we showed that the macroscopic decrease in correlation variations during WM task was indeed a combined effect of more monotonic state repertoire, less frequent state alternations, and increased spatial consistency across various brain patterns.

(3) We noticed a salient similarity between the dominant WM-CAPs and REST-CAPs, whether the reproducible CAPs and their corresponding temporal fractions could serve as robust biomarkers in neuroscience investigations warrants explorations in broader population and mental states.

Acknowledgements: Funding support was provided by NIH P41 EB15891. **References:** [1] Chen et al., ISMRM 2013; [2] Liu et al., PNAS, 2013; [3] Glover & Law, MRM 2001; [4] Glover et al., 2000; [5] Chang et al., NI 2009; [6] Normalized-cut toolbox: http://www.cis.upenn.edu/~jshi/software/

Figure 1



Variability (stdev) over the sequence of 1-min sliding-window correlations between the network seeds and each voxel (averaged across 17 subjects, (a) DMN, (b) ECN)

Figure 2

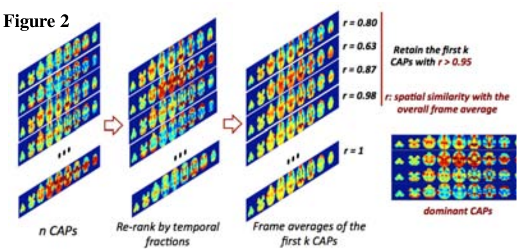
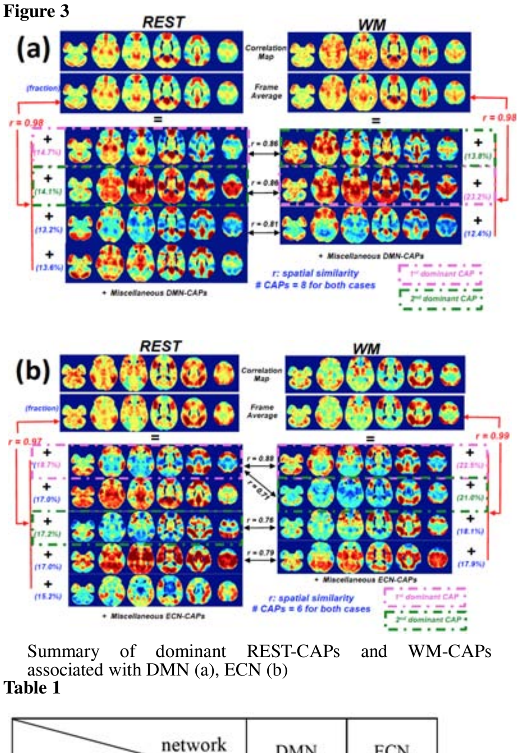


Figure 3



Summary of dominant REST-CAPs and WM-CAPs associated with DMN (a), ECN (b)

Table 1

network / # of CAPs	DMN	ECN
k=2	0.0237	0.0033
k=8 for DMN, k=6 for ECN	0.0130	0.2652

P values of paired-t tests: the temporal fraction of the 1st dominant REST-CAP vs. the 1st dominant WM-CAP