International Journal of Basic and Applied Sciences, 1 (2) (2012) 100-108
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Prediction of Possible conversion from MCI to AD using Machine learning[1]

Rahila Umer[1], Sohrab Khan[2], Aftab Ahmed[3], Khaled Rasheed[4], Tianming Liu[5]

[1]Assistant Professor,
Department of Computer Science,
BUITEMS, Quetta.
rahilaumer@buitms.edu.pk

[2]Assistant Professor,
Department of Computer Systems Engineering & Sciences,
BUET, *Khuzdar*
sohrab@buetk.edu.pk

[3]Associate Professor,
Department of Computer Science,
BUITEMS, Quetta.
Aftab.ahmed@buitms.edu.pk

[4]Associate Professor,
Department of Computer Science, University of Georgia
Athens, GA 30602, USA
khaled@cs.uga.edu

[5]Assistant Professor,
Department of Computer Science, University of Georgia
Athens, GA 30602, USA
tliu@cs.uga.edu

[1] Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu/ADNI). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://www.loni.ucla.edu\ADNI\ Collaboration\ADNI_Authorship_list.pdf

Abstract

Alzheimer's is an irreversible brain disease that impairs memory, thinking and behavior and leads ultimately to death. It is a major public health problem in the elder population and has a huge impact on society. It is useful to diagnose AD as early as possible, in order to improve the quality of life of the patient and their care takers. In this study we analyze the performance of different machine learning methods to predict the possible conversion from MCI to AD. We conducted many experiments with various learning algorithms and achieved performance levels comparable to the published results in this domain. The results are very promising and demonstrate the utility of machine learning methods in this domain.

Keywords: *Alzheimer's disease, Mild cognitive Impairment, Machine learning, Neural network Support vector machine.*

1 Introduction

There is an active research going on to delay the onset or slow down the progression of AD. Early diagnosis of AD helps both the patients and their caregivers to improve the quality of their lives. There are treatments that slow down the disease progression and help in prevention [1]. However this is only possible if the AD is diagnosed with high accuracy in its early symptomatic stage.

Many scientists believe that there is a transitional stage between normal aging and AD termed as mild cognitive impairment (MCI). During this stage a person experiences more memory loss that cannot be linked to age problems but also not severe enough to point to probable AD. MCI has high chance to turn to AD. Research shows that there is evidence that 10% to 15% of MCI subjects turn to probable AD per year [2]. While for a healthy person it is just 1% to 2%. As a result MCI got more attention among researchers.

One of the major objectives of ADNI (Alzheimer's Disease Neuroimaging Initiative) is to find bioglocial biomarkers to measure the progression of MCI and probable AD. For that they are using advanced brain imaging techniques and clinical and neurological assessments to assess the progression of the disease. Finding biomarkers will help in the early diagnosis of AD and in the development of treatments.

MCI does not fulfill the criteria for probable AD that makes it more challenging to predict the prior conversion from MCI to probable AD. Most of the researchers are focusing on brain imaging techniques to predict the conversion of MCI to probable AD.

2 Previous Work

This section briefly surveys the previous work done in this domain.

The Classification of different stages of Alzheimer's disease using machine learning methods was addressed in [3]. Stages of AD are divided as Mild, Moderate and Severe AD. The dataset used in that paper was collected at the National Institute on Aging NIA. Many machine learning algorithms are compared based on accuracy and run time. For the evaluation of the classifier they used a testing set. In that study, the highest accuracy achieved was 99.55%.

In [4] a predictive model is developed using machine learning methods where focus is to identify the possible conversion from MCI to AD. The dataset used in the study was from the ADNI database. They used the Area under the ROC curve (AUC) as a metric of performance measurement for the classification. The highest accuracy they got was 0.887 AUC. However they are using an oversampling technique called SMOTE which produces new (hypothetical) instances for the rare class and which may not be authentic in a biomedical domain.

In [5] Support vector machines (SVM) are used to distinguish between subjects as AD or elderly control subjects by using whole brain Magnetic Resonance Images (MRI). The dataset was comprised of 16 subjects with AD and 22 elderly control subjects. The highest classification accuracy obtained was 94.5% with specificity of 96.6% and sensitivity of 91.5%.

In [6] the authors proposed a computer aided diagnosis system for the early diagnosis of Alzheimer's disease using Single Emission Computed Tomography (SPECT) images. The proposed method is based on random forests as a predictor. With the help of feature extraction algorithms, the highest accuracy achieved is 96.9% with sensitivity of 100% and specificity of 92.7%.

In [7] Support vector machines with an SVM based feature selection method were trained to differentiate between AD and healthy controls, then this trained model is used to predict possible conversion from MCI to AD. This classification was based on the Structural Magnetic Resonance Imaging data**.** The highest accuracy achieved was 90.5% for classifying AD and healthy control, and 72.3% accuracy for predicting MCI conversion to AD.

The goal of our study is to predict the probable conversion of MCI to AD based on only clinical data using machine learning methods.

3 Prediction dataset

The data set used for this study is comprised of clinical information about each subject including recruitment, demographic, physical and neurological examination, cognitive assessments, patient medical history and baseline diagnosis and symptoms. For the prediction dataset we have two types of datasets.

3.1 Training Dataset

For training classifiers we have a dataset where the subjects are diagnosed in month 06 as Normal or MCI or AD. We have a total of 732 subjects' data and their diagnosis in month 06. 212 subjects are diagnosed as Normal, 341 as MCI

and 179 are diagnosed as AD. However in the training dataset we will just include the data for subjects that are diagnosed as normal and AD, excluding the MCI subjects. We name this the *Baseline* dataset.

3.2 Testing Dataset

For testing purposes we have three datasets each dataset is the follow up diagnosis of the subject for three years after baseline. Each dataset is comprised of two groups, *MCI stable:* All subjects that were diagnosed MCI in baseline and remained MCI till three years and *MCI converters:* Subjects that were diagnosed MCI in baseline and they turned to AD in later stages. Table 1 shows the details of each group.

Table 1: Prediction Dataset Details

Baseline	**Normal**	**MCI**		**AD**
		MCI-S	**MCI-C**	
Baseline	212	NILL		179
Month 12		294	43	
Month 24		236	92	
Month 36		9	7	

4 Experimental Setup

Our main objective in this study is to improve the prediction performance (sensitivity and specificity) by evaluating all available diagnostic information with machine learning techniques.

We used the University of Waikato's WEKA [8] software package, to run the experiments. In the current study we use multiple machine learning methods and compare their accuracy for prediction of subjects that are diagnosed as MCI in baseline, predicting either they will remain MCI or will turn to probable AD. We used the training dataset that is already discussed in previous section-termed as *baseline*. For testing purposes we have three datasets that are the diagnoses of the subjects after baseline - i.e. month 12, month 24 and month 36, each of these datasets are representing the diagnosis at different stages.

We train the classifier using the baseline dataset that is comprised of the subjects diagnosed as purely healthy and pure AD and test it with follow up diagnosis of MCI subjects after the baseline, where we have subjects from two groups MCI stable (those who will remain MCI) and MCI converted (those who turned to AD

after baseline). We also include the subjects that were MCI in base line and turned to Normal in MCI stable. In both datasets we have two classes: 1 represents that the subject will not turn to AD and 0 represents that the subject will turn to AD.

5 Performance Measurement

Our main focus of this study is to measure the classifier's performance to predict the probable conversion from MCI to AD. It is a binary classification problem but we are more interested in one class (i.e. to predict probable AD conversion from MCI). In such cases overall classification accuracy is not the most important measure of performance. We use metrics such as Sensitivity and Specificity and the Area Under the Curve (AUC) to evaluate the performance of learning algorithms. All of those metrics are functions of the confusion matrix.
A completely random predictor would generate a straight line at an angle of 45 degrees with the horizontal, from bottom left to top right. Classifiers with ROC curves higher than this straight line are better than a random classifier. The statistic that is most commonly calculated from the ROC for comparing classifier performance is the Area under ROC Curve (AUC).

Fig 1: Month 12 Prediction accuracy comparison

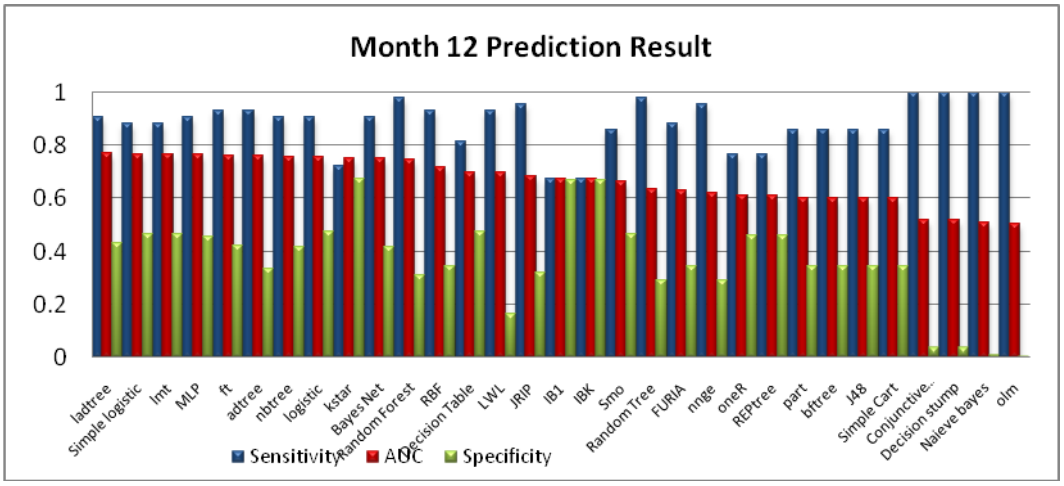


Fig 2: Month 24 Prediction accuracy comparison

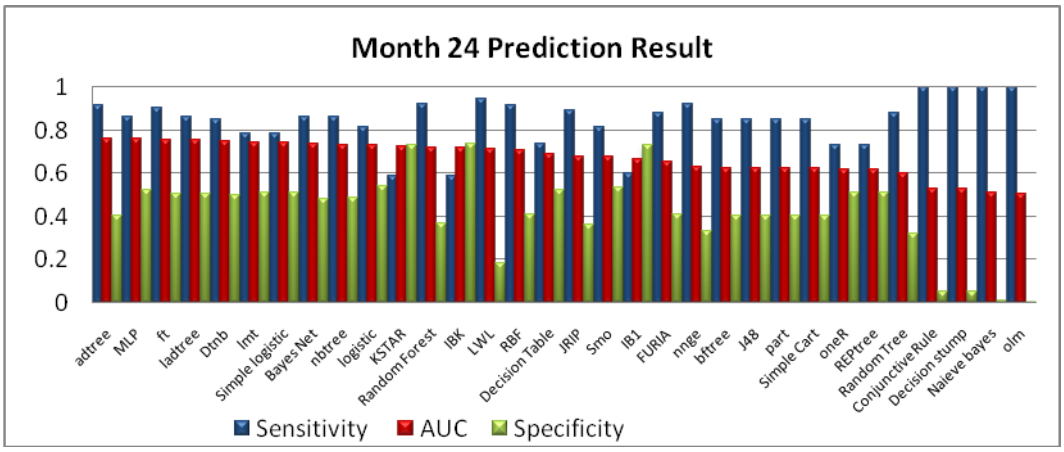
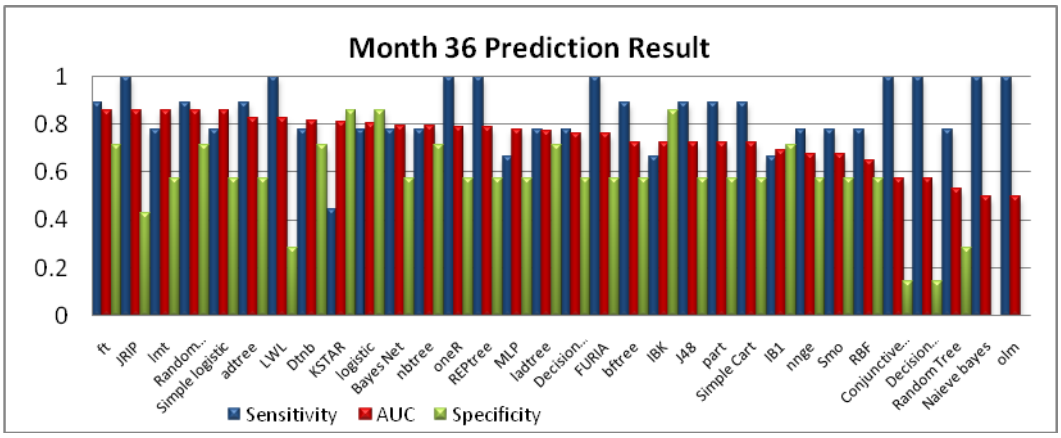


Fig 3: Month 36 Prediction accuracy comparison



6 Prediction Result

Figures 1 through 3 show the prediction accuracy of different machine learning algorithms based on sensitivity, specificity and AUC. In the figures, the learning algorithms are sorted in descending order of AUC.
The results show that for all classifiers there is a tradeoff between sensitivity and specificity. In our case our testing class is imbalanced and the rare class is of more interest. Thus it is desirable to have a classifier that gives high prediction accuracy over the rare class (AD), while keeping reasonable accuracy for the majority class (NOT AD). We used all of these metrics to get a classifier that gives best result.
As we discussed earlier, overall accuracy is not important in the current scenario. Prediction results show that all classifiers' sensitivity is higher than specificity for all datasets. LADTree, ADTree and FT classifiers are selected as best classifiers based on AUC for Month 12, Month 24 and Month 36 accordingly. We can see that there are classifiers with higher sensitivity (i.e. 100%) but their specificity values are very low and so are their AUCs.

7 Conclusion

This study applies a variety of models for the prediction of possible conversion of MCI to Alzheimer's disease, based on different cognitive tests, physical examinations, age, mental status examination and neuropsychiatry assessments. For the prediction of MCI to probable AD conversion, our results are promising. We get up to 87% sensitivity but there is a trade-off between sensitivity and specificity which can be controlled using cost-sensitive classifiers. Considering sensitivity, specificity and AUC we still get very promising results. These results are very helpful for predicting the future diagnosis of MCI patients that either they will remain MCI or will convert to AD. However, we cannot directly compare our results to the few other published papers in this domain as our datasets and methods are different.

ACKNOWLEDGEMENTS

Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904). ADNI is funded by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, and through generous contributions from the following: Abbott, AstraZeneca AB, Bayer Schering Pharma AG, Bristol-Myers Squibb, Eisai Global Clinical Development, Elan Corporation, Genentech, GE Healthcare, GlaxoSmithKline, Innogenetics, Johnson and Johnson, Eli Lilly and Co.,Medpace, Inc.,Merck and Co., Inc., Novartis AG, Pfizer Inc., F. Hoffman-La Roche, Schering-Plough, Synarc, Inc., as well as non-profit partners the Alzheimer's Association and Alzheimer's Drug Discovery

Foundation, with participation from the U.S. Food and Drug Administration. Private sector contributions to ADNI are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Disease Cooperative Study at the University of California, San Diego. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of California, Los Angeles. The support of the Alzheimer's Disease Neuroimaging Initiative (ADNI) is very much acknowledged by the authors.

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