Mapping Functional Connectome Changes of the Human Brain across the Life Span

Miao Cao[1], Zhengjia Dai[1], Fengmei Fan[2], Lili Jiang[2], Xiaoyan Cao[2], Mingrui Xia[1], Ni Shu[1], Xinian Zuo[2], and Yong He[1]

[1]*National Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, Beijing, China, People's Republic of,* [2]*Institue of Psychology, Chinese Academy of Sciences, Beijing, Beijing, China, People's Republic of*

Introduction:

Uncovering the lifespan changes of the human brain is definitely thrilling and a fundamental goal in discovery neuroscience. The lifespan trajectory coding both normal developing and aging stages of the brain has reflected dramatic changes both its structure [1-3] and function [4-6]. It has been commonly accepted that human brain is structurally and functionally organized into a complex network allowing the segregation and integration of information processing [7,8]. In particular, the brain network, describing the interaction between different brain regions, has demonstrated consistent non-trivial properties and reliable changes throughout normal development, aging and in various pathological conditions. Beyond these advances, how the brain network is reorganized through the whole lifespan or its lifespan trajectory has been rarely studied. Here, armed with the graph theory, we aim to chart the lifespan trajectory of human whole-brain functional networks based on resting-state functional MRI (R-fMRI) datasets from 150 subjects collected from the same scanner.

Materials and Methods:

Participants and Data acquisition: A public R-fMRI dataset including total 150 right-handed healthy people (males, 87; females, 63; age range, 7-85 years) from the NKI/Rockland sample (http://fcon_1000.projects.nitrc.org/indi/pro/nki.html) was employed. All subjects have no history of neurological and psychiatric disorders. The resting state fMRI scans were performed on the Siemens Trio^{TM} 3.0 Tesla MRI scanner using an echo-planar imaging (EPI) sequence (TR/TE=2500/30 ms, FA=80°, FOV=216 mm, matrix=256×256, slices=38, thickness=3.0 mm, 260 volumes). High-resolutionT1-weighted images were also collected by magnetization-prepared rapid gradient echo (MPRAGE) sequence (TR/TE=2500/3.5 ms, FA=8°, thickness=1.0 mm, slices=192, matrix=256×256, FOV=256mm). Functional data preprocessing: Data preprocessing was similar to as implemented in [6], producing individual residual timeseries in the MNI152 standard space. Network Construction: A group mask in standard space was made which includes all voxels with non-zeros standard deviation of bold time series and gray matter tissue probability greater than 20%. A high-resolution parcellation template was generated by randomly partitioning the group mask into 1024 contiguous and uniform regions using an algorithm described in [9]. Resting state functional connectivity (RSFC) for each pair of 1024 regions of interest was obtained by computing Pearson correlation coefficients of their representative (i.e., mean across all voxels) time series. Each subject's weighted functional connectivity network was then constructed based on a Bonforroni correction procedure. Network properties analysis: We studied the age-related variation trends of the following regional characteristic and connection property: 1) the regional correlation strength which measures the average correlation extent by which a given region, i, is connected to the rest of the network. Regions with correlation strength greater than the mean and two standard deviations of the global network correlation strength were defined as hubs in every person. 2) The anatomical distance of the connection between region i and region j is defined as the Euclidean distance between centroids of the two regions. The percentages of long-distance (>75mm) and short-distance (≤75mm) connection of the functional connectome were computed for each subject.

Results:

The probability map of hubs in population was gotten and several specific regions including default-mode network regions, attention network regions, motor-related regions and visual cortex were detected to be functional hubs consistently (Figure 1.A). Besides, we observed significantly linear decreases of RSFC strength with age primarily located in several default-mode (e.g., medial frontal and parietal cortex, lateral temporal and parietal cortex) and attention network regions (e.g., insula, dorsal anterior cingulate cortex, lateral frontal cortex and temporal-parietal conjunction) while few regions including SMA and temporal pole showed significantly linear increases ($p<0.05$, FDR corrected) (Figure 1.B). Meanwhile, significant quadratic trajectories of RSFC strength on age were also detected within the left hippocampus and bilateral superior temporal gyrus ($p<0.01$, uncorrected) (Figure 1.C). The network sparsity (i.e., number of graph edges or network connections showing significant RSFC) between brain regions demonstrated a linear trend of decrease with age (not significant) through the lifespan ($p=0.10$). The percentage of long-distance connections was found increase up to age 42 and then decrease while the short-distance connections showed an inverse trajectory ($p=0.01$) (Figure 2).

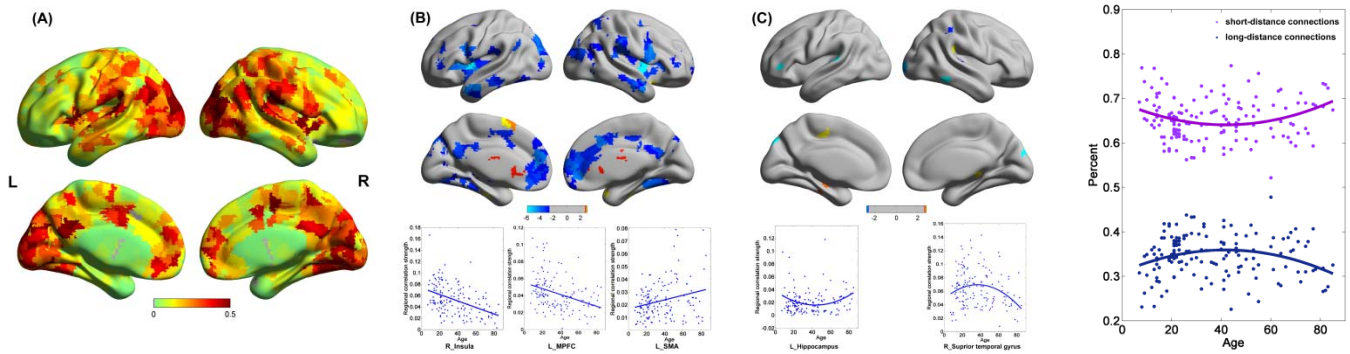

Fig 1 (left) The regional correlation strength results. (A) Probability map of the hubs in the group. The color bar stands for the probability of being hubs for every region. (B) Regions exhibit significantly linearly changes with age. The bottom three charts show the regress lines of typical regions: R-Insula, L-MPFC and SMA. (C) Regions exhibit significantly quadratic changes with age. The bottom three charts show the regress curves of typical regions: L-hippocampus, R-superior temporal gyrus.
Fig 2 (right) The change curve of the percent of long-distance connections and short-distance connections with age.

Conclusion:

In this study, we explored the brain's resting-state functional network changes during the whole lifespan. The hub regions we found in the all age group were consistent with former studies [6]. Importantly, significant age-related changes were mainly occurred to the hub regions. Changes of long-distance and short-distance were found to follow a quadratic trajectory, indicating that the organization of the functional network shifts from a local anatomical emphasis during childhood to a more broadly distributed architecture during adulthood and then turn back in the senescence [10]. We argue these characterizations have important implications for understanding the lifespan changes of neural systems underlying cognition and minds.

Reference: [1] Sowell ER et al. Nat Neurosci 2003;6:309-15. [2] Gong G et al. J Neurosci 2009;29:15684-93. [3] Hagmann P et al. Proc Natl Acad Sci U S A 2010;107:19067-72. [4] Biswal BB et al. Proc Natl Acad Sci U S A 2010;107:4734-9. [5] Zuo XN et al. J Neurosci 2010;30:15034-43. [6] Zuo XN et al. Cereb Cortex 2011. [7] Bullmore and Sporns Nat Rev Neurosci 2009;10:186-98. [8] He Y et al. Curr Opin Neurol 2010:1. [9] Zalesky A et al. Neuroimage 2010;50:970-83. [10] Fair DA et al. PLoS Comput Biol 2009;5:e1000381.