

A Comparison Study of CMBHC and ICA Methods for Human Functional Connectivity Analysis

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Introduction

Functional connectivity of the brain, measured by spatiotemporal correlations between spontaneous BOLD signals, has been found to indicate many resting-state networks [1]. Several methods have been used for functional connectivity analysis; and among them, seed-based correlation analysis and independent component analysis (ICA) are two of the most popular approaches. However, the seed-based correlation analysis needs priori information about seed locations, can only generate one correlation map at one time, and may have biases due to seed selection. The ICA gives results hard to be directly linked to the coherent strength of functional connectivity; and its implied model assumption may still need to be validated.

Recently, we proposed a correlation-matrix-based hierarchical clustering (CMBHC) method, which combines advantages of the seed-based correlation analysis and ICA, for extracting spatial correlation structures from spontaneous BOLD signals. It has been used to identify multiple interesting patterns, including some cortico-subcortical connections, from a single resting-state BOLD dataset acquired from the rat brain [2]. The previous study is, however, limited by the spatial coverage of BOLD signals (only in the somatosensory region) and the anesthesia complication. In this study, the effectiveness of the CMBHC method was further evaluated using human resting-state datasets and the results were compared with those obtained using ICA.

Methods

The human data from 4 subjects, which have been published by other lab [3], were downloaded from BrainScape website (www.brainscape.org). In summary, the data were acquired on a 3T Siemens scanner with following parameters: FOV = 256×256 mm²; TR/TE = 3013/25 ms; 64×64 matrix; 4 mm thickness; and 110 image volumes for each run. For each subject, only three runs under eyes-closed condition were used for analysis. For more information about the data, please refer to the previous publication [3].

The data were first preprocessed using the following steps: motion correction, slice timing correction, brain extraction, spatial smoothing, detrending, and temporal band-pass (0.01–0.1 Hz) filtering. The CMBHC and ICA (MELODIC in FSL) were then performed on the preprocessed data at different level: single-run data, multi-run data from same subjects, and group analysis on all subjects.

Results

Results of the multi-run (3 runs) CMBHC analysis and ICA from a representative subject are shown in Figure 1. A total of 50 clusters and 38 independent components (ICs) were identified, and only parts of them were demonstrated herein with selected image slices due to space limitation. The similar networks identified by both the CMBHC and ICA methods, e.g. default mode network (DMN, C1 & I1 in Figure 1), are compared side by side in Figure 1A. The CMBHC was able to detect many subcortical structures (white arrows in Figure 1) having relatively weak connections with cortical regions, which were, however, largely missed by the ICA. This difference is not due to the displaying threshold, because the observation holds even using lower thresholds. Furthermore, the CMBHC extracted many patterns (Figure 1B) that were not clearly shown in the ICA results, for example, the clusters C6 showing correlations between cerebellum and anterior part of the thalamus. Generally, the difference of effectiveness between the CMBHC and ICA described above was even bigger when they were applied to a single-run data, and became relatively smaller for the group analysis on all subjects.

Discussion

With modeling BOLD signal as a linear mixture of independent source signals (from different networks), the ICA decomposes spontaneous BOLD dataset into multiple spatial components by maximizing their non-Gaussianity, and this may help it reliably detect networks with distinct (independent) spatial and temporal patterns, e.g., DMN. The functional connectivity of the brain, however, may not be always distinct over the whole brain: some networks may be connected to their subcortical components with a relatively weak connection while others may intrinsically show weak but consistent connectivity. The results of the present study suggest that the ICA is a relatively conservative method and has limited sensitivity (statistical power), especially with less data average (single run or single subject), to identify the weak functional connectivity across brain regions. In contrast, the CMBHC demonstrated a better balance of statistical sensitivity and specificity, and identify those weak connections reliably even at a single subject level. The overall results suggest that the CMBHC can serve as a complementary and improved tool for investigating resting-state connectivity, especially for studies focusing on single subject's data.

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References [1] Biswal B. et al. *MRM* 1995; [2] Liu X. et al. *ISMRM* 2011 p3556; [3] For MD. et al. *PNAS* 2005.

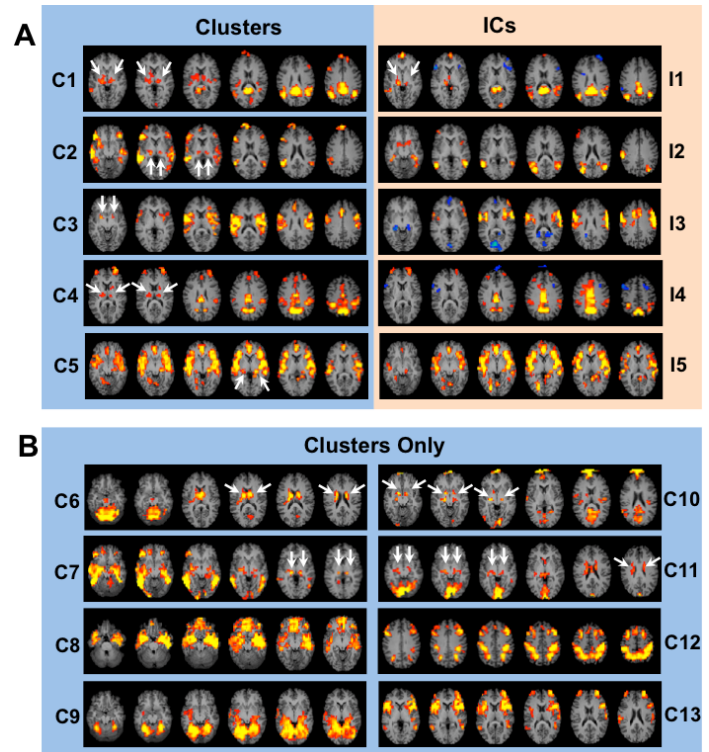


Fig. 1 Cluster and IC maps from a representative subject. Similar patterns identified by both CMBHC (C1~C5) and ICA (I1~I5) are compared directly at the same row (A), while patterns exclusively found by the CMBHC (C6~C13) are shown separately (B). The threshold for each color map was automatically determined to cover 8% of whole brain region. White arrows point out subcortical structures in the maps.