

# Shape Analysis of Human Brain with Cognitive Disorders

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**Abstract.** In this paper, we present some of our current studies on how human brain structures are influenced by cognitive disorders occurred from various neurological and psychiatric diseases based on magnetic resonance imaging (MRI). We first give a brief introduction about computational neuroanatomy, which is the basis of these studies. In Section 2, several novel methods on segmentations of brain tissue and anatomical substructures were presented. Section 3 presented some studies on brain image registration, which plays a core role in computational neuroanatomy. Shape analysis of substructures, cerebral cortical thickness and complexity was presented in Section 4. Finally, some prospects and future research directions in this field are also given.

## 1 Introduction

Computational neuroanatomy here aims at computationally demanding quantitative neuroanatomic analyses, and computational modeling of brain structure and spatial organization based on such quantitative data. It has played an essential role in the study of cognitive disorders, especially on relationships between anatomical abnormalities and cognitive disorders [1]. The basic research topics in this field include brain tissue segmentation of MR images, intra- and inter-modality image registration, automatic lesion detection and segmentation, brain structure segmentation, registration and shape analysis and so on.

In recent years, more and more studies show their interest in these directions and also achieve satisfying results [1][3]. In this paper, we will present some advances of our current studies on detection of the anatomical abnormalities of human brain with neurological and psychiatric diseases based on magnetic resonance imaging (MRI). First, several novel methods on segmentations of brain tissue and anatomical substructures, brain image registration, and computation of cerebral cortical thickness and complexity will be presented. Then, we will present some interesting findings on anatomical abnormalities when these methods were applied to human brain with various cognitive disorders, including Alzheimer's diseases, Schizophrenia, Attention Deficit Hyperactivity Disorder, early blind and deaf, compared with matched normal controls. Finally, some prospects and future research directions in this field are also given.

## 2 Segmentation of Brain Image

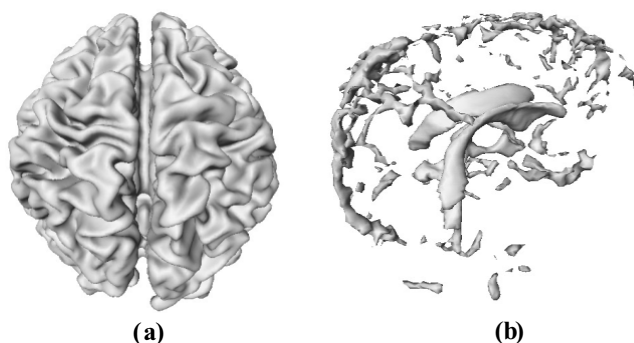
Image segmentation is a process of separating an image into several disjoint regions in which characteristics are similar such as intensity, color, texture, or other attributes. In the field of brain image analysis, we are mainly concerning with brain tissue segmentation and brain substructure segmentation, which are also the mainly preprocessing step in many medical research and clinical applications.

**Brain Tissue Segmentation:** In MR images, intensity inhomogeneity is a very common phenomenon which can change the absolute intensity for a given voxel in different locations. So it becomes a major obstacle to any automatic methods for MR image segmentation and makes it difficult to obtain accurate segmentation results. In order to address this issue, we proposed a novel method called Multi-Context Fuzzy Clustering (MCFC) based on a local image model for classifying 3D MR data into tissues of white matter, gray matter, and cerebral spinal fluid automatically [3]. Experimental results on both simulated volumetric MR data and real MR images showed that the MCFC outperforms the classic method of fuzzy c-means (FCM) as well as other segmentation methods that deal with intensity inhomogeneity.

Another related work is pixon-based adaptive scale method for image segmentation. Markov random fields (MRF)-based methods are of great importance in image segmentation, for their ability to model a prior belief about the continuity of image features such as region labels, textures, edges. However, the main disadvantage of MRF-based methods is that the objective function associated with most nontrivial MRF problems is extremely nonconvex, which makes the corresponding minimization problem very time consuming. We combined a pixon-based image model with a Markov random field (MRF) model under a Bayesian framework [4]. The anisotropic diffusion equation was successfully used to form the pixons in our new pixon scheme. Experimental results demonstrated that the proposed method performs fairly well and computational costs decrease dramatically compared with the pixel-based MRF algorithm.

**Brain Substructure Segmentation:** We also proposed another variational based segmentation algorithm. The originality of formulation was on the use of J-divergence (symmetrized Kullback-Leibler divergence) for the dissimilarity measure between local and global regions. The intensity of a local region was assumed to obey Gaussian distribution. Thus, two features mean and variance of the distribution of every voxel were used to ensure the robustness of the algorithm when the noise appeared. J-divergence was then employed to measure the distance between two distributions [5]. The proposed method was verified on synthetic and real medical images and experimental results indicated that it had the ability to segment brain substructure robustly.

Accurate segmentation of brain structures such as the brain ventricles is needed for some clinic applications. In recent years, the active-models-based segmentation methods have been extensively studied and widely employed in medical image segmentation and have achieved considerable success. However, the current techniques are going to be trapped in undesired minimum due to the image noise and pseudoedges. We proposed a parallel genetic algorithm-based active model method and applied it to segment the lateral ventricles from magnetic resonance brain images



**Fig. 1.** Brain cortex segmentation results. (a) Inner surface of cerebral cortex. (b) CSF surface

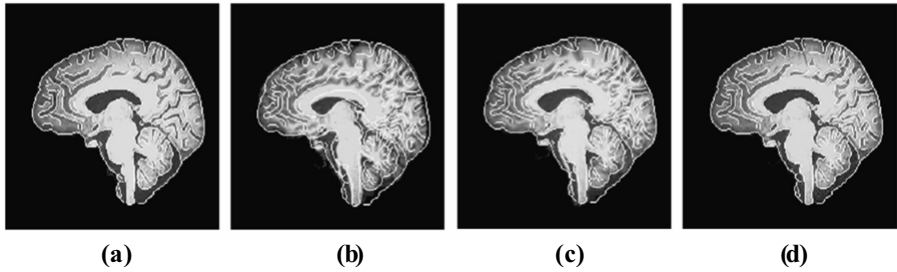
[6]. The proposed method was demonstrated successfully to overcome numerical instability and was capable of generating an accurate and robust anatomic descriptor for complex objects in the human brain as lateral ventricles.

### 3 Registration of Brain Image

Image registration plays major role in computational neuroanatomy. In terms of satisfying the technical requirements of robustness and accuracy with minimal user interaction, rigid registration has been applied to many applications including multimodality and inter-subject registration. However, due to the nonlinear morphometric variability between subjects. The requirement of both global and local registration accuracy asks for non-rigid registration. The method of non-rigid medical image registration usually include physics-based and geometry-based. We have made our effort on both of them.

**Physics-Based Method:** A non-rigid Medical Image Registration by Viscoelastic Model was presented in [7], by assuming the local shape variations were satisfied the property of Maxwell model of viscoelasticity, the deformable fields were constrained by the corresponding partial differential equations. Applications of the proposed method to synthetic images and inter-subject registration of brain anatomical structure images illustrate the high efficiency and accuracy.

**Geometry-Based Method:** We also proposed an efficient registration framework which has feature of multiresolution and multigrid [8]. In contrast to the existing registration algorithms, Free-Form Deformations based NURBS (Nonuniform Rational B Spline) are used to acquire nonrigid transformation. This can provide a competitive alternative to Free-Form Deformations based B spline on flexibility and accuracy. Subdivision of NURBS is extended to 3D and is used in hierarchical optimization to speed up the registration and avoid local minima. The performance of this method is numerically evaluated on simulated images and real images. Compared with the registration method using uniform Free-Form Deformations based B spline, this method can successfully register images with improved performance.



**Fig. 2.** Registration results on MRI images. Contours of the reference image (white line) were overlaid on the resulting images as a reference of registration accuracy. (a) Reference image, (b) result image using affine registration, (c) result image using FFD registration, (d) result image using NFFD registration.

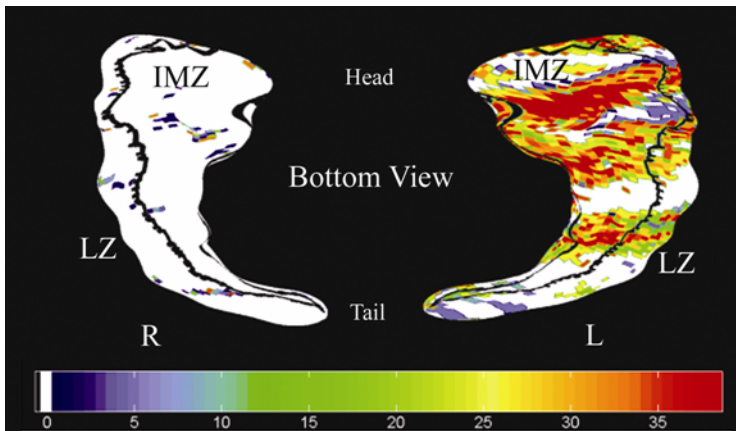
**Deformation Based Morphometry:** Deformation based morphometry (DBM) derived a voxel-wise estimation of regional tissue volume change from the deformation field required to warp subject to the template image. By using this technique, anatomic differences in boys with Attention-Deficit/Hyperactivity Disorder (ADHD) was characterized [9]. The statistical results reveal some pronounced volume alterations in the brains of ADHD, which confirm that there are widespread abnormalities in volume of boys suffering by ADHD.

## 4 Shape Analysis

Cognitive disorders can cause the variations of anatomical shape in human brain. Statistical Shape Analysis (SSA) is a powerful tool for noninvasive studies of pathophysiology and diagnosis of brain diseases. It is another key component of computational neuroanatomy. The population-based shape analysis not only reveals the difference between the healthy and diseased subjects, but also provides the dynamic variations of the patients' brain structures over time.

**Hippocampus Shape Analysis:** We proposed a new method which incorporated shape-based landmarks into parameterization of banana-like 3D brain structures to address this problem [10]. The triangulated surface of the object was firstly obtained and two landmarks were extracted from the mesh, i.e. the ends of the banana-like object. Then the surface was parameterized by creating a continuous and bijective mapping from the surface to a spherical surface based on a heat conduction model. The correspondence of shapes was achieved by mapping the two landmarks to the north and south poles of the sphere. The proposed method was applied in a Alzheimer's disease (AD) study [11]. The machine learning methods were used to characterize shape variations in AD based on these surface-based shape measures. Correct prediction rate were above 80% in bilateral hippocampi with leave-one-out cross validation.

**Cortical Morphometry Analysis:** We proposed a 3-phase variational segmentation model for extraction of inner and outer surfaces of cerebral cortex [6]. As the brain



**Fig. 3.** Visualization of surface shape variations of hippocampi in AD compared to healthy controls

tissue can be decomposed into white matter, grey matter and cerebrospinal fluid, any two tissues have boundaries. Thus competition should be introduced for any two regions. The proposed 3-phase model based on our J-divergence active contour model and designed specifically for three regions segmentation. It has been successfully applied to cerebral cortex reconstruction. Cortical thickness analysis has also been performed for finding abnormal pattern of brain structure between normal controls and early blind patients. The T-average was used as cortical thickness definition. After statistics analysis, the final results showed us that normal people had more thinner cortical thickness for part of occipital region. This may be caused by absent usage of this brain region during development of brain.

Besides cortical thickness, there is another widely used measurement of cortical morphometry. Cortical complexity, which is usually employed to describe the degree of cortical convolution or gyrification, is often assessed by using fractal dimension. We developed a voxel based method to compute information dimension of cortical pial surface and applied to subjects with attention-deficit/hyperactivity disorder. A left-greater-than-right prefrontal cortical convolution complexity pattern was found in both groups.

## 5 Conclusions and Future Directions

In this paper, we have presented some representative techniques to detect the anatomical abnormalities of human brain with neurological and psychiatric diseases. We have been applying various modern neuroimaging techniques to combat the neurological and psychiatric diseases, especially Alzheimer's Diseases and Attention Deficit Hyperactivity Disorder. Our long-term goal is to find the early markers for the neurological and psychiatric diseases based on not only neuroimages and but also genome datasets. It would be very interesting to identify the genetic basis of the anatomical and functional abnormalities of human brain with neurological and

psychiatric diseases. Anatomical and functional abnormalities of human brain with neurological and psychiatric disorders are very promising endophenotypes for these disorders. In fact, several publications have been available and a new field - imaging genomics, named by Hariri and Weinberger, has emerged [13]. It is at its infant stage and we expect a lot of important progress can be made in the future.

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