## Network discovery with fMRI: analytic choices and their implications

**OUTLINE:**

   I.   Approaches for defining networks (ICA, seeds, ROIs)

  II.   Processing issues (motion, autocorrelation, filtering)

 III.   Other issues (task vs rest, overlap of networks)

 IV.   Applications (diagnostic, prediction)

  V.   Time-varying networks

 VI.   Summary

**TAKE-HOME MESSAGES/WHAT YOU SHOULD KNOW:**

1.     Awareness of various ways of defining a brain network
2.     The importance of various processing choices and corrections connectivity results
3.     Uses of the multivariate group ICA approach in extracting and analyzing brain networks

**SUGGESTED READING:**

V. D. Calhoun and T. Adalı, "Multi-subject Independent Component Analysis of fMRI: A Decade of Intrinsic Networks, Default Mode, and Neurodiagnostic Discovery," IEEE Reviews in Biomedical Engineering, vol. 5, pp. 60-73, 2012.

E. Erhardt, E. Allen, E. Damaraju, and V. D. Calhoun, "On network derivation, classification, and visualization: a response to Habeck and Moeller," Brain Connectivity, vol. 1, pp. 1-19, 2011.

R. M. Hutchison, T. Womelsdorf, E. A. Allen, P. Bandettini, V. D. Calhoun, M. Corbetta, S. D. Penna, J. Duyn, G. Glover, J. Gonzalez-Castillo, D. A. Handwerker, S. D. Keilholz, V. Kiviniemi, D. A. Leopold, F. de Pasquale, O. Sporns, M. Walter, and C. Chang, "Dynamic functional connectivity: promises, issues, and interpretations," NeuroImage, vol. 80, pp. 360-378, 2013.

**Overview:**
From region of interest (ROI) to seed-based correlations to approaches like independent component analysis (ICA) and graph theory, there are many ways to define a brain network and every paper seems to use the word differently. We will discuss common definitions of the word brain network and briefly discuss several of the main approaches. One approach which is being used with increasing frequency is independent component analysis (ICA). Independent component analysis is a statistical method used to discover hidden factors (sources or features) from a set of measurements or observed data such that the sources are maximally independent. Typically, it assumes a generative model where observations are assumed to be linear mixtures of independent sources, and unlike principal component analysis (PCA) which uncorrelates the data, ICA works with higher-order statistics to achieve independence.

ICA has demonstrated considerable promise in characterizing functional magnetic resonance imaging (fMRI) data, primarily due to its intuitive nature and ability for flexible characterization of the brain function. As typically applied, spatial brain networks are assumed to be systematically non-overlapping. Often temporal coherence of brain networks is also assumed, although convolutive and other models can be utilized to relax this assumption. ICA has been successfully utilized in a number of exciting fMRI applications including the identification of various signal-types such as resting-state networks (RSNs, e.g., Figure 2), task and transiently task-related components, and physiology-related signals in the spatial or temporal domain.

Unlike univariate methods (e.g., seed or regression analysis, Kolmogorov–Smirnov statistics), ICA does not naturally generalize to a method suitable for drawing inferences about groups of subjects. For example, when using the general linear model, the investigator specifies the regressors of interest, and so drawing inferences about group data comes naturally, since all individuals in the group share the same regressors. In ICA, by contrast, different individuals in the group will have different time courses, and they will be sorted differently, so it is not immediately clear how to draw inferences about group data using ICA. To address these issues, several multi-subject ICA approaches have been proposed that differ in the organization of data and subsequent assumptions of spatial and/or temporal consistency across subjects. I will discuss several of these approaches and present evidence that the commonly-used "temporal concatenation" approach provides excellent estimates of subject activations which can be used to make inferences about an individual or at the group level (e.g., Figure 3).
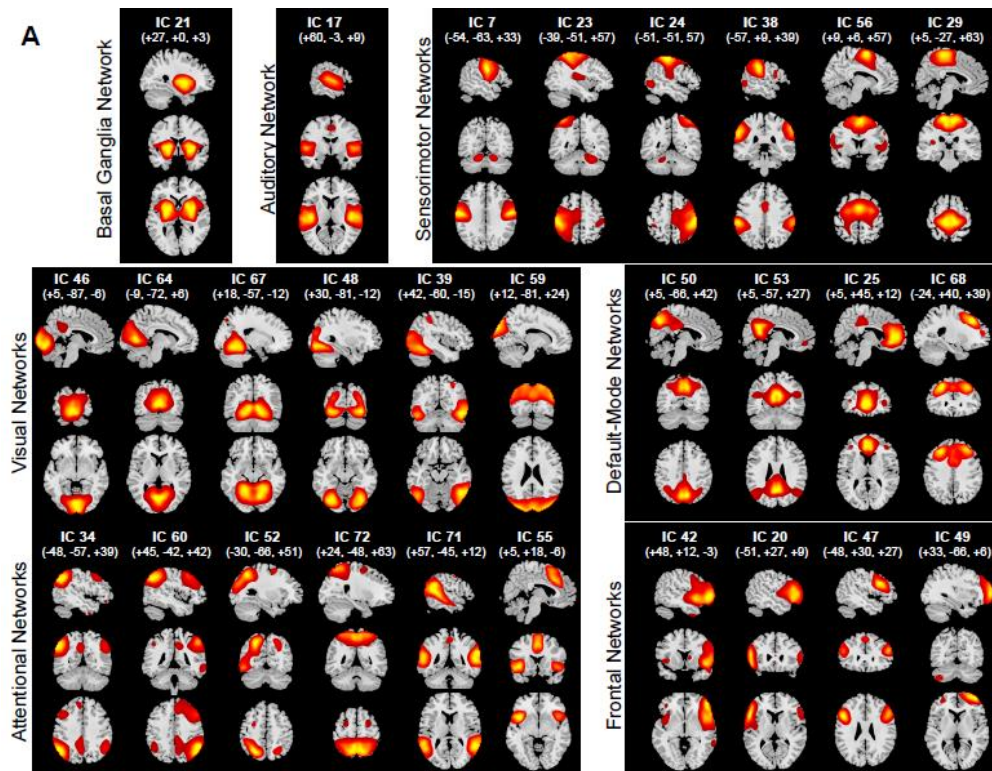


**Figure 2.** Select components obtained by applying ICA to resting-state fMRI data. From Allen et al., Frontiers in Systems Neuroscience (2011).

2
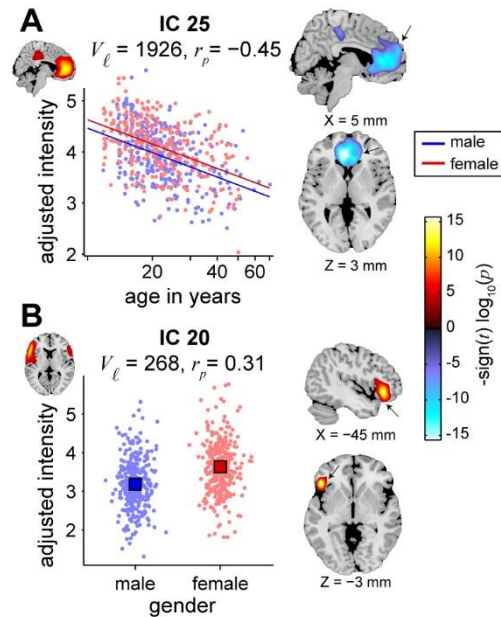
**Figure 3.** Examples of age (A) and gender (B) effects on the intensity of spatial maps. Group ICA of resting-state data from 603 subjects was performed using the "temporal concatenation" approach. Spatial maps for individual subjects were estimated with direct back-projection. From Allen et al., Frontiers in Systems Neuroscience (2011).

This lecture will also focus on the impact of preprocessing steps. This includes, for ICA, things like 1) the choice of model order (i.e., number of components to estimate), and 2) selecting and interpreting components "of interest". But it also include other general areas such as motion correction, whether to correct for autocorrelation, physiologic signal regression, etc.

In the last section of this lecture we will discuss the rapidly growing area of capturing time-varying connectivity patterns in brain imaging data. This is a promising field and especially important in analyzing resting fMRI data, for example, which is unlikely to have a consistent pattern of connectivity throughout due to the lack of a tightly controlled experimental condition. The use of dynamic connectivity approaches is a promising way to avoid averaging changing networks together and may significantly increase our ability to utilize these networks for characterizing healthy and diseased brain.

3