Behavioral relevance of the temporal dynamics of the functional brain connectome

Hao Jia[1], Xiaoping Hu[2], and Gopikrishna Deshpande[1,3]

[1]*MRI Research Center, Department of Electrical and Computer Engineering, Auburn University, Auburn, Alabama, United States,* [2]*Biomedical Imaging Technology Center, Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, Georgia, United States,* [3]*Department of Psychology, Auburn University, Auburn, Alabama, United States*

Introduction: Dynamic functional connectivity (FC) analysis has received increasing attention in the past few years [1-4], since it is hoped that dynamics of FC could provide potentially more information than its static counterpart, which can benefit both neuroscientific and clinical research. Previous studies have shown that abnormality in behavioral variables of patients can be predicted by brain FC aberration [5]. Recent works have shown that static FC is quite informative in predicting behavior [6] and notably the link between connectivity dynamics and behavioral variability has come into consideration [7]. However, the key question that is yet to be answered is whether connectivity dynamics has any behavioral relevance over and above that obtained from static FC. In this work, we describe a principled framework for calculating dynamic FC metrics from the whole brain using data-driven adaptive windows and evolutionary clustering. In addition, we demonstrate that dynamic FC explains more variance in behavior as compared to static FC metrics.

Methods: Resting state fMRI data obtained from the Human Connectome Project (http://humanconnectome.org; HCP Q3 release, minimally preprocessed data of session1, 40 healthy subjects) were employed for this work. Additional preprocessing included mean and linear trend removal, bandpass filtering (0.01~0.1Hz), and regressing out motion, white matter and CSF signals. Mean fMRI time series were extracted from 190 functionally homogeneous regions from whole brain [8]. Then, we employed sliding window correlation method to calculate dynamic FC, with the length of the sliding window determined by augmented Dickey-Fuller test (ADF). ADF tests the existence of unit root for a given time series through which stationarity can be inferred. The Pearson's correlation coefficient X was used to represent FC, and we used $1-|X|$ as the distance measure between regions. This resulted in a time-varying similarity matrix which was clustered over regions at each time instant using adaptive evolutionary clustering algorithm [9]. The number of clusters was set to 10 in accordance with previous studies which have shown the existence of 10 resting state networks (RSNs) [10]. Also, we calculated static FC using Pearson's correlation of entire time series for comparison. Next, we defined three metrics to represent dynamic FC based on the clustering result. The first is the mean time that two regions are in connected (or disconnected) state before transitioning into a disconnected (or connected) state, called mean time before state transition (MTST). The second is standard deviation of the time before state transition (SDTST). The third is called CFP (clustering frequency percentage), which measures the percentage of total time that two regions are clustered relative to total scanning time. The final metric was just the static FC value (SFC). Next, dynamic and static FC metrics were input into a general linear model with behavioral measures obtained from the HCP as dependent variables.

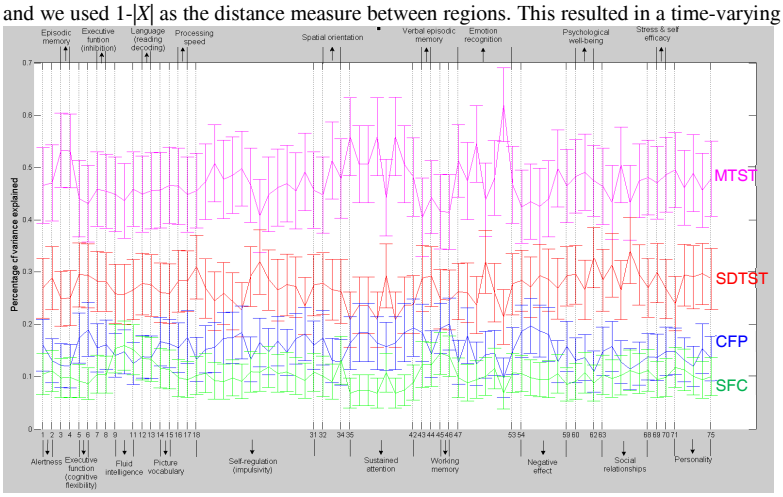

Fig. 1 *Percent variance in different behaviors explained by dynamic and static FC*

Results and Discussion: Fig.1 compares the relative percentage of variances explained by dynamic and static FC metrics for scores from various behavioral domains in HCP data. The behavioral scores include alertness, cognition, emotion, and personality. It is noteworthy that the variances explained by MTST and SDTST were clearly higher than those by CFP and SFC for each and every behavioral measure. MTST was by far the best performer. This is significant because it implies that dynamics of FC can explain more variance in behavior than static FC. This provides the basis for the need to study dynamics of FC, and points to the potential of dynamic FC in providing improved sensitivity to connectional abnormalities in brain disorders. Fig.2 shows paths with top and bottom 0.1% of interregional MTSTs. The connectivity of rectus in Broadmann area 11 with many regions outside the frontal cortex had the longest mean times before connectivity state transitions. This region is generally considered a part of the gating circuit for higher cognition [11]. The blue paths indicating quickest state transitions involved paths between the mid frontal area, anterior and mid cingulate, insula, supplemental motor area (SMA) and paths within the cerebellum. This may involve cognitive control in the frontal areas, timing circuits within the cerebellum and their common role in autobiographical episodes [12,13]. Fig.3 shows regions with highest and lowest mean MTST and CFP, calculated by considering all paths associated with the given region (top and bottom 30%). Brainstem, orbito-frontal area and rectus (parts of BA 11) had higher mean MTST and lower mean CFP (Figs.3 A and D) indicating that they were mostly disconnected and became connected only intermittently. Regions of the default mode (DMN), dorsal attention (DAN) and fronto-parietal control (FPCN) networks had lowest mean MTST (Fig.3B), indicating faster dynamics in these networks. Regions in superior frontal, parietal, temporal, and occipital cortices had higher mean CFP (Fig. 3D), indicating that they were connected to other regions most of the times. However, note that only regions of the DMN, DAN and FPCN were connected in the majority of the time and in addition, displayed faster dynamics in terms of state transitions.

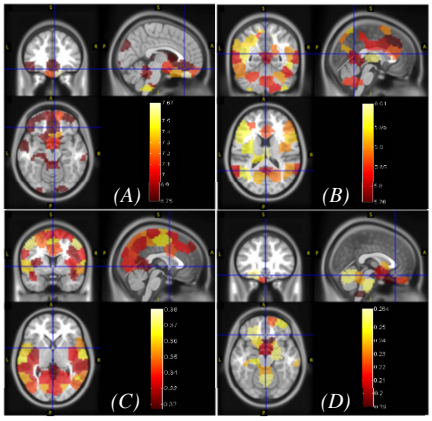

Fig. 3 *(A) Regions with highest mean MTST (top 30%). (B) Regions with lowest mean MTST (bottom 30%). (C) Regions with highest mean CFP (top 30%). (D) Regions with lowest mean CFP (bottom 30%).*

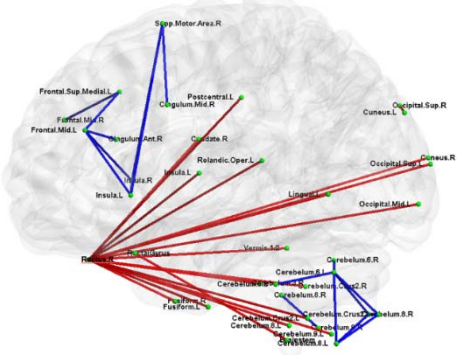

Fig. 2 *Paths with most and least interregional MTSTs. Red paths represent interregional MTSTs whose values are among the top 0.1% of all MTSTs, and blue paths represent interregional MTSTs whose values are among the bottom 0.1% of all MTSTs.*

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