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Computerized Technique for Computer-Aided Diagnosis of Dementia Based on Structural MRI Data

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ABSTRACT

Neurodegenerative diseases are frequently associated with structural changes in the brain. Magnetic Resonance Imaging (MRI) scans can show these variations and therefore be used as a supportive feature for a number of neurodegenerative diseases. The hippocampus has been known to be a biomarker for Alzheimers disease and other neurological and psychiatric diseases. However, it requires accurate, robust and reproducible delineation of hippocampal structures. This work utilises a datasets consisting of MR images shared by EADC-ADNI working group . Hippocampus volume is a feature used in this analysis. For the other features we used publicly available brain segmentation package FreeSurfer v.5.1 (FS) (freesurfer.nmr.mgh.harvard.edu) [17] to process the structural brain MRI scans and compute morphological measurements. The FreeSurfer pipeline is fully automatic and provides 184 features per MRI scan in total. Volumes of cortical and sub-cortical structures such as the caudate and average thickness measurements within cortical regions, such as the precuneus. We use the FS features but for hippocampus volume we use the segmentation proposed in [16]. For the diagnosis classification we passed all the features to a C-Support Vector Classifier (C-SVC) with a linear kernel on a 5-fold cross validation. The goal is evaluating the performance of an algorithms for multi-class classification: AD, MCI and controls. Methods that are developed for binary classification can be used for three-way classification by using either a one-vs-one (ovo) or one-vs-all (ova) strategy. In this approach, three classifiers are trained for the three binary problems using the ovo methodology and thereafter their outputs are combined into three predictions.

I. INTRODUCTION

In the last few years the enormous development of neuroimaging has deeply altered the research and clinical prospects in the field of neurodegenerative disorders. This has been particularly relevant for Alzheimerss disease (AD), the most common dementia in the world, affecting currently over 36 millions of people (World Alzheimer Report 2011), a number destined to grow due to the increasing aging population. AD is characterised by the formation and deposition of abnormal proteins in the brain, with subsequent functional disruption, neuronal suffering and cell death (neurodegeneration), the latter ultimately translated into a loss of brain volume (atrophy). The cognitive decline is related to the degree of brain atrophy, which accelerates with the progression of the disease, as detected on MRI at a rate of 2% per year for the whole brain (versus 0.2 − 0.5% in normal aging), and at a rate of 5% per year for the hippocampus, a complex structure located in the medial temporal lobe with a primary role in

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memory and learning, thus making hippocampal atrophy the most important imaging biomarker of the condition [2]. It is not surprising, then, that the accurate measurement of hippocampal volume, is of crucial importance and has become the focus of an increasingly large body of work. Until recently the segmentation of the hippocampus, i.e. its identification and separation from surrounding brain structures, had been performed mainly manually or with semi-automated techniques, followed by manual editing. This is obviously time-consuming and subject to investigator variability, so a number of automated segmentation methods have been developed. These have relied so far mainly on image intensity-based methods, often adopting multi-atlas registration approaches, in order to minimize errors due to individual anatomical variation.

More recently, though, a number of methods that exploit shape information have been developed, based on preliminary work carried out in the nineties with the Active Shape Models (ASM) [1] and the Active Appearance Models (AAM) [3]). ASM address the issue of identifying objects of a known shape in a digital image when the shape is characterized by a certain degree of variability, as in the case of anatomical structures. AAM combine grey-level information with shape information provided by a training set, but this may fail to capture the intrinsic variability of biological structures, a limit attempted to overcome by the use of the wavelet transform and the principal component analysis (PCA) [4]. Alternative methods have used deformable representations or deformable M-reps [5]. Also, algorithms that associate geometric information (obtained by expert priors or learning procedures in a Bayesian framework) to powerful statistical tools, such as region competition algorithms (Zhu and Yuille, 1996) have been combined with homotopic deformations in automated hippocampal segmentation methods[6]. Recent work has employed probabilistic tree frames for brain segmentation [7], at times adopting specific models such as Markovian random fields or graphical cuts [8]. The use of machine learning techniques enables the processing of high-dimensional feature vectors without time-consuming computations thanks to optimization procedures.

II MATERIALS

This work utilises two datasets named DB − 1 and DB − 2. DB − 1 consists of 98 MR images and their corresponding expert manual labels. The dataset is shared by EADC-ADNI working group using a standard harmonized protocol (www.hippocampal-protocol.net). The most inclusive definition of the Harmonized protocol [12] may limit the inconsistencies due to the use of arbitrary lines and tissue exclusion of the currently available manual segmentation protocols. The second dataset used -DB − 2, is from ADNI screening images and cosists of 160 MR images.

III METHODS

Statistical classification is an active area of pattern recognition and computer vision research in which scalar- or vector-valued observations are automatically assigned to specific groups, often based on a training set of previously labeled examples. In medical imaging, different types of classification tasks are performed, e.g., classifying image voxels as belonging to a certain anatomical structure, or classifying an individual scanned into one of several diagnostic groups (disease versus normal, semantic dementia versus Alzheimers disease, for example). We use a

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fully automated method for voxel classification in a brain MRI scan as belonging to the hippocampus versus not. In this method a procedure of training dataset selection based on active learning machine is used during learning of voxel classification according to their Haar-like features, variables that describe complex images based on a statistical analysis of adjacent groups of voxels. The system consists of three processing levels: (a) linear registration of all brains to a standard template and automated method to capture the global shape of the hippocampus. (b) Feature extraction: all voxels included in the previously selected volume were characterized by 315 features computed from local information. (c) Voxel classification: a Random Forests algorithm was used to classify voxels as belonging or not belonging to the hippocampus.

IV. COMPUTATIONAL INFRASTRUCTURE

The method is developed in ITK and MATLAB framework for hippocampus segmentation and we use FS to brain feature extraction. The computational resources required is about 13 hour per image. Therefore the availability of distributed computing software environments and adequate infrastructures was of fundamental importance. In this study, the LONI pipeline processing environment [21, 22] was used: a user-friendly and efficient software for complex data analyses, available at http://pipeline.loni.ucla.edu. The present study was carried out using the local computer farm BC2S 3 : a distributed computing infrastructure consisting of about 5000 CPU and allowing up to 1,8 PB storage. A further study for grid deployment was also performed, with the aim of creating a pipeline tool suitable for large clinical trials. It was carried out on the European Grid Infrastructure (EGI) which consists of about 300 geographically distributed sites around the world. In particular all the results presented in this study were obtained on the BC2S using the 484 MR images at our disposal. the run-time reduction with the grid implementation allowed to produce results in a reasonable time with respect to the application execution as a sequential process on limited resources. The advantages of the grid execution are evident since we obtained the 90% of the analysis of 484 images after less than 16 hours.

V. CONCLUSION

Compute our estimates of the performance metrics (ACC, AUC) for 5-fold cross validation extracting random the test set. Results showed that our method performs very good in discriminating the three classes (CTRL, MCI, and AD), in line with those of literature.

The proposed fully automated approach may be suitable for large-scale research studies, in the first instance on Alzheimers disease, where the hippocampal volume and morphological changes are important biomarkers, potentially also on other brain disorders in which atrophy and structural brain changes plays a relevant pathogenetic role.

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