Resting state network and human intelligence, and fMRI study

C. Tang[1], D. Carpenter[2], E. Eaves[2], J. Ng[2], C. A. Condon[3], D. H. Schroeder[3], R. Colom[4], and R. Haier[5]
[1]Radiology & Psychiatry, Mt. Sinai School of Medicine, New York, NY, United States, [2]Radiology, Mt. Sinai School of Medicine, New York, NY, United States, [3]Johnson O'Connor Research Foundation, Chicago, Il, United States, [4]Psychology, Universidad Autonoma de Madrid, Madrid, Spain, [5]School of Medicine (Emeritus), UC Irvine, Irvine, Ca, United States

Abstract
Resting state networks are an emerging target for functional MRI researchers. In this study we sought to investigate the relationship between cognitive factors and features of brain activity at baseline. We obtained a set of cognitive measures on 40 normal control subjects. Subjects received fMRI scans while at rest as well as while performing a working memory task. Correlations were computed between indices of the resting state networks and cognitive factor scores. In addition the loci of the resting state networks were also analyzed while the subjects performed the working memory tasks.

Method - Subjects:
The subjects were screened for medical and psychiatric illnesses including a history of head injury and substance abuse. Included were 21 males and 19 females, aged 18-35 years (mean age = 26.6, *SD = 4.9; mean age for male is 26 and for female is 27).* The subjects completed eight tests of the Johnson O'Connor Research Foundation (JOCRF): Inductive Speed (IS), Analytical Reasoning (AR), Number Series (NS), Number Facility (NF), Wiggly Block (WB), Paper Folding (PF), Verbal-Associative Memory (VAM), and Number Memory (NM). Previous research[(1)] showed that these tests load on four cognitive factors – Speed of Reasoning (IS and AR), Numerical (NS and NF), Spatial (WB and PF), and Memory (VAM and NM) in addition to a *general factor*. These tests have been used in research on various aspects of cognition and intelligence[(2)]. For the present study, test scores were separated for sex and age in order to eliminate nuisance variance.

Paradigm:
For the resting state scans the subjects were told to lie quietly and close their eyes. For the working memory task we used a modified N-Back paradigm. Based on a single letter N-back paradigm, a multi-back paradigm was developed using E-Prime (PST Inc., Pittsburgh, PA). Six trials of different N-back stimuli were presented where N∈{0,1,2,3}. Each trial was preceded by a 2s instruction screen indicating which N-back was to follow. Each trial lasted for 30 seconds. In between the trials was a 20 seconds rest period where the subjects were presented with a fixation screen. All subjects received instructions on the task before the imaging session.

Imaging:
Imaging was performed using a Siemens 3T Allegra MRI. Imaging protocols: Axial 3D-MPRage (TR = 2500 ms, TE = 4.4 ms, FOV = 23 cm, matrix size = 256x256, 208 slices with thickness = 0.9 mm). EPI Bold scans were acquired using a GE-EPI sequence with the parameters: TR=2s, TE=27ms, FOV=21cm, 2.5mm thick, skip = 0.5mm, Matrix size=64x64, 34 slices, 246 measurements with a total scan time of about 8 minutes. The resting state scans used the same acquisition protocol but with 120 measurements.

Analysis:
N-Back BOLD data was processed using SPM5. Functional data was slice-time corrected by interpolation to the middle slice prior to motion correction. Anatomical images were coregistered to each subjects' mean functional image. Coregistered anatomical images were then segmented to produce the parameters used for normalization into MNI space. Images were spatially smoothed using a 6 mm isotropic Gaussian smoothing kernel. Individual contrast images were produced in the context of the general linear model using a boxcar function [0-back versus 1,2,3-back] convolved with a canonical hemodynamic response function. Activation maps thresholded at p<0.001 were computed. The following clusters of activation were identified: Anterior Cingulate (ACC), Prefrontal Cortex (PFC), Parietal cortex (PC), Insular Cortex (IC) and visual cortex (VC) (Fig 1). These group activation clusters loci were then used for individual functional connectivity analysis. R-values were computed between each of these clusters and fisher transformed. Correlations were then computed between these r-values and the cognitive performance scores. Resting state scans were motion corrected and temporally smoothed and then analyzed using a K-Means clustering algorithm, random seedpoints were generated for 10 clusters. The resting state network that encompasses the posterior cingulate cortex (PCC) and the parietal cortices (PC) was selected for analysis (Fig 2). A cluster tightness index was computed as a function of the average Euclidean distance of the of each timecourse signal vector to the mean timecourse vector of the cluster.

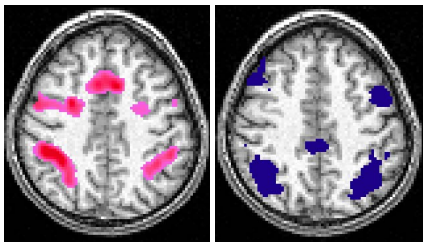

Fig 1a. N-Back group activation map showing PC,DLPFC and ACC.
Fig 1b: Resting state network showing PC, PCC and DLPFC

Results
The resting state data showed a significant correlation between the tightness of the cluster and the spatial (r=0.39,p<0.015) and memory (r=-0.48, p<0.003) factor scores. Functional connectivity analysis between these regions while the subjects were performing a working memory task showed no significant correlations between the fisher transformed connectivity r-values and the spatial (r=0.08, p<0.630) or memory (r=0.038, p<0.821) factor scores. Instead, the connectivity r-values between the parietal cortex and the dlpfc showed a significant correlation with the general factor scores: right PC- right DLPFC: r=0.412, p<0.010 and left PC-left DLPFC: r=0.464, p<0.003).

Discussion
Several studies have shown aberrant characteristics of the resting state network in various psychiatric disorders such as Alzheimer's and schizophrenia[(3,4)]. The resting state network that consist of the PC and PCC is also the complementary network that is turned off when engaged in a working memory task[(5)]. Here we have used this technique to study this network in normal controls as a function of their cognitive performance scores. We showed that the coherence of this resting state as measured by the tightness index is correlated with several cognitive indices. In addition we found a significant correlation between the functional connectivity between the parietal cortex and the DLPFC with the general factor scores, consistent with the Parietal-Frontal Integration Theory (P-FIT) [(6)].

Grant Support: Johnson O'Connor Research Support Corporation

1) Condon C.A., Schroeder D.H. 2003. Establishing the factor structure of the Johnson O'Connor Research Foundation's test battery. In Annual Meeting of the International Society for Intelligence Research, Newport Beach, CA.
2) Haier RJ, Colom R, Schroeder D, Condon C, Tang C, Eaves E, & Head K. Gray Matter and Intelligence Factors: Is there a neuro-g? Intelligence, 37(2), 136-144, 2009.
3) Greicius M.D., Srivastava G., Reiss A.L., Menon V., 2004 Default-mode network activity distinguished Alzheimer's disease from healthy aging: Evidence from functional MRI. PNAS V101,13 p4637-4642.
4) Jafri M.J., Pearlson G.D., Stevens M., Calhoun V.D., 2007, A method for functional network connectivity amoung spatially independent resting state components in schizophrenia. Neuroimage, V39, 4, P1666-1681.
5) Greicius M.D., Krasnow B., Reiss A.L., Menon V., 2003, Functional connectivity in the resting brain: A Network analysis of the default mode hypothesis, PNAS V100,1, p253-258.
6) Jung R.E. & Haier, R.J., The Parieto-Frontal Integration Theory (P-FIT) of Intelligence: Converging Neuroimaging Evidence. Behavioral and Brain Sciences , 30, 135-187, 2007