Using Contiguous Bi-Clustering for data driven temporal analysis of fMRI based functional connectivity

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Background: Functional connectivity is a commonly used approach in human brain imaging for revealing inter- and intra-regional relationships under various conditions and tasks as well as at rest. Since 1990 several approaches to functional connectivity analysis have been proposed, some hypothesis-driven and others data driven. Data-driven approaches have included factor analysis methods such as ICA and PCA as well as clustering methods such as hierarchical clustering, K-means and FCA (Fuzzy clustering analysis). All these methods share a common basic assumption that the connectivity-maps/networks in the brain are stationary and thus seek functional connectivity over all time points. Based on recent findings, we find this assumption is too restrictive, and postulate that network's dynamics can be revealed by considering subsets of the measured time points. In addition, most of the data-driven methods partition the segregated voxel populations (i.e. regions) into disjoint sets, while in fact one region may play a role in more than one network.

Method: Here we present ConBic (Contiguous Bi-Clustering) – a data driven novel computational method for detecting dynamism in functional brain networks using fMRI data. Unlike previous data-driven approaches, this method identifies changes over time in inter- and intra-regional functional connectivity. Moreover, ConBic does not impose a disjoint partition on the voxels/regions, but rather allows networks to overlap, so that one region may be involved in more than one functional network under different time points or conditions. The method models voxels by an undirected graph whose edges represent spatial proximity. First, on each time window, seed nodes are selected and a search procedure from each seed identifies homogenous regions. Various region evaluation measurements are used, including clustering coefficient, region homogeneity and anatomic atlas annotation. In the next stage bi-clustering approaches are

used in order to reconcile and group time periods in which spatially similar regions were detected, as well as regions that share a similar signal in a single time period.

Results: Preliminary tests were performed on four motor fMRI data sets obtained from healthy young adults during moving right and left foot alternating for 3 minutes. These tests have shown the ability of the method to identify de-novo the corresponding primary motor regions as well as correlated secondary regions involved in motor cognition. Intra-regional connectivity (i.e. homogeneity) in locations that are known to be related to leg movements was higher when performed the corresponding tasks than during rest periods. In addition, though right and left hemispheres were analyzed separately, there was bilateral symmetry in many of the identified regions in both cortical and subcrotical locations. Further tests and validations are currently performed on motor datasets of moving left and right hand as well as on resting state data.

Conclusion: ConBic is a promising new data-driven computational method for detecting highly connected, functional networks in the brain. Importantly, it can effectively reveal intra- and inter-regional functional connections as well as temporal changes in these connections.

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