The "foot-print" of memory encoding on the brain

Deng Mao[1], Kuang-Chi Tung[1], Peiying Liu[1], Yong He[2], Jinhui Wang[2], and Hanzhang Lu[1]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [2]*State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China, People's Republic of*

INTRODUCTION: An interesting application of rest-state fMRI (or fcMRI) is that this technique can be used to study connectivity changes before and after a task or training, i.e. the "foot-print" that a task left behind on the brain. The ability to quantify this change potentially provides a novel biomarker for brain plasticity and may find applications in brain aging, Alzheimer's Disease, or stroke. A number of evidences have suggested that the resting brain can be modulated by recent experience [1-5]. However, few reports have demonstrated the feasibility to measure brain changes after merely minutes of use. Here, we used a 20-min memory encoding task to stimulate the brain, and collected fcMRI data (under resting state) before and after the task. We compared resting brain network between these two time points to identify any connectivity changes. Finally, we tested the hypothesis that, across individuals, the extent of connectivity change is correlated with the behavioral data of memory scores.

METHODS: BOLD fMRI data (3.4x3.4x5mm^3 voxels, TE 25ms, TR 1000ms) were acquired in 11 healthy right-handed adults (24.8±1.8yo, 8males) using a 3T Philip MR scanner. The experimental session for each subject started with a 5 min resting state scan (*Pre-training scan*) (Fig. 1), in which they were instructed to fixate on a white crosshair. This was followed by a 20-min *task period*, during which the subject was shown 200 color pictures of equal number of indoor and outdoor scenes (presented one at a time for 3 s). They were instructed to determine whether it is an indoor or outdoor scene by pressing one of the two buttons in two hands. This was followed by another 5 min resting state (*Post-training scan*). After the MRI session, subjects were given a surprising memory test in which 200 new pictures with equal number of indoor and outdoor scenes were randomly mixed with the 200 pictures they viewed in previous task. Subject's response of yes or no to questions if they have seen the picture before was used as the memory score.

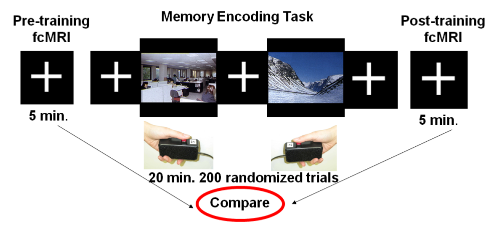

Figure 1. Experimental paradigm to compare resting networks before and after memory encoding task.

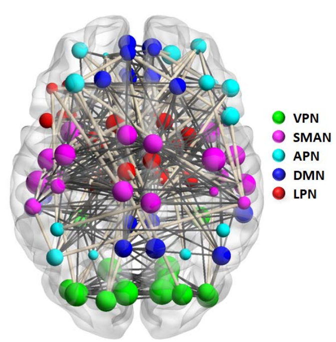

Figure 2. Node assignments of brain regions.

Data processing: Imaging data were preprocessed (realigned, normalized, smoothed and band-pass filtered (0.01-0.1 Hz) and detrended) in SPM. Then the whole brain was divided into 90 cortical and subcortical regions of interest according to anatomical automatic labeling (AAL) atlas and the mean time course for each region was extracted by GRETNA toolbox [6]. Each time course was corrected for respiration, multiple fluctuations (whole brain, white matter and CSF) and motion. Correlation coefficient (CC) was calculated between the time courses of every pair of regions, yielding a 90 by 90 correlation matrix. To reduce the number of multiple comparisons, the correlation matrix was consolidated to a 5 by 5 matrix by averaging entries that belonged to the same networks defined in literature [6]. These networks corresponded to Default-mode network (DMN), Attention processing network (APN), Visual processing network (VPN), Limbic and paralimbic network (LPN) and Somatosensory-motor-auditory network (SMAN) (Fig. 2). Pre- and Post-training comparisons were made for intra-network and inter-network connections.

RESULTS and DISCUSSION: We first confirmed the validity of the node assignments by applying the method described in [6] to our Pre-training data, and the results (Fig. 2) showed high consistency in network identification (86% of nodes overlapping with reports in [6]). The pre vs. post comparison still used node assignments in [6] in order to avoid bias. Comparison between pre- and post-training CC values revealed significant alterations in brain connectivity following a memory task as short as 20 min (Fig. 3). Default mode network (DMN) (corrected P=0.005) and attention process network (APN) (corrected P=0.05) showed significantly reduction in intra-network connectivity after training. For inter-network connectivity, a trend of reduction was also seen between DMN and APN (uncorrected, P=0.027) and between APN and LPN (uncorrected P=0.038). Furthermore, across individuals, the degree of connectivity reduction was correlated with the memory score (mixed effect analysis, P=0.0037). An individual with a larger reduction in connectivity tended to show a poorer memory score (Fig. 4). To our knowledge, this is the first demonstration that fcMRI brain networks can be modified in the acute phase using a memory task. We showed that resting state connectivities among nodes within DMN and those within APN were reduced after 20 minute of scene encoding. Interestingly, these spatial regions are virtually identical to those activated or deactivated by an encoding task [7], supporting the notion that these findings represent a "foot-print" from previous brain usage. Our findings cannot be attributed to the possibility that the subject was still performing an "imaginary" memory task during the post-training fcMRI, as DMN and APN would have shown opposite changes according fMRI literature (encoding task activates APN, but deactivates DMN). This method may provide a new approach to study brain plasticity in humans and may find applications in studies of aging and neurodegenerative diseases.

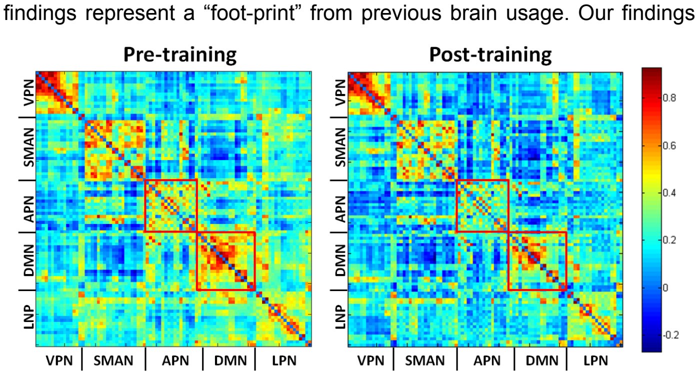

Figure 3. Comparison of Pre-training and Post-training correlation matrices. The areas inside red boxes are the intra-network connectivity of APN and DMN respectively. The color bar shows the CC.

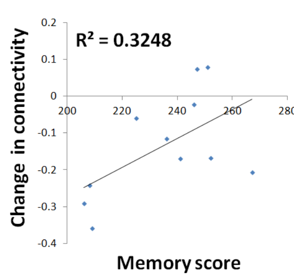

Figure 4. Changes in intra-network connectivity within DMN (post-pre) predict memory score.

REFERENCE: 1. Waites *et al*. HBM. 24:59(2005). 2. Stevens *et al*. Cereb. Cortex. 20:1997(2009). 3. Albert *et al*. Curr. Biol. 19:1023(2009). 4. Lewis *et al*. PNAS. 106:17558(2009). 5. Hasson *et al*. PNAS. 106:10841(2009). 6. He *et al*. Plos. One. 4:5226(2009). 7. Liu *et al*. ISMRM #1648 2010.