A SURVEY OF COMPUTER-ASSISTED METHODS FOR THE DIAGNOSIS OF MEMORY-RELATED DISORDERS

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Abstract

The segmentation of human brain and its parts is needed to analyze brain-related disorders. Hippocampus is a paired structure present on either side of the temporal lobe of a human brain. It is a curve like structure responsible for processing memory. Any abnormality in the size and volume of hippocampus leads to dementia-related disorders. Hippocampus is a bio-marker for Alzheimer's, one of the memory-related diseases referred to as AD. An analysis of this type of disorder needs segmented images of hippocampus from brain images. When the segmentation is manually done by the physicians, takes a lot of time since the volume of data sets is high. Hence, an automatic or semi-automatic system is needed to segment hippocampus from large data sets. This paper presents a complete survey of the existing techniques for automatic and semi-automatic segmentation of hippocampus.

Keywords: Human brain, Segmentation, Hippocampus, Alzheimer's disease.

1. Introduction

Various types of imaging techniques are used nowadays to take images of the human body. Magnetic Resonance Imaging (MRI) is one of the important imaging methods to obtain a detailed image of the human brain tissues. The function of hippocampus (Hc) in human brain is to form new memories and retrieves them when needed, and the study of Hc is needed to analyze diseases related with memory. The Hc is segmented manually by the clinical experts to study its size, volume etc. The techniques to segment human brain are divided into three categories such as i) Manual ii) Automatic and iii) Semi-automatic methods.

1.1 Manual Segmentation

The segmentation of Hc manually by the clinicians [1] is called the gold standard. This manually-segmented images are used as a reference to assess the performance of segmentation methods. MIDAS is a software package developed by Free borough [2] to segment Hc manually. By this tool, an expert finds boundaries of the region of interest using two orthogonal views. The combination of alveus, subiculum, hippocampus and dentate gyrus is defined as a region of interest. The cerebral-spinal-fluid (CSF) is excluded by applying a threshold value, which is 70% of mean brain intensity.

Achten et al. [3] proposed a manual ray-tracing tool to measure the volume of Hc manually. The dataset for this manual segmentation consisted of 11 normal patients and 12 patients who are affected with presumed complex partial seizures. Starting from left, the manual contour was taken and ended with right side of the hippocampus. But, the contours produced variability because of poor definition in the areas of superolateral borders. Pruessner et al. [4] developed a protocol for manual segmentation from the database of 40 healthy subjects. Boccardiet al. [5] proposed EADC harmonized protocol for manual segmentation. Special care was taken to determine caudal and rostral slices. A new method was developed by Niloofar Hashempour et al. [6] for manual segmentation of hippocampus and amygdala from neonate MRI. The neonate images have multiple contrasts when compared to adult brain MRI. The manual

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segmentation results are compared with automatic method-iBEAT toolbox, and inter-rater, intra-rater variabilities are measured. In this approach, a protocol is derived to segment hippocampus and amygdala from T2-W neonatal MRI. The data set consists of 31 healthy participants of age between 2 to 5 weeks. Inter-rater and intra-rater reliabilities were measured in 12 MR images which are randomly selected. The coefficients such as intra class correlation and dice similarity are measured for comparison. The method finally concluded that the clear procedures and protocols were to be developed for automatic segmentation.

The manual segmentation was done by marking the needed boundary directly on the raw image. The clinical people then picked up the intensity of a particular structure by pointing to the corresponding pixels. This method needed more human resources and also produced intra-rater and inter-rater variability. To address these problems, researchers tried to develop semi-automatic and automatic segmentation methods.

1.2 Semi-automatic segmentation

Semi-automatic segmentation techniques offered a good solution to the problems of manual segmentation methods, and a greater number of semi-automatic techniques were adopted. Most of the problems were solved in the field of neurological research. In terms of sub-cortical segmentation like hippocampus extraction, prior knowledge about the size and location of Hcwere taken as parameters to achieve segmentation. An AFDM-Adaptive Focus Deformable Model was developed by Shen et al. [7] which incorporated three kinds of information to extract the portion of Hc from MRI. The information dealt with the geometric structure and properties of Hc boundary, characterization of shape and statistical variation to derive prior knowledge and the boundary points of Hc which were manually derived. This information was collectively taken for initialization of seed point in an input image.

Features such as gray-level intensity and shape were used by Duchesne et al. [8] to develop a method for segmentation of Hc. Then a 3D deformation vector analysis was taken for further description of Hc. This method was tested with the data of 80 normal subjects, and its performance was compared with manually-segmented data and automatic segmentation method-ANIMAL, which is a non-linear registration. This method was developed with an application for analyzing shape deformation, and had a good processing time, which is six times faster than that of ANMAL. Another deformable model, which was based on knowledge-guided approach, was developed by Pitiot et al. [9]. The knowledge about textural and shape of a target structure was considered as a parameter. To get this parameter, implicit knowledge such as appearance, size, shape of Hc and explicit knowledge such as relative distance of Hc from other structures of human brain were considered. Kavitha et al. [10] presented a method using clustering technique. The K-means clustering approach was experimented with the data set obtained from Penn Hippocampus Atlas (PHA). The method was experimented using 39 MR images of two different data sets. As the boundary of Hc is vague and fuzzy, its boundary was improved using trimmed mean filter. The filtered image was then converted into a binary one using the threshold value calculated by K-means clustering. The value of K was chosen as four using trial and error method. The performance of the method was measured by calculating quantitative metrics jaccard and dice co-efficient,and these results were compared with ITK-SNAP, another semi-automaticmethod.

A semi-automatic technique called FAST SURF was developed by Fabian Bartel et al [11] by simulations. A sparse delineation derived from manually-segmented results was served as an input for simulation. The method incorporated mesh-processing techniques, which were inexpensive in terms of computation and it didn’t need prior knowledge about Hc such as atlas or a model. There was a small change when the cross sections of Hc moved slice by slice. Using this constraint, the shape of Hc was reconstructed by manual segmentation. The performance of the method was validated by three different types of data sets collected from NKI-AvL and ADNI. Indices such as Jaccard, Percentage Volume Differences (PVD) were also computed.

Semi-automatic techniques needed human intervention. In the deformable models, accuracy depended on the initialization of seed point. This was considered a drawback of semi-automatic segmentation techniques.

1.3 Automatic segmentation

The problems arise in semi-automatic segmentation techniques led to the development of fully automated methods. Automatic segmentation methods became more helpful when the size and availability of MRI databases was high. They did not suffer with inter- and intra-rater variabilities, and able to computea large amount of database without the intervention of humans.

An image registration method was used by Webb et al [12] to find atrophy in Hc region automatically. The differences in image intensities between controls and patients within a volume of interest (VOI) were analyzed and taken as a parameter. The changes in the volume of Hc found by using non-linear warping approach were proposed by Crum et al [13]. In this technique, three-dimensional voxel-level fluid registration was calculated. The result produced by this method wascompared with the datasets of fifteen controls and twelveare diagnosed with Alzheimer’s disease. For quantitative analysis, the results were compared with manual segmentations done by clinical experts.

A boundary-shift integral and registration techniques were used to create a hippocampal mask [14]. In this method, a group of hippocampi (controls and the patients diagnosed with AD) was taken, and by using this group, single subject template was generated. Then, affine (rotation, translation and scaling functions) brain registrations were done, and the templates of Hc region resliced. Finally, hippocampus was aligned more accurately using affine hippocampus-hippocampus registrations. An automatic method which segmented sub-cortical brain structures was developed by Khan et al. [15]. This method was initialized with a semi-automatic tool –FreeSurfer. A label propagation that combined Large Deformation Diffeomorphic Metric Mapping (LDDMM) and FreeSurferwere applied. FreeSurfer provided coarse-to-fine information in template-based segmentation.

Knowledge about anatomical landmarks [16] and probabilistic atlas of hippocampus were used to develop an automatic method to segment Hc from MRI. A tool SPM5 (Statistical Parametric Mapping) was used to register the probabilistic atlases which are formed from 16 healthy subjects. The initial object and bounding box were initialized automatically using probabilistic information. This information wasmodeled from high and low likelihood zones. The zones are derived by iso-probability regions that consisted of pixels belonging to Hc. The method was experimented with the dataset of healthy controls and the patients diagnosed with hippocampal sclerosis.

A multi-atlas segmentation framework with some modifications was proposed by Lotjonen et al. [17]. The multi-atlas framework consisted of three steps. In step 1, both the data and atlas were non-rigidly registered to a template. In the template space, the most similar atlases were calculated by normalized mutual information. In step 2, non-rigid transformation was done between selected atlas and unseen data. In step 3, the tissue was classified by standard Expectation Maximization (EM) framework. The EM in the proposed method allowed statistical modeling of tissue intensities and priori spatial information. An appearance-based modeling scheme was developed by Shiyan Hu et al. [18] for the segmentation of Hc automatically from MRI of human brain. In this method, multi-contrast images such as

T1W, T2W and PDW MRI were combined to improve the performance of segmentation. The alignments such as linear alignment of volume of interest (VOI), linear alignment of whole brain and non-linear alignment of local VOI were compared. For optimization, the difference in intensity values of synthesized image and test image was taken as an objective function.

Costafreda et al. [19] proposed an automatic method by analyzing the shape of hippocampus. This method was developed to diagnose dementia in mild cognitive impairment (MCI). 3D shape morphology of hippocampus was extracted from MR scans by analysis and mapping. The conversion of MCI into AD was predicted using machine learning classification. An auto context model

(ACM) based on atlas approach was developed by Minjeong Kim et al. [20]. This method segmented hippocampus automatically from MRI scans of 7.0 Tesla. The sequence of location adaptive classifier was constructed iteratively in each atlas by ACM. The classification is done by the integration of local context features and image appearance. The advanced features of texture were obtained from texture information and combined into ACM in the training stage. The segmentation was done by the fusion of labeling from all the atlases, and each of the atlases was obtained by ACM based classifiers.

The atlas-based method was combined with graph cuts algorithm by Kichang Kwak et al [21] to develop an automatic segmentation technique. The region of hippocampus was used in graph cuts algorithm to derive priori information. The templates of hippocampus were available in International Consortium for Brain Mapping (ICBM). By using the templates, the physician manually segmented the region of hippocampus and this region was used as an atlas of Hc. The morphological operations were also used to remove imperfections in the segmentation results. The method was applied to 3D T1W MRI.

Ting Guo et al. [22] developed a protocol to validate an automatic segmentation of hippocampus from preterm born neonates. The protocol developed was based on MAGeT-Brain (Multiple Automatically Generated Templates). It consisted of three steps. In step 1, the boundary of hippocampus was estimated initially using 25 slices in coronal view. In step 2, the segmentations which had been completed in coronal slices were verified with sagittal view, and voxels labeled incorrectly were corrected. In step 3, a 3D surface was used to represent the segmented hippocampus. To validate the performance of the method, the experimentation was done with 22 early-in-life and 22 term images. The volumetric and spatial overlap was measured using Dice co-efficient.

An automatic framework was developed by Manhua Liu et al. [23] to classify and segment hippocampus in AD. The method was based on a multi-model deep learning approach using convolutional neural network (CNN). Initially, a CNN model was generated for segmentation and classification. After that, a 3D CNN was constructed to learn the features of a hippocampus. Finally, the generated features were incorporated for disease classification. The method was evaluated with T1W structural MR images collected from ADNI database. The database consisted of 97 AD, 233 mild cognitive impairment and 119 normal subjects. The method produced the coefficient of 87% of hippocampal segmentation for Dice index.

Every method has some drawbacks so that, a method that produces good results for a particular dataset may not give better results for another type of datasets. Table 1gives a summary of segmentation methods that extract hippocampus from MRI of human brain scans.

Table 1. Summary of Segmentation methods

S.No	Segmentation techniques	Reference	Brain Structures	MRI type
1	Single-Atlas based	Kwak et al.	Hippocampus	T1
2	Multiple-Atlas based	Collins et al.	Hippocampus and Amygdala	T1
3	Active appearance models	Hu et al.	Hippocampus and Amygdala	T1 and T2
4	Geometric deformable models	Shen et al.	Hippocampus	T1
5	Machine learning - ANN	Hult et al.	Hippocampus	T1 and T2
6	Machine learning - SVM	Morra et al.	Hippocampus	T1

Conclusion

The survey of various techniques shows that all segmentation methods possess merits and demerits. All types of segmentation such as manual, semi-automatic and automatic methods and their contributions are presented. Automatic methods such as atlas-based and neural network-based have been discussed briefly. The short-comings and limitations in these methods are taken into consideration.

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