Task modulation of intrinsic low-frequency temporal connectivity in the brain default mode network

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Introduction:

Recent neuroimaging studies have led to the proposal that a specific set of regions, referred to as the default mode network (DMN), is engaged when individuals are at rest. Temporal activity within the network is characterized by spontaneous intrinsic low-frequency fluctuations. However, it is still unclear how the low-frequency temporal connectivity within DMN regions changes under different types of external task modulation. In particular, while previous studies have examined the behavior of the DMN at rest or under continuous, attention-demanding tasks that deactivate the DMN [1,2], it is not known how DMN connectivity is modulated by tasks that *activate* major nodes of the DMN. In the current study, we use both cluster analysis and marginal/partial correlation analysis to quantify and compare how low-frequency temporal connectivity of the DMN changes during sustained tasks that activate and deactivate major regions of the DMN.

Methods:

Subjects: 7 healthy subjects (5 females, aged = 26.4 ± 8.9 year) 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:*** We used a two-back working memory task [4,5] to deactivate DMN and a self-referential task [6-9] to activate DMN. In the deactivation task, subjects were instructed to indicate via button-press whether the currently-present letter was identical to the one presented 2 letters back. In the self-referential task, subjects were instructed to judge whether or not a presented adjective 'seldom, sometimes, or often' describes them. Each task consisted of two 3-min continuous runs, during which the letters/phrases were continuously presented every 3/6 sec. A 5-min block design (block duration=24s) version of each task was performed prior to the continuous runs in order to detect activation/deactivation effects. In addition, each subject underwent an 8-min resting scan. Experimental sequences were counterbalanced among subjects. ***Data analysis:*** (i) Pre-processing consisted of physiological noise correction [10], 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. In addition, to isolate the intrinsic low frequency signals, temporal signals were band pass filtered (pass band 0.008 - 0.12Hz). (ii) For each scan, we first used Normed-cut methods [11] to do cluster analysis and selected the best-fit DMN cluster according to anatomical priors. By calculating correlation coefficients between the weighted-average time course of DMN cluster and time courses of all gray matter voxels, we obtained a DMN-correlation map for each state at individual-subject level. For the group analysis, individual-subject correlation maps were thresholded at r>0.2 and transformed to z-scores, two-sample t-tests were employed to make comparisons between different states. (iii) Further, by separating DMN into different sub-regions and calculating marginal/partial correlation inside these regions [2], we attempted to address the low-frequency temporal connectivity on a node-by-node basis for each condition.

Results & Discussion:

According to the block design results, the working memory task successfully deactivated major regions inside DMN for all subjects, while the self-referential task only clearly activated DMN in 2 out of 7 subjects. Continuous data of valid scans were utilized to do cluster analysis. We found that major regions of the DMN were grouped in the same cluster for all valid scans, indicating the persistence of low-frequency temporal connectivity inside the network when subjects performed both activation and deactivation tasks. The correlation map with the weighted-average time-series of the DMN cluster reveals the strong temporal correlations in a clearer way. Fig. 1 shows the DMN-correlation map of a representative subject. Fig. 2 shows the t-score ($p<0.01$) map of the group level comparison between deactivation and resting state. It appears that more prefrontal areas were engaged in the low-frequency temporal connectivity network under working memory task modulation. Based on the clustering results for the resting state scan, 9 regions (precuneus/posterior cingulated cortex (PCC), dorsal/ventral medial prefrontal cortex (d/vMPFC), left/right inferior parietal lob (l/rIPL), left/right temporal cortex (l/rTC) and left/right medial temporal lobe (l/rMTL)) were chosen for a subsequent marginal/partial correlation analysis. Fig. 3 shows the group level results of this analysis.

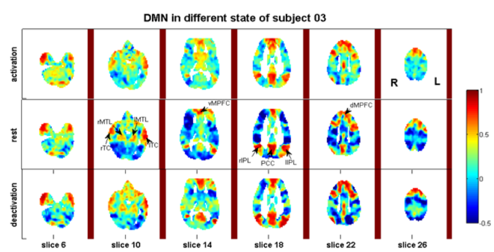

Fig. 1 DMN-correlation map of subject 03

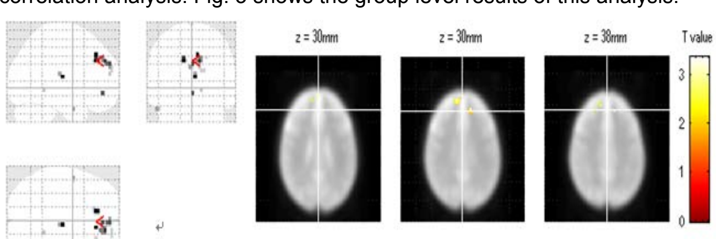

Fig. 2 (top) Two-sample t-test group comparison of DMN-correlation map: (deactivation > rest, p < 0.01).

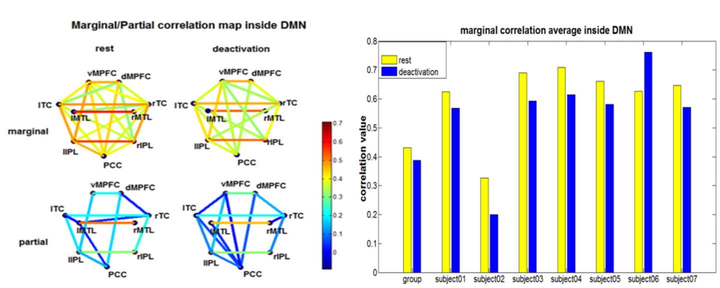

Fig.3 (left) The left panel shows the marginal/partial correlation map inside DMN in network graph format at group level. Each node corresponds to a specific region of the DMN, and the correlation strength between any two nodes is indicated by the colorbar; only network links that are larger than 0.4/0.1 ($p<0.05$) for marginal/partial map are shown. The right panel plots the histogram of average marginal correlation values inside DMN.

Conclusion:

In current study, we used cluster analysis, rather than correlations with single PCC seed time course [1] to obtain a comprehensive view of the low-frequency temporal connectivity network profile under continuous task modulation. Notably and unlike previous studies, we examined DMN connectivity throughout a continuous task designed to elicit activation, rather than only deactivation, of major DMN regions. Combining marginal and partial correlation analysis, we found that low-frequency temporal connectivity was not extinguished but attenuated within most major regions of DMN under tasks that deactivate its nodes relative to rest, and that more prefrontal regions were engaged in the network under such task modulation. Moreover, we noticed the persistence of low-frequency temporal connectivity in subjects whose DMN was activated by external task, providing evidence for the existence of intrinsic activity within the DMN in broader mental states. In further study, a larger subject population will be needed to validate these conclusions.

References:

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