BOLD Signal Changes in Resting State Networks are Related to Performance on a Vigilance Task

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ABSTRACT

Purpose and Background: Recent research has shown that spatially separated brain regions often display functional synchrony that relates to brain state and human performance. Two important anti-correlated functional networks that are seen with resting state functional magnetic resonance imaging (fMRI) are the default mode network (DMN) and the task positive network (TPN). Analytically defining these two networks to better understand their behavior may have a critical impact on understanding higher level function and human performance.

Methods: 17 participants were scanned using fMRI in two different states: while performing the psychomotor vigilance task (PVT) and while in resting state. Using seed based correlation defined networks, the behavior of the TPN and DMN were tested for dynamic behavior after the onset of the task and the shifts in the magnitude of the signal in each network was compared to reaction time on the PVT using a linear regression.

Results and conclusion: The signal in each network changed significantly in response to the task (TPN increased with a peak at 6 seconds, DMN decreased with a peak at 12 seconds). The magnitude of the increase in the signal within the TPN was significantly related to response time on the PVT. This study validates a network generation technique that can be used in future studies to further investigate the behavior of functional networks, and it shows a relationship between shifts within the TPN and behavior on this vigilance task.

INTRODUCTION

One of the principle goals of biomedical research in the past decade has been to reverse engineer the human brain. Traditional cognitive research has focused on localizing functions to specific brain regions, and as a result several techniques have been developed to Determine where specific functions are mapped in various regions of the brain. These techniques include the observation of brain injury patients, functional neuro-imaging, and neurostimulation. Functional magnetic resonance imaging (fMRI) is one of the tools that has been crucial for this type of analysis. By taking repeated MRI scans, fMRI produces a time array of images where the relative contrast in each image is related to the proportion of oxygenated blood. Neural activity requires energy, and energy production requires oxygen, so when neural activity rises, oxygenated blood flows to that region in order to meet the need of the cell. These changes in blood oxygenation level can be deceted with spatial resolution as small as a few millimeters.

Although functional localization has provided valuable information about basic neurological processes, it is now clear that higher level processing relies on the interactions across brain regions (Friston 2011). Biswal, et al. (1995) were the first to characterize the functional relationship between spatially separated regions.

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By selecting a specific seed region and determining the voxels with the greatest correlation to that seed, Biswal discovered that at very low frequencies (0.08-0.1 Hz) spatially separated brain regions activate in a temporally synchronous manner. These resting networks were related to behavior through comparison with traditional task based fMRI analysis to show that the regions associated with performance of a specific task were also correlated in time during resting state scans. Since the initial study by Biswal, et al., many studies have used seed based correlation as well as other analysis methods to explore functional interactions within the brain. In 2001, Raichle discovered a "default mode network" (DMN) in the brain using functional neuroimaging positron emission tomography (Raichle et al. 2001). The default mode network is one the most prominent functional networks in the brain comprised of the precuneus, angular gyri, and medial prefrontal cortex. The DMN was found to be anti-correlated with the "task positive network" (TPN) which becomes active when people perform cognitively demanding tasks (ie. attention or working memory tasks). Anatomical nodes of the TPN include the dorsal lateral prefrontal cortex, the promoter cortex, and the inferior parietal cortex (Fransson 2005).

The psychomotor vigilance task (PVT) is a reaction time task that is used to assess sustained attention. It is a basic vigilance test that involves fixating on a dot that undergoes a slight shift in color at random times. Participants are instructed to signal as quickly as possible when the dot shifts colors. Within well rested subjects, previous studies have related performance on the PVT to specific brain regions using fMRI and the general linear model. Activation in the regions of the brain associated with the TPN has been shown to relate to faster performance, and activation within the regions of the brain associated with the DMN has been associated with slower performance (Drummond et al. 2005). In this work we expand on previous work by using seed based correlation to define the default mode network and task positive network. We show that both resting-state networks change in response to the onset of a task, and that the extent of this change is related to performance as defined by reaction time on the PVT.

METHODS

Several healthy individuals were recruited (9 males and 8 females) with ages ranging from 18 to 26. Data was acquired at Georgia Institute of Technology/ Georgia State University Center for Advanced Brain Imaging, and all studies were performed in compliance with the Georgia Institute of Technology Institutional Review Board. fMRI was performed on all 17 individuals using a Siemens Trio 3T whole body MRI scanner (Echo-planar imaging, number of slices= 4, slice thickness = 2mm, repetition time = 300ms, echo time = 30ms) while simultaneously performing a PVT. The simultaneous image and task paradigm was repeated for four fMRI runs. During each run, the subject was instructed to look at a centrally located black dot and respond immediately by pressing a button when the dot changed color to navy blue. Delay time between task onsets were randomly assigned between 10 and 480 seconds. In addition to the four task fMRI runs, each subject participated in two resting state scans where they were instructed to lie still and fixate on a black dot. Participants were informed that the dot would not change color during resting state scans. The overall order of the scans was counter balanced between order options to control for time effects (Option 1: Resting State-PVT-PVT-Resting State-PVT or Option 2: PVT-PVT-Resting State-PVT-PVT-Resting State).

Preprocessing is the initial step in fMRI data analysis. Preprocessing was conducted using Matlab and the Matlab programs SPM8 and AFNI. During this process, image sequences were aligned with relevant anatomical regions and adjusted to compensate for variance due to time and motion. T1 weighted anatomical images for each subject were segmented into white matter, grey matter, and cerebrospinal fluid maps. Motion parameters and mean signal in white matter were regressed from EPI data. Each voxel's time course was normalized to mean zero and unit variance. The left precuneus was reverse normalized from the MNI brain to be registered to the functional EPI scans and then later be used as a seed region. EPI sequences were slice time corrected and motion corrected using AFNI. The initial 100 TRs (30 s) were removed to account for stabilization time, and the EPI images were spatially blurred with a Gaussian sigma 2x2x1 voxels and size 3x3x1 voxels. The EPI time sequence was then band pass filtered using a finite impulse response (FIR) filter to 0.01 to 0.08 Hz. Finally, the EPI sequences were normalized and detrended according to Thompson et al. (2012). Scans were excluded from analysis for excessive movement (greater than 3.4 mm) or failure to respond to the task.

In order to generate and analyze the functional networks, the Pearson product-moment correlation coefficient (r) was calculated between the mean normalized time course for a seed region (the left precuneus in the most dorsal image) and each voxel's normalized time course for the entire fMRI run. The 1,639 voxels in gray matter most correlated with the seed (1,630 voxels / 10% of all voxels) in gray matter were used to define the DMN, and the 1,639 voxels in gray matter least correlated with the seed were considered the TPN (see fig.2). This network generation technique was chosen because the precuneus is an easily identifiable region in the default mode, and the task positive mode is assumed to be anti-correlated with the default mode (Fransson 2005). The mean activity in the DMN and TPN was evaluated in 2 s windows beginning at the onset of the stimulus through 24 s post stimulus. The resulting Blood oxygenation level dependent (BOLD) signal from each time window after the task onset was compared to the mean BOLD signal between 16 and 0 seconds prior to the onset of the task within each network. A linear regression comparing BOLD signal change within each network to the response time for that trial was then performed for each time window.

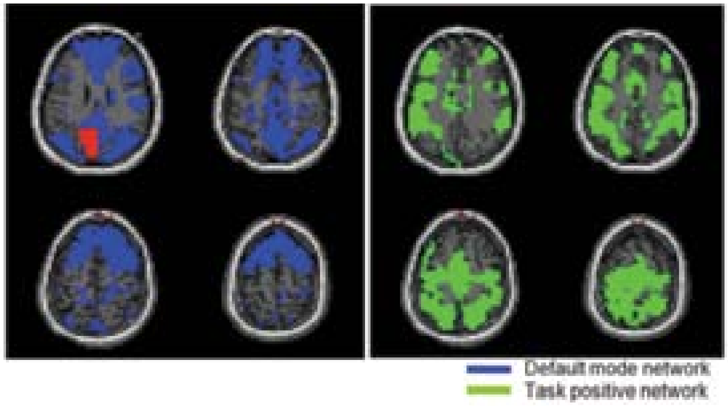

Figure 1: Images of the default mode (left) and the task positve mode (right) for one representative subject. The red highlighted region represents the seed region.

RESULTS

A summary of the results can be seen in figure 2. Both networks changed significantly in response to the task onset (alpha value of 0.05 adjusted for multiple comparisons with Sequential Goodness of Fit, multiple T tests). The mean BOLD signal in the default mode network decreased in magnitude after the onset of the task. This reduction in signal intensity was significantly non-zero at 8, 10, 12, and 14 seconds after the task peaking at 12 seconds. Figure 1 shows the dynamics of both networks after the onset of the task. Conversely, the mean BOLD signal in the task positive network increased in magnitude after the onset of the task. This increase was significantly positive at 6, 8 and 10 seconds after the task peaking at 6 seconds. Using a linear regression, the change in signal within the task positive network was significantly related to performance in terms of reaction time at time shifts 6 and 8 (p-value<.05).

DISCUSSION

The present study shows that performance on the PVT is related to changes within resting state defined networks. This supports previous findings regarding the neural correlates of the PVT, and validates the use of seed based correlation to define the default mode network and task positive network during the PVT. Thompson et al. (2012) used the network defining method presented in this work to relate the correlation between the two networks to trial by trial performance both inter- and intra- individually. The present analysis provides validity to the network generation technique used in Thompson's work by showing that the behavior of both functional networks are similar to the response characteristics seen in networks defined using the General Linear Model (Drummond, 2005). Furthermore, the present study contributes to a larger body of research suggesting that resting state functional network analysis is critical for understanding and predicting human behavior.

An interesting and unexplored result of this study is the difference in the response time for each network. The DMN peak response was 12 seconds after the onset of the task whereas the

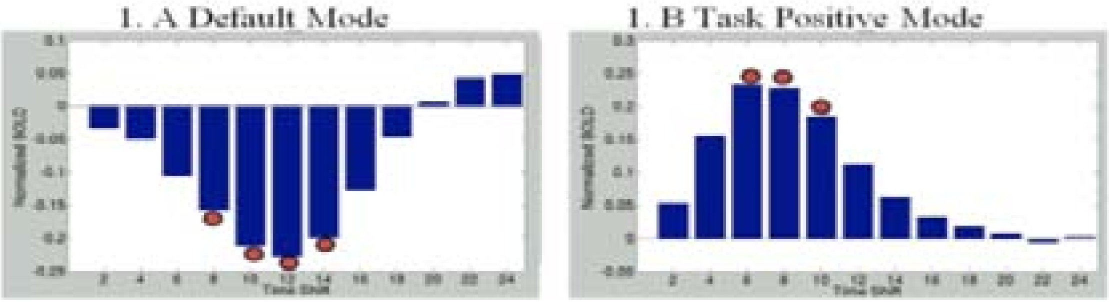

Figure 2: The BOLD signal shift within each network after the onset of the task.

TPN peak response was only 6 seconds after the onset of the task. While this delay does not appear to be related to performance on the task, it may suggest a different hemodynamic response function of negative DMN and positive TPN, or it may relate to a relationship between the spatiotemporal structures of the two networks. The delay also may be related to the pathway by which the task triggers each network. Further work with greater spatial resolution may be necessary to better understand this phenomenon.

FUTURE WORK

This study opens the door for two types of follow up work: 1. Work to better understand functional neural networks. 2. Work to modulate functional neural networks in a beneficial way.

To better understand the networks, future studies may use more complicated performance metrics and full brain scanning rather than four slice scans to better understand the extent of each network spatially, and to what extent each of the networks relates to human behavior. Within this framework, more advanced analysis methods may reveal interesting characteristics of resting state networks. For example, several techniques including wavelet analysis and sliding window correlation are being developed in order to characterize the dynamic behavior of functional networks in time.

Finally future studies may attempt to modulate the behavior of these functional networks with stimulation techniques such as transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS), or transcranial alternating current stimulation (tACS). TDCS and tACS use small amounts of electrical current (<2 mA) in order to alter cortical excitability. Specifically the tDCS animal set up that is currently being developed in the Keilholz lab may be used in future work to understand how brain stimulation alters resting state network behavior.

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