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PH. D. THESIS ABSTRACT

Development and Validation of a New Method for the Adjustment of Human Brain Atlases

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Abstract

Brain atlases constitute one of the most important aid systems for neurosurgeons and neuroradiologists in their daily clinical work. Some of the atlas types with more relevance today are the deformable atlases. In this paper the implementation of a new graphical system for the handling and adjustment of brain atlases is presented. Different options are included. The most relevant is the new developed method of adjustment. In it 6 different approaches have been implemented, 3 of them novel who use vectorial fields to make the adjustment. In addition, the system allows the placement of the patient in the Talairach coordinate system. It automatically locates the Mid Sagittal Plane and the Anterior and Posterior Commissures. The new adjustment method offers an average precision of 2.734 mm. The system satisfactorily locates the Mid Sagittal Plane and the Anterior and Posterior Commissures.

Keywords: Human brain atlases, Deformable atlases, Vectorial field, Automatic localization, Mid sagittal plane, Anterior commissure, Posterior commissure, Talairach coordinate system

1 Introduction

The neurosurgeons and neuroradiologists are two groups that need to accurately identify certain points or structures in a patient's brain. Different systems are used to aid in this identification. One of them is the brain atlas. Since the appearance of printed atlases, atlases have evolved and have become into more and more sophisticated computer programs like digitalized, deformable and probabilistic atlases. The deformable and probabilistic brain atlases form part of a widely studied line of research (Thompson and Toga, (1996), Toga and Thompson, (2000)). This article will focus on deformable atlases, where the new developed adjustment method is formed.

Deformable brain atlases part from two sets of images, one in the atlas and another one in the patient's brain. The objective is to find the homologous atlas points or structures on the patient or the other way around. Different techniques exist for this. A first classification could be linear and nonlinear. In the linear classification, translations, rotations and scalings are made. The rest of the deformations are included in the nonlinear classification. The most extended are the warping techniques. Toga and Thompson, 1998, 2000 and Thompson, 2000, established a classification of warping algorithms directed by intensity and directed by the model. The first matches intensity patterns by regions in each slice based on mathematical or statistical criteria. In this case, different approximations also exist. On the contrary, in the algorithms directed by the model, the models are explicitly built first, representing separately the identifiable anatomical elements in each one of the slices to be matched. In this case, the approaches are determined based on the explicit geometry of the structures. Models are formed using points, curves or surfaces of the structures. The new adjustment method would be included within the deformable atlases, nonlinear transformations, warping directed by the model and created using points. To extend the concepts treated here consult Toga and Thompson, 1998, 2000 and Thompson, 2000.

The description of the new adjustment method and the rest of the options of the system are presented in section 2. Section 3 includes the obtained results after processing 10 patients. Lastly, section 4 gives the conclusions and section 5 mentions future works.

2 Material and Methods

2.1 New Adjustment Method

The new adjustment method consists of 6 different approaches, 2 of them already used previously, 3 of them new, and the other one is an improved version of a well-known technique. It is worked with two sets of points in it. One is identified in the atlas and it is denoted as a_i. The other one is identified in the patient's brain and is denoted as c_i. The composition of two applications is used (*f* or *g*) to obtain this adjustment; *f* is the affine transformation and *g* uses 5 different approaches.

The first of the approaches, only applies to the affine transformation. Among all the affine applications, the one being searched for is the one for which the sum of the squares of the distances between $f(a_i)$ and c_i for i=1..N

is minimum. This means, $\sum_{i=1}^{N}(b_i-c_i)^2$, where $b_i=f(a_i)$.

In the second approach, application *g* is defined by a displacement measured from the inverse of the relative distance to the reference points. g is obtained in the following manner:

$$g(x)=x+\frac{1}{q(x)}\sum_{i=1}^{N}q_i(x)(c_i-b_i),$$

$$q_i(x)=|x-b_1|^2..|x-b_i|^2..|x-b_N|^2,\quad q(x)=\sum_{i=1}^{N}q_i(x),$$

where $|\ |^2$ indicates that the factor is suppressed.

In the third approach, *g* is obtained using a similar idea, but in this case a system of equations is solved. Let $s_i=c_i-b_i$. In this case, g is searched for so that $g(b_i)=c_i$, g=identity+h, where h will be a transformation for $h(b_i)=s_i$, i=1,...,N. Let b_i be the center of a deformation d_i that in a point, q, has the following value: $d_i(q)=\frac{k^2u_i}{k^2+(q-b_i).(q-b_i)}$, where u_i is a vector that corresponds to the displacement of the point b_i, given that $q=b_i \rightarrow d_i(b_i)=u_i$. k is a scaling factor and must be interpreted in the following manner: If the distance between q and b_i is k, then
$(q-b_i).(q-b_i)=k^2$ and $d_i(q)=u_i/2$. h is defined as: $h(q)=\sum_{i=1}^{N}d_i(q)=\sum_{i=1}^{N}\frac{k^2u_i}{k^2+(q-b_i).(q-b_i)}$.

In the last approaches, application *g* uses displacements that approximately conserve the volume using three different vectorial fields.

A vectorial field $W(x,y,z)=u(x,y,z)(-y,x,0)$ is considered where $u(x,y,z)$ is a function to choose. *W* is a vectorial field, whose value in point (x,y,z), knowing $W(x,y,z)$, is given by $u(x,y,z)(-y,x,0)=(-u(x,y,z)y,u(x,y,z)x,0)$, so that it is completely defined by the function *u* of R^3 in *R*.

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Figure 1.a shows the tangential lines to the displacements of this first vectorial field.

The second vectorial field used is: $Y(x,y,z)=\frac{(xz,yz,1-x^2-y^2)}{e^{x^2+y^2+z^2}}$, which was obtained by taking $u(x,y,z)=\frac{1}{2e^{x^2+y^2+z^2}}$. Figure 1.b shows the tangential lines to the displacements of this second vectorial field. The third vectorial field used is: $Z(x,y,z)=\frac{(2xz,2yz,1-x^2-y^2+z^2)}{(1+x^2+y^2+z^2)^3}$, which was obtained by taking $u(x,y,z)=\dfrac{1}{2(1+x^2+y^2+z^2)^2}$.

Figure 1.c shows the tangential lines to the displacements of this third vectorial field.

In the previous fields there is one scaling factor missing that establishes the velocity with which the displacement is cushioned as it moves away from the generating point. For the first vectorial field each coordinate is multiplied by $1/k$, the resulting formula is:

$$X(x,y,z)=\left(\frac{k^2xz}{(k^2+x^2+y^2+z^2)^2},\frac{k^2yz}{(k^2+x^2+y^2+z^2)^2},\frac{k^2(k^2+z^2)}{(k^2+x^2+y^2+z^2)^2}\right)$$

k expresses the distance to which the displacement amplitude is reduced in half. In the other two vectorial fields k is also used.

The constant k considerably influences in the results. In the implementation, k is obtained by $k=cte*value$. To calculate this constant, a fixed k (2-50) and a variable k have been used.

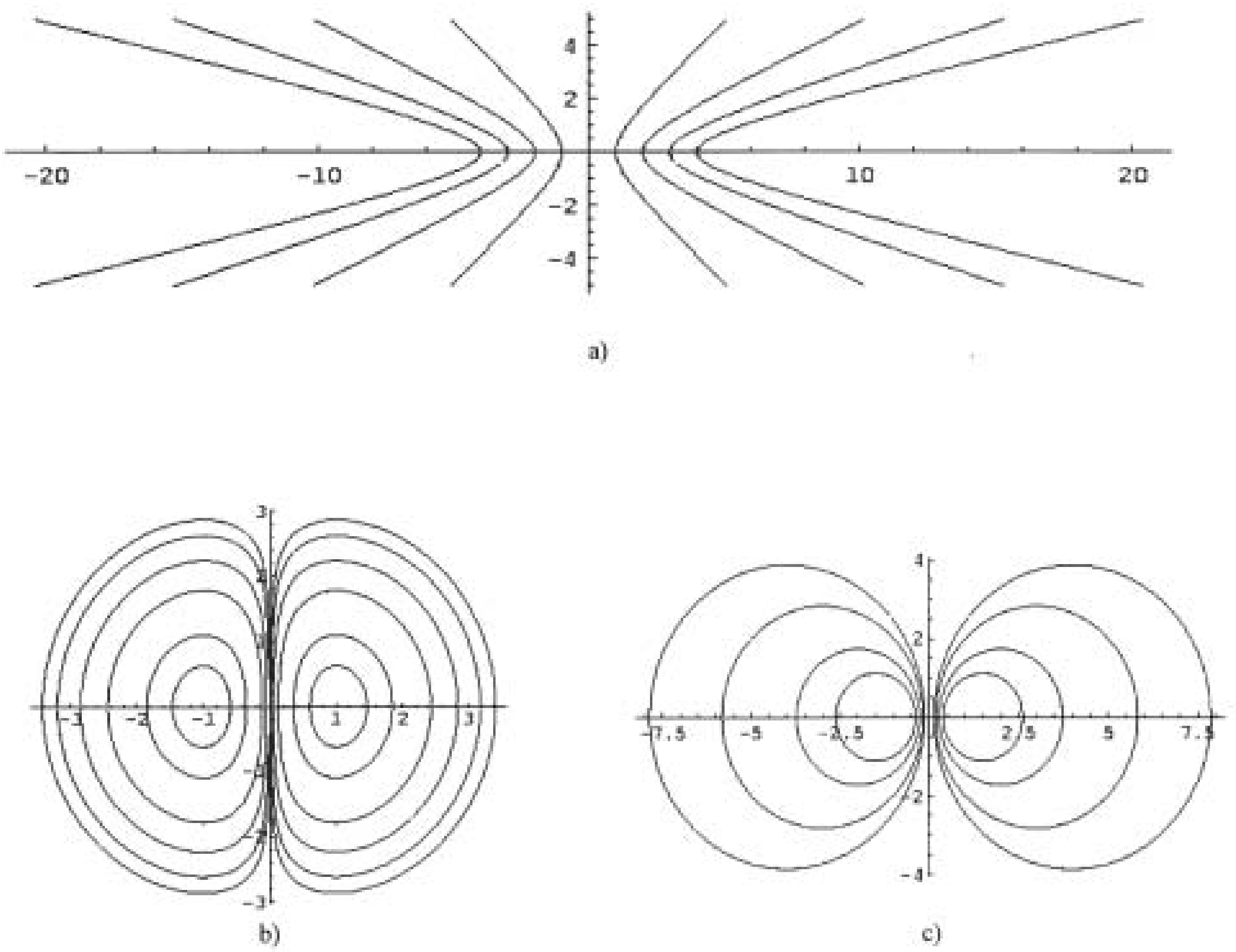


Figure 1. Tangential lines to the displacements of the three vectorial fields

Better results have been obtained for the k variable. In the case where the k variable is used, *cte* has been varied between 0.5 and 3. To obtain *value*, four different strategies have been used. In the first and second strategies, the Euclidean, average and minimum distance is respectively calculated between the points of the patient and the atlas. In the last two strategies, the displacement is centered in some of the points that intervene in the adjustment, taking this point, the minimum and maximum are respectively obtained of the Euclidean distances between the point in which the displacement is centered and the points that intervene in the adjustment.
The number of points used in the adjustment must be greater or equal to five for the system to function correctly.

2.2 Other System Options

Another utility of the system allows the location of the patient in the Talairach stereotactical coordinate system. For this, the necessary points to correctly locate the system are selected. After this step, the slices of the patient are visualized in their habitual orientations (axial, sagittal or coronal) with the grid superimposed, dividing each slice according to this stereotactical system. In addition, using a special affine transformation it locates points or structures identified in another volume taken as an atlas. In this case the atlas used has been the Talairach-Tournoux Oriented to References, Talairach and Tornoux, 1993.

In the new adjustment method, points are used that must be identified in the images of the patients like the one used to locate the patient in the Talairach coordinate system. The idea is to automatize the manual identification of these points. The first step initiated in this sense constitutes the automatic identification of the Mid Sagittal Plane (MSP) and the Anterior (AC) and Posterior (PC) Commissures.

The implemented automatic localization algorithm of the MSP was based on the Ardekani et al. algorithm (1997). In it the maximum symmetry plane between both hemispheres is obtained. To obtain this objective, the mass center of the image is first calculated. Next, N points are identified in a sphere of unitary radius and center in the mass center calculated. Following, the symmetry of all these planes is obtained and it is determined which one of them presents the maximum symmetry. This localization is made in the complete image and in the reduced images.

The Verard et al. algorithm (1997) has been implemented to automatically locate the AC and PC; to which numerous modifications have been made to adapt it to the type of images used (Magnetic Resonance Images). In it an analysis of the scene by steps is made. It parts from the Mid Sagittal Plane, which is calculated with the previous algorithm. Thresholding, 8-connected components search and filtering on the original image is made. From this point, two 8-connected components are obtained that correspond to two easily identifiable structures as are the Callous Body and the Brain Stem. Two convolution masks are applied to an intermediate window identified thanks to the two previous 8-connected components and the PC is identified. Lastly, the AC is identified attending to the relative positions between the two commissures.

3 Results

In this section, the results obtained from processing 10 patients with the different system options are summarized. Magnetic Resonance images of 256x256 pixels were acquired from each patient, with a distance between pixels of 0.859375 mm. and a total of 96 slices with a distance between them of 1mm. The equipment in which these images were taken is: Philips Gyroscan ACS-NT (Best, Holanda) equipped wih a superconductor magnet of 1.5 Teslas and field gradients of 15mT/m.

In order to validate the new adjustment method 11 points have been used in addition (Posterior Commissure, Anterior Commissure, left mammilary tubercle, right mammilary tubercle, pineal gland, posterior angle of the fourth ventricle, rostrum of the callous body, center of the superior-left quadrigeminal tubercle, center of the superior-right quadrigeminal tubercle, center of the inferior-left quadrigeminal tubercle, center of the inferior-right quadrigeminal tubercle). Between 5 and 10 points from these have been taken in the adjustment and another point has been used as a target.
Two studies have been made to estimate the error committed by neuroradiologists in the identification of points. The aim was to obtain a value with which to compare the error committed by the system. In a first study, two experienced neuroradiologists marked the same points in a patient, the average error committed was of 2.91 mm. In the second study, a same experienced neuroradiologist marked the same patient in two different days the same points and in this case the average error was of 3.84 mm.

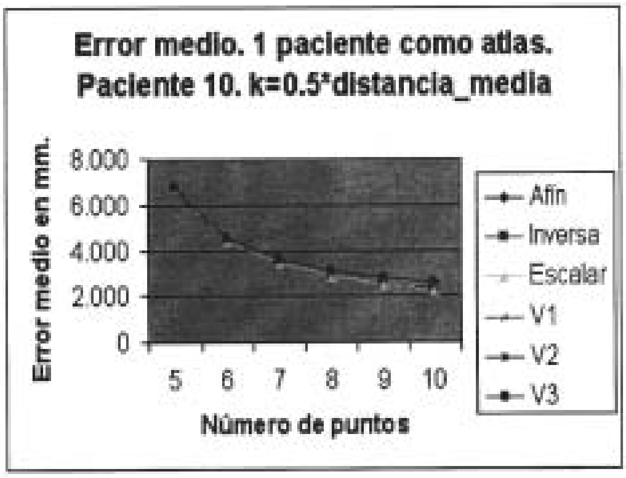
The operation of the system was verified after identifying these values. First, the images of the ten patients were verified and used as atlas the brains numerated XXVII and LXXXV from the Schaltenbrand-Bailey atlas. The results were not the awaited ones. The average error committed was of 15 mm. This error is inadmissible, considering that the error expected is between 2 and 3 mm. A determinant factor exists that influences excessively in this result. The separation between the slices used of these brains is excessive (4.5-7mm.). This causes the identification of homologous points to present a very large error and influences in the terrible results obtained with this method.

Next, different patients were used as atlas. In this manner the new adjustment method obtains an average error of 2.734 mm. (inferior to the error committed by the neuroradiologists) and a success percentage of about 90%. That is to say, that in 90% of the points used, errors would be obtained smaller to the error considered acceptable (5mm.). All the approaches behave better by increasing the number of points used in the adjustment, figure 2a. All of the patients present a similar behavior, figure 2b. Better results are obtained with the *k* variable (the new adjustment method constant). Among the 5 methods used to calculate this *k*, the best one is the one that uses the minimum Euclidean distance and centers the displacement in the different points that intervene in the adjustment, figure 2c.

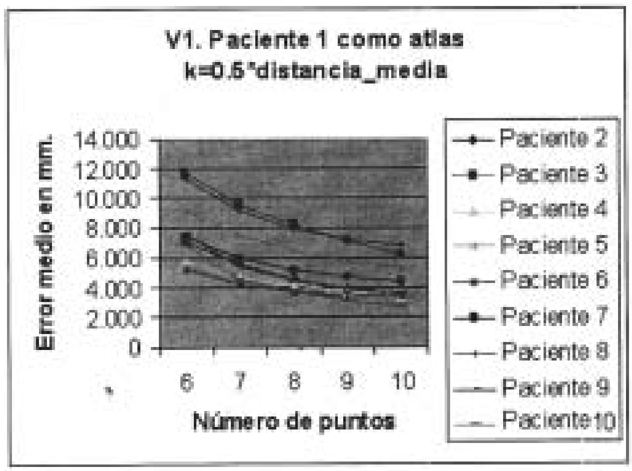
Figures 3a and 3b show two results obtained when processing the same patient with different inclination with the system option to automatically locate the MSP. In figure 3a, the result after processing a patient rotated 20 degrees and with different sizes can be observed. Figure 3b, presents the same patient rotated 40 degrees using as a constant $q=40$ (constant that determines the set of planes to use). In figure 3c the average time in seconds used by the system to obtain the MSP for the images of ten patients for $q=10$ can be seen. Figure 3d shows the average time consumed in minutes by the system to obtain the MSP in images of 256x256 pixels for the images of 10 patients with a different q.

The algorithm of automatic localization of the MSP has adequately located the MSP in the 10 patients studied and as can be deduced from the graphs, the execution time diminishes by reducing the image size.

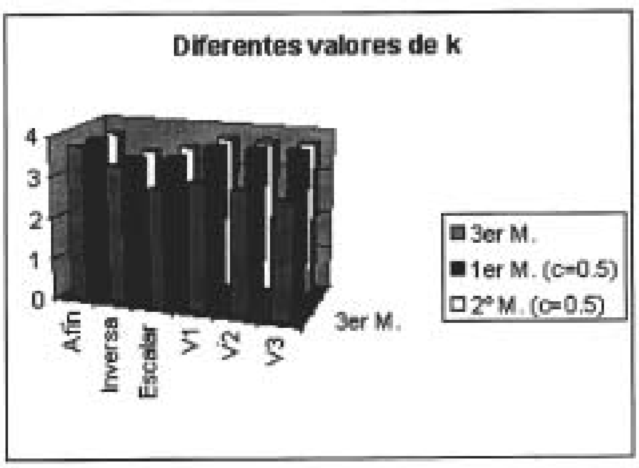
Figures 4a and 4b show the result after processing a patient with the system option for the automatic localization of the AC and PC. This option identifies with an error smaller to the one considered as acceptable the AC in 10 of the patients studied (100%) and the PC in 7 of the 10 patients (70%). Figures 4c, 4d and 4e present the location of the same patient in the Talairach coordinate system.



a)



b)



c)

Fig. 2. Average error for the different patients and approaches, using the first patient as atlas and 10 reference points. (a) Different approaches (b) Different patients and approaches of the first vectorial field (c) Comparing different k

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$$g(x) = x + \frac{1}{q(x)}\sum_{i=1}^{N} q_i(x)(c_i - b_i),$$

$$q_i(x) = |x-b_1|^2 \ldots |x-b_i|^2 \ldots |x-b_N|^2, \quad q(x) = \sum_{i=1}^{N} q_i(x),$$

where $|\ |^2$ indicates that the factor is suppressed.

In the third approach, *g* is obtained using a similar idea, but in this case a system of equations is solved. Let $s_i = c_i - b_i$. In this case, g is searched for so that $g(b_i) = c_i$, g=identity+h, where h will be a transformation for $h(b_i) = s_i$, i=1,...,N. Let b_i be the center of a deformation d_i that in a point, q, has the following value: $d_i(q) = \frac{k^2 u_i}{k^2 + (q-b_i).(q-b_i)}$, where u_i is a vector that corresponds to the displacement of the point b_i, given that $q=b_i \rightarrow d_i(b_i)=u_i$. k is a scaling factor and must be interpreted in the following manner: If the distance between q and b_i is k, then $(q-b_i).(q-b_i)=k^2$ and $d_i(q)=u_i/2$. h is defined as:

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is obtained by taking $u(x,y,z) = \frac{1}{2(1+x^2+y^2+z^2)}$.

Figure 1.a shows the tangential lines to the displacements of this first vectorial field.

The second vectorial field used is: $Y(x,y,z) = \frac{(xz, yz, 1-x^2-y^2)}{e^{x^2+y^2+z^2}}$, which was obtained by taking $u(x,y,z) = \frac{1}{2e^{x^2+y^2+z^2}}$. Figure 1.b shows the tangential lines to the displacements of this second vectorial field. The third vectorial field used is: $Z(x,y,z) = \frac{(2xz, 2yz, 1-x^2-y^2+z^2)}{(1+x^2+y^2+z^2)^3}$, which was

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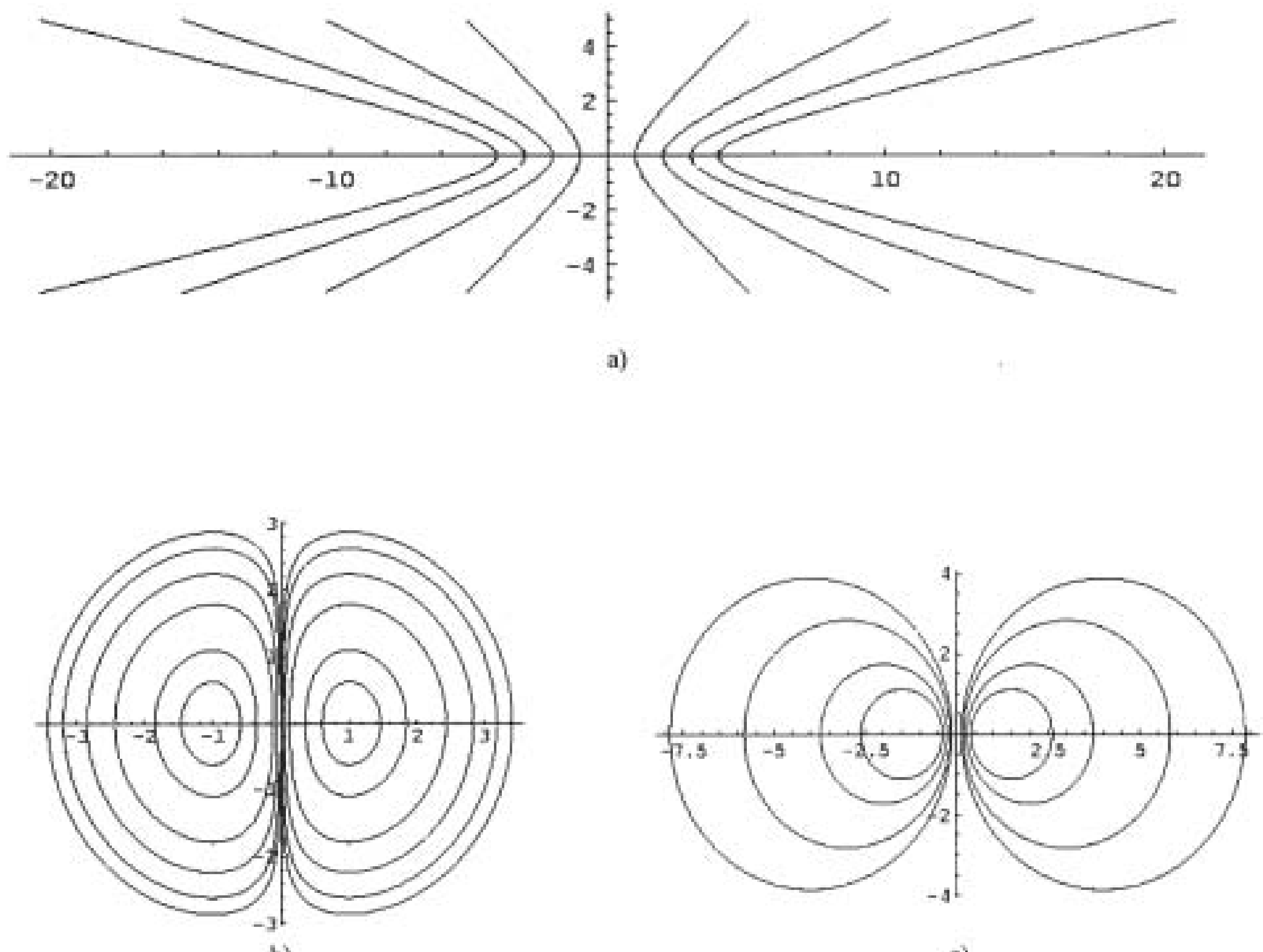

Figure 1. Tangential lines to the displacements of the three vectorial fields

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In order to validate the new adjustment method 11 points have been used in addition (Posterior Commissure, Anterior Commissure, left mammilary tubercle, right mammilary tubercle, pineal gland, posterior angle of the fourth ventricle, rostrum of the callous body, center of the superior-left quadrigeminal tubercle, center of the superior-right quadrigeminal tubercle, center of the inferior-left quadrigeminal tubercle, center of the inferior-right quadrigeminal tubercle). Between 5 and 10 points from these have been taken in the adjustment and another point has been used as a target.

Two studies have been made to estimate the error committed by neuroradiologists in the identification of points. The aim was to obtain a value with which to compare the error committed by the system. In a first study, two experienced neuroradiologists marked the same points in a patient, the average error committed was of 2.91 mm. In the second study, a same experienced neuroradiologist marked the same patient in two different days the same points and in this case the average error was of 3.84 mm.

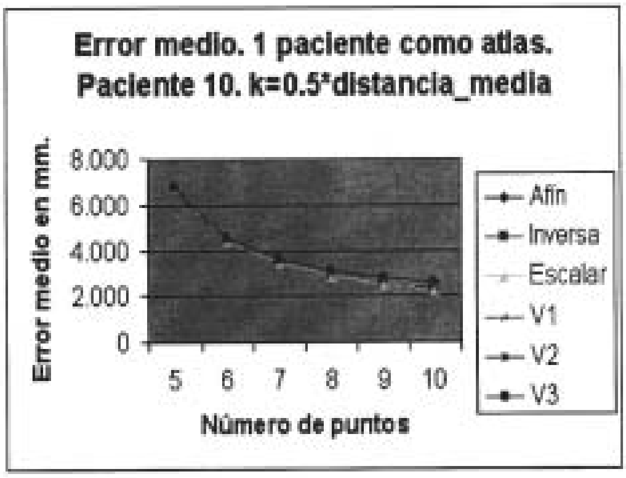
The operation of the system was verified after identifying these values. First, the images of the ten patients were verified and used as atlas the brains numerated XXVII and LXXXV from the Schaltenbrand-Bailey atlas. The results were not the awaited ones. The average error committed was of 15 mm. This error is inadmissible, considering that the error expected is between 2 and 3 mm. A determinant factor exists that influences excessively in this result. The separation between the slices used of these brains is excessive (4.5-7mm.). This causes the identification of homologous points to present a very large error and influences in the terrible results obtained with this method.

Next, different patients were used as atlas. In this manner the new adjustment method obtains an average error of 2.734 mm. (inferior to the error committed by the neuroradiologists) and a success percentage of about 90%. That is to say, that in 90% of the points used, errors would be obtained smaller to the error considered acceptable (5mm.). All the approaches behave better by increasing the number of points used in the adjustment, figure 2a. All of the patients present a similar behavior, figure 2b. Better results are obtained with the *k* variable (the new adjustment method constant). Among the 5 methods used to calculate this *k*, the best one is the one that uses the minimum Euclidean distance and centers the displacement in the different points that intervene in the adjustment, figure 2c.

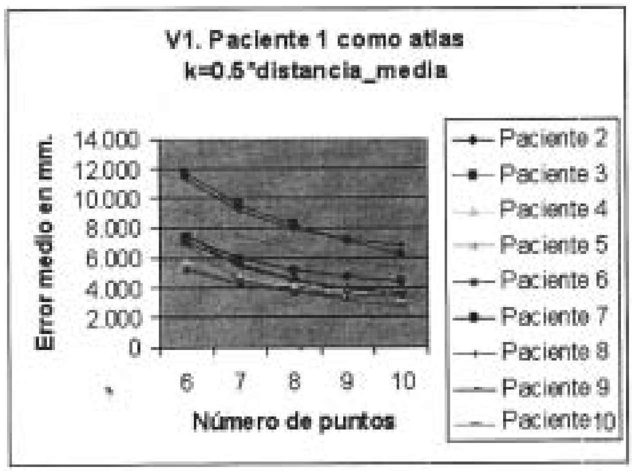
Figures 3a and 3b show two results obtained when processing the same patient with different inclination with the system option to automatically locate the MSP. In figure 3a, the result after processing a patient rotated 20 degrees and with different sizes can be observed. Figure 3b, presents the same patient rotated 40 degrees using as a constant $q=40$ (constant that determines the set of planes to use). In figure 3c the average time in seconds used by the system to obtain the MSP for the images of ten patients for $q=10$ can be seen. Figure 3d shows the average time consumed in minutes by the system to obtain the MSP in images of 256x256 pixels for the images of 10 patients with a different q.

The algorithm of automatic localization of the MSP has adequately located the MSP in the 10 patients studied and as can be deduced from the graphs, the execution time diminishes by reducing the image size.

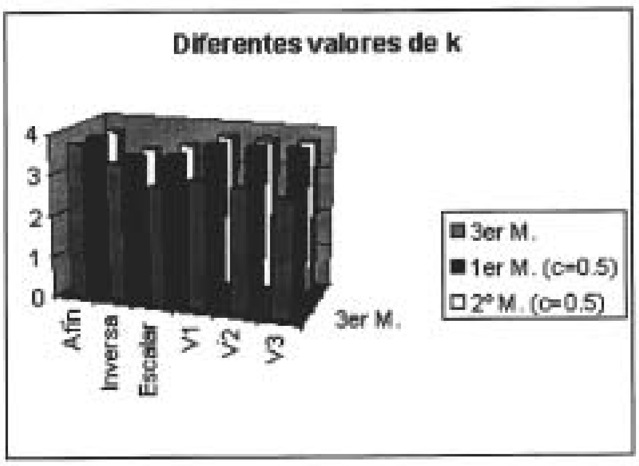
Figures 4a and 4b show the result after processing a patient with the system option for the automatic localization of the AC and PC. This option identifies with an error smaller to the one considered as acceptable the AC in 10 of the patients studied (100%) and the PC in 7 of the 10 patients (70%). Figures 4c, 4d and 4e present the location of the same patient in the Talairach coordinate system.



a)

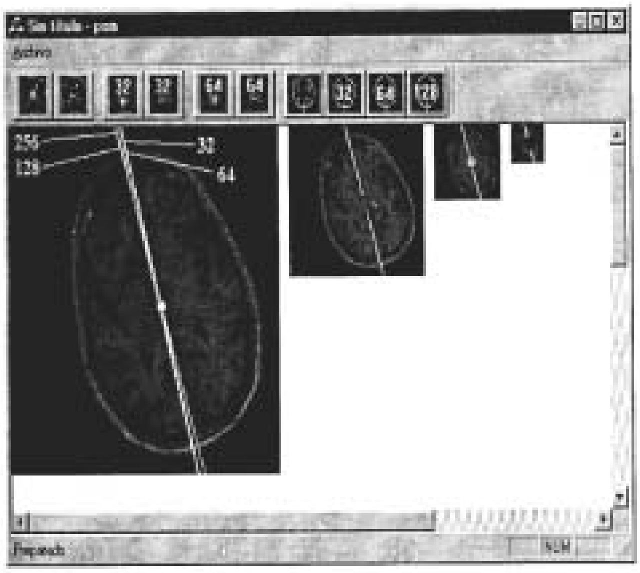


b)

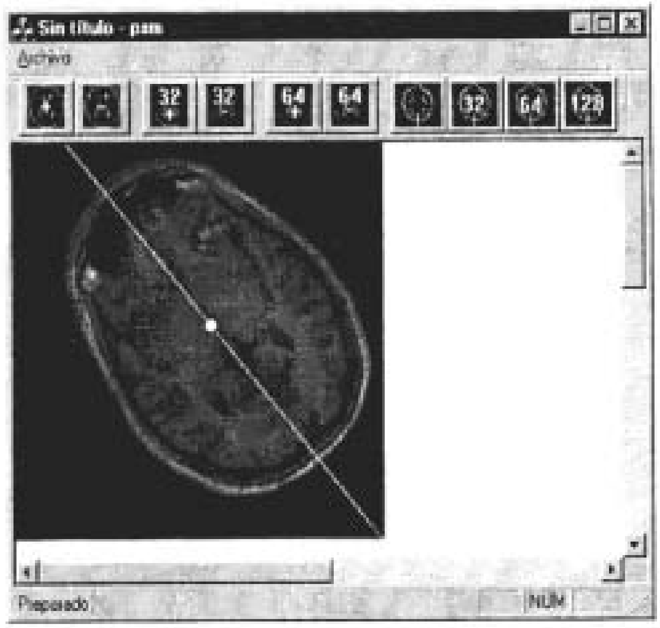


c)

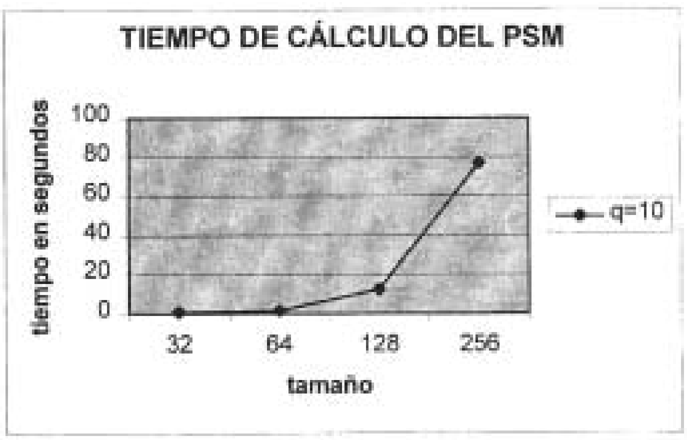
Fig. 2. Average error for the different patients and approaches, using the first patient as atlas and 10 reference points. (a) Different approaches (b) Different patients and approaches of the first vectorial field (c) Comparing different k



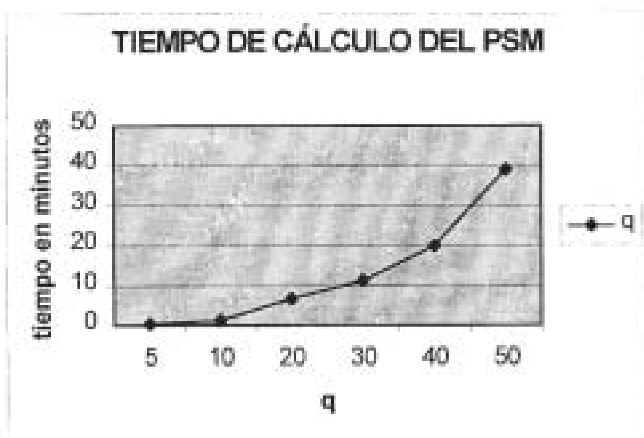
a)



b)

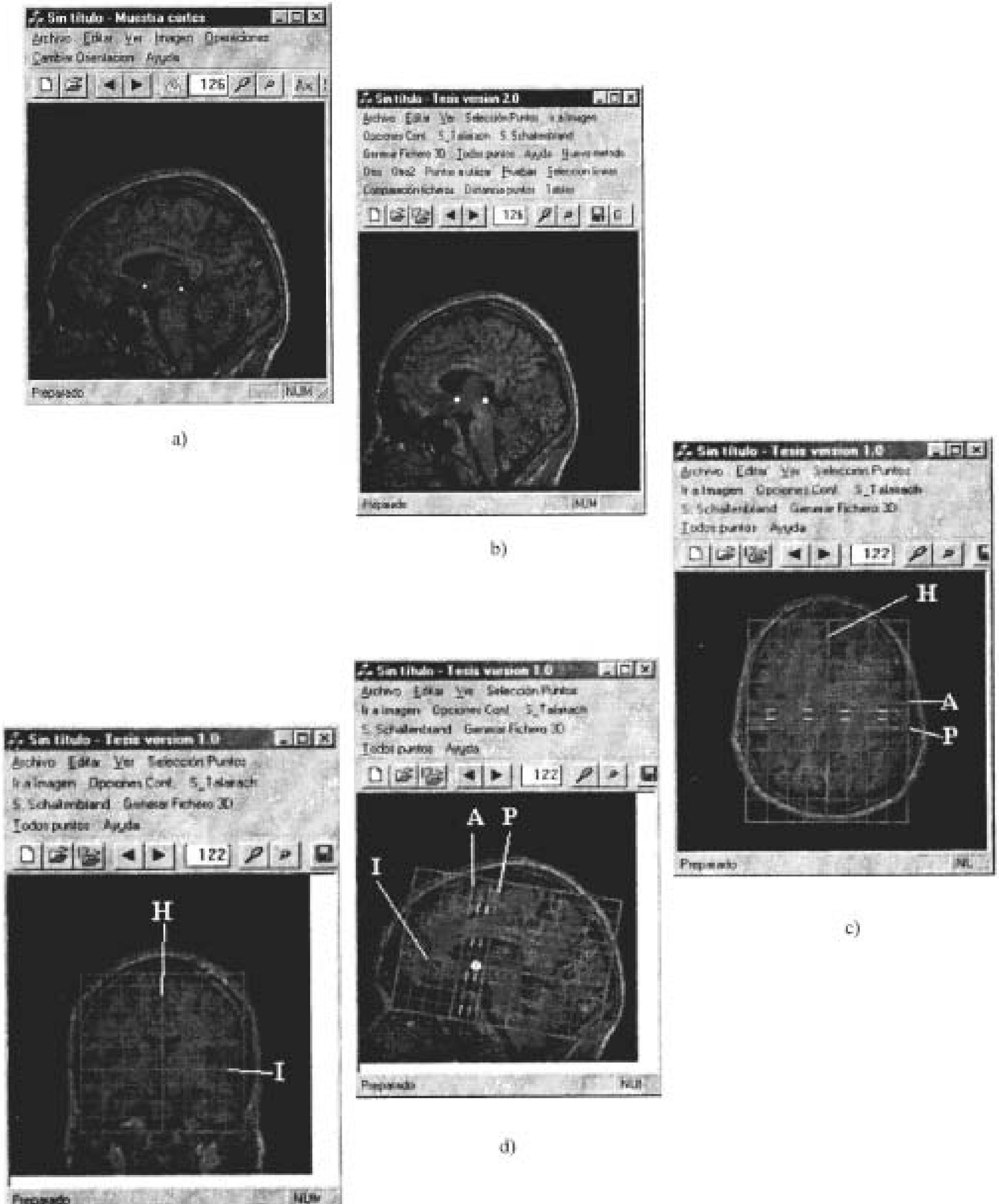


c)



d)

Figure 3. (a) and (b) Results with the system option to automatically locate the MSP.
(c) and (d) Times obtained by the system



e)

Fig.4. (a) and (b) Automatic localization of the AC and PC. (a) Result given by the system. (b) Points identified by the experts.(c), (d) and (e) Talairach coordinate system (c) Axial slice (d) Sagittal slice (e) Coronal slice

4 Conclusions

In this article a new graphical system for the handling and adjustment of human brain atlases has been presented. The main innovation presented is a new adjustment method. This new method consists of 6 different approaches. Three of them new that use vectorial fields.

The system allows the localization of the patient in the Talairach coordinate system. As much as in the new method as in the Talairach coordinate system it is necessary to locate different points. The automatization of this process with the MSP and the AC and PC has been initiated.

The results obtained with the system have been validated by neurosurgeons and neuroradiologist and are considered as very satisfactory. The average error committed by the new adjustment method is of 2.734 mm. Therefore, the new method locates the points with an error lower to the one which an neuroradiologist expert could make. The probability that the error committed in the localization of a point be less than 5 mm. is around 90%. Reason why the system can be considered reliable.

The system also located adequately the MSP in the 10 patients processed (100%), the AC in 10 (100%) and PC in 7 (70%) of these patients with an acceptable error.

Future Works

A common continuation in all the system options susceptible to validation would be to test the system with more patients.

The new adjustment method is being tested with more points. We also want to study more methods to calculate k.

An idea to retake is to use for an atlas a printed or digitilized atlas. It would be specially interesting to use the brains numbered LXVIII and LXXVIII in the Schaltenbrand-Bailey atlas to consist of microscopic slices of the central zone of the brain. A maximum advantage could be taken if the system were used with these slices. This is where the real utility of the system lies, since points and structures could be identified that are not easily identifiable, not even by expert neuroradiologists,.

An interesting idea that will be implemented in a future is the creation of a probabilistic atlas.

The Talairach coordinate system is predicted to be used for spatial localization of zones of brain activition by stimulus.

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