Incorporation of regional homogeneity in seed definition for the resting-state functional MRI analysis

F-X. Yan[1], Y-Y. Hsu[2], S-Y. Cheng[1], K-E. Lim[2], and H-L. Liu[1,3]

[1]Department of Medical Imaging and Radiological Sciences, Chang Gung University, Kwei-Shan, Tao-Yuan, Taiwan, [2]Department of Medical Imaging, Buddhist Tzu Chi General Hospital, Taipei, Taiwan, [3]Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital, Tao-Yuan, Taiwan

Introduction

Recently, studies of human brain connectivity using resting-state (RS) functional MRI (fMRI) have attracted increasing attention (1).   Many studies used a seed-based correlation analysis on resting-state data to assess the functional connectivity of default mode network (DMN), anti-correlation network of DMN (2), mesocorticolimbic system such as amygdala (3) and others.   In addition, the regional homogeneity (ReHo) method based on calculation of Kendall coefficient of concordance (KCC) was developed to measure the temporal similarity of a given voxel with its nearest neighbors in the RS-fMRI data (4).   This study proposed a method for improving the sensitivity of the conventional seed-based correlation analysis (SCA_C) by incorporating the ReHo information (SCA_{ReHo}) in the seed selection.
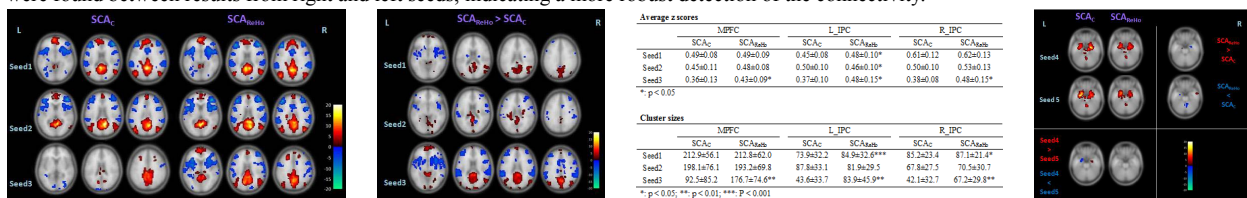
Methods

Twelve young healthy volunteers (6 females; 23 to 28 years of age) participated in this study. During the RS-fMRI scan, subjects lay supine in the scanner with their head fixed.   They were instructed to keep their eyes closed, to remain awake, to think of nothing, and to perform no specific task during the scan.

The RS-fMRI experiments were performed on a 3 Tesla GE HDx scanner (GE Healthcare Systems, Milwaukee, WI) with a T_2*-weighted single-shot gradient-echo echo-planar imaging (EPI) sequence (TR/TE/FA = 2000 ms/ 30 ms/90°, in-plane matrix = 64 x 64, slice thickness = 3 mm with 1 mm gap).   For each participant, twenty-eight continuous axial slices per volume and a total of 325 volumes were acquired.

After discarding the first 10 volumes, the following 180 volumes (six minutes) of data were included in the analysis. Data preprocessing included head motion correction, spatial normalization to the Montreal Neurologic Institute (MNI) template with a resampled resolution of $3\times3\times3$ mm^3, and then spatial smoothing with a 6-mm Gaussian kernel. Functional connectivity within the DMN and amygdala was analyzed using REST (by SONG Xiaowei, YAN Chaogan et al., http://resting-fmri.sourceforge.net).   The preprocessed data were analyzed using SCA_C by computing the correlation coefficients between the reference time course obtained from each of the five seed regions found in literatures (PCC seeds for DMN: seed1: (0,-51,30), radius=4mm; seed2: (12,-54,15), radius=6mm; seed3: (-3,-45,45), radius=10mm; Amygdala seeds: seed4: right side (27, -6, -21), radius=3mm; seed5: left side (-24, -6, -21), radius=3mm) and the time course of each voxel across the whole-brain.   For SCA_{ReHo}, first KCC maps were computed for each subject and then the reference time curve of each seed were obtained from the common voxels of the above seed ROI and the KCC mask (KCC > 0.5).   The resulting correlations were transformed to approximate Gaussian distribution using Fisher's z transformation and then analyzed with one-sample t-test ($p_{corrected} < 0.05$, with p<0.001 and a minimum cluster size of 13 voxels) to identify voxels showing significant correlations.   Paired t-tests were performed to assess group differences between SCA_C and SCA_{ReHo} results for each seed (p < 0.005, uncorrected with a minimum cluster size of 10 voxels).   For the amygdala, two-sample t-tests were used to assess the similarity between the connectivity maps obtained by using the right vs. left sides of the seeds (p < 0.005, uncorrected).   In addition, in order to assess the sensitivities of two methods, the average z scores and cluster sizes were calculated in three ROIs in the DMN results: medial prefrontal cortex (MPFC), left and right inferior parietal cortex (L_IPC, R_IPC).

Results

Figure 1 shows the group results of the DMN connectivity obtained by the SCA_C and SCA_{ReHo} methods for each seed ROI within PCC.   In SCA_C, variations in seed selection have significant impacts on the resultant DMN connectivity. In contrast, more consistent patterns were found with the SCA_{ReHo} method. Figure 2 shows pair t-test results of the DMN connectivity compared between SCA_C with SCA_{ReHo} methods. In general, SCA_{ReHo} leads to stronger connectivity results than SCA_C in the DMN regions.In consistent with Fig. 2, quantitative analyses demonstrated significantly stronger connectivity with greater spatial extents (p<0.05) with SCA_{ReHo} as comparing to SCA_C (for z-score: MPFC with seed3, L_IPC with seeds 1, 2 and 3, and R_IPC with seed3; for cluster size: MPFC with seed3, L_IPC with seeds 1 and 3, and R_IPC with seeds 1 and 3).Figure 3 shows group results of the amygdala connectivity (left upper side), pair t-test between two methods (right upper side), and two-sample t-test between right (seed 4) vs. left (seed 5) seeds (left lower side). SCA_C was found to bias on the sides of seed selection. With SCA_{ReHo}, no significant differences were found between results from right and left seeds, indicating a more robust detection of the connectivity.

Average z scores

	MPFC		L_IPC		R_IPC	
	SCA_C	SCA_{ReHo}	SCA_C	SCA_{ReHo}	SCA_C	SCA_{ReHo}
Seed1	0.49±0.08	0.49±0.09	0.45±0.08	0.48±0.10*	0.61±0.12	0.62±0.13
Seed2	0.45±0.11	0.48±0.08	0.50±0.10	0.46±0.10*	0.50±0.10	0.53±0.13
Seed3	0.36±0.13	0.43±0.09*	0.37±0.10	0.48±0.15*	0.38±0.08	0.48±0.15*

*: p < 0.05

Cluster sizes

	MPFC		L_IPC		R_IPC	
	SCA_C	SCA_{ReHo}	SCA_C	SCA_{ReHo}	SCA_C	SCA_{ReHo}
Seed1	212.9±56.1	212.8±62.0	73.9±33.2	84.9±32.6***	85.2±23.4	87.1±21.4*
Seed2	198.1±76.1	193.2±69.8	87.8±33.1	81.9±29.5	67.8±27.5	70.5±30.7
Seed3	92.5±85.2	176.7±74.6**	43.6±33.7	83.9±45.9**	42.1±32.7	67.2±29.8**

*: p < 0.05; **: p < 0.01; ***: P < 0.001

Conclusion

This study proposed a novel method of RS-fMRI network analysis by incorporating ReHo in the seed definition. This method was showed to be more sensitive in detecting connectivity and less subject to seed locations, thus may be particular helpful when subjects exhibit distinct functional anatomy compared with normal populations.

References

1. Long X.Y., et. al. J. Neurosci. Methods 2008; 171: 349-355. **2.** Uddin L.Q., et. al. Hum Brain Mapp 2009; 30(2): 625-37. **3.** Gu H., et. al. Neuroimage 2010; 53(2):593-601. **4.** Zang Y.F., et. al. Neuroimage 2004; 22:394–400.