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A METHOD FOR DETECTING INTERSTRUCTURAL ATROPHY CORRELATION IN MRI BRAIN IMAGES

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ABSTRACT

Distinguishing neurodegenerative diseased patients (e.g., suffering from Alzheimer's Disease (AD)) from healthy individuals with the aid of MRI images is one of the challenges that need to be addressed in the field of Computational Anatomy (CA). A crucial feature in the analysis is the rate of atrophy of brain structures like the hippocampus or the ventricles. Until recently, analysis of atrophy rate has been restricted mainly to 'localized atrophy', i.e. atrophy within one brain structure. Distinguishing correlations of atrophy rates between different brain structures could possibly provide additional information about the disease process. Therefore, in this paper, we propose a method to measure and analyze correlations of atrophy rate between hippocampus and ventricles with the aid of some correlation parameters. We combine the parameters that we thus obtain with some local atrophy rate parameters into a multidimensional vector, and use various vector classification methods to analyze the atrophy process with the aid of MRI brain volumes from the ADNI database. We obtain a good agreement between our classification results and the ground truth data. The analysis is facilitated with the aid of a specially designed graphical user interface.

Index Terms— Computational Anatomy, Non-local atrophy correlation, Vector classification methods, Segmentation of ventricles, Chan-Vese method.

1. INTRODUCTION

Alzheimer's disease (AD) is one of the most costly diseases for society in Europe and the United States, and with the aging population its importance will increase in the future. Therefore, quick and reliable diagnostic tools will be of great importance. Nowadays, Alzheimer's disease can be diagnosed non-invasively with the aid of MRI brain images. When the brain ages, cells die and are replaced by cerebrospinal fluid (CSF), a process known as atrophy. In AD patients, atrophy occurs at a faster rate than in normal persons, initially especially in the hippocampus and the ventricles. In order to determine brain atrophy, one or more scans are used, that are usually taken at intervals of several months. The diagnosis of AD is being performed by a radiologist, comparing these scans "by eye". For a more quantitative, reliable and reproducible procedure, automation of the diagnostic process would be very useful.

In order to compare two MRI images (referred to often by "Template" and "Study" images) a number of steps are needed [3]: 1. The bias field needs to be corrected. 2. There should be intensity scaling and/or histogram equalization to remove the differences in intensity that are not due to structural differences. 3. Rigid (or affine) registration needs to be performed to remove misalignment of the images. 4. A local registration needs to be performed, through which the true anatomical differences can be revealed by the deformation field $\vec{u}(r)$. 5. "Diagnostic" parameters can give more insight into the (local or global) characteristics of the deformation field. Step 4 and 5 typically belong to the field of "Computational Anatomy" (CA), a term introduced Grenander and Miller in 1998 [1]. Many methods to perform local registration have already been developed [1, 5]. In our work described here we use a method based on fluid-dynamical equations developed by Christensen [2]. Many diagnostic parameters have also been proposed [1, 5]. Most often used are the deformation magnitude $|\vec{u}|$ and the Jacobian determinant JD, both parameters that are measured at positions within various brain structures, like, especially in the case of AD research, the hippocampus and the ventricles. It is very probable, however, that correlations exist between the parameters measured in different structures, and that measuring these correlations will provide additional information about the development of the illness.

In a previous work [3] we enhanced the ability to evaluate local parameters by introducing two new spaces to monitor the (virtual) time evolution of the deformation calculated by a deformation algorithm, viz. the $(J', |\vec{u}|)$, and (θ, φ) space (where we indicate $J' = JD - 1$ as the "Jacobian displacement" is the size of the deformation vector, and (θ, φ) are the polar angles of the deformation vectors), and

designed a user interface that enabled a quick interpretation of the data. Application of these features to a set of MRI brain volumes of the ADNI [4] database revealed new possibilities of pattern analysis, but a clear distinction between sets of AD and NL subjects could not yet be made, possibly due to effects like imperfect rigid registration.

In this paper we introduce the possibility of measuring non-local properties through the introduction of a number of "correlation parameters". In addition we measured already existing parameters like the divergence. We extended the functionality of our user interface to include these functions. Then we performed an analysis using vector classification methods on the same dataset we used for the analysis of [3], to examine whether differences between AD and NL subjects could be identified. It appeared that such differences did indeed occur, and that a good correspondence was achieved between the diagnosis and the ground truth data.

This paper is organized as follows: In Section 2, we describe the diagnostic parameters. In Section 3 we describe some aspects of the new user interface, particularly the part that facilitates the selection of the regions that can be studied. Section 4 describes the different vector classification methods to distinguish AD from NL with the aid of our diagnostic parameters. In Section 5 we present the experimental results, and we conclude in Section 6.

2. DIVERGENCE AND CORRELATION PARAMETERS

In this section we introduce the parameters we added to our diagnostic set, to further enhance the analysis of the deformation process, and give a short motivation for their use.

1. The divergence of the deformation

$$\nabla . \vec{u} = \frac{\partial u_x}{\partial x} + \frac{\partial u_y}{\partial y} + \frac{\partial u_z}{\partial z} \qquad (1)$$

An integration of this quantity over a certain region can show whether sources of compression or expansion appear within this region, and can thus be used to identify atrophy.

2. The directional correlation coefficient

$$f_{corr\_coef}(R,R') = \frac{1}{N_R \times N_{R'}} \sum_{r \in R} \sum_{r' \in R'} \frac{\langle \vec{u}(r), \vec{u}(r') \rangle}{\|\vec{u}(r)\| \times \|\vec{u}(r')\|} \qquad (2)$$

Here, N_R is the number of points inside region R, $\vec{u}(r)$ is the deformation vector at point r, $<\vec{u}(r), \vec{u}(r')>$ is the scalar product for two vectors $\vec{u}(r)$ and $\vec{u}(r')$.

The correlation coefficient is 1 when the deformation is in the same direction, and 0 when the deformation directions are random, and can thus provide an indication to distinguish a large global deformation (that can be due to imperfect rigid registration) from local deformations.

3. Mean Inproduct Correlation.

$$f_{corr}(R,R') = \frac{1}{N_R \times N_{R'}} \sum_{r \in R} \sum_{r' \in R'} \langle \vec{u}(r), \vec{u}(r') \rangle \qquad (3)$$

This parameter yields an indication of the relation of the size and the direction of the deformation of two structures.

4. Mean Jacobian Displacement Correlation

$$f_{J'\_Corr}(R,R') = \frac{1}{N_R \times N_{R'}} \sum_{r \in R} \sum_{r' \in R'} J'(r) \times J'(r') \qquad (4)$$

This gives an indication of whether the joint deformation of two regions is large for both regions, and whether it is in the same direction, e.g. it will be large and positive if there is mainly expansion or contraction in both regions.

5. Mean Jacobian Displacement Sign Correlation

$$f_{J'\_Sign\_Corr}(R,R') = \frac{1}{N_R \times N_{R'}} \sum_{r \in R} \sum_{r' \in R'} Sign(J'(r)) \times Sign(J'(r')) \qquad (5)$$

This coefficient will yield an indication about whether there will be mainly contraction or expansion in both of the regions, and their correlation.

3. VISUALIZATION ENVIRONMENT

We implemented the enhanced Graphical User Interface in Matlab. Below we describe some of its functionality

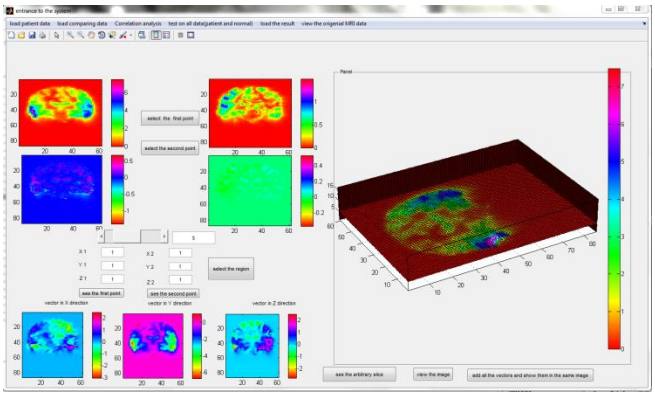

Fig.1. *Starting window of the user interface. Left side: top two images: $|\vec{u}|$ for two slices; middle two images: J' for two slices; bottom 3 slices: x, y, and z component of the deformation field. Right side: an arbitrary slice can be selected to display the displacement field (shown by colored glyphs).*

3.1. Region of Interest (ROI)

In the user interface, the starting screen shows pictures of the displacement $\vec{u}$, as well as pictures of the Jacobian displacement J′, and a 3D vector plot of deformation of a

slice (Fig.1). The regions that are used to calculate the correlation coefficients mentioned above can be selected from this window either manually, or automatically, using the data of a predefined atlas. In addition, the ventricles can be segmented automatically with the Chan-Vese method, where we use convexity and edge conditions for correction of initially imperfect results. The result for a volume of 16 coronal slices is shown in Fig.2

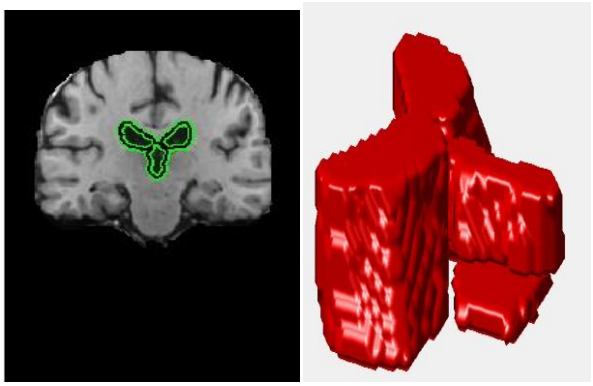

Fig. 2. *Ventricle segmentation result: (left) in 2D view, (right) in 3D view*

3.2. Deformation View of ROI

Once the ROI is selected, the deformation vectors can be shown in a separate window (see Fig. 3 for the a region within the ventricles). In this way, the distribution within the selected structure can be monitored, which yields additional information about the deformation.

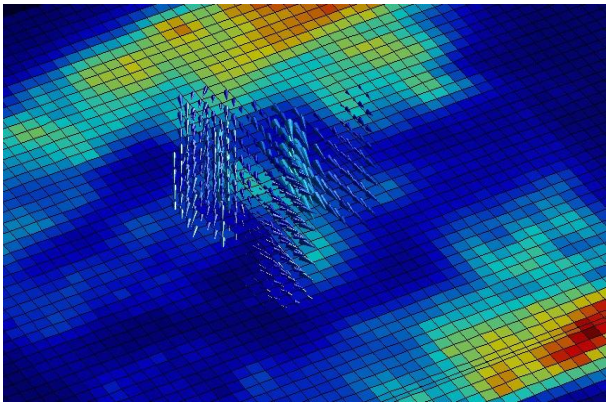

Fig. 3. *Deformation vector plot of 3D ventricle regions in the brain.*

4. VECTOR CLASSIFICATION METHODS

In our present study we have a large number of analytical parameters, whose effectiveness still has to be examined. The results of the measurement of the parameters can be written down into a vector. (In the experiments below we used a seven-component vector). In order to investigate whether information about the difference between AD and NL could be derived from these vectors, we performed several experiments using automated vector classification methods. It is not clear beforehand which method would yield the best results. Therefore we tested three of them, viz. Linear Discriminant Analysis (LDA), K-nearest neighbour (KNN) and Support Vector Machine (SVM).
The LDA method is a way to find a linear combination of features which discriminate two or more classes of objects. The KNN method is a method for classifying objects based on closest training examples in the feature space. KNN is a type of instance-based learning, it is a kind of voting method. The SVM method is used to find an optimal boundary based on a few feature points (support vectors), and it can map non-linear separable features into a higher dimension space and make it linearly-separable. The study we describe below should give a first indication of whether the application of such a method could be developed further and studied in greater detail, for which the discerning effects should be significantly present.

5. EXPERIMENTS AND RESULTS

In our experiments, we used brain MRI data from the ADNI database [4]. We used 19 groups of NL subjects' longitudinal brain MRI images and 12 groups of AD patients' longitudinal brain MRI images as input to compute the displacement field and Jacobian determinant by the 3D Christensen method. Following ref. [3], For each pair of images we applied the method to 16 central slices of a coronal image [3]. For each longitudinal group of data and their derived deformation field and Jacobian determinant, we computed the coefficients given in Eqs. (2)-(5), of the ventricle and hippocampus, and ventricle region size as well as ventricle and hippocampus region divergence as a seven components feature vector. The sizes of the features may play a role. Therefore we study them both in their original range (NonScaled), and with all of them scaled between 0 and 1 (Scaled). As it is not obvious which combination of feature components is the best, we tested these three methods on different combinations of the input features. In addition, we used the leave-one-out cross validation method to test the usefulness of both the features and the classification methods. From the LDA method, we find that for the best combination, the accuracy of the classification for all the data set is 87.1% . When either only AD or only NL are considered, the accuracy is 75% and 94.74%. Thus considering the percentage of AD and NL in our whole dataset(12 in 31, and 19 in 31), it becomes clear that the optimal values cannot be reached when all subjects are considered simultaneously, as is shown in Table 1.

Table 1. optimal classification accuracy for LDA method with different scaled feature

	AD	NL	ALL
NonScaled	75%	94.74%.	87.1%
Scaled	75%	94.74%.	87.1%

For the KNN classification method, we choose the parameter K=2, and from the result, we find that this method can achieve a higher best feature combination classification accuracy (for over all, the optimal accuracy is 93.55%), shown in Table 2. However, it still has the same problem as the LDA method, viz. that the optimal AD, NL and overall optimal accuracy do not occur at the same time. This is because some of the combinations can lead to a very high accuracy in either AD and NL case, but a lower accuracy of the other case. As a result, the optimal overall accuracy can be smaller than both the optimal AD patient accuracy and the optimal NL accuracy. As shown in Table 2, the scale of the features will largely affect the accuracy.

Table 2. optimal classification accuracy for KNN method with different scaled feature

	AD	NL	ALL
NonScaled	100%	90.32%	83.33%
Scaled	91.67%	100%	93.55%

A better solution, that keeps both high accuracy and the simultaneous optimal accuracy for AD, NL and overall data, was obtained by the SVM method with a Quadratic kernel function. From the result, which is shown in Table 3, we can see that it has a high accuracy (90.32% for all sets), while the optimal AD and NL accuracy rate can be achieved at the same time for the original feature data and the Scaled feature data, as shown in Table 3. Thus, in our experiment, the SVM performs better than the LDA and KNN methods. When the SVM method attains its optimal accuracy, the best combination of the input features is**:** Directional Correlation Coefficient of the ventricle and hippocampus, Mean Jacobian Displacement Correlation of the ventricle and hippocampus and Ventricle Region size.

Table 3. optimal classification accuracy for SVM method and Quadratic Kernel function P with different scaled feature

	AD	NL	ALL
NonScaled	75%	100%	90.32%
Scaled	75%	100%	90.32%

6. CONCLUSIONS

In most studies about the effects of AD on the development in time of brain atrophy, the investigation is restricted to the measurement of local effects of diagnostic parameters like the size of the brain deformation or the Jacobian determinant on brain structures like the hippocampus or the ventricles. It is very likely, however, that inter-structural correlations exist in the process of brain aging. Therefore, in this work, we performed a study of the relation of the deformation when correlations between the hippocampus and the ventricles are made. We combined the correlation parameters together with some local deformation parameters into a seven-dimensional vector, and performed a number of vector-classification methods to investigate if such vectors could yield diagnoses that are in agreement with the ground truth data. In order to facilitate the diagnostic analysis, we built a user interface that can visualize the deformation within the structures we want to study, and can facilitate the selection of the regions for which we want to measure the local and inter-structural effects of atrophy. We performed the analysis of the seven-dimensional vectors with the aid of three vector-classification methods, and used them to analyze data from the ADNI database. All three vector methods showed good agreement of the diagnosis with the ground truth data, but the SVM method yielded the best results. We also performed a cross validation to see which parameters were most useful for the diagnosis. We find that the Directional Correlation Coefficient of the ventricle and hippocampus, Mean Jacobian Displacement Correlation of the ventricle and hippocampus and Ventricle Region size are the most useful.

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