Resting-state connections in prefrontal cortex indicate cognitive network efficiency during working memoryτ

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INTRODUCTION

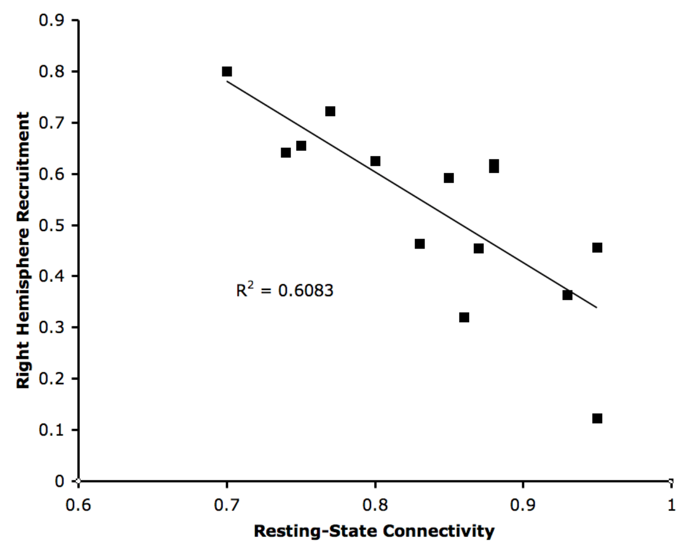
Working memory is crucial for many cognitive abilities, including learning [1], and results from the dynamic interplay between a number of brain regions [2,3]. Of particular interest is the dorsolateral prefrontal cortex (DLPFC), which has consistently been identified as critical for working memory [4], especially as task difficulty increases [5]. Previous fMRI studies have shown that these regions exhibit a significant correlation during the resting-state [6], and patient fMRI studies have demonstrated that abnormal patterns of brain activity during working memory tasks, as well as decreased resting-state correlations between DLPFC and other regions are associated with decreased cognitive performance [7]. This suggests there may be a relationship between resting-state connections and the efficiency of cognitive networks during task performance, which could further our understanding of the mechanisms underlying cognitive function in both health and disease. Therefore, the aim of the current study was to investigate the relationship between resting-state connectivity and cognitive network efficiency during performance of a working memory task in healthy human subjects.

METHODS

Fourteen healthy volunteers (11 males) underwent two scans each of resting-state and working memory fMRI, both of which used a GRE-EPI sequence (TR/TE = 1500/30ms; flip angle = 65°; 64x64 matrix; 24-cm field of view; twenty-four 5-mm thick slices). All images were acquired using a 3 Tesla MR scanner (Signa Excite; GE Healthcare, Waukesha, WI). Resting-state scans consisted of five minutes of scanning while the subject relaxed and fixated on a cross at the centre of a projection screen (Avotec, Inc., Stuart, FL). Working memory fMRI followed, consisting of 15 seconds of rest followed by twelve 40-second epochs of the *n*-back task. Each task epoch was at one of three difficulty levels (n = 1, 2, or 4); each repeated four times in random order. Subjects were presented single numerical digits at three-second intervals, and were asked to press a button when the presented digit was the same as that presented n digits previously. Each epoch commenced with a visual cue as to which task level was to be performed. All data analysis was performed using FSL (http://www.fmrib.ox.ac.uk/fsl) and the General Linear Model to determine the mean brain activity across all task difficulty levels, as well as significant differences in activity between the n=4 and n=1 difficulty levels (i.e., the complexity map). Anatomical images were also collected for registration of fMRI data. The group average complexity map was used to identify a cluster of activity (Z>2.3) within the DLPFC of the left (seed) and right (target) hemispheres for analysis of the resting-state data. For each participant's resting-state data, the average time series of signal intensity was recorded for the seed and target, and a temporal cross-correlation was performed. The median of the cross-correlation was recorded rather than the mean, as the median is less susceptible to intermittent disruptions of the resting state. Right hemisphere recruitment of DLPFC during the n-back task was defined for each subject as the ratio of the mean Z-statistic within the right DLPFC in the complexity map to the Z-statistic in the mean activity map.

RESULTS

Working memory related activation was consistent with previous findings, showing significant activation within the DLPFC and increased right-hemisphere involvement as task difficulty increased. As the figure shows, there was a significant negative linear relationship between recruitment of the right DLPFC as task difficulty increased and resting-state connectivity between right and left DLPFC.



DISCUSSION

Subjects exhibiting greater inter-hemispheric communication in the DLPFC during the resting-state recruit DLPFC in the right hemisphere to a lesser degree during the performance of a working memory task, as the task becomes more complex. One possible explanation for this observed relationship is that brain regions strongly connected to the DLPFC in the left hemisphere during rest act silently during performance of a working memory task, permitting the cognitive network to work more efficiently. In contrast, when the cognitive areas are not strongly connected between the hemispheres during rest, the right hemisphere is recruited more to help perform the task, resulting in a less efficient network.

REFERENCES

[1] D'Esposito M. *Philos Trans R Soc Lond B Biol Sci* 2007; 362: 761-72.
[2] Sinnen SP, et al. *Trands Cogn Sci* 2004; 8: 18-25.
[3] Rogers BP, et al. *Magn Reson Imaging* 2007; 25: 1347-57.
[4] Curtis CE, et al. *Trends Cogn Sci* 2003; 7: 415-23.
[5] Rypma B, et al. *Neuroimage* 1999; 9:216-26.
[6] Biswal B, et al. *Magn Reson Med* 1995; 34: 537-41
[7] Yoon JH, et al. *Am J Psychiatry* 2008; 165: 1006-14.