A Semi-Automatic Atlas-Based Method for Segmentation of the Hippocampus from the mid slices of brain MRI

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ABSTRACT

In this paper, we present a semi-automated tool which can segment the hippocampus from the mid slices in coronal orientation of the T1 weighted brain MRI. This is an atlas based method which reaches the hippocampus from the middle point of the brain. This method is a tool which needs no human intervention during processing. If the middle hippocampus slice is provided as an input to this tool it segments the left and right hippocampus separately.

Key words: Hippocampus, amygdale, Alzheimer disease, MRI, segmentation.

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INTRODUCTION

Alzheimer’s disease (AD), the most common type of dementia, is associated with the pathological accumulation of amyloid plaques and neurofibrillary tangles in the brain. Using MRI at millimeter resolution, subtle hippocampal changes may be resolved. However, isolating the hippocampus in a large number of MRI scans is time consuming, and most studies still rely on manual tracing guided by expert knowledge of the location and shape of each region of interest (ROI). Some automated methods have been proposed for hippocampal segmentation [1, 2, 3, 4].

In [1], multiple-atlas propagation and segmentation (MAPS) has been introduced to library-based segmentation technique. This technique uses non-linear registration of the best-matched templates from manually segmented library to generate multiple segmentations and combines them using the simultaneous truth and performance level estimation (STAPLE) algorithm. Change in volume over 12 months (MAPS-HBSI) was measured by applying the boundary shift integral using MAPS regions. Methods were developed and validated against manual measures using subsets from Alzheimer's Disease Neuroimaging Initiative (ADNI). In [2], a fully automatic method using probabilistic and anatomical priors for hippocampus segmentation has been proposed. Probabilistic information is derived from 16 young controls and anatomical knowledge is modeled with automatically detected landmarks. The results were previously evaluated by comparison with manual segmentation on data from the 16 young healthy controls, with a leave-one-out strategy, and eight patients with AD. In [3], a segmentation method based on the minimization of an energy functional with intensity and prior terms, which are derived from manually labelled training images was proposed. The intensity energy is based on a statistical intensity model that is learned from the training images. The prior energy
consists of a spatial and regularity term. The spatial prior is obtained from a probabilistic atlas created by registering the training images to the unlabelled target image, and deforming and averaging the training labels. The regularity prior energy encourages smooth segmentations. The resulting energy functional is globally minimized using graph cuts.

In [4], an assessment for the performance of standard image registration techniques for automated MRI-based segmentation of the hippocampus in elderly subjects with Alzheimer’s Disease (AD) and mild cognitive impairment (MCI) was presented. In this method, structural MR images of 54 age- and gender-matched healthy elderly individuals, subjects with probable AD, and subjects with MCI were collected at the University of Pittsburgh Alzheimer’s Disease Research Center. Hippocampi in subject images were automatically segmented by using AIR, SPM, FLIRT, and the fully-deformable method of Chen to align the images to the Harvard atlas, MNI atlas, and randomly-selected, manually-labeled subject images. Mixed-effects statistical models analyzed the effects of side of the brain, disease state, registration method, choice of atlas, and manual tracing protocol on the agreement between automated segmentations and expert manual segmentations. In [5-20], the various segmentation methods and the hippocampus features were discussed.

In this paper we present an automated tool to segment the hippocampus from the MRI head scans in coronal orientation. Our method segments the hippocampus more accurately compared with the existing methods. This is a hybrid method which is partly atlas based for reaching the hippocampus and partly intensity based for detecting the correct boundary of the hippocampus. The remaining part of the paper is organized as follows. In section 2, we present the methods and the materials. In section 3, the results and discussion are given. Finally in section 4, the conclusion is given.

MATERIALS AND METHODS

Materials used

The image data set for this work has been collected from NITRC. The slices are T2 weighted and are of 3mm thickness.

Methods used

The proposed method can be applied for the MRI of head scans of any size mid slices(10-15) in the coronal view. The flowchart of the proposed method is shown in Fig.1.

The proposed method is meant for segmenting only the hippocampus and so the input slices should be the MRI of head scans containing the hippocampus. This method automatically detects whether the input slices are mid slices and suitable for hippocampus segmentation by comparing the input slice with that of the mid slices containing the hippocampus. The slice is taken for segmentation if there is a match with any one of the existing. If the slice is a valid input containing the hippocampus then it is taken to the second step of segmentation which is a 3-phase enhancement. The 3-phase enhancement is needed for the following reason. The hippocampus is a critical structure present in the brain and its boundaries are not easily recognizable with the human eye. To make it
visually prominent as well as to make the boundaries distinguishable from the neighboring areas so as to make the segmentation process comparatively easier the following techniques are applied to enhance the original image.

In the first phase the median filter with the [2,3] neighborhood matrix is applied. Median filtering is a nonlinear operation often used in image processing to reduce "salt and pepper" noise. A median filter is more effective than convolution when the goal is to simultaneously reduce noise and preserve edges. Each output pixel contains the median value in the m-by-n neighborhood around the corresponding pixel in the input image.

The next step is to make the hippocampus prominent by using bottom hat filtering. For this, a flat, disk-shaped structuring element (SE) is created, with the radius r. r must be a nonnegative integer. In our method the radius is 20. The disk-shaped structuring element is approximated by a sequence of N periodic-line structuring elements. When N equals 0, no approximation is used, and the structuring element members consist of all pixels whose centers are no greater than r away from the origin. If k is replaced by the real number πr/n, then kα can be found from equation (3). Equation (1) produces a square when n=2, hexagon when n=3 and octagon when n=4. In Proposed method the value of N is 4. Radial decomposition of the image is done using a structuring element SE.

The radial decomposition of a disc D_r of radius r is replaced by a cascade Nε {2,3,...,∞} line structuring elements as given below(1).

\[ D_r \approx L_α_1 k_α_1 \Theta L_α_2 k_α_2 \Theta \ldots \Theta L_α_N k_α_N \]  

where kα is the length of the linear structuring element , α is the orientation .

\[ α_i = \frac{i \pi}{n}, n \varepsilon \{2,3, \ldots, \infty\} \]  

\[ kα = \text{round}(k*0.5*\max(|\cos α|,|\sin α|)+0.5)*2+1. \]  

The final phase makes the edges of hippocampus distinguishable than the neighborhood areas. This is done by top-hat filtering and bottom-hat filtering, which can be used together to enhance contrast in an image. Add the original image to the top-hat filtered image, and then subtract the bottom-hat filtered image.

The third step is the elimination of the non-ROI. To make the segmentation process further easier, some of the unwanted brain portions(non-ROI) which disturb the hippocampus segmentation process are removed by Otsu’s thresholding method which works as follows. In this method we exhaustively search for the threshold that minimizes the intra-class variance, defined as a weighted sum of variances of the two classes:

\[ \sigma_w^2(t) = \omega_1(t)\sigma_1^2(t) + \omega_2(t)\sigma_2^2(t) \]  

where \( \omega_i \) are the probabilities of the two classes separated by a threshold t and \( \sigma_i^2 \) variances of these classes. Otsu shows that minimizing the intra-class variance is the same as maximizing inter-class variance:

\[ \sigma_b^2(t) = \sigma^2 - \sigma_w^2(t) = \omega_1(t)\omega_2(t) [\mu_1(t) - \mu_2(t)]^2 \]  

(5)
Start

Input the slice

Hippocampus present?

3-phase Enhancement (prominent hippocampus)

Non ROI elimination

Right block extraction

Binary image conversion

Edge detection

labeling

Detect hippocampus (right)

segmented hippocampus (right)

Extract ROI (left block)

Binary image conversion

Edge detection

labeling

Detect hippocampus (left)

segmented hippocampus

End of slices

Stop

No

Yes

Fig 1: Flowchart of the proposed method
where $\omega_i$ are the class probabilities and $\mu_i$ are the class means. The equation (3) can be iterated to get maximum $\sigma^2_h(t)$. Desired threshold $T$ corresponds to the maximum $\sigma^2_h(t)$.

The original image is converted into binary using the threshold value obtained from the above process. The parts which are black as a result of this operation are clearly analysed and they are the non-ROI region. This region is removed from the enhanced image by comparing the binary image with the enhanced image. The resultant image is an enhanced image with prominent hippocampus without some non-ROI.

The next step is the extraction of region of interest (ROI). Our ROI is not a single region, since the hippocampus appears as two separate components on the left and right sides of the brain MRI near the ears, in the coronal view. So the left block (containing the hippocampus on left side) and the right block (containing the hippocampus on the right side) are extracted and they are processed separately as follows.

The proposed method first segments the right hippocampus. The right block is retrieved as follows. The hippocampus is present vertically in the middle separated by a minimal distance horizontally from the center point of the brain. So, first the method locates the center point of the slice independent of the size of the slice. A block which completely encloses the hippocampus on the right side is the right block. The boundaries for this block are determined by comparing all the slices in the coronal orientation containing the hippocampus. This right block is extracted by traveling from the midpoint of the block towards all the sides until the boundaries are reached.

The next step is to convert the image into its binary form using the block mean thresholding. If $f(x,y)$ denotes the intensity of pixel at $(x,y)$, in a block of $m \times n$ pixels, then the threshold value $T$ of the block can be calculated as:

$$T = \frac{\sum_{x=1}^{m} \sum_{y=1}^{n} f(x,y)}{m \times n}$$

(6)

The binary image $G$ is obtained as

$$G(x, y) = \begin{cases} 0, & \text{if } f(x, y) < T \\ 1, & \text{otherwise} \end{cases}$$

(7)

The resultant binary image is then used for edge detection. The proposed method uses the Canny edge detection method. The Canny method makes use of two thresholds to detect the gradient: a high threshold for low edge sensitivity and a low threshold for high edge sensitivity. Edge starts with the low sensitivity result and then grows it to include connected edge pixels from the high sensitivity result. This helps to fill in the gaps in the detected edges. The resultant image is then labeled in order to extract the ROI. We follow the labeling procedure given in Milan Sonkar[6]. This labeling process results in a matrix $L$, of the same size as the black and white image, containing labels for the connected objects in the binary image. From the labeled connected component image the label for the hippocampus is detected by trial and error method and retrieved using the identified label. Since the middle portion of the hippocampus contains a dark tissue, the intensity is dark and so a hole found in the middle and the edge is not a closed one. In order to construct a complete mask for the hippocampus, the hole in the identified component is filled. A hole is a set of background pixels that cannot be reached by filling in the background from the edge of the image. As a final step the hippocampus in the right block is segmented using the mask. The resultant images of the above processes are shown in fig 1.

The proposed method next segments the left hippocampus. For this operation the input image is the 3-phase enhanced image without non-ROI elimination. The left block is
retrieved as follows. The hippocampus is present vertically in the middle separated by a minimal distance horizontally from the center point of the brain. So, first the method locates the center point of the slice independent of the size of the slice. A block which completely encloses the hippocampus on the left side is the left block. The boundaries for this block are determined by comparing all the slices in the coronal orientation containing the hippocampus. This left block is extracted by traveling from the midpoint of the block towards all the sides until the boundaries are reached.

The next step is to convert this image into binary form. This is done with the fixed threshold value which is found by trial and error method. In fixed (or global) thresholding, the threshold value is held constant throughout the image, determining a single threshold value by treating each pixel independently of its neighbourhood. Fixed thresholding is of the form (7).

The resultant image is of the binary form. As a next step labeling is applied similar to the right block. The label for the left hippocampus is identified by trial and error method. The hippocampus mask is retrieved by using the corresponding label. Finally the left hippocampus is segmented using the mask. The results for the above process for the sample slice 14 are shown in Fig.2.

Fig 2: Manual Vs Proposed method Segmented Results for Slice 14.
RESULTS AND DISCUSSION

Performance analysis

We carried out experiments using our method at the stack of 20 slices obtained from the data base in NITRC[b]. This set contains hand segmented gold standard. For quantitative analysis we computed the false positive rate (FPR), false negative rate (FNR), sensitivity (S), specificity (Sp), Jaccard coefficient (J) and Dice coefficient (D) which are calculated as follows.

The Jaccard coefficient (Jaccard, 1912) is given by:

\[ J (A, B) = \frac{A \cap B}{A \cup B} \]  

(8)

The Dice coefficient (D) (Zijdenbos et al., 1994) is given by

\[ D (A, B) = \frac{2|A \cap B|}{|A| + |B|} \]  

(9)

where A and B are two data sets. The value J as well as D varies from 0 for complete disagreement to 1 for complete agreement, between A and B. The coefficients J and D are related and are given by (Shattuck et al., 2001):

\[ D = \frac{2J}{J + 1} \]  

(10)

The quantitative evaluation based on sensitivity (S), specificity (Sp) and predictive accuracy (PA), as given in equations (10), (11) and (12), are performed between the region of interest (ROI) hand drawn by the experts and the respective portions produced by the proposed methods. These parameters are used to measure the performance of an algorithm against the manual extraction. The sensitivity (S) is the percentage of ROI voxels recognized by an algorithm and specificity (Sp) is the percentage of non-ROI voxels recognized by an algorithm using the True Positive (TP), False Positive (FP), True Negative (TN) and False Negative (FN) values extracted by an algorithm. Here ROI is the left or right hippocampus.

The predictive accuracy (PA) is the percentage of both ROI and non-ROI regions recognized by the proposed methods. TP and FP are the total number of pixels correctly and incorrectly classified as ROI by the automated algorithm. TN and FN are defined as the total pixels correctly and incorrectly classified as non-ROI tissue by an automated algorithm.

\[ S = \frac{TP}{TP+FN} \]  

(11)

\[ Sp = \frac{TN}{TN+FP} \]  

(12)

\[ PA = 100 \times \frac{TP+TN}{TP+TN+FP+FN} \]  

(13)
Finally, false positive rate (FPR) and false negative rate (FNR) are used to measure the misclassification done by an algorithm. FPR is the number of voxels incorrectly classified as ROI by the automated algorithm divided by manually segmented ROI and is given by:

$$FPR = \frac{FP}{TP + FN}$$  \hspace{1cm} (14)

FNR is the number of voxels incorrectly classified as non-ROI by the automated algorithm divided by manually segmented ROI and is given by:

$$FNR = \frac{FN}{TP + FN}$$  \hspace{1cm} (15)

The FPR represents the degree of under segmentation and the FNR the degree of over segmentation.

The segmented image by the proposed algorithm is compared with the manual segmented image using various metrics discussed above and the results are presented in the following table.

Table 1. Performance analysis

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Slice</th>
<th>Metric</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Jaccard</td>
</tr>
<tr>
<td>1</td>
<td>tse_native.nii-0014(RIGHT)</td>
<td>0.6577</td>
</tr>
<tr>
<td>2</td>
<td>tse_native.nii-0014(LEFT)</td>
<td>0.7034</td>
</tr>
<tr>
<td>3</td>
<td>tse_native.nii-0015(RIGHT)</td>
<td>0.6907</td>
</tr>
<tr>
<td>4</td>
<td>tse_native.nii-0015(LEFT)</td>
<td>0.5102</td>
</tr>
</tbody>
</table>

The above said approach, a hybrid method for automatic segmentation of the hippocampus has its own merits and demerits. The performance analysis has revealed that it is comparatively better than the manual segmentation, which is a time consuming process and it needs human intervention. Our method comparatively requires only the input set provided manually and no further human intervention is needed. The predictive accuracy in shape compared to the manual segmentation is 99.97 at an average and it can be easily understood from the shown result. Further work is going on to implement the same on the real data set for all slices for a single patient which is obtained from the clinical laboratory containing the images of both the normal and diseased persons and available at NITRC.
CONCLUSION

In this paper we have proposed a semi-automatic, atlas based technique for segmenting the hippocampus from the NITRC. However, this method requires the human intervention to input only the selected mid slices for segmentation process. Further work is in progress to isolate the slices containing the hippocampus from the entire volume and extract the hippocampus.

REFERENCES


Authors

Somasundaram .K was born in the year 1953. He received the M.Sc degree in Physics from University of Madras, Chennai, India in 1976, the Post Graduate Diploma in Computer Methods from Madurai Kamaraj University, Madurai, India in 1989 and the Ph.D degree in theoretical Physics from Indian Institute of Science, Bangalore, India in 1984. He is presently the Professor and Head of the Department of Computer Science and Applications, and Head, Computer Centre at Gandhigram Rural Institute, Gandhigram, India. From 1976 to 1989, he was a Professor with the Department of Physics at the same Institute. He was previously a Researcher at an International Centre for Theoretical Physics, Trieste, Italy and a Development Fellow of Commonwealth Universities at the school of Multimedia, Edith Cowan University, Australia. His research interests are in image processing, image compression and medical imaging. He is a Life member of Indian Society for Technical Education and Telemedicine Society of India. He is also an annual member in ACM, USA and IEEE Computer Society, USA.

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