Steady State Functional Connectivity Modulated by Demand in Working Memory

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Introduction Steady state correlations in low frequency blood oxygen level dependent (BOLD) signals have been interpreted as revealing functional connectivity between regions within the human brain. While measurements of these correlations in a resting state have been fruitful [1,2], it is still not well understood how they may change as a function of cognitive demand, or whether they are a general feature of cognitive networks. Working memory involves a distributed network of regions including pre-frontal cortex. The goal of the research presented here is to address the question of whether inter-regional correlations in low frequency BOLD signals change as a function of cognitive demand using the N-back task.

Methods Healthy, normal subjects (N=5) were imaged using a Philips Achieva 3T MR scanner. Functional data were collected using a gradient echo EPI pulse sequence (TE=35ms) making use of an eight channel SENSE coil (SENSE factor=1.8). All images covered a 240x240x122.5mm field of view in which voxel dimensions measured 3.75x3.75x3.5mm. All functional data were corrected for slice timing and motion and co-registered within each subject using SPM2. [3] High resolution anatomic images were acquired as well using conventional parameters.

In order to address the influence of task demand on steady state inter-regional correlations, three steady state data sets were acquired. The first consisted of images acquired in a resting condition. The subject did not provide any response and was instructed to lie still with their eyes closed. The second steady state data set was collected while the subject performed a 1-back letter identity task, and responses were recorded using a button pad on the right hand. The third steady state data set was collected while the subject performed a 2-back letter identity task, and responses were again recorded using a button pad on the right hand. The order of the steady state N-back tasks was randomized across subjects to prevent practice effects. All three steady state data sets consisted of 100 images acquired over 200s.

In order to identify a seed region and target region for analysis, regions of interest (ROIs) were first generated. ROIs were identified using a blocked design task alternating between the 2-back condition and the 0-back condition, where the 0 back task is when the subject responded to a pre-determined target letter. Blocks consisted of 15 letters each containing three targets per block. Five blocks for each task were arranged in alternating order. Activation maps were generated using SPM2 setting statistical thresholds at p=0.001, and minimum cluster sizes of five voxels. Maps were not corrected for multiple comparisons. A target ROI was defined around activation in the anterior cingulate (green as seen in Figure 1) and the seed region was defined around activation in the left prefrontal cortex (cyan in Figure 1) for each subject.

Functional connectivity analysis was performed on all three steady state data sets. This consisted of measuring the mean low frequency signal (<0.1Hz) of the seed ROI, and correlating that to the low frequency signal of each voxel individually. Partial correlations were used in order to remove the effects of global low frequency variations present throughout the entire brain. The mean partial correlation (MPC) of the left prefrontal ROI to the anterior cingulate ROI was then calculated.

Results A significant difference was found between the MPC of the left prefrontal cortex to the anterior cingulate during rest as compared to while the task was performed. This can be seen in Figure 1 (bottom right). Paired t-tests confirmed that the differences in means across subjects were significant (p<0.001 for both task conditions). However, no significant difference was found in MPC between steady state performance of the 1back task as compared to the 2back task (p=0.59). Representative slices showing the ROIs overlaid on partial correlation maps can be seen in Figure 1 (upper right, upper left, bottom left).

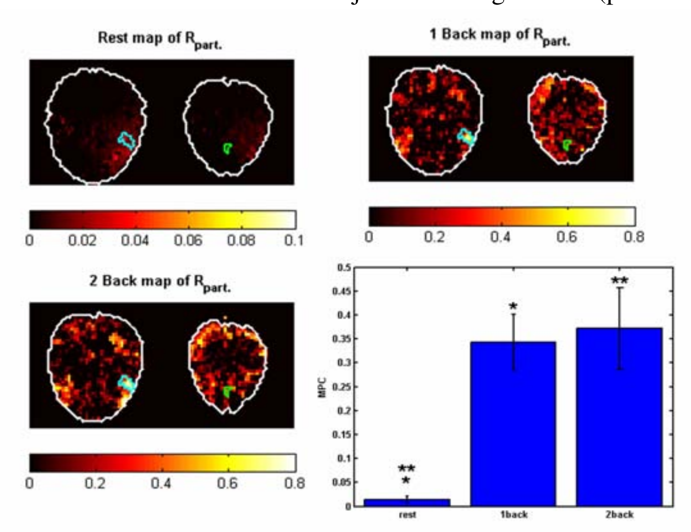

Figure 1: Maps of partial correlation coefficients to the seed region, marked in cyan, for the Rest, 1 and 2Back condition (upper left, right, and lower left respectively). Lower right is the average MPC across subjects. Error bars represent the standard deviation.*,** = p<0.001.

Conclusions These preliminary data suggest that inter-regional correlations of BOLD data in the working memory network correspond to regions that were also activated during conventional working memory tasks. Furthermore, these data confirm that the demand introduced by a higher order cognitive task increase the low frequency correlations between regions known to be involved in the task. These results are in agreement with Honey et.al. who addressed a similar question via path analysis. [4] However, these correlations may not change continuously with increasing demand, perhaps because of ceiling effects or other causes that remain to be investigated.

References

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