Small-World Brain Networks in Resting State in Typically Developing Children and Adolescents

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Introduction

Low-frequency (0.01-0.1 Hz) BOLD signals at rest have been hypothesized to reveal the brain's intrinsic neural activity. Temporally correlated activation of brain regions at rest suggests functional connectivity among these regions (rs-fcMRI) [1], which may reflect underlying structural connectivity or the prior history of co-activation. Graph theory-based complex network analysis qualitatively and quantitatively characterize the organization of complex brain networks [2]. Applying graph theory analyses to resting state brain functional activity [3,4], we sought to examine the efficiency and pattern of brain networks in typically developing children and adolescents.

Materials and Methods

One hundred thirty-two healthy volunteers participated in this study: 76F/56M (female/male), age = 14.19 ± 2.10 years (range 10-18 years), IQ = 111.21 ± 12.90, 121 right handed/11 left handed, parents' social economic status = 3.19 ± 1.47, no history of neurological or psychiatric disease or brain injury. This study was approved by the University of Illinois at Chicago's Institutional Review Board (IRB). Informed consent was obtained from at least one parent, and assent was obtained from all participants.

The participants were scanned on 3.0 Tesla GE Signa HDx scanner (General Electric Health Care, Waukesha, Wisconsin) with a quadrature head coil. Axial T1-weighted image was acquired with FSPGR BRAVO: FOV = 240x240 mm^2, 512x512 matrix, 120 slices, slice thickness = 1.5mm, gap = 0mm, TR = 11.58ms, TE = 4.96ms, TI = 450ms, flip angle = 13°. Resting state fMRI images sensitive to BOLD contrast were acquired: TE = 25ms; flip angle = 90°; FOV = 20 × 20 cm2; matrix = 64 × 64; TR = 2.5s; 5-mm slice thickness with 1-mm gap, 200 time frames).

The resting state fMRI data were preprocessed in SPM for slice timing correction, motion correction and smoothed (isotropic Gaussian kernel FWHM=6mm). The data were then subsequently band-pass filtered using a bandpass filter of 0.009 to 0.08 Hz to extract the low-frequency resting-state BOLD signal. Nuisance signals from white matter, cerebrospinal fluid (CSF), the global signals, and six motion parameters were removed by regression. Individual T1 image was parcellated into 82 cortical and subcortical regions of interest (ROI) using FreeSurfer and mapped to the corresponding fMRI space through co-registration. For each participant, regional resting state timeseries were extracted from the 82 ROIs, and were used to construct the correlation matrix M(82x82), where M(i,j) represents the timeserie correlation of regional i and j. The correlation matrix was then threholded at different cost/density (K) to generate 82-node binarized graphs for each subject. Graph theoretic metrices including small-worldness, global/local efficiency, clustering coefficient, and node degree were computed and correlated with age to characterize developmental changes in the topological organization of the functional connectivity network.

Results and Discussion

Using the graph theory-based approach, the resting state brain networks in children and adolescents consistently showed a small-world architecture in low-cost to medium-cost networks (0.05<cost < 0.25, 1.5<small-worldness<4.39, Fig. 1A), which facilities efficient information processing at a low cost. Global and local efficiency increased as a function of cost (K), and the cost efficiency reached its maximum at K = 0.22, as shown in Fig. 1B.

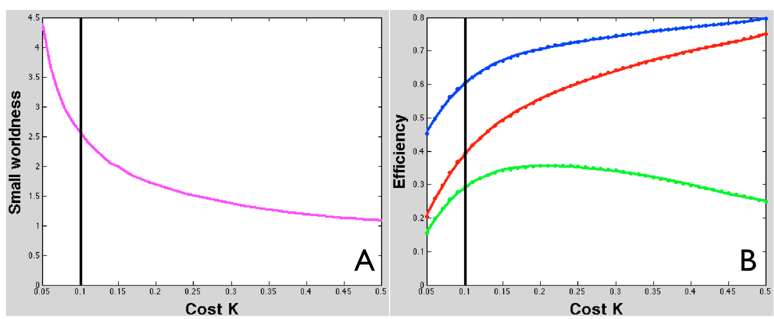

Fig. 1.A. Small-worldness (magenta). B. global efficiency (red), local efficiency(blue), and cost efficiency (green) as a function of cost K.

We examined the developmental changes on the topology of sparse functional networks at low-cost threshold K = 0.1 (shown in Fig. 1A as the black vertical line), which preserved the top 10% of strongest resting connectivity. No significant correlation was found between age and small-worldness or global efficiency at $p < 0.05$. Significant positive correlation was found between age and local efficiency at right lingual gyrus; and node degree for left medial orbitofrontal area (OFC), pericalcarine, anterior cingulate gyri (ACC). Significant negative correlation between age and node degree at right premotor, superior temporal gyrus and insula at $p < 0.05$. These age-related changes at node level may suggest topological fine tuning of resting state brain networks in children and adolescents.

Increased local efficiency at right lingual gyrus and increased node degree for pericalcarine gyrus may increase the efficiency of scanning or visual accuracy with age; and Increased local efficiency at the OFC and ACC may mean better emotion regulation with age. Less node degree at insula may relate to less arousal with negative emotions with progress in age; similarly the motor and auditory, sensory and visuospatial perceptual arousal may decrease with age with less connectivity at the right premotor and superior temporal regions. While our findings are in line with the documented behavioural developmental features [5], examining topological reconfiguration of brain networks in task-based fMRI activity alongside resting state acitivity would be definitive.

References

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