Evaluating the Variability of Local and Distant Functional Connectivity Fluctuation in Task-free Human Brains

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Purpose

Recently, dynamic task-free functional connectivity, believed to provide greater insight into fundamental properties of large-scale functional brain networks, has received increasing attention [1]. However, previous studies did not take into account cortical distance of the dynamics networks. From an information system perspective, local specific neuronal populations perform elementary operations, whereas complex functions result from the integration of the distributed local operations throughout the brain. Inspired by this hierarchical processing model, we hypothesized that local and distant functional connectivities may have differential dynamic property in task-free states, and tested this hypothesis by characterizing the variability in dynamics in local and distant task-free functional connectivity measures, respectively with a sliding windows approach and connectivity degree measures.

Method

Analyses were performed on a group of subjects (n = 198 [76M/122F]; ages: 18-26; TR = 2s; # slices = 33; # timepoints = 225) from a separate site (Beijing_Zang) of the 1000 Functional Connectomes Project, an open-access repository of resting-state functional MRI datasets (www.nitrc.org/projects/fcon_1000). Resting-state functional MRI images were preprocessed using SPM8 software package (http://www.fil.ion.ucl.ac.uk/spm), including registering and re-slicing for head motion, normalizing to standard MNI space, spatially smoothing with a Gaussian filter with 8 mm FWHM kernel, and filtering using a Chebyshev band-pass filter (0.01-0.08Hz). The time series at each voxel were further corrected by regressing out head motion, global signals, white matter and cerebrospinal fluid average signals. A sliding time window approach was used to divide rs-fMRI signals into temporal segments with the window size of 18 volumes (36 s) (Fig.1A). For each window of an individual subject, we estimated functional connectivity between each pair of voxels using Pearson's correlation coefficient (Fig.1B). Subsequently, a graph-based computational approach was used to map the degree of functional connectivity [2], taking into account topographical neighborhood information for distinguishing local and distant connections (with correlation threshold of r>0.26, and neighborhood radius of 14 mm), resulting in the undirected and unweighted local and distant functional connectivity degree (lFCD and dFCD) maps over time (Fig.1C). These maps were further standardized by Z-score transformation so that maps across subjects were averaged and compared. Finally, the amplitude in the time domain (AM), and average low-frequency fluctuation (ALFF) measure [3] were used to evaluate the variability of dFCD oscillations.

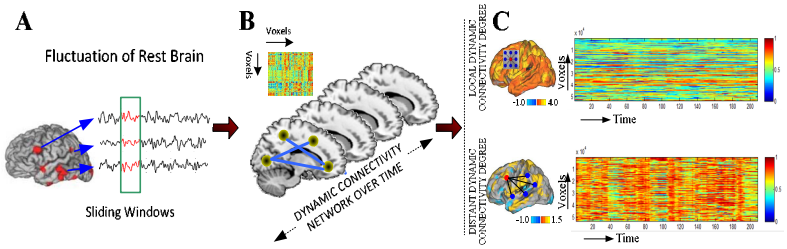

Fig.1 Dynamic fluctuation of local and distant functional connectivity degrees.

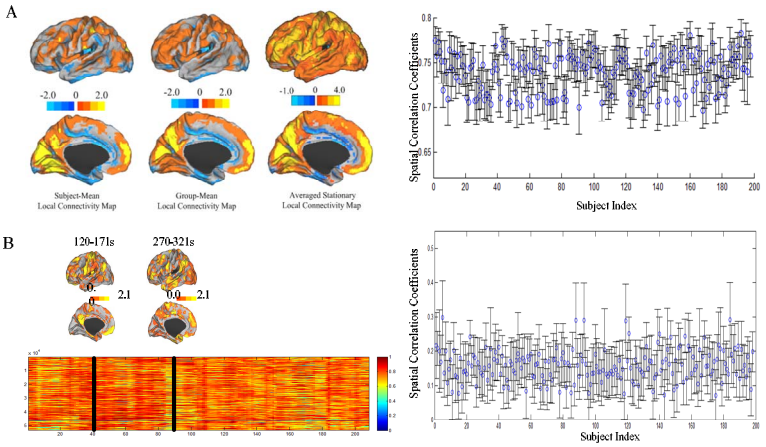

Fig. 2 Dynamics of lFCD maps (A) and dFCD maps (B). (A) Left panel: Averaged lFCD map over time of a randomly selected subject (left column), averaged lFCD map for all the 198 subjects (middle column) and the averaged stationary lFCD map over subjects. Right panel: The mean (blue dots) and standard deviation (error bars) of spatial correlation coefficients of local connectivity maps in response to all 208×198 sliding windows with averaged stationary lFCD map over subjects. (B) Left panel: Time series of dFCD for a randomly selected subject. Significantly differential long-distance connectivity patterns in two sliding windows are presented. Right panel: For each subject, the mean (blue dot) and standard deviation (error bars) of spatial correlation coefficients of sliced dFCD maps at different time with the stationary dFCD map were plotted.

Results

lFCD maps demonstrated high similarity with averaged stationary local connectivity map (Fig.2A), suggesting a stable local modular organization pattern distributed in whole brains throughout the scan (Fig.2A). In contrast, dFCD maps exhibit intensive fluctuation over time (Fig.2B). In particular, we found that the sensory and motor cortices, including motor, somatosensory, auditory cortex, and some parts of visual cortex, showed the most variable dFCD, whereas the default mode network (DN) as the hubs and central system of long-distance cortical-cortical interactions, and anatomically adjacent frontoparietal network demonstrated relatively stable dFCD (Fig.3A). ALFF measures in dFCD maps were further assessed within 7 specific brain networks [4], indicting that the default mode and frontoparietal control networks possess low fluctuation amplitude, and in contrast, the somatosensory network exhibits the highest magnitude of oscillation in dFCD maps (Fig.3B). In particular, the vision network shows a high inconsistency across subjects.

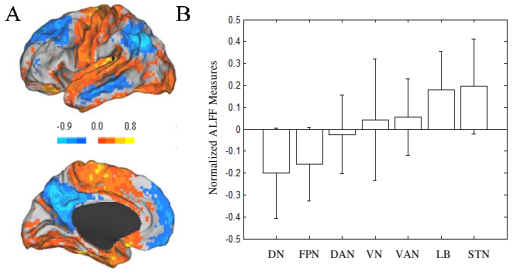

Fig.3 Demonstration of differential strength of low frequency dFCD oscillation within distinct cortical regions. (A) Spatial topography of an averaged ALFF map over subjects. (B) Mean amplitude of ALFF within the distinct cortical networks based on recent parcellation of the cerebrum [4], including the frontoparietal control (FPN), ventral and dorsal attention (DAN, VAN), default (DN), limbic (LB), somatomotor (STN), and visual network (VN).

Conclusion

Compared with local connectivity, distant connectivity exhibited significantly more intensive fluctuation, suggesting that functional connectivity dynamics may be mostly accounted for by long-distance functional interactions across widely distributed regions. Furthermore, the observation regarding variability of dFCD reveals a dynamic property of cortical network architecture that divides processing between parallel systems with extensive local processing and transnetwork regions that serve as hubs connecting these local systems. These findings also shed new lights on functional organization principle of dynamic functional connectivity in task-free human brains.

References

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