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Hippocampal volumetry for lateralization of temporal lobe epilepsy: automated versus manual methods

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Abstract

The hippocampus has been the primary region of interest in the preoperative imaging investigations of mesial temporal lobe epilepsy (mTLE). Hippocampal imaging and electroencephalographic features may be sufficient in several cases to declare the epileptogenic focus. In particular, hippocampal atrophy, as appreciated on T1-weighted (T1W) magnetic resonance (MR) images, may suggest a mesial temporal sclerosis. Qualitative visual assessment of hippocampal volume, however, is influenced by head position in the magnet and the amount of atrophy in different parts of the hippocampus. An entropy-based segmentation algorithm for subcortical brain structures (LocalInfo) was developed and supplemented by both a new multiple atlas strategy and a free-form deformation step to capture structural variability. Manually segmented T1-weighted magnetic resonance (MR) images of 10 non-epileptic subjects were used as atlases for the proposed automatic segmentation protocol which was applied to a cohort of 46 mTLE patients. The segmentation and lateralization accuracies of the proposed technique were compared with those of two other available programs, HAMMER and FreeSurfer, in addition to the manual method. The Dice coefficient for the proposed method was 11% ($p < 10^{-5}$) and 14% ($p < 10^{-4}$) higher in comparison with the HAMMER and FreeSurfer, respectively. Mean and Hausdorff distances in the proposed method were also 14% ($p < 0.2$) and 26% ($p < 10^{-3}$) lower in comparison with HAMMER and 8% ($p < 0.8$) and 48% ($p < 10^{-5}$) lower in comparison with FreeSurfer, respectively. LocalInfo proved to have higher concordance (87%) with the manual segmentation method than either HAMMER (85%) or FreeSurfer (83%). The accuracy of lateralization by volumetry in this study with LocalInfo was 74% compared to 78% with the manual segmentation method. LocalInfo yields a closer approximation to that of manual segmentation and may therefore prove to be more reliable than currently published automatic segmentation algorithms.

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Introduction

Localization of the epileptogenic site is an important task in the preoperative evaluation of patients with intractable mesial temporal lobe epilepsy (mTLE). The hippocampus is frequently the site of imaging abnormality with the characteristic feature being that of sclerosis. This is defined by a loss of volume, increased signal intensity particularly with fluid-attenuated inversion recovery (FLAIR) images and curvature alteration and will often lateralize the site of epileptogenicity (Cendes et al., 1993; Jack et al., 1990). Although quantitative studies have shown that a reduced hippocampal volume strongly correlates with an ipsilateral mTLE, 15–30% of mTLE cases show no evidence of asymmetry despite clear indication of a unilateral ictal origin (Carne et al., 2004; Jackson et al., 1994; Van Paesschen, 1997). Hippocampal atrophy is conventionally detected by visual assessment of T1-weighted (T1W) MR images. Proper assessment may be compromised, however, by head position in the magnet and the variable degree of atrophy found along the two hippocampi. Head tilt, for instance, may cause one hippocampus to look inadvertently smaller, although the image may be reoriented to correct this effect. Quantitative manual efforts, on the other hand, necessitate the outline of individual coronal images and are time-consuming. Automated segmentation algorithms are thus of special interest.

Automatic segmentation of the hippocampus in mTLE presents certain challenges because of changes in size and shape along its longitudinal axis. Although a number of such segmentation techniques have been proposed in the literature, they have been largely tested in nonepileptic subjects. To the best of our knowledge, there is only one report of automatic hippocampal segmentation in cases of mTLE (Pardoe et al., 2009). In this study, both FreeSurfer and FSL-FIRST were applied in a cohort of 10 mTLE patients and in 10 nonepileptic subjects.

There are several review articles on automatic segmentation techniques for a variety of brain structures (Angelini et al., 2005; Cremers et al., 2007; Rouainia and Doghmane, 2008; Suri et al., 2002; Trichili et al., 2003). Generally, in many of the segmentation methods, there is an energy function, a shape model and an optimization algorithm. Each of these plays an important role in the design of a segmentation algorithm. Almost all of the new methods in the literature use some form of prior knowledge (Chupin et al., 2007; Dambreville et al., 2008; Tejos et al., 2009; Yan and Kassim, 2006). In an attempt to improve upon the segmentation technique, we have applied a principal component analysis (PCA) to extract the shape relation between different structures in the training dataset (Akhondi-Asl and Soltanian-Zadeh, 2009).

Furthermore, in unpublished work, a probabilistic energy function was introduced based on intensity, tissue type, and location information of a given structure using a single atlas and rigid registration. To find the local minimum of the energy function, a two-step optimization algorithm was employed. In the first step, shape parameters were optimized based on the first derivative of the energy function with respect to each parameter. In the second step, the shapes of individual structures were fine-tuned using a level set method. The method was used for hippocampal segmentation in a limited number of mTLE patients. Although the segmentation quality was superior compared with that of some of the state-of-the-art techniques, lateralization accuracy was not satisfactory compared to that of manual segmentation.

In this paper, a local information-based multiple-atlas method (LocalInfo) is employed to determine whether the segmentation method may be improved further. Generally, the single atlas-based methods have limitations because of dissimilarities with the atlas image provided. To circumvent this, multiple atlases may be used to improve upon the likelihood

of finding a closer approximation of images. Some methods described in the literature have employed a multiple atlas approach for segmentation purposes (Artachevarria et al., 2009; Isgum et al., 2009; Rohlfing et al., 2004; van Rikxoort et al.). The approach described herein, however, uses local information for atlas selection unlike these other methods. The appropriate atlas is chosen for a specified region of interest and is used for shape model and location information extraction. The approach has been further modified at the stage of initialization and with the use of non-rigid coregistration. The proposed method is applied to the MR images of 46 mTLE patients in whom laterality is well-defined and compared with two of the state-of-the-art segmentation techniques, namely HAMMER (Shen and Davatzikos, 2002) and FreeSurfer (Fischl et al., 2002).

Methods

Patients

From an archival review of patients operated for mTLE, 46 patients (17 males, 29 females; age range 19-66y, mean 41y) with preoperative T1-weighted MR images and sufficient clinical follow-up to declare Engel class Ia outcomes were selected for study. The epileptic focus resided on the right in 20 cases and on the left in 26. Definitive preoperative localization and surgical outcomes provided a pure culture of cases harboring a mTLE. None of the patients harbored a distinct lesion associated with their epilepsy.

Imaging

Magnetic resonance images were acquired with a 3T General Electric Signa system (GE Medical Systems, Milwaukee, WI, USA). All patients underwent coronal T1-weighted MR study using a spoiled gradient-echo (SPGR) sequence with TR /TI /TE = 7.6/1.7/ 500 ms, flip angle = 20°, field of view (FOV) = 200×200 mm², matrix size = 256×256, pixel size = 0.781×0.781 mm², and slice thickness = 2.0mm. The regions of interest (ROIs) encompassing the hippocampi were outlined manually for segmentation using sequential coronal T1-weighted MR images. A single investigator (KJ) outlined all coronal hippocampal contours (usually 20 slices/case) using Eigentool, an in-house software (<http://www.radiologyresearch.org/eigentool.htm>). These were then verified by another investigator (KE).

Segmentation

Ten T1-weighted images of healthy subjects were manually segmented and used in the training process. Each of these ten T1-weighted images was coregistered to all of the 46 T1-weighted images of mTLE patients to construct the shape models and location information. A sub-volume region-of-interest (ROI) was chosen and processed to improve speed and robustness of the algorithm. The ROI was defined as 1.05 times of the smallest cube that covered all the desired structures in all of the training datasets. The additional 5% confidence interval has been sufficient for the image segmentation phase in our experiments. The T1-weighted MR images of all hippocampi were segmented by the proposed method as well as with two other methods, HAMMER (Shen and Davatzikos, 2002) and FreeSurfer (Fischl et al., 2002), two publicly available software tools.

Discrepancies among automatic segmentation outcomes regarding volumetric measures are attributable to their respective software tools as all are established by comparison with manual outlines. A measure of the segmentation accuracy of the individual methods was therefore made by comparison with that of manual hippocampal segmentation in cases of mTLE with known postoperative seizure-free outcomes.

The Dice coefficient (k), mean distance, and Hausdorff distance were used to evaluate segmentation accuracy. The Dice coefficient is a similarity index widely used for segmentation evaluation, whereas, the Hausdorff distance (H) represents the maximum of the minimum distances between the corresponding surface points of two volumes. Due to outliers, the 95 percentile of the Hausdorff distance (H_{95}) was used in this study.

The proposed multiple atlas-based segmentation method (LocalInfo) is described here. The application of a number of atlases provides a greater opportunity to approximate a chosen MR image with its desired atlas counterpart for segmentation purposes. The segmentation method is schematized in its entirety in Fig. 1. Suppose that we want to simultaneously segment m different structures in a skull-stripped image $I(x)$ and have n skull-stripped training intensity images $I_{Tr}^i(x) i \in \{1, \dots, n\}$ and their corresponding training label maps $L_{Tr}^i(x) i \in \{1, \dots, n\}$ in which all of the m structures are segmented and labeled with $l \in \{0, \dots, m\}$. Label 0 is assigned to the background.

For each voxel x in the image, we define the probability of belonging to the region Ω_k as $p(x \in \Omega_k) = p_k(x) \times p_{fk}(x) \times p_{sk}(x)$ where $k \in \{1, \dots, m+1\}$ indicates the region index with $m+1$ is the background index. In this definition, $p_{sk}(x)$, $p_{fk}(x)$, and $p_k(x)$ specify the probability that the point x belongs to the region Ω_k based on its location, tissue type, and intensity, respectively. To compute $p_{sk}(x)$, and $p_{fk}(x)$, we register $I_{Tr}^i(x) i \in \{1, \dots, n\}$ to $I(x)$ with a non-rigid registration method. We use a local weight for each structure based on the similarity of $I_{Tr}^i(x) i \in \{1, \dots, n\}$ with $I(x)$. For each $I_{Tr}^i(x)$, we show the transformation of the non-rigid registration by T^i . We apply these transforms to $L_{Tr}^i(x) i \in \{1, \dots, n\}$ to get $T^i L_{Tr}^i(x)$ (transformation of $L_{Tr}^i(x)$ with T^i). In the next step, for each structure k , we select a region of interest (ROI), R_k , based on the registered datasets to speed up the process. We use $(I(x))_{R_k}$ to show the selected part of the image $I(x)$ based on R_k . Then, we use $M_k^i = MI\left(\left(T^i L_{Tr}^i(x)\right)_{R_k}, (I(x))_{R_k}\right)$ to find the similarity between structures of the training datasets and the test image within R_k , where $MI(A, B)$ show the mutual information between the images A and B . If $M_k^{i_1} > M_k^i, \forall i = 1 \dots m, i \neq i_1$, then, images i_1 and $I(x)$ have the highest similarity in the structure k based on the mutual information metric. Next, for each label, we find the following image.

$$\bar{\phi}_k^s(x) = \sum_{i=1}^n M_k^i \times S\left(\delta_k\left(T^i L_{Tr}^i(x)\right)\right), \quad k=1 \dots m \quad (1)$$

where $\delta_k(u) = \begin{cases} 1 & \text{if } u=k \\ 0 & \text{if } u \neq k \end{cases}$ and S shows the sign distance function (SDF) of the binary image. This image has the property that provides for a point with a lower value to have a higher probability of being inside the structure. Thus, using $\bar{\phi}_k^s(x)$, we define $p_{sk}(x)$ for the structure k as:

$$p_{sk}(x) = \begin{cases} \ln\left(\left(e - e^{0.5}\right)\left(\frac{\bar{\phi}_k^s(x)}{\min(\bar{\phi}_k^s(x))}\right) + e^{0.5}\right) & \text{if } \frac{\bar{\phi}_k^s(x)}{\min(\bar{\phi}_k^s(x))} > \frac{e^e - e^{0.5}}{e - e^{0.5}} \\ \varepsilon & \text{otherwise} \end{cases} \quad (2)$$

This function is 1 when $\bar{\phi}_k^s(x)$ is at minimum and 0.5 when $\bar{\phi}_k^s(x)=0$. In equation (2), a nonzero ε is used to avoid numerical problems. To calculate $p_{fk}(x)$, we construct the probability mass function (pmf) by performing intensity clustering twice with 3 and 10 clusters (Akhondi-Asl and Soltanian-Zadeh, 2010). The 3-class clustering captures the global intensity information of the tissues while the 10-class clustering captures the local or fine intensity information. Each label in the 10-class segmentation is called a tissue type. We model the pmf of each structure versus tissue type as follows:

$$p_{fk}(x) = \begin{cases} \varepsilon & l(x) \leq L1 - 3, l(x) \geq L2 + 3 \\ \frac{1}{4} & l(x) = L1 - 2, l(x) = L2 + 2 \\ \frac{1}{4} & l(x) = L1 - 1, l(x) = L2 + 1 \\ 1 & L1 \leq l(x) \leq L2 \end{cases} \quad (3)$$

where parameters $L1$ and $L2$ are estimated using:

$$\begin{cases} L1 = \arg \min_{1 \leq i \leq 10} \text{abs}(C_3(2) - C_{10}(i)) \\ L2 = \arg \min_{1 \leq i \leq 10} \text{abs}(C_3(3) - C_{10}(i)) - 2 \end{cases} \quad (4)$$

In this equation, $C_N(t)$ shows the cluster center for the t -th class (cluster) in the N -class clustering. For the background (region $m+1$), we use:

$$p_{fm+1}(x) = \begin{cases} 1 - p_{f1}(x) & \text{if } \forall k, k' \neq k \in \{1, \dots, m\} \quad p_{fk}(x) = p_{fk'}(x) \\ 0.5 & \text{otherwise} \end{cases} \quad (5)$$

For $p_k(x)$, we use the Parzen window estimator defined as

$$p_k(x) = \frac{1}{|\Omega_k|} \int_{\Omega_k} K(I(x) - I(\bar{x})) d\bar{x} \quad (\text{Akhondi-Asl and Soltanian-Zadeh, 2009})$$

where K is the Gaussian kernel. Finally, we write the energy function as:

$$J(\Omega_1, \dots, \Omega_m) = \sum_{k=1}^{m+1} \int_{\Omega_k} F(p(x \in \Omega_k)) dx = \sum_{k=1}^{m+1} \int_{\Omega_k} F(p_k(x) \times p_{fk}(x) \times p_{sk}(x)) dx \quad (6)$$

We use the decreasing function $F(p) = -\ln(p)$ which makes the optimization a minimization problem. To find the best segmentation, we need to find the regions $(\Omega_1, \dots, \Omega_m)$ that optimize equation (6). It should be noticed that Ω_{m+1} is a function of the other regions and thus is not an independent region. When all of the regions are as uniform as possible, are in the correct tissue as much as possible, and are in the proper locations, the energy function is at its optimum. To optimize this function, a shape (region) representation method is needed. We use the training dataset to find a shape model which considers the shape relation between different structures.

Sign distance function is one of the most effective shape representation methods in the literature (Malladi et al., 1995). Important information about shape and the relation between structures can be used for segmentation. We have used these relations and have shown their effectiveness in a previous publication (Akhondi-Asl and Soltanian-Zadeh, 2009). In the present circumstance, suppose that we define a SDF $\phi_k(x)$ which is negative inside the region for each region $k \in \{1, 2, \dots, m\}$. To extract shape relations among different structures,

for each structure, we register the binary images (produced from the label images) of all of the training datasets to the one with the highest similarity with $(I(x))_{R_k}$ in order to find the transform A_k^i . Each A_k^i is an affine transform with 12 parameters. Thus, for each structure k , we need to find $12 \times (n-1)$ parameters. A similar method is now used as in our previous publication (Akhondi-Asl and Soltanian-Zadeh, 2009) to model shape priors using PCA. In this method, we calculate the shape basis function (ϕ_j) weights w_i that minimize the energy function. To consider the pose variances in the segmentation process, an individual affine transformation is used for each structure. These transformations give flexibility to the regions and are used for local alignment. In this case, for each region, we add 12 parameters to the problem. Thus, we have $l + 12 \times m$ parameters which we put in the vector $\mathbf{P}$ (l shows the number of principal shapes used for the shape representation). Finally, we have the following energy function:

$$\min_{\mathbf{P}} J(\mathbf{P}) = \sum_{j=1}^m \int_{\Omega} H(-\phi_j(x)) F(p_j(x) \times p_{fj}(x) \times p_{sj}(x)) dx + \int_{\Omega} \prod_{k=1}^m H(\phi_k(x)) F(p_{m+1}(x) \times p_{fm+1}(x) \times p_{sm+1}(x)) dx \quad (7)$$

where H is the heavy side function. For the initialization and optimization, we use the same strategy as before (Akhondi-Asl and Soltanian-Zadeh, 2009). Thus, we must compute first order derivatives of the energy function for the parameters in the $\mathbf{P}$. It can be shown that the derivative of the function J with respect to a parameter ω is:

$$\frac{\partial J(\mathbf{P})}{\partial \omega} = \sum_{j=1}^m \oint_{\Gamma_j} \frac{\partial \phi_j(\bar{x})}{\partial \omega} \times \left\{ \prod_{\substack{l=1 \\ l \neq j}}^m H(\phi_l(\bar{x})) \times F(\widehat{p}_{m+1}(\bar{x})) - F(\widehat{p}_j(\bar{x})) + \frac{1}{\sum_{k \in S_j} |\Omega_k|} \int_{\{\Omega_k | k \in S_j\}} F'(\widehat{p}_j(x)) \times p_{tj}(x) \times (p_j(x) - K(I(x) - I(\bar{x}))) dx \right. \\ \left. - \frac{1}{|\Omega_{m+1}|} \int_{\Omega_{m+1}} F'(\widehat{p}_{m+1}(x)) p_{tm+1}(x) \prod_{\substack{l=1 \\ l \neq j}}^m H(\phi_l(\bar{x})) (p_{m+1}(x) - K(I(x) - I(\bar{x}))) dx \right\} d\bar{x} \quad (8)$$

In this equation, $p_{ij}(x) = p_{fj}(x) p_{sj}(x)$ and $\widehat{p}_j(x) = p_j(x) p_{ij}(x)$. In addition, Γ_j is the

boundary of the region j . For computing the desired derivatives, we must compute $\frac{\partial \phi_j(\bar{x})}{\partial \omega}$ (Akhondi-Asl and Soltanian-Zadeh, 2009). In the next step and also after optimization of the parameters of the energy function, in order to capture details of the structures that cannot be extracted from the principal shapes, we remove shape dependency related to the principal shapes and define the following function:

$$\min J(\phi_1, \phi_2, \dots, \phi_m) = \sum_{j=1}^{m+1} \int_{\Omega_j} F(p_j(x) \times p_{fj}(x) \times p_{sj}(x)) dx \quad (9)$$

In this function, there are m level set functions that should be optimized. Thus, we can use the following energy function where the second term is for the smoothness of the shapes.

$$E = \sum_{j=1}^{m+1} \int_{\Omega_j} F(p_j(x) \times p_{fj}(x) \times p_{sj}(x)) dx + \sum_{j=1}^m \mu_j \int_{\Omega} \delta(\phi_j(x)) |\nabla \phi_j(x)| dx \quad (10)$$

Using the following equation, we can update each shape iteratively.

$$\begin{aligned} \frac{\partial \phi_j(\bar{x})}{\partial t} = & |\nabla(\phi_j(\bar{x}))| \left\{ F(\bar{p}_j(\bar{x})) - \prod_{\substack{l=1 \\ l \neq j}}^m H(\phi_l(\bar{x})) \times F(\bar{p}_{m+1}(\bar{x})) \right. \\ & - \int_{\{\Omega_k | k \in S_j\}} \frac{F'(\bar{p}_j(x))}{\sum_{k \in S_j} |\Omega_k|} p_{tj}(x) (p_j(x) - K(I(x) - I(\bar{x}))) dx \\ & \left. + \int_{\Omega_{m+1}} \frac{F'(\bar{p}_{m+1}(x))}{|\Omega_{m+1}|} p_{m+1}(x) \prod_{\substack{l=1 \\ l \neq j}}^m H(\phi_l(\bar{x})) (p_{m+1}(x) - K(I(x) - I(\bar{x}))) dx + \mu_j \operatorname{div} \left(\frac{\phi_j(\bar{x})}{|\nabla \phi_j(\bar{x})|} \right) \right\} \end{aligned} \quad (11)$$

The final segmentation is the output of the above optimization process.

Results

Table 1 reports the segmentation evaluation metrics for the patients. The Dice coefficient for LocalInfo is 11% ($p < 10^{-5}$) and 14% ($p < 10^{-4}$) higher compared to HAMMER and FreeSurfer, respectively (Fig. 2). Also, mean and Hausdorff distances for LocalInfo is 14% ($p < 0.2$) and 26% ($p < 10^{-3}$) lower compared to HAMMER and 8% ($p < 0.8$) and 48% ($p < 10^{-5}$) lower compared to FreeSurfer, respectively. The cases are then sorted according to values of the Dice coefficient of LocalInfo. In 87% of cases, LocalInfo had the highest Dice coefficient followed by HAMMER (85%) and FreeSurfer (83%). Segmentation accuracy of each of the automatic segmentation methods is compared schematically with outline overlays on coronal MR images. Visual comparisons demonstrate the closer approximations achieved with LocalInfo relative to that of HAMMER (Fig. 3) and FreeSurfer (Fig. 4) with the manual segmentation method. These disparities are accentuated in select cases for each of the two automatic segmentation methods, HAMMER (Fig. 5) and FreeSurfer (Fig. 6). These demonstrate the more extreme diversions from the actual hippocampal outlines in this cohort of cases.

Hippocampal volumes on both sides were calculated for all patients using the outlines obtained with each of the automatic segmentation methods (i.e., LocalInfo, HAMMER, FreeSurfer) as well as the manual method. Each case was then expressed as a ratio (i.e., right/left) to provide an indication of possible laterality of epileptogenicity based on a result greater than or less than unity. Scatter plots provide a visual display of the distribution of individual cases for each of the automatic segmentation techniques compared to that for the manual method (Fig. 7). A discriminator line, $y = x + b$, is provided, where 'b' is the bias parameter set as the difference between the averages of each of the left and right hippocampal volumes. The distribution of values is more concentrated and situated lower along the discriminator line with LocalInfo than with either HAMMER or FreeSurfer. This is also the case with manual segmentation although a wider disparity of ratios here indicates a clearer separation of volume measures. The average values for the left and right hippocampal volume measures using FreeSurfer were 50% and 44% higher, respectively, than that obtained by manual segmentation (Table 2). With HAMMER, a significant volume

discrepancy arose only on the left side with the hippocampal volume calculated to be 37% higher than that obtained with manual segmentation. With the values available in the current study, the accuracy of lateralization was greatest with manual segmentation (78%) and subsequently for both LocalInfo and FreeSurfer (74%) and finally for HAMMER (72%).

Discussion

A new segmentation algorithm using a local information-based multiple atlas method (LocalInfo) is proposed. Its performance compared with two publicly available segmentation methods was measured in a population of 46 mTLE patients using the hippocampus as the target volume. LocalInfo is shown by the Dice coefficient and both the mean distance and the Hausdorff distance methods to be superior to the two currently published automatic segmentation methods. This superiority is attributable to: (i) the use of multiple atlases to find the most suitable for the image of interest; and (ii) a fine-tuning step used to capture details of structures that cannot be extracted from their principal shapes. Moreover, in each of the 87% of mTLE cases, the Dice coefficient was found to be higher with application of LocalInfo than with the other automatic methods.

Because of higher segmentation accuracy with LocalInfo, a higher concordance with the manual segmentation method was achieved in lateralizing the epileptogenic side. Volumetric analysis itself fails to establish laterality in mTLE in 15 – 30% of cases as volumetric asymmetry is not established in all proven cases (Carne et al., 2004; Jackson et al., 1994; Van Paesschen, 1997). Hence, despite the fact that agreement with the manual segmentation method is most evident with LocalInfo, this approach alone lacks sufficient reliability on its own to declare a focus.

Inasmuch as actual lateralization accuracy was achieved in this study cohort of 46 patients, both LocalInfo and FreeSurfer attained a level of 74% compared to the manual segmentation method which lateralized correctly in 78% of cases. Despite relatively poorer segmentation concordance for both HAMMER and FreeSurfer, lateralization of the epileptogenic side was still possible in some cases allowing a reasonable approximation of that achieved with the manual method. One might expect that with a larger cohort of cases of mTLE of a known laterality, a greater separation in lateralization would be achieved between LocalInfo and the other automatic methods. Although the lateralization accuracy achieved with LocalInfo more closely approximated that found with the manual method, those obtained with both HAMMER and FreeSurfer were close behind and reflect, in part, the size of the study population. It is possible that the segmentation inaccuracy peculiar to any given methodology may affect the volume estimation of each of the two hippocampi similarly resulting in a volume ratio that is not markedly different. This would render a situation in which the segmentation outcomes would be different yet the lateralization accuracies remain similar. Nevertheless, an accurate segmentation will, in most cases, ensure that the lateralization accuracy will approximate that achieved with manual segmentation.

Automatic hippocampal segmentation was studied for a cohort of 10 temporal lobe epilepsy patients in a previous study (Pardoe et al., 2009). Lateralization in this study, however, was based on the presence of significant unilateral hippocampal atrophy, an impression not uniformly apparent in all mTLE cases. Dice coefficients of 0.66 ± 0.042 and 0.62 ± 0.057 (mean $\pm$ SD) were reported for FreeSurfer and FSL-FIRST, respectively. Lateralization accuracies of 90%, 70%, and 30% were reported for the manual method, FreeSurfer and FSL-FIRST, respectively. In the current study, a Dice coefficient of 0.63 ± 0.12 and a lateralization accuracy of 74% were obtained using FreeSurfer in a dataset of 46 patients. Volume ratios were used to better reflect the circumstances of the clinical presentation in cases of mTLE.

Lateralization accuracy using volumetric analysis carried out by automatic segmentation methods in cases of mTLE remains less than with manual segmentation. Although volumetry does not ideally distinguish the epileptogenic side in all cases of mTLE, it remains an integral part of the investigational approach in this condition. In this regard, automatic segmentation methods must undergo continuous modification to render the most reliable estimates, particularly in circumstances where volumetric disparity between the hippocampi is not obvious.

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Fig. 1.
Flowchart of the proposed multiple-atlas segmentation method.

Fig. 2. Dice coefficients of the three methods of automatic segmentation (LocalInfo, HAMMER, FreeSurfer) by case number for all mTLE patients. The cases have been sorted according to the value of the Dice coefficient obtained for the proposed method (LocalInfo) in each case.

Fig. 3. Comparison of segmentation results for the hippocampus generated by LocalInfo (red), HAMMER (blue), and expert manual segmentation (white) in a series of coronal MR images of a sample mTLE case dataset.

Fig. 4. Comparison of segmentation results for the hippocampus generated by LocalInfo (red), FreeSurfer (green), and expert manual segmentation (white) in a series of coronal MR images of a sample mTLE case dataset. The average Dice coefficient for this case was 0.00 using FreeSurfer and 0.70 using LocalInfo.

Fig. 5.

Comparison of segmentation results for the hippocampus generated by LocalInfo (red), HAMMER (blue), and expert manual segmentation (white) in a series of coronal MR images of a sample case with a poor segmentation outcome using HAMMER. The average Dice coefficients for this subject using LocalInfo and HAMMER were 0.62 and 0.39, respectively.

Fig. 6. Comparison of segmentation results for the hippocampus generated by LocalInfo (red), FreeSurfer (green), and expert manual segmentation (white) in a series of coronal MR images of a sample case with a poor segmentation outcome using FreeSurfer. The average Dice coefficients for this subject using LocalInfo and FreeSurfer were 0.70 and 0.00, respectively.

Fig. 7. Scatter plots of hippocampal volumes for (A) manual segmentation, (B) LocalInfo, (C) HAMMER, and (D) FreeSurfer. The symbols, 'R' and 'L', respectively, correspond to patients with right-and left-sided mTLE.

Table 1

The mean and standard deviations of the Dice coefficients (k) and the mean (M) and the Hausdorff (H_{95}) distances for the hippocampal segmentations of 46 mTLE patients by LocalInfo, HAMMER (Shen and Davatzikos, 2002), and FreeSurfer (Fischl et al., 2002). Statistically significantly different values are printed in bold.

	k	M	H₉₅
LocalInfo	0.72±0.09	0.77±0.50	3.09±1.42
HAMMER	0.64±0.09	0.90±0.47	4.19±1.54
FreeSurfer	0.63±0.12	0.84±1.79	5.89±3.19

Table 2

Average volumetric measurements (mean $\pm$ SD, mm³) for the left and right hippocampi of 46 mTLE patients reported with lateralization accuracy, sensitivity, and specificity for manual segmentation, LocalInfo, HAMMER (Shen and Davatzikos, 2002), and FreeSurfer (Fischl et al., 2002).

	Left Average Volume (mm ³)		Right Average Volume (mm ³)		Lateralization		
		Difference Percentage Compared with Manual		Difference Percentage Compared with Manual	Accuracy	Sensitivity	Specificity
Manual	2271 $\pm$ 734	–	2533 $\pm$ 631	–	78%	0.750	0.808
LocalInfo	2337 $\pm$ 681	-1%	2400 $\pm$ 640	-5%	74%	0.682	0.792
HAMMER	3105 $\pm$ 840	35%	2565 $\pm$ 612	1%	72%	0.640	0.810
FreeSurfer	3417 $\pm$ 854	46%	3656 $\pm$ 802	44%	74%	0.667	0.818