Using intelligent system for medical decision-making to magnetic resonance imaging

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Abstract. A new methodology for classification of MR images is proposed using a large data base (more than one thousand patient), for the classification of MCI patients, especially in the case of MCI-C and MCI-NC, using simultaneously all kind of features is proposed. An important goal in this paper is the identification and classification between normal subjects, MCI (Middle Cognitive Impairment) patients and AD patients, and finally, and a very interesting objective is the possibility to classify between Middle Cognitive Impairment Converters (MCI-C, this is, people that suffer a MCI and in the future will have Alzheimer's disease, within 18 months), and Middle Cognitive Impairment Non Converters (MCI-NC, this is, people that suffer a MCI and in the future will not have Alzheimer's disease). Besides, throughout the entire paper different techniques and methods are tested to compare them and determine which those that offer better results are.

1 Introduction

According to the World Health Organization (WHO), in almost every country, the proportion of people aged over 60 years is growing faster than any other age group, as a result of both longer life expectancy and declining fertility rates. This population aging can be seen as a success story for public health policies and for socioeconomic development, but it also challenges society to adapt, in order to maximize the health and functional capacity of older people as well as their social participation and security. Statistics say that from 2000 until 2050, the population of the world aged 60 and over will more than triple from 600 million to 2 billion.

Most of this increase is occurring in less developed countries, where the number of older people will rise from 400 million in 2000 to 1.7 billion by 2050. In Spain, according to the National Institute of Statistic ("Instituto Nacional de Estadística", INE) the population aged over 64 will double in 40 years, being this age group the 30% of the total population in 2049.

Now, focusing on Alzheimer's disease (AD), interesting data and statistics are shown in the "World Alzheimer Report 2011" (ADI, 2011). There are an estimated 35.6 million people in the world with dementia, and this number is expected to increase to 65.7 million in 2030 and 115.4 million in 2050. Already 58% of people with dementia live in developing countries, but by 2050 this will rise to 71%. It is important to note, that neuroimaging, using mainly magnetic resonance, is a powerful tool that adds a positive predictive value to the diagnosis and includes measurements using structural MRI to evaluate medial temporal lobe atrophy and positron emission

tomography using fluorodeoxyglucose (FDG) or amyloid markers [1]. Many studies have focused on quantifying focal atrophy in the temporal lobe [2], [3] and even exist visual scales to quantify the degree of atrophy, which are quick and easy to use. Recently have been published validations of computerized methods to measure the degree of temporal atrophy. In comparison, these methods have a similar discriminatory power [4] with the advantage that they would facilitate measurements and would provide more objective results by standardizing the methods of analysis [5].

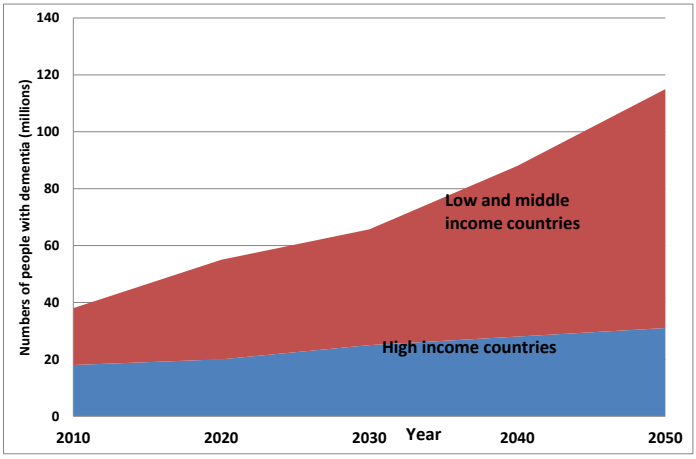


Fig. 1. Evolution of the numbers of people with dementia in low, middle and high income countries in the next years.

There are new development automatic classification systems based on computer intelligent paradigms, mainly such as support vector machine (SVM), that present new diagnostic tools based on T1-weighted MRI [7][8][9][10][11][12]. These approaches can be divided into three different categories, taking into account the type of features extracted from the MRI (voxel-based, vertex-based or ROI-based) [1]. For the voxel-based, the features are the probability of the different tissue classes in a given voxel [13][14]. In the second category, vertex-based, the features are defined at the vertex-level on the cortical surface [12][15]. Finally, the method based on ROI, include mainly the analysis of the hippocampus (study of the of the volume, shape and specific characteristic of the hippocampus) [16][17].

Even these approaches achieve high accuracy (over 85%) , however, they were calculated on different study populations (in fact, the variability between evaluations statistically increased mainly in case where the number of subject is small, typically, there are several approaches that just only less than one hundred subjects are used) making it difficult to compare the obtained results. It is important to note that most the articles published to date for the use of intelligent classification systems Alzheimer's disease has three major drawbacks: a) low number of patients and images; b) Small number of classes to be classified and c) only one type of feature is used.

All these problem are solved in the presented methodology, in which more than 2600 images of MRI are taking into account to classify: Normal patient, MCI-C and MCI-NC patient and finally AD patient.

2 Alzheimer's disease on magnetic resonance imaging

The hippocampus is a major component of the brain. It belongs to the limbic system and plays important roles in the consolidation of information from short-term memory to long-term memory and spatial navigation. The hippocampus is closely associated with the cerebral cortex, and is located in the medial temporal lobe, underneath the cortical surface.

In AD, the hippocampus is one of the first regions of the brain to suffer damage; memory problems and disorientation appear among the first symptoms. The hippocampus can be observed on MRI coronal and axial view, respectively, as it is indicated on the following figure.

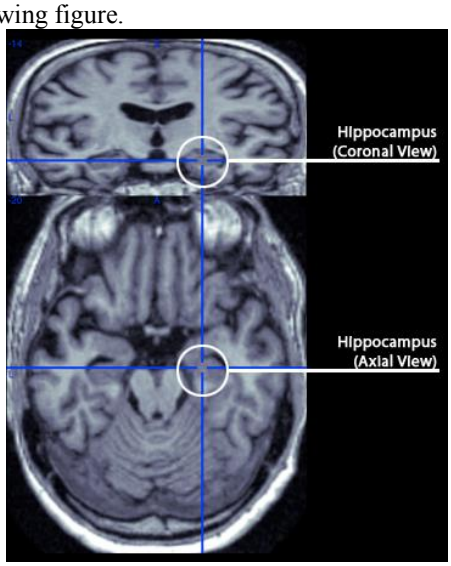


Fig. 2. MRI coronal and axial views of the hippocampus

The structural imaging of the brain with cranial MRI has become a fundamental part of the evaluation of patients suspected of having cognitive impairment or dementia; therefore, it has been included in the new research criteria for AD [2].

In the last decade has increased exponentially the number of neuroimaging studies of degenerative dementias. The main goal of neuroimaging in clinical practice is the identification and exclusion of potentially treatable causes such as brain tumors, hydrocephalus and subdural hematomas. However, imaging techniques can play a key role in other issues of clinical practice such as early detection of patients who can develop dementia, the differential diagnose of distinct dementias or monitoring the disease progression.

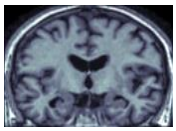
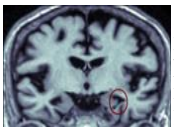
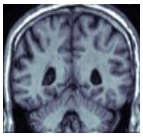
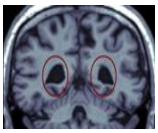
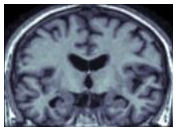
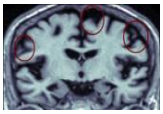
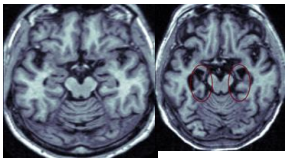
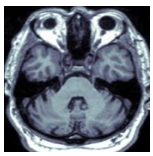
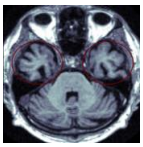
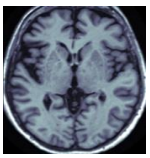
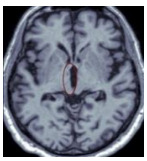
Healthy Patient	Patient with AD	Comment	Healthy Patient	Patient with AD	Comment
		In clinical practice, the width of the horn of the lateral ventricle is the most reproducible measure to asses the atrophy.			Dilatation of the ventricular system as a result of general atrophy.
		Cortical volume loss. General atrophy of the cortex.			Atrophy in the hippocampal region.
		Atrophy of the temporal lobes.			It is possible to observe the dilatation of the third ventricle.

Table 1. Alzheimer's disease on MRI

The structural imaging of the brain with cranial MRI has become a fundamental part of the evaluation of patients suspected of having cognitive impairment or dementia; therefore, it has been included in the new research criteria for AD [2]. So patients with significant episodic memory impairment and temporal lobe atrophy evaluated with MRI may be diagnosed as probable AD. This is a significant step for the detection of the disease in early stages, with the medical, psychological and social advantages that suppose to the patient and the caregiver. Nevertheless, despite many articles have set the relevance of cerebrospinal fluid biomarkers for early and prodomal diagnose of AD, few studies have determined the characteristic changes in MRI of prodomal AD group according to the new proposed criteria which establish the pattern of atrophy in those patients with a pattern of amnesia typical of AD and positive biomarkers [7].

3 Data used

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.ucla.edu). The ADNI was launched in 2003 by the National Institute on Aging (NIA), the National Institute of Biomedical Imaging and Bioengineering (NIBIB), the Food and Drug Administration (FDA), private pharmaceutical companies and non-profit organizations, as a $60 million, 5-year public–private partnership. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography

(PET), other biological markers, and clinical and neuropsychological assessments can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD) [1]. ADNI is a multisite longitudinal clinical/ imaging/ genetic/ biospecimen/biomarker study. Its goal is to determine the characteristics of AD as the pathology that evolves from normal aging to mild symptoms, to MCI, to dementia. ADNI is committed to establishing standardized methods for imaging/biomarker collection and analysis for use in clinical trials.

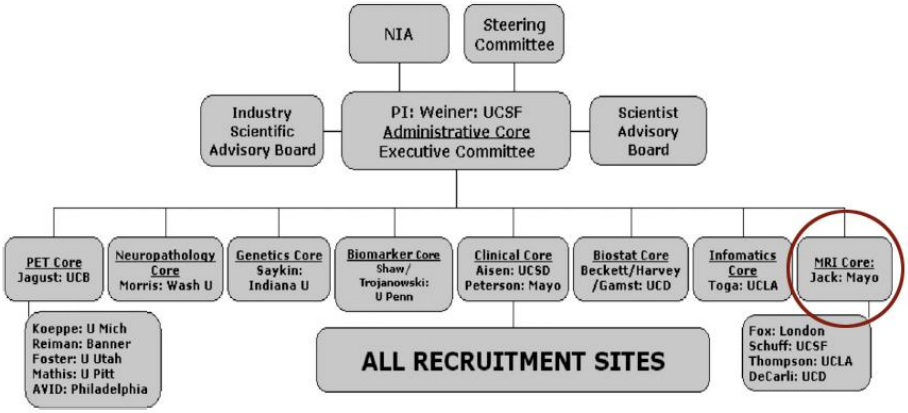


Fig. 3. Governance and organization of ADNI

In this paper, images from 1.5-T and 3-T were simultaneously used. It is important to note, that a pre-processing (normalization) of all the images obtained is carried out, and all the images were visualized one by one, taking into account both the normal image, the gray matter and white matter. Abnormal or defectives images were considered corrupted and therefore discarded. More than 2600 images of different patients (Normal, MCI-C, MCI-NC and AD) were considered.

4 Feature Extraction

In this paper, we need to extract from an image the feature vector that characterizes it. Thus, our features are the approximate wavelet coefficients, using them to generate a classification rule to assist with diagnosis. As described in the following sections the number of features is not as important as robustness to get the best classification accuracy, being robustness in an image application understood as the consistency of the results that certain feature provides across the entire application. Wavelets are mathematical functions that decompose data into different frequency components and then study each component with a resolution matched to its scale. While the Fourier Transform only provides representation of an image based on its frequency content, so it loses time information of the signal, the Wavelet Transform provides both time and frequency information. Therefore, the Wavelet Transform is a better tool for feature extraction from images. The Discrete Wavelet Transform (DWT) is a linear

transformation that operates on a data vector whose length is an integer power of two, transforming it into a numerically different frequency components, and then studies each component with resolution matched to its scale.

Supposed *x(t)* a square-integrable function, then the continuous wavelet transform of *x(t)* relative to a given wavelet ψ(t) is defined as:

$$(1)\ W_{\Psi}(a,b) = \int_{-\infty}^{\infty} x(t)\,\psi_{a,b}(t)dt$$

where

$$(2)\ \psi_{a,b}(t) = \frac{1}{\sqrt{a}}\psi\left(\frac{t-a}{b}\right)$$

To get the DWT, previous equation can be discretized by restraining a and b to a discrete lattice (a = 2b; a > 0; a, b ∈ ℜ). Then, the DWT can be expressed as follows:

$$ca_{j,k}(n) = DS\left[\sum_{n} x(n)g_j^*(n-2^j k)\right]$$

$$cd_{j,k}(n) = DS\left[\sum_{n} x(n)h_j^*(n-2^j k)\right]$$

Here $ca_{j,k}$ and $cd_{j,k}$ refer to the coefficients of the approximation components and detail components, respectively. *g(n)* and *h(n)* denote the low-pass filter and high-pass filter, respectively. *j* and *k* represent the wavelet scale and translation factors, respectively; and *DS* operator means the down sampling. The above decomposition process can be iterated decomposing successively the approximations in turn, so that the signal is broken down into various levels of resolution. In case of images, the DWT is applied to each dimension separately, decomposing an image into four sub-bands which are low-low (LL), low-high (LH), high-high (HH) and high-low (HL); where the LL sub-band can be regarded as the approximation component and it is used for the next level of the 2D-DWT, meanwhile the other sub-bands would be regarded as the detailed component of the image. A 2D-DWT scheme is shown in the following figure.

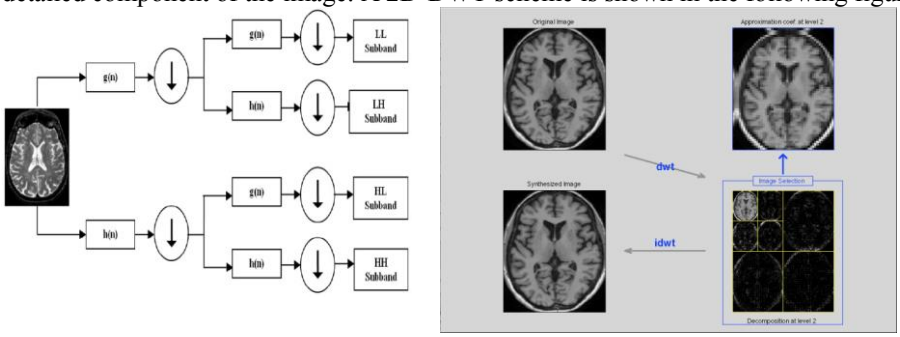


Fig. 4. *A) 2D DWT decomposition scheme; B) Level 2 decomposition of an image using DWT*

At each decomposition level, the half band filters produce signals spanning only half the frequency bands. This makes the frequency resolution two when the

indetermination in frequency becomes a half less, the size of the first level approximation coefficients of an N by N image is N/2 by N/2, the second level is N/4 by N/4 and so on. As the level decomposition is increased, a more compact and less resolution image is obtained.

6 Using Principal Component Analysis for Feature Selection

PCA is a mathematical procedure that uses an orthogonal transformation to convert a set of observations of possibly correlated variables into a set of values of uncorrelated variables called principal components. The number of principal components is less than or equal to the number of original variables.

In other words, PCA finds the lower dimensional representation of the data such that the variance of the reconstructed data is preserved. In this project, PCA help us to minimize the length of the feature vectors, which in addition to increase computation times and storage memory, it also could make classification more complicated (this is known as "the course of dimensionality").

Thus, introducing the feature matrix composed of the wavelet coefficients into the PCA algorithm we obtain a reduced matrix with fewer columns composed of the principal components ordered so that those with the largest variation come first and where the components that contributes the least to the variation in the data set are eliminated.

7 Simulations Results

For the classification of the MR images we used Support Vector Machines technique. In particular, the LIBSVM, which is an integrated software for SVM classification with a MATLAB extension. The best enhancement that LIBSVM provides is the multi-class classification, while most of SVM tools only can classify between two classes. Firstly, we defined the procedure to follow. In the first place, we use the 2D-DWT to perform the feature extraction, then we develop a feature selection algorithm based on PCA and finally we use an SVM classifier. The structure of the procedure is schematically shown at Fig. 5.

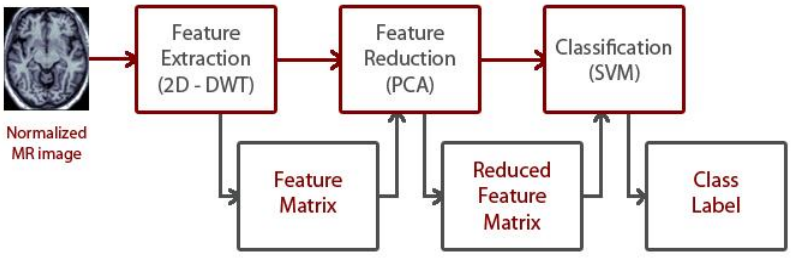


Fig. 5. *Structure of Experiment schematically*

Once the procedure was decided, we had to know what slice or slices where the best to extract the wavelets from them. According to this, we proposed two starting points: a first in which we have no medical expert help and a second in which Doctor Ignacio García Basterra (Neurologist) advises us the slices where the AD can be diagnosed. Thus, in the first option, we have applied the complete procedure shown in Fig. 5 to every slice of every image to set up a ranking of accuracy. Then we used the top 20 slices in the experiment.

Also, in this experiment, we would like to compare the behavior of SVM, against other classifier. For a human expert (an especially for a doctor expert in MRI) it is not easy to understand the knowledge within the model of a SVM. However, there are other types of classifier, than even the precision is lower, the interpretability is more clear (for example, decision trees) and therefore, this classifier are very important to extract the knowledge within the weights associated and understand (from the point of view of a human expert) the rules for the classification carried out.

In this paper, decision trees (DT), linear discriminant analysis (LDA), quadratic discriminant analysis (QDA), naive bayes (NB), support vector machines (SVM) and Radial basic function neural networks (RN) were used.

We will also compare the behavior of these classifiers in four different scenarios: a) using information from the wavelet transform (denoted as D42); b) using information from morphological features (there are a total 100 features, denoted as MRF100); using the 50 more relevant morphological features (MRF50) or the 10 more relevant morphological features (MRF10).

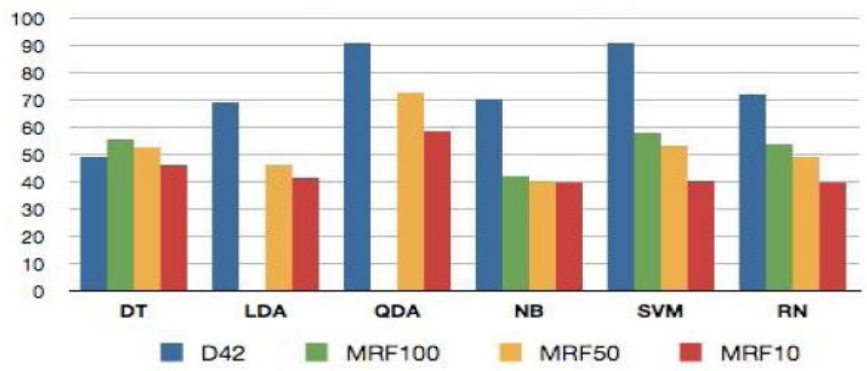


Fig. 6. Comparison of different classifier for classification of the four groups (Normal, AD, MCI-N and MIC-NC).

A second analysis was carried out, but in this case with the purpose of classify two different groups: MCI-N and MCI-NC. The best classifier was the SVM, with the results presented in the following table:

	Maximum	Minimum	Mean	STD
Wavelet	99,25	95,11	97,41	1,17
Morphol. 100	96,27	91,79	94,55	1,52
Morphol. 50	98,13	89,93	94,14	2,50
Morphol. 10	93,28	85,82	90,19	2,31

Table 4. Results of the SVM classifier for the problem MCI-N, and MCI-NC

8. Conclusion

In this papers an advanced classifier that is able to combine different source of information (features) is proposed and compare for different scenarios: the first one where a classification method is focused in obtain normal subjects, MCI-NC, MCI-N patients and AD patients, and finally, and a very interesting goal is the possibility to classify between MCI-N and MCI-NC.

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