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Functional magnetic resonance imaging (fMRI) is increasingly used to characterize functional connectivity between brain regions. Given the vast number of between-voxel interactions in high-dimensional fMRI data, it is an ongoing challenge to detect stable and generalizable functional connectivity in the brain among groups of subjects. Component models can be used to define subspace representations of functional connectivity that are more interpretable. It is, however, unclear which component model provides the optimal representation of functional networks for multi-subject fMRI datasets. A flexible cross-validation approach that assesses the ability of the models to predict voxel-wise covariance in new data, using three different measures of generalization was proposed. This framework is used to compare a range of component models with varying degrees of flexibility in their representation of functional connectivity, evaluated on both simulated and experimental resting-state fMRI data. It was demonstrated that highly flexible subject-specific component subspaces, as well as very constrained average models, are poor predictors of whole-brain functional connectivity, whereas the best-generalizing models account for subject variability within a common spatial subspace. Within this set of models, spatial Independent Component Analysis (sICA) on concatenated data provides more interpretable brain patterns, whereas a consistent-covariance model that accounts for subject-specific network scaling (PARAFAC2) provides greater stability in functional connectivity relationships between components and their spatial representations. The proposed evaluation framework is a promising quantitative approach to evaluating component models, and reveals important differences between subspace models in terms of predictability, robustness, characterization of subject variability, and interpretability of the model parameters. Hum Brain Mapp, 2016.

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