Modulation of the Inverse Functional Relation of Resting and Working Memory Networks

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Introduction

Functional brain imaging studies traditionally focus on task related increases in neuronal activity. Several studies have shown regions where activity is higher during rest than tasks. A number of regions including the posterior cingulate cortex (PCC) are active during rest. It is proposed that these structures make up a resting state network that is active in a default mode of function and disrupted during externally cued cognitive tasks [1]. It is important to understand how this network is modulated under different degrees of cognitive demand and how key structures subserving different states of function modulate the activity of one another.

The work presented here describes aspects of the interaction of two seemingly opposing networks; the complimentary activity of the dorsal lateral prefrontal cortex (DLPFC) and the PCC is investigated here. The role of the DLPFC in subserving working memory is very well documented. The n-back working memory task is used in many studies to elicit activation of the DLPFC. An attractive feature of the n-back task is the ability to scale the task difficulty and elicit a range of DLPFC activation [2]. We capitalized on this feature to investigate how changing DLPFC activation relates to the interaction between the two structures.

Methods

Five healthy right-handed subjects with no history of neurological disorder participated in this study after giving informed consent in accordance with Mount Sinai's Institutional Review Board. All imaging was performed on a 3T Allegra MRI scanner (Siemens, Ehrlangen, Germany). BOLD fMRI was acquired with a gradient echo-planar using the following protocol: 32 axial slices, 3mm skip 1mm, TR=2s, TE=30 ms, flip angle=90°, FOV=21 cm, matrix size=64x64. Five different levels of the N-back working memory task using letters were performed by each subject. BOLD scans were obtained on each subject using the n-back activation condition (40s) contrasted with a baseline resting period (20s) repeated 5 times. Images were motion corrected, spatially (6x6x6mm^3) and temporally (4s) smoothed using Brain Voyager (Brain Innovation B.V., The Netherlands). The percent activation was calculated as the percent increase in signal between rest and task. Functional connectivity (FC) between two voxels or regions of interest was described as the degree to which the fluctuations of their time series correlate. The correlation coefficients were Fisher transformed to normalize the distributions.

Results

Activation maps were generated (Fig 1). As expected, all levels of the n-back task caused at least some degree of activation of the DLPFC for every subject. The PCC showed most significant deactivation during more difficult levels of the task. The time series from the two regions (Fig 2) showed a FC that was proportional to the amount of activation of the DLPFC and deactivation of the PCC (Fig 3 and 4). Three of the five subjects showed significant correlations between DLPFC activation and PCC-DLPFC FC (Table 1). One showed a trend while the fifth was not significant. Upon examining PCC activation and PCC-DLPFC FC three of five subject show significant correlations, and two showed a trend.

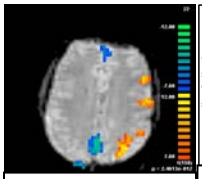


Fig 1. Activation map.

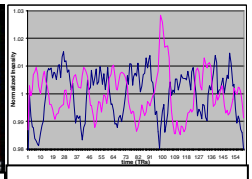
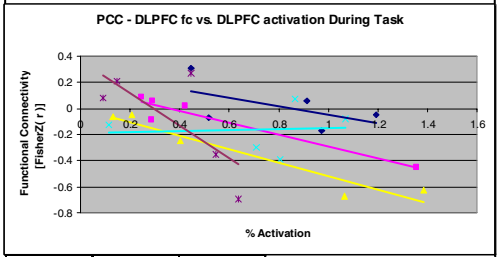


Fig 2. PCC and DLPFC time course

Conclusions

This study combined two analytical techniques, canonical activation and functional connectivity, to investigate how changing task related activity modulates the functional connectivity of two key structures of the resting and working memory networks. It is shown above that the PCC and DLPFC are coupled and that this degree of coupling increases as task related neuronal activity increases.

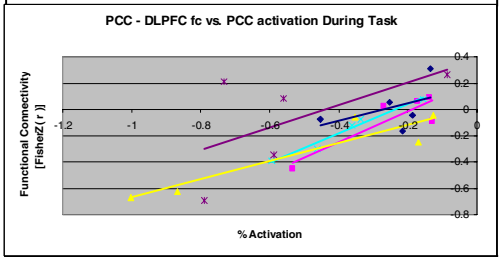
Fig 3. Functional Connectivity vs. DLPFC



Subject	r Value	p Value
Subject 1	-0.56	0.250
Subject 2	-0.95	0.004
Subject 3	-0.96	0.002
Subject 4	0.08	ns
Subject 5	-0.73	0.099

Table 1. Correlation between DLPFC activation and DLPFC-PCC FC.

Fig 4. Functional Connectivity vs. PCC activation



Subject	r Value	p Value
Subject 1	0.46	0.359
Subject 2	0.88	0.021
Subject 3	0.93	0.007
Subject 4	0.98	0.001
Subject 5	0.58	0.223

Table 2. Correlation between PCC activation and DLPFC-PCC FC.

1. Greicius, M.D., et al., Proc Natl Acad Sci U S A, 2003. **100**(1): p. 253-8.
2. Manoach, D.S., Schizophr Res., 2003. **60**(2-3):p.285-98.