Functional Connectivity in the Resting Brain Revealed by Group-Level Independent Component Analysis

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Introduction

Functional connectivity in the brain has been investigated using synchronized low-frequency fluctuations in resting-state fMRI data (1). Various applications of resting-state fMRI have been demonstrated recently, including studies of Alzheimer's disease (2), antidepressant effects (3), and "default mode" of brain networks (4). In the majority of these studies, patterns of brain connectivity were obtained from cross-correlation analysis of the resting-state signal against the time course of "seed points" selected from stimulation-induced activation maps and/or *a prior* knowledge of neural networks. These seed-point based methods require relatively subjective assumptions for choosing reference points, and may have limitations in revealing unknown brain networks. To alleviate this problem, independent component analysis (ICA), a data-driven method, has been recently used to reveal resting-state functional networks without the requirement of seed points (5). A potential challenge in analyzing resting data using ICA, particularly at group level, is the lack of synchronization in resting time courses between subjects. In this study, we used simulated and experimental data to assess the feasibility and efficacy of group-level ICA (gICA) in analyzing group resting-state fMRI data.

Methods

Resting-State fMRI Experiments. MRI experiments were performed on 14 healthy and right-handed volunteers (all male, 30±6 yrs) in two sessions (2 days apart) on a 3T Siemens Allegra scanner. In each session, whole brain resting-state images (39 sagittal slices, 4 mm in thickness) were acquired, and the subjects were instructed to close their eyes and not to think anything in particular. Echo-planar imaging (EPI) was used for image acquisition with FOV of 22 cm^2, matrix size of 64×64, TE of 27ms, TR of 2160 ms, and 90 repetitions.

Simulated Resting-State fMRI Data. Computer simulation was used to evaluate the effectiveness of gICA in the analysis of resting-state fMRI data. Simulated "group" resting data were generated based on 5 experimental resting EPI data sets (22 oblique axial slices, 5mm in thickness, FOV = 22 cm^2, matrix size = 64×64, TE = 27ms, TR = 2s, and repetitions = 180) collected on a subject. Each synthetic data set consisted of a baseline, Gaussian-distributed noise, and artificial signal. The artificial signal was obtained from a gray matter voxel of the experimental data set, and added to a region of interest (ROI) of 5×5×22 voxels. A total of 5 synthetic data sets were generated using the artificial signals from the 5 experimental data sets.

Group ICA. Resting-state EPI data were spatially normalized to Talairach space, and temporally filtered by a low-pass digital filter (0.1 Hz). Group ICA was performed on temporally concatenated data sets, following the procedures of Calhoun et al (6). For each gICA component, voxels were considered as "activated" if their intensities significantly deviated from the mean intensity of the component ($z>2.5$; $p<0.01$) and their cluster sizes were greater than 8. Time courses corresponding to constituent components were reconstructed.

Results and Discussion

The computer simulation results are illustrated in Fig.1. The synthetic time courses (in red) added to the brain ROI and the reconstructed time courses (in blue) corresponding to constituent ICA components are shown in Fig.1a. These two time courses are correlated extremely well. Fig.1b shows a slice of the gICA component maps corresponding to the reconstructed time courses. Perfect "activation" areas (the same as assigned) are detected in the maps. These results indicate that gICA is able to identify activated regions and reconstruct time courses for group resting data, even through the data lack temoral synchronization between subjects.

For the experimental data, consistent gICA component maps were obtained from the group resting-state fMRI data collected in the two sessions. Consistency was assessed by a spatial cross correlation method, in which cross-correlation coefficients (CC) between each component map from one session and the component maps from another session were calculated. Fig.2 shows the gICA component maps with highest CC (>0.4) from session 1 and 2. Excellent consistency between the two sessions can be observed. These component maps include (ordered by CC value) a) medial occipital cortices, b) areas around brain stem, c) temporal cortices and anterior cingulate cortex, d) posterior cingulate cortex, anterior cingulate cortex, and bilateral inferior parietal cortex (default-mode circuit (4)), e) medial and lateral frontal cortices, f) lateral occipital cortices, and g) lateral frontal and parietal cortices. The component map (d), described as a default-mode brain network, has been investigated using the conventional seed-point method (4).

In summary, the simulation study has demonstrated that gICA is feasible to analyze group resting-state fMRI data, even through there is no temporal coherence between the data sets. The experimental results showed that gICA can extract consistent patterns of brain connectivity from group resting-state fMRI data.

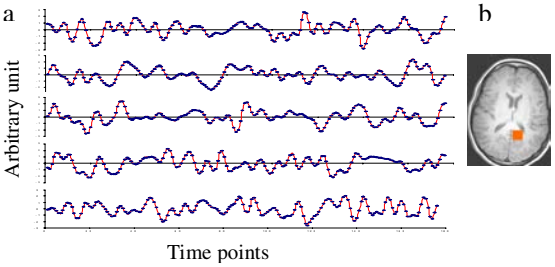

Fig.1 (a) Synthetic time courses (in red) added to the brain ROI and reconstructed time courses (in blue) corresponding to constituent ICA components. (b) A slice of the gICA component map.

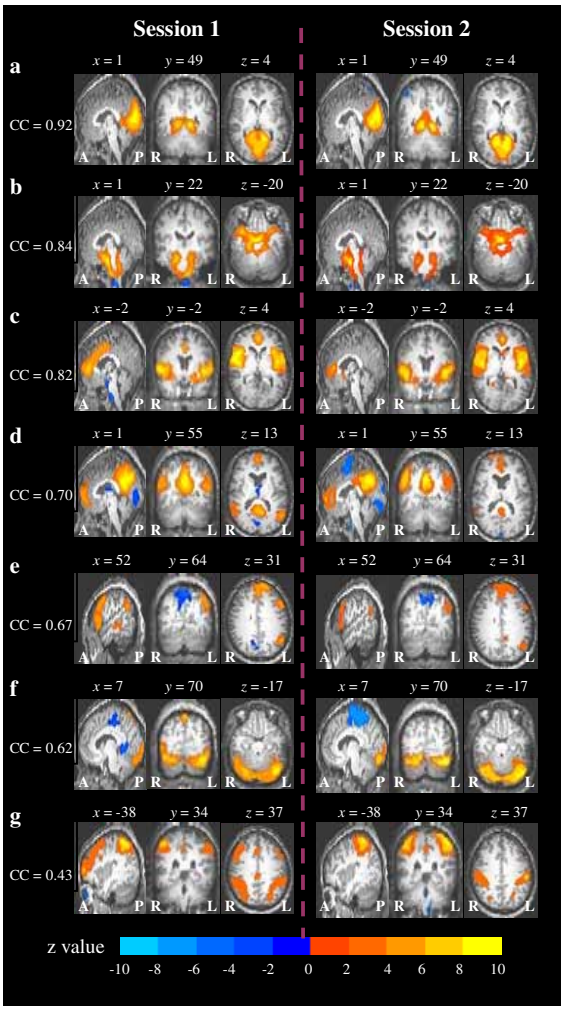

Fig.2 Group ICA component maps from sessions 1 and 2, and spatial cross-correlation coefficients (CC) between the two sessions.

References

1. Biswal et al, Magn Reson Med 1994; 34: 537-541. **2.** Li et al., Ragiology 2002; 225: 253-259. **3.** Anand et al., Neuropsychopharmacology 2005; 30: 1334-1344. **4.** Greicius et al., PNAS 2003; 100: 253-258. **5.** Beckmann et al, Phil. Trans. R. Soc. B 2005; 360: 1001-1013. **6.** Calhoun et al., Human Brain Mapping 2001; 14: 140-151.