HIPPOCAMPUS SEGMENTATION TECHNIQUES: A SURVEY

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Abstract: The segmentation of the hippocampus in Magnetic Resonance Imaging (MRI) has been an important procedure to diagnose and monitor several clinical situations. The precise delineation of the borders of this brain structure makes it possible to obtain a measure of the volume and estimate its shape, which can be used to diagnose some diseases, such as Alzheimer’s disease, schizophrenia and epilepsy. As the manual segmentation procedure in three-dimensional images is highly time consuming and the reproducibility is low, automated methods introduce substantial gains. Image segmentation is essential in numerous medicinal imaging applications. We are presenting some survey and review of the current technologies and approaches of semi-automated and automated methods for the segmentation of medical images. Some essential issues in restorative picture division have been talked about in this paper. Audits related with therapeutic picture division and issue distinguishing proof about those papers has been secured.


I. INTRODUCTION

Hippocampal volumetry is a marker sensitive to disease state and progression in Alzheimer’s disease (AD). The proposal for revised diagnostic criteria [1] posits that, even in the preclinical stages of the disease, the presence of hippocampal atrophy on magnetic resonance imaging (MR) is a marker suggestive of AD, the others being temporo-parietal hypometabolism on FDG PET, abnormal CSF tau and Abeta42 proteins, cerebral amyloidosis on molecular PET imaging. Currently, hippocampal volumetry is included as a secondary outcome measure in several clinical trials of disease modifying drugs to support the claim of disease modification [2]. Manual outlining on MR images by trained raters is presently the most accurate, validated and used procedure to measure hippocampal volumes [3–6], and the gold standard for the validation of automated segmentation algorithms [7–12]. However, a large number of protocols for the manual segmentation of the hippocampus is available and adopted in different fields of neuroscience research, including those investigating a variety of psychiatric and neurodegenerative conditions [13, 14]. These segmentation protocols differ in their definition of anatomical boundaries and tracing procedures, thus originating hippocampal volume estimates that cannot be straightforwardly compared. Indeed, the mean volume for a normal hippocampus can range from 2 to 5.3 cm\(^3\) [14] across laboratories worldwide. Even if individual differences in head size are taken into account, this range is far too broad to accept hippocampal volumetry as a valid marker for any neurological condition. Although these differences are in part caused by heterogeneities in image acquisition and preprocessing, heterogeneities in the landmark definitions are major contributors. Heterogeneity was found in the definition of the most rostral and most caudal slices, in the criteria for inclusion or exclusion of hippocampal white matter (alveus and fimbria), in the definition of boundary lines with adjacent anatomical structures [13, 14]. This heterogeneity prevents a direct comparison of the
outcome of different studies, and slows down the transfer of the marker from the research laboratory to the clinical setting. Standard operational procedures (SOPs) are clearly required for manual hippocampal volumetry to be transferred to routine diagnostic settings and gain status as a surrogate outcome in clinical trials for disease modifying drugs. SOPs will promote the large use of hippocampal atrophy measurements for the early diagnosis of AD and allow the comparison of the effect of different drugs in clinical trials. Moreover, the automated approaches need to be validated using a gold standard, for a given clinical population. SOPs may represent the gold standard for the many automated algorithms aiming to extract hippocampal volume with minimal or no human input that are presently under development [15, 16]. The aim of this study is to survey a selection of the most popular protocols for hippocampal segmentation used in AD research, in order to extract commonalities and differences. Importantly, we sought explicit input from protocol authors to check for proper understanding of their work. This survey is the first step of a larger project aiming to develop an internationally harmonized protocol for hippocampal segmentation.

A. Manual segmentation

Manual division alludes to the procedure whereby a specialist transcriber portions and marks a discourse document by hand, alluding just to the spectrogram and additionally waveform. The manual method is believed to be more accurate. Also, the use of a human transcriber ensures that the segment boundaries and labels (at least at the narrow phonetic level) are perceptually valid. However, there is a requirement for express division criteria to guarantee both between and intra-transcriber consistency, together with (in a perfect world) some type of checking system. Sets of guidelines for manual segmentation have been developed by various projects. One such is Hieronymus et al. (1990), which uses the four levels of underlying phonemic, broad phonetic, narrow phonetic and acoustic. It also retains the same base phonemic symbol even at the acoustic level, to facilitate the automatic determination of boundaries at the phonetic level once the boundaries at the acoustic level have been determined. One should not expect more than 90% agreement between experts.

B. Thresholding segmentation

Threshold-based method is a simple and effective segmentation method by comparing their intensities with one or more intensity thresholds. At present, threshold-based methods are classified into global and local thresholding. If an image contains objects with homogeneous intensity or the contrast between the objects and the background is high, global thresholding is the best choice to segment the objects and the backgrounds. When the contrast of an image is low, threshold selection will become difficult. Local thresholding can be determined by estimating a threshold value for the different regions from the intensity histogram. The threshold values of local thresholding are generally estimated by using the local statistical properties such as the mean intensity value in T1w MRI, by the prior knowledge and by calculating partial volumes of each region to determine the threshold for the segmentation of each component [21]. In addition, the Gaussian distribution was applied to determine the thresholds in normal brain MRI image [22] Because of the uncommon structure of mind tumor, worldwide and neighborhood thressholdings are chiefly used to decide the inexact area of cerebrum tumor in the mind. In most cases, thresholding is used as the first step in the segmentation process of brain tumor.

C. Watershed segmentation

The Watershed Transform is an extraordinary strategy for portioning computerized pictures that uses a kind of area developing technique in light of a picture angle.
The concept of Watershed Transform is based on visualizing an image in three dimensions: two spatial coordinates versus gray levels. In such a "topographic" elucidation, we consider three sorts of focuses:

A. Points belonging to a regional minimum. B. Points at which a drop of water, if placed at the location of any of those points, would fall with certainty to a single minimum. C. Points at which water would be equally likely to fall to more than one such minimum. For a particular regional minimum, the set of points satisfying condition (B) is called the catchment basin or watershed of that minimum.

The focuses fulfilling condition (C) shape peak lines on the topographic surface and are named isolate lines or watershed lines.

The principal objective of segmentation algorithms based on these concepts is to find the watershed lines.

**Advantages of Watershed Transform**

The Watershed Transform effectively combines elements from both the discontinuity and similarity based methods. Since its unique improvement with dark scale pictures, the Watershed Transform has been reached out to a computationally proficient frame (utilizing FIFO lines) and connected to shading pictures.

The main advantages of the Watershed method over other previously developed segmentation methods are:

A. The resulting boundaries form closed and connected regions. Conventional edge based strategies frequently shape separated limits that need present preparing on create shut areas.

B. The boundaries of the resulting regions always correspond to contours which appear in the image as obvious contours of objects. This is in contrast to split and merge methods where the first splitting is often a simple regular sectioning of the image leading sometimes too unstable results.

C. The union of all the regions forms the entire image region.

**D. Snake model based segmentation**

The snake is an energy minimizing parametric contour deforms over a series of time steps or iteration. Consequently each element $x$ along the contour depends on two parameters as in (1), which is $c$ curve (space) parameter and commonly varies between 0 and 1, is $t$ iteration (time) parameter.

$$x = x(c, t) \quad (1)$$

The total energy of the model is defined as sum of the energy for the individual snake elements:

$$E_{\text{snake}} = \int_0^1 E_{\text{element}}(x(c))dc \quad (2)$$

The integral notation used in (2) implies an open-ended snake; but joining the first and last elements makes the snake into a closed loop as shown in Fig. 1. Over a series of time steps the snake moves into alignment with the nearest edge. The contour is determined by three forces or constrains; internal, external, and image. Internal constrains give the model elasticity and rigidity, external constraints come from initialization procedures. Image energy is pushing the model towards the edges. We can rewrite the (2) in terms of three basic energy functions:

$$E_{\text{snake}} = \int_0^1 E_{\text{internal}}(x) dc + \int_0^1 E_{\text{external}}(x) dc + \int_0^1 E_{\text{image}}(x) dc \quad (3)$$
i. Internal energy

The below equations defined the internal energy of a snake model. This energy contains two order terms; first-order term and second-order terms controlled by $\alpha(c)$ and $\beta(c)$ respectively.

$$E_{\text{internal}} = E_{\text{elasticity}} + E_{\text{rigidity}}$$

$$E_{\text{elasticity}} = \alpha(c) \| x_c(c) \|^2$$

$$E_{\text{rigidity}} = \beta(s) \| x_s(c) \|^2 \quad (4)$$

The first-order term makes the snake act like a rubber band representing elasticity; the second-order term makes it resist bending by producing rigidity in [9] and [10]. If the other terms were not given the contour it will keep shrinking to a single spot. Changing the weights $\alpha(c)$ and $\beta(c)$ controls the relative importance of the elasticity and rigidity terms. If we set $\beta(s)$ to zero meaning that the second order is continuous will the model to have a corner.

ii. External energy

The external energy of a snake model discussed by Xu and Prince in [11], it is responsible for putting the snake near the desired local minimum [8], the initialization procedures are applied to control both of attraction and repulsion forces which hold the active contour models to or from the desired features. The external energy term representing the attraction and repulsion in the next equation respectively:

$$E_{\text{external}}(x) = k \| x - l \|^2$$

$$E_{\text{external}}(x) = k \frac{1}{\| x - l \|^2} \quad (5)$$

The attraction force we can say it is like spring force and the repulsion energy like a volcano pushing out. They are generated between a snake element and a point $i$ in an image. In the attraction force case.
the energy is minimal when \( x = i \), and it takes the value of \( k \) when \( i - x = \pm 1 \), but in the repulsion energy case the energy is maximum when \( x = i \). The repulsion term must be stopped as \( i - x \to 0 \).

**iii. Image (Potential) energy**

There are three image energies \( E_{\text{image}} \); lines, edges and terminations. It is produced by the processing of the image \( I(x, y) \) results a force that is used to control snakes towards the features of interest. The total image energy can be expressed as a weighted combination of lines, edges and termination functions:

\[
P = E_{\text{image}} = w_{\text{line}}E_{\text{line}} + w_{\text{edge}}E_{\text{edge}} + w_{\text{term}}E_{\text{term}}
\]

The lines, edges and terminations energy shown in the next equation respectively:

\[
E_{\text{line}} = \int_0^1 \dot{I}(x(c))dc
\]

\[
E_{\text{edge}} = -\left| \nabla I(x(c)) \right|^2
\]

\[
E_{\text{term}} = \int_0^1 \frac{\partial \theta}{\partial n} dc = \int_0^1 \frac{\partial^2 C}{\partial n^2} dc
\]

\[
E_{\text{term}} = \int_0^1 \frac{C_x C_x + C_y C_y - 2C_x C_y C_x C_y}{(C_x^2 + C_y^2)^{3/2}} dc
\]

**D. Segmentation based on level set**

The level set method, originally used as numerical technique for tracking interfaces and shapes developed by Stanley Osher and James A. Sethian in 1988 [8]. Now days this technique is increasingly applied to image segmentation. The benefit of the level set technique is that, one can perform numerical calculations including bends and surfaces on a settled Cartesian network without characterizing the items. Few advantages of Level set methods are: implicit, parameter free, provides geometric properties of the evolving structure, allows for change of topology, and is intrinsic. In 1988 David Mumford and Jayant Shah [9] created Level set techniques (district based model) in view of a general piecewise smooth (PS) detailing used to set up an ideal criteria for fragmenting a picture into sub-areas. Level set approach is numerically most stable implicit representation. This method defines problem in one higher dimension. Which are acts as a great tool for modeling time varying objects. The level set method amounts to representing a closed curve using auxiliary function called as zero level set. The formulation of level set implies that the level set value of a point on the contour with motion must of level set suggests that the level set estimation of a point on the form with movement should dependably be zero. The level set method is boundary driven and region driven model free segmentation.

**E. Atlas-based segmentation**

Atlas–based segmentation is a widely used technique for supervised methods. It depends on a series of reference images in which the tissues have been segmented by hand. To segment the tumor of medical image, it needs to register the atlas correspondence to the volume by point to point [13]. A finite-element method [14], optical-flow [15], and elasticity of transform [16, 18] are used in these
segmentation. Kyriacou et al. [14] choose a biomechanical model of the brain using the finite-element method. The soft tissue deformation was first modeled, and, then, the anatomical atlas was registered with a transformed patient image. Dawant et al. [15] employed an approach relied on optical-flows-Thirion’s demons algorithm [4]-for both tumor growth modeling and atlas matching deformations. This approach is called seeded atlas deformation (SAD), as they put a seed with the same intensity properties as the lesion in the atlas image, and then compute the non-rigid registration [13]. However, this requires a large seed to masks atlas structures. Bach et al. and Polio [17, 18] made a further improvement that minimizes the amount of atlas information that is masked by using a specific model of tumor growth inside the tumor area, which rely on the assumption that the tumor growth radial from a single voxel seed. However, Atlas-based segmentation methods are limited used in presence of large space-occupying lesions, for the damaged areas in the atlas-based area have no correspondence to the atlas. Mutual information flow registration [13] is combined with the pattern presented by Bath et al [17] to overcome the limitation in presence of large space-occupying lesions.

I. Clinical Application of Hippocampal Segmentation

The analysis of the morphometric characteristics of the hippocampus has been used as important biomarker in many clinical applications, including temporal lobe epilepsy, Alzheimer’s disease (AD) and mild cognitive impairment (MCI), schizophrenia, major depression, bipolar disorder, and many other neurological and psychiatric disorders (Geuze et al. 2005). Given the wide clinical applicability of hippocampal measurements, methods that can reliably segment the hippocampus in a variety of different brain shape and sizes need to be developed. Through the use of structural T1-weighted MRI scans, the atrophy of the hippocampus has been shown as a predictive biomarker for patients with MCI that will progress to AD (Convit et al. 1997; Jack et al. 1999). A manuscript by Frisoni et al. (Frisoni et al. 2010) presents a thorough applicability of structural MRI as part of the clinical routine in patients with suspected AD. The volumetric measurement of the hippocampus is also used to monitor the progression of AD and to assess outcomes with the use of potential diseasemodifying drugs. Through a large cohort of subjects (N=160), Laakso et al. 1998, indicated that assessing the volume of the hippocampus through an MRI, it is possible to obtain overall correct classification accuracy of 92 % (sensitivity=94 %, specificity 90 %), when comparing AD patients vs. healthy elderly controls. Asymmetry in hippocampal volumes (atrophy of the hippocampus in one hemisphere) has been shown as a predictor of the lateralization of epileptic abnormalities (Cook et al. 1992; Cendes et al. 1993). Atrophy of the hippocampus has also been used to measure the progression of the disease (Cendes 2005). Atrophy of the hippocampus has also been related to several other diseases, where this measurement has not yet been validated a clinical biomarker. These include, but are not limited to; schizophrenia (Nelson et al. 1997), post-traumatic stress syndrome (Bremner et al. 1997), depression (Bremner et al. 2000), and bipolar disorder (Blumberg et al. 2003) and may others (Geuze et al. 2005).

II. SEGMENTATION PROCEDURES

The definition of segmentation procedures involved:
(a) Segmentation of the hippocampal head from the amygdala in the most rostral slices (proposed from round 1): panelists were asked whether, in their opinion, the currently available 3D navigation tools enable satisfactory discrimination of the boundaries between the amygdala and the hippocampal head;
(b) Segmentation of internal CSF pools (proposed from round 1): panelists were asked whether internal pools should be segmented, and using what criteria (e.g., only when connected to external CSF, or in every case);
(c) segmentation of structures that cannot always be clearly visualized on MR scans, but are expected in specific locations based on a priori anatomical knowledge, as it happens for the subiculum in very atrophic subjects (proposed from round 1);
(d) MR image orientation (proposed from round 1) panelists were asked whether the MR scans should be oriented along the anterior commissure (AC) to the posterior commissure (PC) line, along the axis of the segmented hippocampus, or along the mean angle between the two hippocampal axes for each subject.

III. LITERATURE SURVEY

A. Manual and Automated tumor segmentation: The classification of Brain tumor segmentation methods can be made depending on the degree of human interaction as:

A.1 Manual segmentation
It involves delineation of the boundaries of tumor manually and representing region of anatomic structures with various labels [4]. Manual segmentation requires software tools for the ease of drawing regions of interest (ROI), is a tedious and exhausting task. MRI scanners produce multiple 2-D slices and the human expert has to mark tumor regions carefully, otherwise it will generate jaggy images that lead to poor segmentation results [2].

A.2 Semi-automatic segmentation
In semi-automatic brain tumor segmentation, human interaction is least as possible. As indicated by Olabarriaga et al.[5], the self-loader or intuitive mind tumor division segments comprise of computational part, intelligent part and the interface. Since it involves both computer and humans ‘expertise, result depends on both the combination. Productive division of cerebrum tumor is conceivable through this procedure yet it is additionally subjected to varieties between master clients and inside same client.

A.3 Fully automatic segmentation
In this method, there is no intervention of human and segmentation of tumor is determined with the help of computer. It involves the human intelligence and is developed with soft computing techniques, which is a difficult task. Brain tumor segmentation has various properties which reduce the advantage of humans over machines. These methods are likely to be used for large batch of images in research environment. However; these methods have not gained popularity for clinical practice, due to lack of transparency and interpretability [6].

B. Supervised and Unsupervised Segmentation
Image segmentation’ objective is to segregate the image into mutually exclusive regions, which are similar with respect to pre-defined subsets. This objective can be accomplished using two methods of segmentation methods- Supervised and Unsupervised methods [7]. The detailed explanations about these methods are as follows:

B.1 Unsupervised segmentation:
If for training input vectors, target output is unknown, training method adopted is unsupervised learning. In the previous years, various unsupervised learning methods such as K-means and fuzzy clustering has gained popularity for brain tumor segmentation[8]. The main aim of this type of segmentation is to segment the image into areas that have similar intensity and has well defined anatomic properties. Unsupervised segmentation of brain tumor achieve its anatomic goal by segmenting the image into at
least two anatomically regions, one is tumor and other is edema. The advantage of this type is that it can handle very difficult tasks such as brain tumor segmentation; it produces an accurate segmentation of different regions present in heterogeneous tumor [9]. Disadvantages of this segmentation are: number of regions is to be known before, tumors may not be specified clearly. This disadvantage can be avoided using skull stripping. Skull stripping is a pre-processing step to wipe out noncerebral tissue such as fat, muscle, skin, skull which are not desired region of interest [10].

B.2 Supervised segmentation
In supervised learning, the network is provided with series of sample inputs and output is compared with expected response. It involves both training phase that uses labelled data that maps features to labels and testing phase is used to map labels to unlabeled data[2]. The advantage of this type is that training set can be changed; it can reduce the manual task by providing labelled data. Irrespective of its advantages, it suffers from disadvantages that it requires patient specific training for brain tumor supervised segmentation and also human variability is also a concern.

C. Segmentation methods
In the segmentation process, accurate delineation of the tumor is responsible for early tumor diagnosis in clinical practice. Manifold approaches for brain tumor segmentation has been proposed. Be that as it may, no standard division method can deliver agreeable outcomes for all imaging applications. When all is said in done, different division systems are as per the following:

C.1 Threshold-based methods
It is the convenient and basic technique of image segmentation. It convert gray scale images into binary images[11]. If we consider g(x,y) as the segmented image, we will get two outputs for the corresponding input image f(x,y). According to this technique, g(x,y)=1; if f(x,y) >= T and g(x,y)=0; if f(x,y)<T, where T corresponds to threshold[12]. Pixels having value 1 is the desired tumor’s area, whose processing is made further using morphological operations. Merit of this technique is that it differentiates between black and white intensity values. Computations required for this technique are not very complex. Drawback of this technique is that we may not get accurate results and the pixels may or may not be connected. It is classified into two types-local and global thresholding. The thresholding in which the value of T is constant or fixed is called global thresholding and otherwise is local thresholding.

C.2 Region-based methods
This method is used to examine pixels by merging neighbourhood pixels to form disjoint regions with homogeneity properties [13]. The region growing and the watershed segmentation methods are types of the region based methods and are mostly used in the process of brain tumor segmentation. Region growing is the simplest region-based segmentation method and is used to extract a connected region of similar pixels from an image. It is a technique that group pixels into a larger region, by appending seeds to neighbourhood pixels[14]. Initialization of the seed point is a main aspect. It may be implemented by Mean or Max-Min algorithms. It aims to group the neighbourhood pixels in such a manner so that homogeneity is maintained. The principle of this algorithm is as follows [14]: 1. Select the points (seed) starting in the image. These points are called germ. 2. Fix a criterion of homogeneity of the region traced for example, the grey level or intensity level. 3. Process is repeated until the desired condition is met, so that no region is grown afterwards.
C.3 Artificial Neural Networks
Artificial Neural Network (ANN) is a system modelled based on the human brain. An ANN is a network of many simple units, each having a local memory. It performs classification by learning from data and do not use any set rules. They perform well on difficult, multivariate, nonlinear and noisy domains such as brain tumor segmentation. This classifier feeds the features through a series of nodes, where mathematical operations are applied to the input nodes and a classification is done at the output nodes. Clarke [15] was the first researcher to propose a supervised classification using an AN approach for brain tumor segmentation in MR images. Executing ANN for cerebrum tumor division catch issues of intricacy, the measure of system turns out to be extensive, tedious process and huge number of pictures are required for preparing the system.

A particular case of ANN is the self-organizing map (SOM). SOM is an unsupervised competitive learning algorithm. SOM automatically organizes itself according to the input data using a similarity factor like Euclidean distance [10]. The brain cortex is organized in such a manner that closer neurons will give answers to the same kind of stimulus; this is one of the reason because of which SOM technique is used in visual pattern recognition. Vijayakumar et al [16] proposed SOM method to segment tumor, necrosis, cysts, edema, and normal tissue in T2 and FLAIR MRI. Murugavalli and Rajamani presented a hybrid technique of a Hierarchical Self Organizing Map (HSOM) and Fuzzy Clustering Mean (FCM) to detect various tissues like white matter, gray matter, CSF and tumor in T1 MR images [17].

C.4 Fuzzy C means (FCM)
FCM is based on clustering which segments one class of data into two or more clusters. It works by casting each data point matching to each cluster centre on the basis of distance between the cluster and the data point. The advantages of FCM algorithm are: (1) It gives best result for overlapped data set (2) It produces comparatively better result than k-means algorithm (3) The application of FCM to MRI data has shown satisfactory results [18].

FCM is gaining popularity in the research area of brain tumor segmentation. This calculation produces division pictures that are clinically neuroanatomic tissue differentiate from crude MRI information. A knowledge-based fuzzy clustering approach was proposed and implemented for the segmentation of the MRI images of brain tumor followed by 3-D connected components to build the tumor shape [19]. To improve the accurate detection of stage and size of tumor, a combined method of the k-means and fuzzy c-means algorithms was proposed to deal with the segmentation of brain tumor [20]. The disadvantages regarding this technique are: (1) It has a takes more computational time (2) It is more sensitive to noise.
Summary table of segmentation method

<table>
<thead>
<tr>
<th>Segmentation Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold Based Method</td>
<td>Easy to use.</td>
<td>Limited capability to segment region sharply.</td>
</tr>
<tr>
<td><strong>Region Based Methods</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Region Growing</td>
<td>Computationally inexpensive.</td>
<td>Requires human interference.</td>
</tr>
<tr>
<td>Watershed method</td>
<td>Ability of completing contours in multiple segmented regions</td>
<td>Needs Pre-processing and pose-processing procedures.</td>
</tr>
<tr>
<td><strong>Pixel Based Classification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuzzy C-means</td>
<td>Defines sharp boundary for segmented region.</td>
<td>Noise sensible.</td>
</tr>
<tr>
<td>Artificial Neural Network</td>
<td>Ability to model critical dependencies.</td>
<td>Slow learning phase.</td>
</tr>
<tr>
<td>Markov Random Field</td>
<td>Ability to handle complex dependencies in multispectral data.</td>
<td>Selection of parameters is crucial.</td>
</tr>
<tr>
<td><strong>Model Based Classification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parametric deforming models</td>
<td>Efficient for building automatic methods.</td>
<td>Can not handle inhomogeneities.</td>
</tr>
<tr>
<td>Geometric deforming models</td>
<td>Can handle inhomogeneities well.</td>
<td>Computationally expensive.</td>
</tr>
</tbody>
</table>

IV. CHALLENGES IN SEGMENTATION OF HIPPOCAMPUS

1. The hippocampus has been known as one of the most important structures referred to as Alzheimer’s disease and other neurological disorders. However, division of the hippocampus from MR pictures is as yet a testing undertaking because of its little size, complex shape, low differentiation, and broken limits. Exact and solid programmed division of average transient projection structures, for example, the hippocampus, is as yet a testing.

2. The complexity of the human hippocampus presents various challenges including its general flexure, being intertwined with dentate gyrus, and most importantly, the inability to distinguish the CA (cornu ammonis) fields with standard MRI.

3. Visualizing the capacity of individual human hippocampal subfields stays testing because of their little sizes and convoluted structures.

V. DISCUSSION AND CONCLUSION

Automated techniques for hippocampal segmentation have been developed in the research community to reduce time-consuming workload and improve upon reproducibility attributable to the variability encountered in the manual method. A reliable, objective and reproducible technique for automated hippocampal segmentation, in particular, would expedite the confident processing of absolute volumes in clinical cases in order to judge the degree of bihemispheric asymmetry and establish the degree of atrophy over time.
REFERENCES


