On the relationship between seed-voxel and ICA measures of functional connectivity

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Background & Introduction: Brain functional connectivity (FC) refers to temporally synchronous signals from spatially distinct regions. Blood oxygenation level dependent (BOLD) functional MRI (fMRI) has been used to evaluate FC, both during task performance and in the "resting" state, yielding reports of FC differences correlated with behavior and diagnosis. Two methodologies are widely used for evaluating FC from BOLD fMRI data: Correlation with the time series of a specified "**seed voxel**" (or small region of interest)[1]; and spatial independent component analysis (**ICA**)[2]. While results from seed-voxel and ICA methodologies are generally similar, they can also differ, and we are unaware of a discussion of the relationship between them. The present study is intended to elucidate and illustrate the relationship between seed-voxel and ICA derived measures of FC.

Theory: Functional connectivity of a voxel x_1 to a seed voxel x_2 can be defined as $C(x_1,x_2)=\int\left[S(x_1,t)S(x_2,t)\right]dt$ where $S(x,t)$ is the detrended BOLD signal from voxel x at time t (ignoring normalization). In ICA, BOLD signals from all voxels are decomposed into components, each comprising a spatial map and a corresponding time course. This can be written as $S(x,t)=\sum_{k=1}^{K}M_k(x)A_k(t)$ where K is the number of spatially independent components, $M(k)$ is the spatial map of component k and $A_k(t)$ is the timecourse of component k. Substituting equation (2) in equation (1) yields after rearranging, $C(x_1,x_2)=\sum_k M_k(x_1)M_k(x_2)\int A_k^2(t)dt+\sum_{k\neq l}M_k(x_1)M_l(x_2)\int A_k(t)A_l(t)dt$ i.e., the seed-voxel computed connectivity is the sum of within network connectivity (as observed in each ICA component spatial map) and between-network connectivity (as introduced by Jafri *et al.*[3]).

Methods: Five healthy volunteers (2 male), age 24-32, gave informed consent to participate in IRB-approved research. BOLD fMRI data were acquired at 3.0 T during six runs of four-minute block design tasks, with three runs of visual stimulation ("visual"), and three runs of visual stimulation with concurrent finger tapping ("visuo-motor"). Data were preprocessed (slice-time correction; realignment; atlas-based normalization; spatial smoothing) using FSL[4], then entered into

1. Correlation with a seed voxel in primary visual cortex (MNI coordinates: -10 -94 0)
2. Spatial ICA using temporal concatenation[5] (using Melodic version 3.0) for visual runs and visuo-motor runs separately. Thirty-five and thirty-seven components were estimated,respectively, for the two tasks. Components corresponding to visual and motor networks were identified in each task. Between network connectivity was computed as the correlation between the timecourse of the two components for each run. Significance was calculated after a Fisher z-transform.

Results: During the visual run, correlation with a seed in primary visual cortex yielded a visual network including primary and secondary visual cortices (Figure 1). During the visuo-motor run, significant correlation with this same seed was found in visual cortices and also in the motor cortex. (Figure 1). Using ICA, in both visual and visuo-motor runs, a component with spatial map consistent with a visual network, and a component with spatial map consistent with a motor network, were separately identified. The connectivity between these two networks was significantly (p<0.001) different between the visual and the visuo-motor run. (Figure 1).

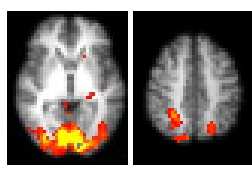
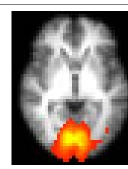
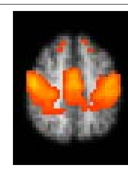
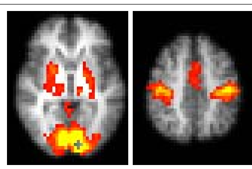
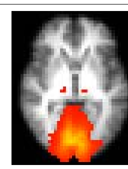
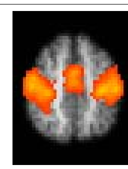
	Seed Voxel Connectivity	ICA: Within-Network Connectivity	ICA: Connectivity Between Visual Network & Motor Network
Visual Run	 Visual connectivity	 Visual Network  Motor Network	r = 0.08 ± 0.26
Visuo-Motor Run	 Visual connectivity	 Visual Network  Motor Network	r = 0.69 ± 0.16

Figure 1: Seed-voxel analysis of visual task data using a visual cortex seed yields a connectivity map that includes only visual cortex, while the same analysis for visuo-motor task data yields significant connectivity in both visual and motor cortex. Using ICA, the visual and the motor components remain distinct in both tasks (column 3), while the correlation between the time courses of the two components, which represents the between-network connectivity, is significantly higher in the visuo-motor run (final column).

Discussion and Conclusions: The purpose of this study was to elucidate the relationship between **seed voxel correlation** and **ICA**, the two predominant methods used for calculating FC from fMRI data. Seed voxel correlation has the same limitation as task activation studies, in that activation of one functional network cannot be distinguished from coactivation of distinct networks[6,7]. During a task (or state) that co-activates two brain networks, voxels from both networks will appear to be connected when using seed-voxel correlation. On the other hand, as we have shown, in a task involving two brain networks, ICA identifies each network distinctly and consistently, and provides a metric of connectivity between the two. In summary, ICA decomposes FC into connectivity **within** each network and connectivity **between** pairs of networks. Thus, the relationship between the seed voxel & ICA approaches to computing FC is similar to the relationship between the general linear model (GLM) and ICA approaches for computing activation, summarized by Friston[8] as the distinction between "modes" and "models": The GLM detects voxels respecting a user-specified temporal model, while ICA yields networks of brain regions displaying synchronous signals or "modes". As seed voxel correlation is essentially a GLM using the time course of the seed voxel, seed voxel FC is essentially a map of the "model" specified by the seed voxel, while ICA based FC distinguishes brain "modes" and the temporal relationships between them.

References
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