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INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team RCCM

RCCM Annual Report 2008

Liama - Beijing - Chine

THEME BIO

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The RCCM was established in the second half of 2008. Its full name is LIAMA Research Center for Computational Medicine, with researches focusing on medical image analysis and the machanisim on how brain works. It is composed by five interactive sub-laboratories. For more informations, please visit our website, http://www.rccm.org.cn.

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2. Overall Objectives

2.1. Overall Objectives

Rapid advances in convergent technologies of information technology, biotechnology, nanotechnology and cognitive science have the great potential to enhance human performance. Especially, combination of information and computational technologies with medicine, biology, chemistry, and so on, creates a number of emerging fields in science and engineering. Computational Medicine is one of such emerging fields, which couples biological models with medical data and practices by applying modern computational techniques to medicine.

LIAMA Center for Computational Medicine will at its stage aim at exploring and understanding how human brain works and how to make machine intelligent by bringing together multidisciplinary expertise in Imaging Science, Cognitive Science, Computer Science, Neurology, Psychiatry, Neuroscience, Mathematics, Physics, and so on. This goal will be achieved through the following five research themes: Computational Anatomy, Biomedical Imaging, Brain-Computer Interface, System Biomedicine and Computer-aided Diagnosis. The center is keen on developing strong academic, clinical and industrial linkages, leading to significant domestic and international collaboration as well as the practical applications of its research. It will become bridge of three communities of information technology, cognitive neuroscience and clinical researchers and practitioners.

2.2. Highlights

With the accumulating knowledge to spontaneous activity observed with functional magnetic resonance imaging (fMRI), the spontaneous activity reveals its potential to locate changes in brain hemodynamics associated with neurological and psychiatric disorders.

We have performed a new regional tempospatial clustering analysis of resting state fMRI data, which is a combined measurement for both the temporal and the spatial patterns of the spontaneous fluctuations. This method is based on the assumption that if a large part of voxels within a specific region reaches a high activity level at certain time points, these time points can be defined as the spontaneous activated time points for this region. These activity pattern could be used in further analysis, such as coactivity in other brain regions [24].

Researchers have long studied the biological basis for intelligence and have found increasing evidence relating high performance on intelligence quotient tests to the coordination of multiple brain regions, utilizing both structural and functional brain imaging techniques. Using resting state fMRI data, we found that brain regions in which the strength of functional connectivity significantly correlated with intelligence scores were distributed in the frontal, parietal, occipital and limbic lobes. This reveals that brain activity may be relevant to differences in intelligence even in the resting state [22].

Functional segregation and integration are two major organizational principles of the human brain. Previous studies have suggested that efficient small-world topology an attractive model for brain functional network. We have demonstrated that the efficient small-world topological properties were disrupted in patients with schizophrenia. This disruption may partially account for the reduced global/local efficiency of information processing within the brain, which may lead to the deficits of cognition and behavior of patients with schizophrenia. Additionally, these altered topological measurements correlate with illness duration in schizophrenia. This study provides further evidences that schizophrenia is a disconnection syndrome [17].

3. Scientific Foundations

3.1. Computational Neuroanatomy

Keywords: *Morphometry*, *Neuroanatomy*, *Registration*, *Segmentation*.

Computational neuroanatomy is one of the main research themes at RCCM. This field combines computer science, mathematics and neuroscience to provide insight that will enable us to quantitatively analyze the variability in neuroanatomical structures. Currently we are primarily concerned with MR images and Diffusion Tensor Images(DTI) analysis.

MR images analysis mainly focus on brain tissue segmentation of MR images, intra- and inter-modality image registration, shape and morphometric analysis of the cerebral cortex, and cortical network analysis. For brain tissue segmentation, we have developed multi-context based brain image segmentation and J-divergence based variational segmentation methods. In addition, a parallel genetic algorithm-based active model has been proposed and applied to segment the lateral ventricles. For image registration, both a viscoelastic based model and a non-uniform B-spline based non-rigid registration approach have been proposed and widely applied to the alignment of individual brains to an average template. As to shape and morphometric analysis, we investigate the cerebral cortex at a different levels from global fractal dimension to local thickness. Various metrics have been used to search for significant differences among different populations. Finally, we build cortical networks by connecting anatomical regions of the cortex using links, the strength of which are determined by correlation coefficients of various metrics (e.g. cortical thickness, voxel-based morphometry) between two regions. Then we apply graph theory, as well as small-world network analysis methods, to the networks, investigating how anatomical changes in a few regions affect the performance of the cortex as a whole.

Diffusion tensor imaging (DTI) is a recently developed MRI technique that can non-invasively measure macroscopic axonal organization in nervous system tissues. With this technique, white matter integrity and fiber connectivity can be evaluated in vivo. Two of the major uses of DTI in the central nervous system are in fiber tracing and quantitative white matter analysis. Our group focuses on developing new methods for analyzing diffusion imaging data and clinical applications of DTI. We have developed a scale-invariant parameterization method by arc-angle for quantitative analysis along the cingulum as an analytical method.This technique can yield a continuous and exact description of any segment of the cingulum and can establish the correspondence in the cinculum between subjects. Through this method, a significant left-greater-than-right asymmetry pattern was obtained in most segments of the cingulum bundle in normal right-handed subjects. A similar method for the quantitative analysis of the pyramidal tract has also been proposed. Clinical applications of DTI in brain development and to neuropsychiatric disorders, such as schizophrenia, Alzheimer disease, depression, multiple scleroses, brain tumors and so on, are also an important part of our work. We attempt to investigate normal and pathologic changes in white matter and brain connectivity over the life span, the white matter abnormalities specific to different brain disorders and the correlation between psychiatric symptoms and white matter lesions. A hot issue in our research recently has been the use of DTI to obtain the anatomical network of the cerebral cortex. This has allowed us to characterize the global architecture of the anatomical connection pattern in the human brain.

3.2. Biomedical Imaging

Keywords: *Brain Activity*, *Complex Brain Network*, *Functional Connectivity*, *fMRI*, *fNIRS*.

Currently, our team is focusing on the study of computational theory and methodology and its application in cognitive disorders based on functional images. Our primary research is in two main areas, as follows:

- **Functional MRI:**
  - **Evaluating Brain Activity:** We are studying brain activity in different states and disorders by combining time and spatial information.
  - **Functional Connectivity Analysis:** Our group is studying the complex relationships among different functional brain regions by developing new functional coherence/consistency measures so as to evaluate the dynamic changes of the connectivity. In addition, this research can be used to help us investigate the alterations in functional connectivity patterns among patients with various cognitive disorders.
  - **Algorithm for Construction and Analysis of Complex Brain Networks:** We are working on constructing an appropriate network model of complex brain systems and on investigating organized brain architecture so as to understand the working pattern of the human brain and to evaluate alterations in patients with cognitive disorders.
- **fNIRS:**
  - **Improve the Distribution of Sources and Detectors:** We currently study new ways to distribute sources and detectors in order to improve the quality of fNIRS images.
  - **Algorithm for Image Reconstruction:** We are working to develop a new reconstruction method in order to improve the depth resolution of NIRS images.
  - **Platform for fNIRS Image Analysis:** We are developing a public platform for the statistical analysis of NIRS signals.

3.3. Systems Biomedicine

Keywords: *Biomarker*, *Complex Biological Networks*, *Imaging Genomics*.

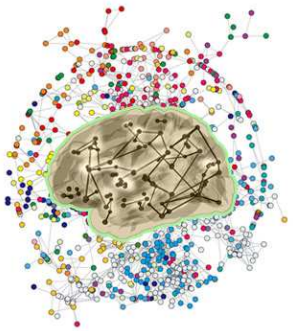

Figure 1. Medical Imaging and Computing Complex Network

Systems biomedicine is a relatively new field that focuses on the study of complex interactions in biological systems at a systemic level. Our goals are to study human diseases especially brain diseases from the systemic view, by combining various data sets. Our main research interests focus on Microarray Data Analysis, Network Biology and Imaging Genetics.

- **Microarray Data Analysis:** Microarray Data Analysis mainly concentrates on developing novel algorithms for classification, clustering and disease feature gene selection from microarrays. We are also interested in discovering microRNA markers of brain diseases from microRNA microarray.
- **Network Biology:** Network Biology includes applying machine learning, data mining and statistics methods to reconstruct and analyze various complex biological networks (Fig.1), incorporating interactome with diverse omics datasets such as transcriptomics and phenomics datasets, and further to find disease-related genes or gene sub-networks.
- **Imaging Genetics:** The theme of Imaging Genomics in this team aims at the genetic basis of anatomical and functional abnormalities in various neurological and psychiatric diseases found by neuroimaging. Our studies are also dedicated to develop and apply novel pattern recognition and machine learning algorithms combining imaging information with genomics data from system-level perspectives to find the biomarker for complex brain disease (such as schizophrenia, Alzheimer's disease, and glioma etc.).

3.4. Brain-computer Interface

Keywords: *Brain-computer Interface*, *EEG*, *NIRS*, *fMRI*.

Brain-computer Interface (BCI) is an emerging technology that is derived from several disciplines, including neuroscience, computer science and biomedical engineering. The combination of techniques from these fields opens the possibility for direct communication between the human brain and the external environment and to manipulate devices without the involvement of muscles or the peripheral nervous system. This field could provide new vistas for some patients with neural damage. Researchers commonly categorize BCI according to the method used to record the brain activity. For example, technologies that are based on an electrical signal include electroencephalography (EEG), and technologies that are based on blood dynamics include fMRI and NIRS. In this laboratory we primarily focus on developing BCI systems and related technologies based on near infrared reflectance spectroscopy (NIRS). NIRS is a non-invasive and portable technology, which can be used in certain clinical applications. Currently, we are exploring the development of a new technology, that is, a responsive brain-computer interface based on near infrared reflectance spectroscopy. We hope that it will be helpful for some patients with severe brain damage by enabling them to communicate with the external environment.

3.5. Computer Aided Detection and Diagnosis

Keywords: *Biomarkers*, *CAD2*, *Diagnosis*, *Prognosticate*.

This team is trying to use the computer program to process a variety of brain images for the sake of (semi-) automatic sub-structure extraction, measurement and quantitative statistical analysis, and thus to incubate a computer aided detection and diagnosis (CAD2) system concentrating on the brain disease and the corresponding change of the sub-structures, which should be promising for guiding the study how the brain works.

Some preliminary research results shows that the alienation or missing of the consciousness or the functions in the brain have corresponding morphologic changes in the brain images. For an instance, the changes of the shape or the volume of the hippocampus could affect the memory function; Some relationships between the diseases and the changes of sub-structures doesnât arrive at a final validation yet, such as the relationship between the losing of the language ability and the changes of the gray matter in the cerebral cortical, or between the intelligence quotient (IQ) and the complexity or the thickness of the cerebral cortical. Therefore, the study for the morphologic changes of the sub-structures inside the brain could give birth to a powerful assistant for the research how the brain works, and form an objective and reliable CAD2 system.

Currently our lab has achieved some promising progress on the extractions and descriptions of some sub-structures of the brain, including the extraction and measurement of the shape and volume for the hippocampus, the tracking and the classification for the white matter fiber, and the definition and measurement of the thickness and the complexity of the cerebral cortical. We will combine the research results from the functional images of the brain, to validate the objectivity and rationality of the above physical description and functional analysis, and extend the research to other critical sub-structures inside the brains and its influences to the brain functions. The destination of our research is to set up a complete (semi-) automatic computer aided detection and diagnosis system for our brain.

4. Application Domains

4.1. Application Domains

The ultimate objectives of our research are to improve our understandings of the pathogenesis of diseases and to find early markers for neurological and psychiatric diseases, based on neuroimages and genome datasets. A long term goal of these studies is to provide objective and quantitative indices for early diagnosis and for evaluating the effect of therapy for cognitive disorders.

In the near future, convenient, noninvasive imaging biomarkers for early prediction and diagnosis of brain disorders will be available as a result of increasing collaboration among multiple centers/institutions as well as datasets that are shared all over the world.

5. Software

5.1. Software for Cortical Shape Analysis

Keywords: *Cortical Networks*, *Shape Analysis*, *Statistical Tests*, *Visualization*.

Participants: Jiefeng JIANG, Yuanchao ZHANG, Lei LIN, Xing MIN, Yongfu HAO, Na ZHANG, Cunlu XU, Zhijun YAO, Sheng WANG, Nianming ZUO, Tianzi JIANG.

The shape analysis of the cerebral cortex is always a hot topic in both neuroscience and computer science. We plan to design software for neuroscientists and doctors to perform shape analysis and statistical tests (Fig.2). It takes morphological measurements computed from other software such as SPM, freesurfer and so on. The software is divided in two parts. One is the shape analysis part, in this part, we try to implement up-to-date shape analysis techniques to extract shape features, as well as establish cortical networks whose vertices and edges are brain regions and correlations among brain regions respectively. After that, statistical tests were performed to test the effect of factors, for example, group, gender, age, IQ and so on. Finally, in order to ensure the findings, multiple comparison corrections algorithms like false discovery rates and random field thoey are applied. The other part is the visualization part, we use VTK and/or OpenGL to render the results of statistical tests. This part has two major functions: displaying scalar values on the cortical surface using a mapping between values and colorbar; and showing cortical network edges using "sticks" connecting different brain regions, the strength of edges are coded by colors and radii of the "sticks".

5.2. Software for DTI analysis

Keywords: *3D Visualization*, *Batch Processing*, *Diffusion Tensor Calculations*, *Fiber Tracking*, *ROI Drawing*.

Participants: Qifeng WANG, Haixia ZHAO, Xiantong ZHEN, Jiefeng JIANG, Ni SHU, Yonghui LI, Xiuchao SUI, Nianming ZUO, Tianzi JIANG.

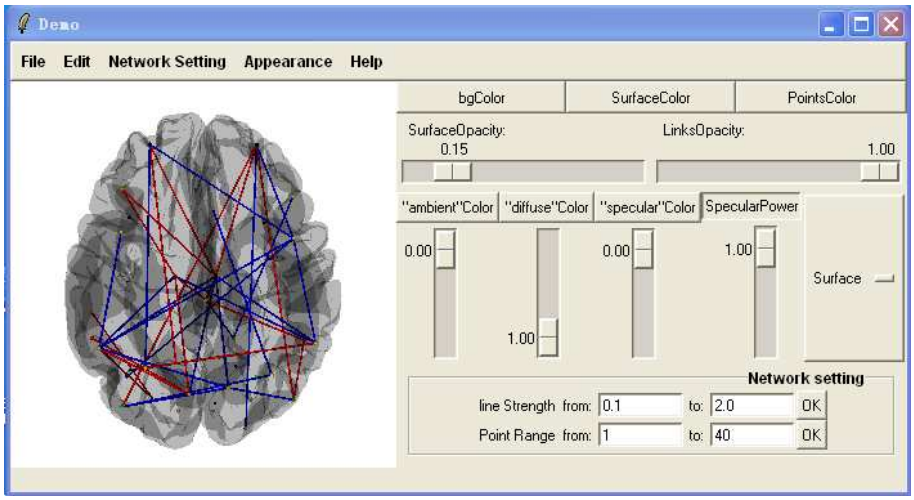

Figure 2. Software for Cortical Shape Analysis

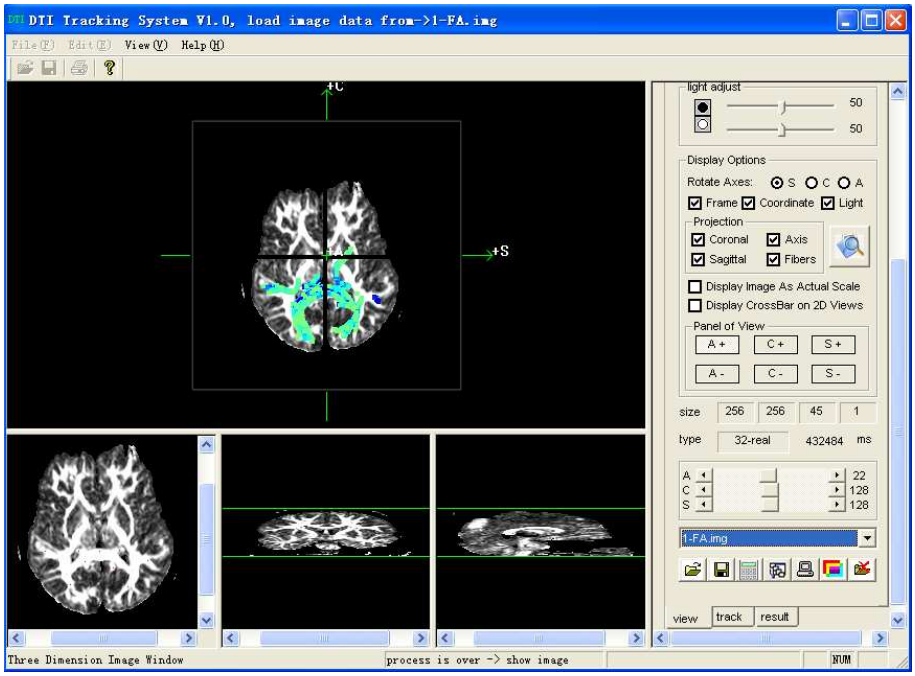

Figure 3. Software for DTI analysis

DTI Tracking System is a diffusion tensor image processing, fiber tracking and 3D visualization program (Fig.3). It is suitable for calculating DTI data, showing and saving tracked fibers and statistics results. DTI Tracking has more user-friendly operational procedures, better deal with abnormal situations. Importantly, it also adds tensor calculation batch processing and fiber tracking batch processing, which are particularly useful operations for avoiding repeated operations, greatly reducing the cost of data analysis time and improving data processing efficiency. The software can be found on our web http://www.rccm.org.cn/download/DTIsoftware.html.

6. New Results

6.1. A Novel Pixon-representation for Image Segmentation Based on Markov Random Field

Participants: Lei LIN [Zhejiang University], Litao ZHU, Faguo YANG, Tianzi JIANG.

In this paper, based on the previous work in our team, we propose a pixon-representation for image segmentation, which is a set of disjoint regions with variable shape and size, named pixon. These pixons combines with their attributes and adjacencies construct a graph, which represents the observed image. Since the characteristics such as intensity, color, texture, etc., of pixels in each pixon are similar, an assumption is taken into account that the pixels in one pixon belong to the same class in the segmented image. A criterion of GOOD pixon-representation has also been presented and a fast QuadTree combination (FQTC) algorithm has been proposed to extract the good pixon-representation. Then the proposed image representation has been applied to image segmentation based on MRF model. Finally the experimental results have demonstrated that our pixon-based algorithm has good performance while reduces the computational cost sharply compared with the pixel-based method [16].

6.2. A Robust and Accurate Algorithm for Estimating the Complexity of the Cortical Surface

Participants: Jiefeng JIANG, Wanlin ZHU, Feng SHI, Yuanchao ZHANG [Zhejiang University], Lei LIN [Zhejiang University], Tianzi JIANG.

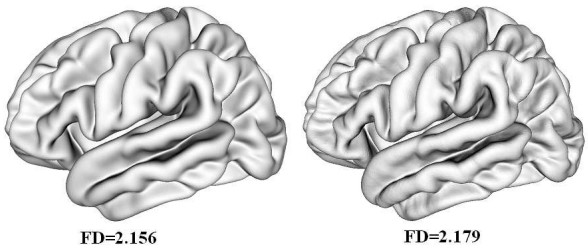

Figure 4. Estimating the Complexity of the Cortical Surface

A fractal dimension (FD) gives a highly compact description of the shape characteristics of the human brain and has been employed in many studies on brain morphology. The accuracy of FD estimation depends on the precision of the input shape description. Facilitated by automatic cerebral cortical surface reconstruction algorithms, the shape of the cerebral cortex can be more precisely modeled using Magnetic Resonance (MR) imaging. Since the reconstructed cortical surface is represented by triangles, rather than by points, as is typical of models that use voxels, the voxel-based FD estimation algorithms that have been used in previous studies do not work when using the cortical surface as the input. Thus designing a new algorithm that is able to estimate the FD from a surface representation becomes of particular interest. We proposed a robust and accurate FD estimation algorithm (Fig.4). The algorithm is based on a box-triangle intersection checking strategy, which is used for the first time in brain analyses, and a box-counting method, which has been widely used in FD computations of the human brain and other natural objects. These two features endowed the algorithm with robustness. The accuracy of the algorithm was validated via several experiments using both manually generated datasets and real MR images. As a result of these features, the algorithm is also suitable for estimating the FD of fractals in addition to that of the cerebral cortex [13].

6.3. COMT Val158Met Modulates Association between Brain White Matter Architecture and IQ

Participants: Jun LI, Chunshui YU [Xuanwu Hospital], Yonghui LI, Bing LIU, Yong LIU, Ni SHU, Ming SONG, Yuan ZHOU, Wanlin ZHU, Kuncheng LI [Xuanwu Hospital], Tianzi JIANG.

The intelligence quotient (IQ) is typically associated with the architecture of gray and white matter in specific brain regions, and this association appears to be genetically based. However, specific sources of genetic variation for the association have not been studied extensively. Using diffusion tensor imaging in 15 mental retardation patients and 80 healthy volunteers, we studied the association between white matter architecture and IQ and also investigated the effects of COMT val158met on this association. The results showed that fractional anisotropy (FA) values in the prefrontal lobe and the hippocampus formation were associated with IQ and that val158met may affect this association. Subjects who were val homozygous showed steeper slopes for regression of the FA value on IQ than met carriers. Our findings suggest that COMT val158met may contribute to intelligence by affecting the association between IQ and the white matter architecture in the prefrontal lobe and the hippocampal formation [15].

6.4. Abnormal Diffusion of Cerebral White Matter in Early Blindness

Participants: Ni SHU, Jun LI, Kuncheng LI [Xuanwu Hospital], Cunshui YU [Xuanwu Hospital], Tianzi JIANG.

Early visual deprivation may lead to both abnormal and plastic changes in the visual and other systems of the brain. Such secondary changes in the gray matter of the early blind have been well studied, but not so well in the cerebral white matter whose subtle changes may be revealed by diffusion tensor imaging (DTI). The first purpose of this study is to explore the possible changed white matter regions of the early blind in whole brain manners, using voxel-based analysis (VBA) and tract-based spatial statistics (TBSS) methods. The second purpose is to investigate the changes of diffusion eigenvalues in the abnormal white matter fiber tracts using tractography based group mapping analysis. From VBA of fractional anisotropy (FA) images, the significant changed white matter regions were the geniculocalcarine tract (GCT) and its adjacent regions. This finding was validated by TBSS method. Then we studied the changes of mean diffusivity (MD), FA, primary ($\lambda 1$) and transverse diffusivities ($\lambda 23$) in the GCT using tractography based group mapping analysis. We found the early blind had significantly lower FA ($P < 0.0001$), higher MD (P = 0.001) and ($\lambda 23$) (P < 0.0001) in the GCT. This pattern of diffusion changes is similar to findings seen in immaturity or axonal degeneration. Thus, we suggest that transneuronal degeneration and/or immaturity may account for the abnormal diffusion changes in the GCT of the early blind [21].

6.5. Brain Spontaneous Functional Connectivity and Intelligence

Participants: Ming SONG, Yuan ZHOU, Jun LI, Yong LIU, Lixia TIAN, Cunshui YU [Xuanwu Hospital], Tianzi JIANG.

Many functional imaging studies have been performed to explore the neural basis of intelligence by detecting brain activity changes induced by intelligence-related tasks, such as reasoning or working memory. However, little is known about whether the spontaneous brain activity at rest is relevant to the differences in intelligence. Here, 59 healthy adult subjects (Wechsler Adult Intelligence Scale score, 90-138) were studied with resting state fMRI. We took the bilateral dorsolateral prefrontal cortices (DLPFC) as the seed regions and investigated the correlations across subjects between individual intelligence scores and the strength of the functional connectivity (FC) between the seed regions and other brain regions. We found that the brain regions in which the strength of the FC significantly correlated with intelligence scores were distributed in the frontal, parietal, occipital and limbic lobes. Stepwise linear regression analysis also revealed that the FCs within the frontal lobe and between the frontal and posterior brain regions were both important predictive factors for the differences in intelligence. These findings support a network view of intelligence, as suggested in previous studies. More importantly, our findings suggest that brain activity may be relevant to the differences in intelligence even in the resting state and in the absence of an explicit cognitive demand. This could provide a new perspective for understanding the neural basis of intelligence [22].

6.6. Disrupted Small-world Networks in Schizophrenia

Participants: Yong LIU, Meng LIANG [Oxford University], Yuan ZHOU, Yong HE [McGill University], Yihui HAO [Xiangya Hospital], Ming SONG, Chunshui YU [Xuanwu Hospital], Haihong LIU [Xiangya Hospital], Zhening LIU [Xiangya Hospital], Tianzi JIANG.

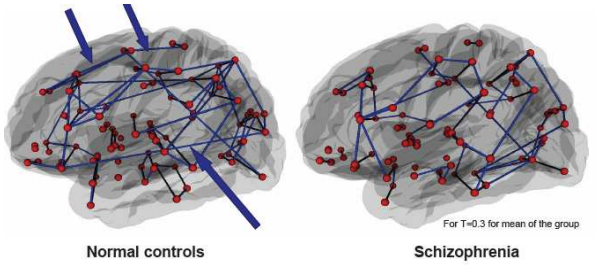

Figure 5. Disrupted Small-world Networks in Schizophrenia

The human brain has been described as a large, sparse, complex network characterized by efficient small-world properties, which assure that the brain generates and integrates informationwith high efficiency. Many previous neuroimaging studies have provided consistent evidence of 'dysfunctional connectivity' among the brain regions in schizophrenia; however, little is known about whether or not this dysfunctional connectivity causes disruption of the topological properties of brain functional networks.

To this end, we investigated the topological properties of human brain functional networks derived from resting-state functional magnetic resonance imaging (fMRI). Data was obtained from 31 schizophrenia patients and 31 healthy subjects; then functional connectivity between 90 cortical and sub-cortical regions was estimated by partial correlation analysis and thresholded to construct aset of undirected graphs. Our findings demonstrated that the brain functional networks had efficient smallworld properties in the healthy subjects; whereas these properties were disrupted in the patients with schizophrenia. Brain functional networks have efficient small-world properties which support efficient parallel information transfer at a relatively low cost. More importantly, in patients with schizophrenia the small-world topological properties are significantly altered in many brain regions in the prefrontal, parietal and temporal lobes (Fig.5). These findings are consistent with a hypothesis of dysfunctional integration of the brain in this illness. Specifically, we found that these altered topological measurements correlate with illness duration in schizophrenia. The correlation between

the topological measures of the efficient small-world attributes and illness duration in schizophrenia leads us to believe that this method could be helpful for understanding the dysfunction syndrome in schizophrenia. Detection and estimation of these alterations could prove helpful for understanding the pathophysiological mechanism as well as for evaluation of the severity of schizophrenia.

This approach may also be able to be used in other disorders such as Alzheimer's disease, which can also be taken as a disconnection syndrome and in which abnormal functional connectivity plays a role[17].

6.7. Altered Resting-state Functional Connectivity and Anatomical Connectivity of Hippocampus in Schizophrenia

Participants: Yuan ZHOU, Ni SHU, Yong LIU, Ming SONG, Yihui HAO [Xiangya Hospital], Haihong LIU [Xiangya Hospital], Chunshui YU [Xuanwu Hospital], Zhening LIU [Xiangya Hospital], Tianzi JIANG.

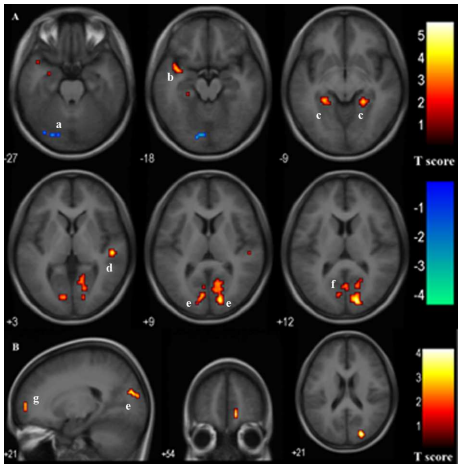

Figure 6. Altered Resting-state Functional Connectivity and Anatomical Connectivity

Hippocampus has been implicated in participating in the pathophysiology of schizophrenia. However, the functional and anatomical connectivities between hippocampus and other regions are rarely concurrently investigated in schizophrenia. In the present study, both functional magnetic resonance imaging (fMRI) during rest and diffusion tensor imaging (DTI) were performed on 17 patients with paranoid schizophrenia and 14 healthy subjects. Resting-state functional connectivities of the bilateral hippocampi were separately analyzed by selecting the anterior hippocampus as region of interest. The fornix body was reconstructed by diffusion tensor tractography, and the integrity of this tract was evaluated using fractional anisotropy (FA). In patients with schizophrenia, the bilateral hippocampi showed reduced functional connectivities to some regions which have been reported to be involved in episodic memory, such as posterior cingulate cortex, extrastriate cortex, medial prefrontal cortex, and parahippocampus gyrus (Fig.6). We speculated that these reduced connectivity may reflect the disconnectivity within a neural network related to the anterior hippocampus in schizophrenia. Meanwhile the mean FA of the fornix body was significantly reduced in patients, indicating the damage in the hippocampal anatomical connectivity in schizophrenia. The concurrence of the functional disconnectivity and damaged anatomical connectivity between the hippocampus and other regions in schizophrenia suggest that the functional-anatomical relationship need to be further investigated.

This study provides a multidisciplinary perspective to investigate underlying mechanism of the abnormality of resting-state functional connectivity in disease state [30].

6.8. Spontaneous Activity Associated with Primary Visual Cortex: A Resting State fMRI Study

Participants: Kun WANG, Tianzi JIANG, Chunshui YU [Xuanwu Hospital], Lixia TIAN, Jun LI, Yong LIU, Yuan ZHOU, Lijuan XU, Ming SONG, Kuncheng LI [Xuanwu Hospital].

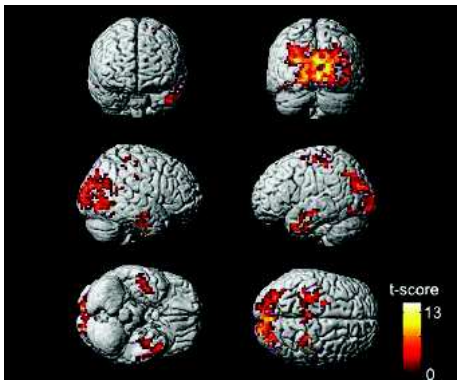

Figure 7. Spontaneous Activity Associated with Primary Visual Cortex

Brain functions during the resting state have attracted considerable attention in the past several years. However, little has been known about spontaneous activity in the sensory cortices in the task-free state. This study used functional magnetic resonance imaging (fMRI) to investigate the existence of spontaneous activity in the primary visual areas (PVA) of normal-sighted subjects and to explore the physiological implications of such activity. Our results revealed that we were able to detect spontaneous activity, which was nonrandom in that it was distinctly clustered both temporally and spatially in the PVA of each subject (Fig.7). In addition, the neural network associated with the PVA-related spontaneous activity included the visual association areas, the precuneus, the precentral/ postcentral gyrus, the middle frontal gyrus, the fusiform gyrus, the inferior/middle temporal gyrus, and the parahippocampal gyrus. After considering the functions of these regions, we speculated that the PVA-related spontaneous activity may be associated with memory-related mental imagery and/or visual memory consolidation processes. These findings confirm the presence of spontaneous activity in the PVA and related brain areas. This confirmation supports the perspective that brain is a system intrinsically operating on its own, and sensory information interacts with rather than determines the operation of the system.[24].

6.9. Modularity in the Genetic Disease-phenotype Network

Participants: Xinpeng JIANG, Bing LIU, Jiefeng JIANG, Huizhi ZHAO, Ming FAN, Jing ZHANG, Zhenjie FAN, Tianzi JIANG.

With the arrival of the post-genomics era, phenotype networks have become a powerful tool for studying gene function and exploring the candidate genes of disease. Similar disease phenotypes are engendered as a result of the modular nature of gene networks; thus we hypothesized that all human genetic disease phenotypes appear in similar modular styles. Network representations of phenotypes make it possible to explore this hypotheses. We investigated the modularity of a network of genetic disease phenotypes. We computationally extracted phenotype modules and found that the modularity is well correlated with a physiological classification of human diseases (Fig.8). We also found correlations between the modularity and functional genomics as well as with drug discovery. The method proposed in this paper reveals the modularity of a phenotype network by systemically analyzing human genetic diseases phenotypes[11].

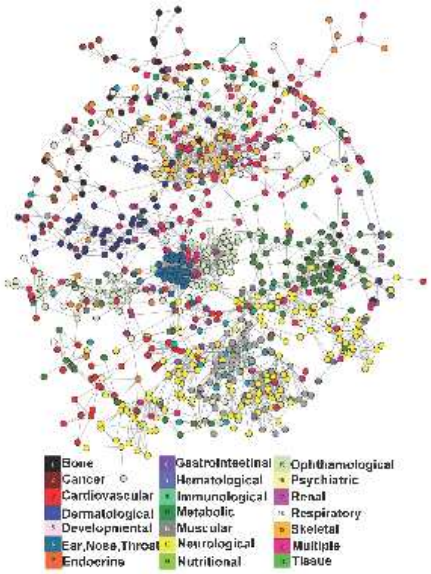

Figure 8. Modularity in the Genetic Disease-phenotype Network

6.10. Improving Image Quality of Diffuse Optical Tomography with a Projection-error-based Adaptive Regularization Method

Participants: Haijing NIU [Beijing Normal University], Ping GUO [Beijing Normal University], Lijun JI, Qing ZHAO, Tianzi JIANG.

Diffuse optical tomography (DOT) reconstructs the images of internal optical parameter distribution using noninvasive boundary measurements. The image reconstruction procedure is known to be an ill-posed problem. In order to solve such a problem, a regularization technique is needed to constrain the solution space. In this study, a projection-error-based adaptive regularization (PAR) technique is proposed to improve the reconstructed image quality. Simulations are performed using a diffusion approximation model and the simulated results demonstrate that the PAR technique can improve reconstruction precision of object more effectively. The method is demonstrated to have low sensitivity to noise at various noise levels. Moreover, with the PAR method, the detectability of an object located both at the center and near the peripheral regions has been increased largely [20].

7. Contracts and Grants with Industry

7.1. Collaborators

Modern imaging scanners from 1.5 to 3.0 Tesla are available in middle-sized and large cities in China, which has the largest population and thus the widest disease spectrum. A formal collaborative network has been established through this center with many hospitals throughout China based on various projects. For example, this center has established its collaboration with Xuanwu Hospital, Huaxi Hospital and China PLA General Hospital to investigate the imaging biomarker for Alzheimer's diseases, with Xiangya Hosptal to study PTSD, depression, and schizophrenia. In fact, the networks of excellence for computational medicine have been established. An incomplete list of our collaborators is as follows.

- Prof. Christian Barillot, CNRS/INRIA, France
- Prof. Qinghua Cui, Peking University, China
- Prof. Rachid Deriche, INRIA at Sophia-Antipolis, France
- Prof. Qiyong Gong and Dr. Ling Zou, West China Hospital, China
- Prof. Yong He, Beijing Normal University, China
- Prof. Tao Jiang, Tiantan Hosptial, China
- Prof. Chong Li, Zhejiang University, China
- Prof. Kuncheng Li and Chunshui Yu, Xuanwu Hospital, China
- Prof. Lingjiang Li, Xiangya Hospital, China
- Prof. Zhening Liu, Xiangya Hosital, China
- Prof. Xin Ma, Anding Hospital, China
- Prof. Max Viergever, Utrecht University, Netherland
- Prof. Dai Zhang, Peking University, China
- Prof. Xi Zhang, China PLA General Hospital, China
- Prof. Yunting Zhang and Dr. Quan Zhang, Tianjin Medical University, China
- Prof. Zhijun Zhang, Southeast University, China
- Prof. Yuemin Zhu, CNRS, France

8. Other Grants and Activities

8.1. Current Grants

- Brain Diseases Oriented Computational Theory and Algorithms for Multimodal Magnetic Resonance Imaging, the Key Project of National Science Foundation of China, 2008-2011.
- Early Diagnosis Systems Based on Brain Imaging for Mild Cognitive Impairment and Alzheimer's Disease, the Key Project of the External Cooperation Program of the Chinese Academy of Sciences, 2008-2011.
- Theory and Methodologies for Digital Context Understanding, National Key Basic Research Projects of China (973), the Ministry of Science and Technology of China, 2004-2009.
- Computational Theory and Methodologies for Brain Imaging and Their Applications to Brain Diseases, the National Distinguished Youth Foundations of China, National Science Foundation of China, 2005-2008.
- Investigation on Key Problems in Information Processing of Clinic Medicine, National Key Basic Research Projects of China (973), The Ministry of Science and Technology of China, 2003-2008.
- Study of Human Uncertain Decision-Making with functional Magnetic Resonance Imaging, National Science Foundation of China, 2007-2009.
- Computational Theory and Methodology of Diffusion Tensor Imaging, National Science Foundation of China, 2006-2008.
- Ontology and Context Related Medical Image Distributed Intelligent Access, Regional Program ICT-Asia, Research Innovation, 2006-2008.

8.2. Journal Editorial Boards

Dr. Tianzi Jiang is an associate editor or a member of editorial board of the following 9 internatioal journals and book series and one chinese journal:

- Associate Editor, IEEE Transactions on Medical Imaging, 2004-present.
- Associate Editor, IEEE Transactions on Autonomous Mental Development, 2008-present.
- Series Editor, Book Series on Computational Imaging and Vision, Springer Verlag, 2006-present.
- Member of Editorial Board, NeuroImage, Elsevier, 2006-present.
- Member of Editorial Board, Cognitive Neurodynamics, Springer Verlag, 2006-present.
- Member of Editorial Board, Genomics, Proteomics & Bioinformatics, Science Press (Beijing) and Elsevier, 2006-present.
- Member of Editorial Board, International Journal of Computer Mathematics, Taylor & Francis, 2000- present.
- Member of Editorial Board, the Open Neuroimaging Journal, Bentham Open, 2007- present.
- Member of Editorial Board, Chinese Journal of Medical Imaging Technology, 2003-present.

8.3. Participation in Scietific Conferences

- Tianzi Jiang, Disrupted Small-world Networks in Cognitive Disorders: Evidence from Rest-state fMRI, International Conference on Statistical Paradigms - Recent Advances And Reconciliations for Platinum Jubilee Celebrations of Indian Statistical Institute, ISI, January 1-4, 2008, Kolkata, India. (Invited report)
- Tianzi Jiang, Complex Brain Networks: From Anatomy to Functional, The 2nd Conference of Agent Theory and its Application, April 19-20, 2008, Nanjing, China. (Invited)
- Tianzi Jiang, Ming Song, Yong Liu, Kun Wang, Yuan Zhou, Lijuan Xu, Yonghui Li and Lei Lin, The 14th International Conference of Organization for Human Brain Mapping (OHBM'08), June 15-19, 2008, Melbourne, Australia.
- Tianzi Jiang, The 5th Symposium for Chinese Neuroscientists Worldwide, July 26-30, 2008, Changsha, China.
- Yuanchao Zhang, The 4th International Workshop on Medical Imaging and Augmented Reality, August 1-3, 2008, Tokyo, Japan.
- Tianzi Jiang, Yong Liu and Yuan Zhou, The 5th Annual meeting of the Chinese Society of Psycho-Neuroscience, August 2-5, 2008, Changchun, China.
- Tianzi Jiang, The 2nd QBI Brain Plasticity, September 9-12, 2008, Queensland Brain Institute, Australia.
- Tianzi Jiang, Disrupted Small-world Networks in Brain Disorders, 2008 International Symposium on Brain Functional Genomics, October 21, 2008, Shanghai, China. (Invited)
- Tianzi Jiang, Brain Networks: From Anatomy to Dynamics, The 10th Shanghai Roundtable "Biomedical Engineering in the 21th Century", November 16-19, 2008, Shanghai, China.
- Ming Song and Nianming Zuo, The 10th Shanghai Roundtable "Biomedical Engineering in the 21th Century", November16-19, 2008, Shanghai, China.
- Tianzi Jiang, 2008 European Information and Communications Technology Conference, November 25-27, 2008, Lyon, France.
- Tianzi Jiang, Visit INRIA-Paris, INRIA-Sophia-Antipolis, INSA-Lyon and Utrecht University, Radbound University, Eindhoven University of Technology, December 1-12, 2008.
- Tianzi Jiang, Cortical Thickness Based on MRI: A Promising Imaging Biomarker for Brain Disorders, CMRMF & OCSMRM Joint Meeting 2008 and ESMRMB Workshop, December 15, 2008, Shenzhen, China.

8.4. Organized Scietific Conferences

- Tianzi Jiang, Chair, International Symposium on Computational Medicine, November 7-8, 2008, Beijing, China (http://www.rccm.org.cn/iscm/iscm2008.htm).
- Tianzi Jiang, Program Committee Member, The 11th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 2008), September 6-10, 2008, New York, USA.
- Tianzi Jiang, Program Committee Member, The 14th International Conference of Organization for Human Brain Mapping (OHBM'08), June 15-19, 2008, Melbourne, Australia.
- Tianzi Jiang, Program Committee Member, International Workshop on Medical Imaging and Augmented Reality (MIAR'08), August 1-2, 2008, Tokyo, Japan.
- Tianzi Jiang, Program Committee Member, International Conference on Image and Signal Processing, July 1-3, 2008, Cherbourg-Octeville, Normandy, France.
- Tianzi Jiang, Program Committee Member, The 21th IEEE International Symposium on Computer-Based Medical Systems (CBMS 2008), June 17-19, 2008.

8.5. Teaching

Tianzi Jiang, Brain Network, Brain Circuits and Information Processing, National Graduate Summer School of Brain Function and Neuro Information, July 2-14, 2008, University of Electronic Science and Technology of China, Chengdu, China.

9. Dissemination

9.1. Student Activity

- All the students together travelled to Huludao City, Liaoning Province, June 1-5, 2008.
- Party for celebrating the graduation of Ming Song, Yong Liu and Feng Shi, June 20, 2008.
- Party for celebrating the Mid-Autumn Festival, September 10, 2008.

9.2. Student Awards

- Yong Liu, President's Scholarship of CAS, 2008.
- Ni Shu, Baogang Scholarship, 2008.
- Fuchun Lin, Outstanding Dissertation of CAS, 2008.
- Yong Liu, Outstanding Graduates of CAS, 2008.
- Ming Song, Outstanding Graduates of CASIA, 2008.
- Jian Cheng, Bourse Doctorales en Alternance (French Government Grant), 2008.
- Lei Lin, INRIA-CAS Fellowship, 2008.
- Lijuan Xu, Travel Award of OHBM , 2008.
- Yong Liu, Travel Award of OHBM , 2008.
- Yuan Zhou, Travel Award of OHBM , 2008.

9.3. New Members

- Yong Fan, Professor.
- Nianming Zuo, Assistant Professor.
- Ming Song, Assistant Professor.

- Yong Liu, Assistant Professor.
- Xing Min, PhD Candidate.
- Maohu Zhu, PhD Candidate.
- Hanbin Hu, PhD Candidate.
- Na Zhang, PhD Candidate.
- Haixia Zhao, Master Candidate.
- Ying Chen, Master Candidate.
- Yongfu Hao, Master Candidate.
- Nanfeng Jie, PhD Candidate.
- Jiajia Li, PhD Candidate.
- Hongming Li, PhD Candidate.
- Baogui Zhang, PhD Candidate.

10. Bibliography

Major publications by the team in recent years

[1] G. GONG, T. JIANG, C. ZHU, Y. ZANG, F. WANG, S. XIE, J. XIAO, X. GUO. *Asymmetry Analysis of Cingulum Based on Scale-Invariant Parameterization by Diffusion Tensor*, in "Human Brain Mapping", vol. 24, 2005, p. 92-98.

[2] T. JIANG, Y. HE, Y. ZANG, X. WENG. *Modulation of Functional Connectivity During the Rest State and the Task State*, in "Human Brain Mapping", vol. 22, 2004, p. 63-71.

[3] M. LIANG, Y. ZHOU, T. JIANG, Z. LIU, L. TIAN, H. LIU, Y. HAO. *Widespread Functional Dysconnectivity in Schizophrenia with Resting-state fMRI*, in "NeuroReport", vol. 17, 2006, p. 209-213.

[4] Y. LIU, M. LIANG, Y. ZHOU, Y. HE, Y. HAO, M. SONG, C. YU, H. LIU, Z. LIU, T. JIANG. *Disrupted Small-world Networks in Schizophrenia*, in "Brain", vol. 131, 2008, p. 945-961.

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[7] K. WANG, T. JIANG, C. YU, L. TIAN, J. LI, Y. LIU, Y. ZHOU, L. XU, M. SONG, K. LI. *Spontaneous Activity Associated with Primary Visual Cortex: a Resting State fMRI Study*, in "Cerebral Cortex", vol. 18, 2008, p. 697-704.

[8] K. WANG, M. LIANG, L. WANG, L. TIAN, X. ZHANG, K. LI, T. JIANG. *Altered Functional Connectivity in Early Alzheimer's Disease: a Resting-state fMRI Study*, in "Human Brain Mapping", vol. 28, 2007, p. 967-978.

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[10] C. ZHU, T. JIANG. *Multi-context Fuzzy Clustering for Separation of Brain Tissues in MR Images*, in "NeuroImage", vol. 18, 2003, p. 685-696.

Year Publications

Articles in International Peer-Reviewed Journal

[11] X. JIANG, B. LIU, J. JIANG, H. ZHAO, M. FAN, J. ZHANG, Z. FAN, T. JIANG. *Modularity in the Genetic Disease-phenotype Network*, in "FEBS Letters", vol. 582, 2008, p. 2549-2554.

[12] T. JIANG, Y. LIU, F. SHI, N. SHU, B. LIU, J. JIANG, Y. ZHOU. *Multimodal Magnetic Resonance Imaging for Brain Disorders: Advances and Perspectives*, in "Brain Imaging and Behavior", in press, 2008.

[13] J. JIANG, W. ZHU, F. SHI, Y. ZHANG, L. LIN, T. JIANG. *A Robust and Accurate Algorithm for Estimating the Complexity of the Cortical Surface*, in "Journal of Neuroscience Methods", vol. 172, 2008, p. 122-130.

[14] S. LI, F. PU, F. SHI, S. XIE, Y. WANG, T. JIANG. *Regional White Matter Decreases in Alzheimer's Disease Using Optimized Voxel-Based Morphometry*, in "Acta Radiologica", vol. 49, 2008, p. 84-90.

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[16] L. LIN, L. ZHU, F. YANG, T. JIANG. *A Novel Pixon-Representation for Image Segmentation Based on Markov Random Field*, in "Image and Vision Computing", vol. 26, 2008, p. 1507-1514.

[17] Y. LIU, M. LIANG, Y. ZHOU, Y. HE, Y. HAO, M. SONG, C. YU, H. LIU, Z. LIU, T. JIANG. *Disrupted Small-world Networks in Schizophrenia*, in "Brain", vol. 131, 2008, p. 945-961.

[18] Y. LIU, K. WANG, C. YU, Y. HE, Y. ZHOU, M. LIANG, L. WANG, T. JIANG. *Regional Homogeneity, Functional Connectivity and Imaging Markers of Alzheimer's Disease: A Review of Resting-state fMRI Studies*, in "Neuropsychologia", vol. 46, 2008, p. 1648-1656.

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