課題番号（Project number）61

Development and aging of human functional and structural brain networks studied with a large brain MRI database

［１］組織（Research group）
代表者（Principal Investigator (PI)）：
瀧　靖之
（東北大学加齢医学研究所）
対応者（Host researcher at IDAC）：
呉　凱
（華南理工大学）
分担者（Co-investigator）：

研究費(Expenditure report of research funds)：
物件費 250,000YEN

［２］研究経過（Research setup）

Graph theoretical analysis of neuroimaging data is growing rapidly and could potentially provide a relatively simple but powerful quantitative framework to describe and compare whole human brain structural and functional networks under diverse experimental and clinical conditions. Prof. Taki's group has built a large-scale of Japanese brain MRI database (around 2500 subjects aged from 6-80) with a variety of imaging modalities, including s-MRI, DTI, and rs-fMRI. Prof. Taki and I proposaled a new research regarding lifespan changes of human brain connectivity, which yields truly integrative and comprehensive descriptions of the structural and functional organization of the human brain. We construct structural brain networks by the measurement of regional gray matter volume (RGMV) using sMRI and the measurement of anatomical connection probabilities using DTI. We employ rs-fMRI to construct functional brain networks by measuring the temporal correlations in time courses (also referred to as functional connectivity).

One of our previous studies demonstrate topological organization of functional brain networks in healthy children using resting-state fMRI and indicate network properties in relation to age, sex, and intelligence [1]. The recent progress of our study was to investigate age- and sex- related differences in structural cortical networks derived from DTI in healthy children.

［３］成果（Research outcomes）

（３－１）研究成果（Results）

The sample consisted of 291 subjects (146 boys, 145 girls; age range, 5.6-18.4 years) [1]. All images were collected using a 3-T Philips Intera Achieva scanner. The diffusion-weighted data were acquired by using a spin-echo EPI sequence. Additionally, a data set with no diffusion weighting (b value=0 s/mm2) (b=0 image) was acquired.

We constructed structural cortical networks using DTI by the methodology described in a previous studies [2]. Briefly, the whole brain was parcellated into 1024 regions with equal size, defined by a high-resolution parcellation of Automated Anatomical Labeling (AAL) atlas [3]. The number of interconnecting fibers was defined as the weight of the network edge, which results in a symmetric 1024*1024 matrix for each subject. Finally, a threshold of (T=3) was set to the weight of the network edge. To characterize the global and regional properties of structural cortical networks, we computed graph measures as follow: clustering coefficient, path length, local efficiency, global efficiency, small-worldness, modularity, mean anatomical distance, regional nodal efficiency, regional strength of anatomical distance [4].

We applied a general linear model (GLM) to analyze the effects of age, sex, and their interaction on the network parameters. To detect the development trajectories of the linear and quadratic age-related changes in each network parameter, we used two multiple linear regressions (Model I and II) that modeled mean value, age, and age2 as predictors, with sex as a covariate. We then determined the best model among the two regressions based on Akaike's information criterion (AIC).

Significant age- and sex-related differences were found in both global and regional network properties. Global efficiency and mean anatomical distance were positive correlated with age, while path length and modularity were negative correlated with age (p<0.05). Girls showed significantly higher values in clustering coefficient, local efficiency, global efficiency, and small-worldness, compared with boys. Boys showed significantly higher values in path length, compared with girls (p<0.05). Global hubs defined by regional nodal efficiency were predominately in frontal and parietal brain regions (Figure 1).

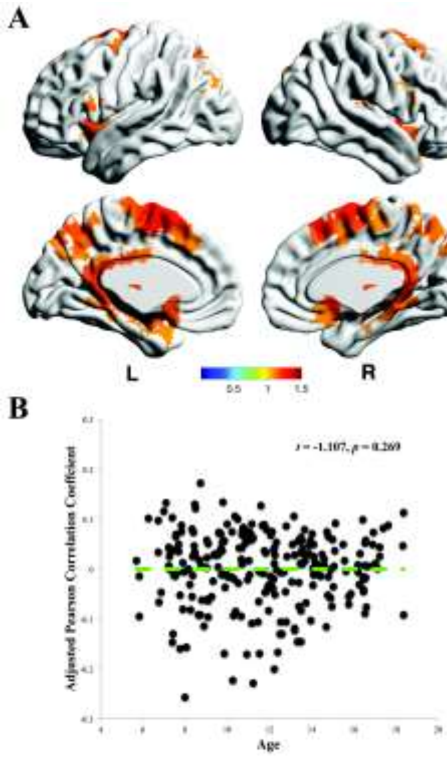

Figure 1. Global hubs in structural cortical networks.

Global hubs defined as the brain regions showing higher values in regional nodal efficiency (> mean + SD). The correlation between age and the Pearson correlation coefficient, which was defined as the association of hub distribution between the global hubs shown in (A) and those in each individual. Note that the results were calculated after adjusting for the effects of brain size and sex, using a general linear model.

Importantly, the global hubs pattern was non-significantly correlated with age and thus kept relatively stable across the age range of 6-18 years. Age-related increases in the regional nodal efficiency were found in the medial prefrontal, lateral frontal, medial temporal, parietal, and occipital brain regions (Figure 2). Significant sex-related differences in the regional nodal efficiency were found in various brain regions, primarily in the medial prefrontal, parietal, and occipital brain regions.

To our knowledge, this is the first study to reveal age- and sex-related changes in topological organization of structural cortical networks in a large number of healthy children. Our findings of the network topology of structural cortical networks with normal development bring new insights into the understanding of brain maturation and cognitive development during childhood and adolescence.

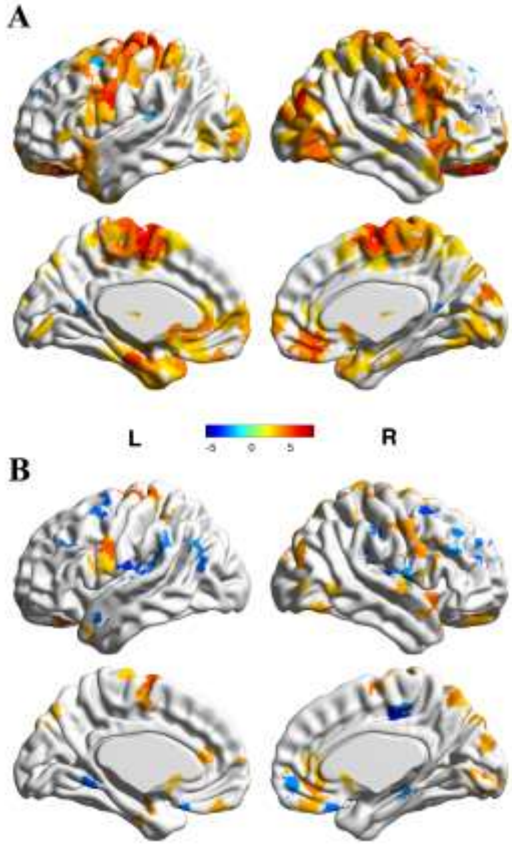

Figure 2. Significant age-related changes in regional nodal properties.

Significant age-related differences in regional nodal efficiency (p<0.05, FDR-corrected). Significant age-related differences in regional strength of anatomical distance (p<0.05, FDR-corrected)

（３－２）波及効果と発展性など（Future perspectives）

With the support of this project, Prof. Taki's group and my group have established a mechanism of international joint research. The group of Prof. Taki focuses on the construction of a huge database of MRI images and its application in the studies of normal aging, development, and life style related topics. My group is engaged in developing new methods of human connectome analysis and machine learning and applying these methods into the studies of healthy subjects and patients with brain diseases. We hope that this kind joint research could be approached in the future.

［4］成果資料（List of Papers）

（1）Wu K , Taki Y, Sato K, Wu X, Xue J, Du X, Takeuchi H, Thyreau B, Fukuda H, Kawashima R. Age- and sex- related differences in structural cortical networks in healthy children. 21st Annual Meeting of the Organization for Human Brain Mapping, June 14-18, 2015, Honolulu, USA.

（２）Chihiro Kondo, Koichi Ito, Kai Wu, Kazunori Sato, Yasuyuki Taki, Hiroshi Fukuda, Takafumi Aoki. Age Estimation Method Using Brain Local Features for T1-Weighted Images.37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, pp. 666--669, August 2015.

（3）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.ADNI データベースの脳ネットワーク解析に関する検討.電子情報通信学会医用画像研究会, Vol. 115, No. 301, pp. 67--72, November2015.

（4）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.脳局所特徴量に基づく年齢推定手法と ADNI データベースを用いた性能評価.電子情報通信学会医用画像研究会, Vol. 115, No. 139, pp. 79--84, July 2015.

（5）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.経時変化のある脳 MRI 画像データベースを用いた年齢推定手法の性能評価.電子情報通信学会医用画像研究会, Vol. 114, No. 482, pp. 23--28, March 2015.

（6）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.脳 MRI 画像の局所特徴量に基づく年齢推定手法と縦断データベースを用いた性能評価.情報処理学会 第 77 回全国大会, pp. 2-359--2-360, March 2015.

（7）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.脳 MRI 画像の局所特徴量に基づく年齢推定手法とその評価.電子情報通信学会医用画像研究会, Vol. 114, No. 311, pp. 11--16, November 2014.

（8）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.脳 MRI 画像の局所特徴量に基づく年齢推定手法の検討.平成 26 年度電気関係学会東北支部連合大会, No. 2H01, p. 208, August 2014.

（9）近藤千裕, 伊藤康一, 呉凱, 佐藤和則, 瀧靖之, 福田寛, 青木孝文.脳局所特徴量に基づく年齢推定手法と脳 MRI 画像データベースを用いた性能評価.映像情報メディア学会技術報告, Vol. 38, No. 32, pp. 15--18, August 2014.

（１０）Minyue Chi, Shengwen Guo, Yuping Ning, Jie Li, Haochen Qi, Minjian Gao, Xiuyong Wu, Junwei Xue, Xin Du, Jiexin Wang, Xiaowei Hu, Yangbo Guo, Yuling Yang, Hongjun Peng, and Kai Wu. Discriminative Analysis of Major Depressive Disorder and Anxious Depression Using Support Vector Machine. J. Comput. Theor. Nanosci. 12(7), 1395-1401, 2015.

（１１）Shengwen Guo, Chunren Lai, Wensheng Wang, Lina Cheng, Kai Wu, Guiying Cen, Minyue Chi. Classification using multiply cortical features of temporal lobe epilepsy patients. Journal of Southeast University (Natural Science Edition). Vol.45, No.6, pp. 1057-1060, 2015.11.

Reference:

1. Wu, K., et al., *Topological organization of functional brain networks in healthy children: differences in relation to age, sex, and intelligence.* PLoS ONE, 2013. **8**(2): p. e55347.
2. Shu, N., et al., *Diffusion Tensor Tractography Reveals Disrupted Topological Efficiency in White Matter Structural Networks in Multiple Sclerosis.* Cereb Cortex, 2011. **21**(11): p. 2565-2577.
3. Zalesky, A., et al., *Whole-brain anatomical networks: does the choice of nodes matter?* Neuroimage, 2010. **50**(3): p. 970-83.
4. Rubinov, M. and O. Sporns, *Complex network measures of brain connectivity: uses and interpretations.* Neuroimage, 2010. **52**(3): p. 1059-69.