

Dynamic Network Analysis of Resting-state Effective Connectivity Based on Multiband fMRI Data

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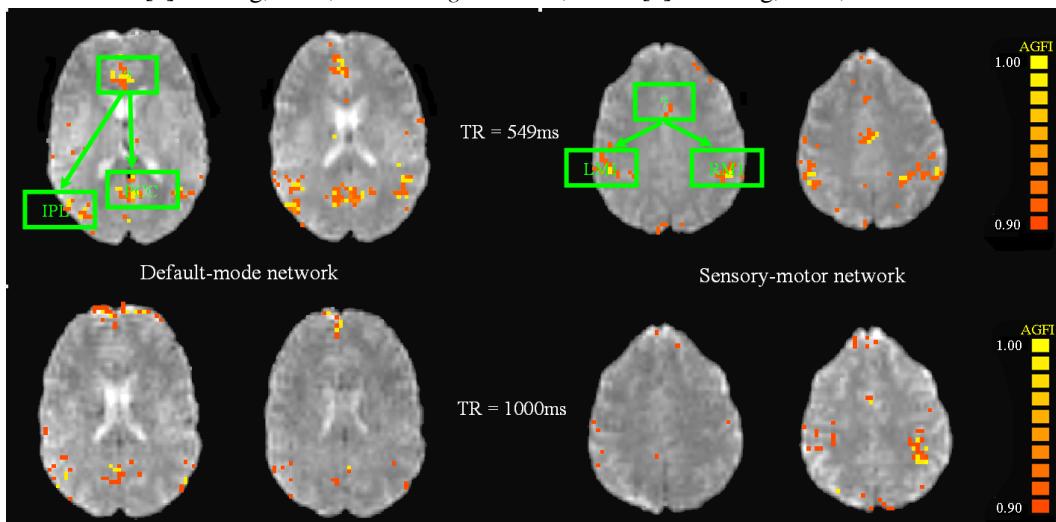
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Introduction Determining connectivity between cortical areas from resting-state fMRI data has become an important tool in neuroscience. Conventional correlation analysis cannot provide causal or directional information between multiple regions in the brain. Previously, we have shown that Structural Equation Modeling (SEM) can be an effective method to ascertain path directions and coefficients from the covariance structure in fMRI data [1]. However, the usefulness of SEM depends on the dynamic content of the data. The recently developed multiband slice-accelerated technique provides higher temporal resolution for measuring the dynamic fluctuation of fMRI BOLD signals than conventional EPI sequence [2]. Here, we test if high-speed slice-accelerated multiband EPI sequence can help to leverage the dynamic content of resting-state BOLD signal for the purpose of inferring effective connectivity network using SEM.

Materials and Methods The fMRI scans were performed on eight healthy and right-handed subjects. They were scanned on a Siemens 3T Trio/Tim system using a multiband EPI sequence [2]. Acquisition parameters were field of view (FOV) = 224 mm, matrix = 64×64 , echo time (TE) = 25 ms, flip angle = 60° and forty-four axial slices (3 mm thick without gap). Four subjects were scanned with repetition time (TR) = 1 sec and slice acceleration factor = 2, and four subjects were scanned with TR = 549 ms and slice acceleration factor = 4. For both groups, the resting-state fMRI scan took about 4 minutes. Subjects were instructed to close their eyes but stay awake. The multiband fMRI data were realigned to correct head motion. Thereafter, the data were regressed with the average signals from CSF and white matter to remove the physiological noises. Two SEM analyses were conducted. In one of them, the left and right primary motor areas (L/R M1) were chosen as two ROIs for the detection of sensory-motor network. In the other, the posterior cingulate cortex (PCC) and inferior parietal lobules (IPL) were selected as two ROIs for the detection of default-mode network. For each analysis, the signal of each voxel within the brain was regarded as the third observation in the SEM, with a time shift Δt iterated between 0, -1TR and -2TR. Each model consists of two connections start from the unknown region to the two predefined ROIs (Fig. 1). For every voxel, the models were estimated based on Adjusted Goodness-of-Fit Index (AGFI) with a significant t-value (>1.96) on each path [1]. The AGFI at each voxel was saved and displayed in the final connectivity map. The model fit indices were compared between connectivity maps obtained from different temporal resolution scans.

Results and Discussion The representative connectivity maps resulted from SEM are illustrated in the Figure 1. The connectivity maps were found to be reproducible across subjects at the higher temporal resolution (TR= 549 ms), but not at the lower temporal resolution (TR=1s). With the higher temporal resolution, we found that the supplementary motor area (SMA) has significant connections to both LM1 and RM1 in the sensory-motor network, and the medial prefrontal cortex (MPFC) link significantly with PCC and IPL in the default-mode network. These results are consistent with the neuroanatomical evidence and existing results from non-directional functional connectivity data. Parts of predefined ROIs shown in the connectivity map can be interpreted as direct interactions between the two ROIs, which is also often found in the previous studies of functional connectivity. The largest standardized residual (the latent variable) obtained from SEM fitting at lower temporal resolution is much larger than that obtained at higher temporal resolution (Table 1), which suggests high-temporal-resolution data enabled by multiband fMRI can provide more robust information about the dynamic characteristics of connectivity networks. The present approach of SEM analysis on the multiband fMRI data allows us to search the possible effective connections at each brain region directly from high temporal resolution signals. When several areas are involved in a network, which is often the case, the connections can become too complicated to be ascertained simply via correlation analysis. In contrast, SEM produces directional maps and estimations that circumvent this difficulty. Multiband fMRI enables data acquisition at high temporal resolution and allows more applications of SEM in inferring effective connectivity.

Reference [1] Zhuang, et al., *Neuroimage* 42: 799, 2008. [2] Feinberg, et al., *PloS ONE*: e15710, 2010.



	TR (ms)	549	1000
Sensory-motor Network	0.0154 (0.0083)	0.0346 (0.0104)	
Default-mode Network	0.0181 (0.0096)	0.0579 (0.0133)	

Table 1. Largest standardized residual averaged (and its standard deviation) from SEM fittings at each network and each scan.

Figure 1. The structural equation models (in green) and resulting connectivity maps on two typical slices from multiband fMRI data.