Spontaneous Low-frequency Functional Connectivity and Temporal Dynamics: Working Memory vs. Rest

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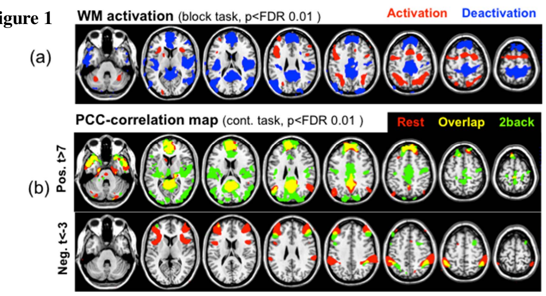
Introduction:

FMRI studies in the past decade have demonstrated that a specific set of brain regions, referred to as the default mode network (DMN), is engaged when people are at rest. The spontaneous low-frequency temporal connectivity within the network has been shown to persist under levels of consciousness and certain task modulations [1,2]. In spite of the rich literature and growing interest in the DMN under broader mental states, the modulation of its static functional connectivity (FC) and temporal dynamics by external, attention-demanding tasks has not been well understood. In the present study, by comparing the temporal behavior of DMN at rest and under a sustained 2-back working memory (WM) task load, we attempt to address three questions: (1) whether steady-state task-induced activation/deactivation can entrain similar patterns in the spontaneous low-frequency temporal connectivity; (2) whether we can observe an attenuation in the global variability with respect to the DMN, as WM baseline mental conditions are hypothesized to be more stable compared to rest, because subjects' attentions are primarily occupied by the imposed WM load; (3) whether the signal intensity in different brain networks exhibits significant changes during the sustained WM task.

Methods:

Subjects: 17 healthy subjects (7 females, aged = 29.0±11.1 years) participated in the study. ***Data acquisition:*** Images 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) an 8-min resting-state scan (relaxed & closed eyes); (2) a continuous working memory (WM) task scan, during which the subjects were instructed to judge whether a currently-present letter was identical to the one presented 2 letters back. Trials were presented sequentially with an inter-stimulus interval (ISI) of 3s. In order to identify the activation pattern, a 6-min block-design (24 sec/block, 7 blocks in total) version was performed prior to the 8-min continuous task. ***Data analysis:*** (1) Pre-processing consisted of physiological noise correction [4,5], slice time correction, detrending, and spatial smoothing (Gaussian FWHM=4mm). Several sources of nuisance covariates (six head motion parameters, signal from the white matter and the CSF) were eliminated using linear regression. With ISI = 3s, TR = 2s, the present stimulus in the continuous WM task was aliased to high frequency (0.16Hz), inducing minimal task-driven BOLD contrast in the collected dataset. To further isolate the spontaneous activity under task conditions: (i) a subject-specific task-waveform, generated by convolving each individual's reaction time sequence with HRF, was regressed out from the continuous WM dataset (results showed that up to 10% variance were explained in the task-activation regions); (ii) temporal signals of both rest and task scans were low-pass filtered (pass band < 0.1Hz); (2) We first performed a seed-based functional network analysis with respect to posterior cingulate cortex (PCC) (MNI -6, -58, 28; 3 mm diameter), a primary node in the DMN. Pearson correlation with the seed ROI across all time points within a scan reflected each voxel's static temporal correlation with PCC; standard derivation of the sliding-window Pearson correlation (window size = 1min, window step = 4s) time-series was utilized to quantify the variability of functional connectivity with PCC across a single scan; (3) To examine the task modulation of the signal intensity in different brain networks, we performed a power spectrum analysis across 0.01-0.08 Hz using amplitude of low-frequency fluctuation (ALFF) index (due to the contamination of task-driven BOLD contrast in the high-frequency band, fractional ALFF index was not analyzed here) [6]. Network ROIs were selected based on the free online functional atlas developed by Stanford FIND lab (http://findlab.stanford.edu/research.html). After normalizing the templates to each subject's native space, an iterative approach was used to extract ROI signals that maximize the intra-network connectivity.

Figure 1



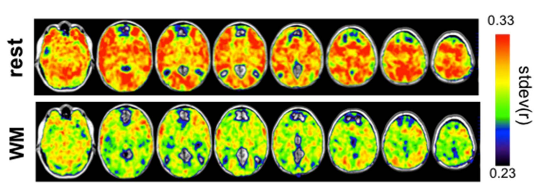


Figure 2, Variability (stdev) over the sequence of 1-min sliding-window correlations between PCC and each voxel (averaged across 17 subjects)

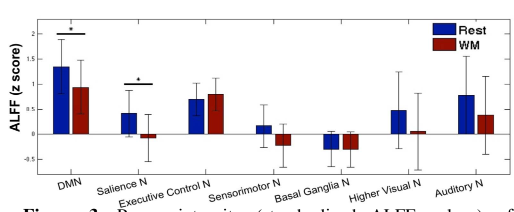


Figure 3, Power intensity (standardized ALFF values) of different brain networks (averaged across ROIs within each network), and 'rest vs. WM' paired t-test result (* = p <0.01).

Results & Conclusions:

The block-design WM results match the typical activation patterns reported in previous WM literatures (Figure 1 (a)) [7,8], and consistent with findings in [2], the spontaneous low-frequency temporal connectivity within the DMN persisted under continuous WM task load (Figure 1 (b), upper).

(1) ***Static FC***: Comparing the PCC-correlation maps of the spontaneous activity under two mental states (rest vs. WM) and contrasting them to the block-design results, we can note a significant *similarity* between the modulated correlations and the activation pattern of the block-design task: regions co-deactivated with PCC by the WM task (Figure 1 (a) blue) showed greater spontaneous low-frequency connectivity with PCC during the sustained task load (Figure 1 (b), upper green); while certain regions of the task positive network (TPN), which were not task-relevant, showed reduced anti-correlations with PCC (Figure 1 (b), lower red). This observation lends supports to a compelling hypothesis that relates the topography of DMN, and other resting-state networks to the history of co-activation between regions inside the same functional network [9].

(2) ***FC Variability***: As has been hypothesized, global variability with PCC was *weaker* during sustained WM task compared to rest (Figure 2), extending findings in a '1-back vs. 2-back' WM comparison in which decreased variability was observed with increasing cognitive load [10], and further implying a possible correlation between the resting-state FC dynamics and subjects' conscious-oriented changes in baseline mental states.

(3) ***Power Intensity****:* ALFF results reflected an attenuation of power intensity across widespread brain regions (not shown). After transforming to z-score, which provides a better view of the 'energy redistribution' within different brain regions, significant power *reductions* were present in the DMN and Salience Network (SN) (Figure 3). Given that the SN is believed to be an important sub-network of TPN, and that the dynamic interplay between DMN and TPN has been argued to be pivotal in cognitive information processing, regional energy reductions in these two networks may likely indicate a more complicated load modulation on the functionality of spontaneous temporal activity and warrants deeper exploration.

Acknowledgments: Funding support was provided by NIH P41 EB15891. **References:** [1] Greicius et al., HBM 2008; [2] Fransson, Neuropsychologia 2006; [3] Glover & Law, MRM 2001; [4] Glover et al., 2000; [5] Chang et al., NI 2009; [6] Hong et al., NI 2007; [7] Owen et al., HBM 2005; [8] Barnes et al., PLOS ONE 2009; [9] Deco et al., The Neuroscientist 2011; [10] Chang et al., OHBM 2011.