ISSN 2278-3091
Volume 8, No.1.4, 2019
International Journal of Advanced Trends in Computer Science and Engineering
Available Online at http://www.warse.org/IJATCSE/static/pdf/file/ijatcse0581.42019.pdf
https://doi.org/10.30534/ijatcse/2019/0581.42019

Early detection of Alzheimer's disease using predictive k-NN instance based approach and T-Test Method

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ABSTRACT

Nowadays various neural network algorithms are used in the classification of clinical data for human conditions such as Alzheimer's disease, which can extract low-to-high-level features. Classification of clinical data for Alzheimer's disease has always been challenging as currently there is no clinical test for Alzheimer's disease. Doctors diagnose it by conducting assessments of patients' cognitive decline. But it's particularly difficult for them to identify mild cognitive impairment at an early stage when symptoms are less obvious. Also, it is difficult to predict whether patients will develop Alzheimer's disease or not. The accurate diagnosis of Alzheimer's disease in the early stage is important in order to take preventive measures and to reduce the severity and progression before irreversible brain damages occur. The effectiveness of abnormality detection depends on the accuracy and robustness of the algorithm used. Different machine learning techniques with different levels of sensitivity, efficiency, and accuracy have been developed. In this paper, a feature selection using T-Test method for joint regression and classification via instance based k-Nearest Neighbor classifier is proposed for Alzheimer's disease detection. Also, we compare the accuracy measures and performance of the proposed method with existing techniques in Alzheimer's disease detection. The new method gives a better accuracy results compared to conventional methods.

Key words: Alzheimer's disease, Machine Learning, Feature Extraction, K-Nearest Neighbor, Pattern Recognition, Data Mining

1. INTRODUCTION

Alzheimer's disease is an accelerating and irremediable neurologic brain disease that slowly destroys brain cells and thereby resulting in memory losses, and ultimately loss of the ability to carry out even the simplest tasks. The cognitive decline caused by this syndrome ultimately leads to dementia [1]. It is the most common form of dementia in adults aged 65 and older. The worldwide prevalence of AD was reported to 50 million in 2019 and is expected to increase twice by 2050. The disease begins with mild degeneration in memory and gets worse. Magnetic Resonance Imaging (MRI) is an efficient imaging technique to detect Alzheimer's disease without using harmful radiations. It is possible to find the shape, size and position of abnormalities using MRI. Detecting Alzheimer's disease by psychologists requires very careful medical analysis along with other physical and neurological exams. It is a strenuous job for the technicians to categorize and analyze these images manually. Hence the use of automatic detection methods became popular. Abnormalities can be easily identified using various neural network methods. Alzheimer's disease progression is classified into seven stages:

Stage 1: No Impairment- During this stage, no memory problems or other symptoms of dementia are evident and hence Alzheimer's disease is not detectable at this stage.

Stage 2: Very Mild Decline- The people aged 65 and above may notice minor memory problems, although not to the point where the memory loss can easily be distinguished from normal age related memory loss.

Stage 3: Mild Decline- At this stage, memory and cognitive problems are noticeable and physicians will be able to detect impaired cognitive function.

Stage 4: Moderate Decline- During the fourth stage of Alzheimer's disease, patients will have short term memory and face difficulty in doing even simple arithmetic.

Stage 5: Moderately Severe Decline- During the fifth stage of Alzheimer's, patients need help to perform daily activities.

Stage 6: Severe Decline- Patients with the sixth stage of Alzheimer's disease need supervision as the ability to perform basic activities of daily life becomes compromised.

Stage 7: Very Severe Decline- In stage seven of the disease, patients lose the ability to respond to their environment or communicate [2]. At this stage, patients require continuous assistance for survival.

In Alzheimer disease, death of brain cells and development of tangles and plaques in brain results in memory loss. Early diagnosis of AD is important for the control of the disease and for preventing the loss of ability to carry out even the simplest tasks. Machine learning techniques uses various algorithms to obtain the required data from MRI images and parse it, learn from it, and make a prediction out of the input data given [3]. So in order to accomplish a particular task, the system is “trained” using algorithms, which provides the ability to learn and perform the task. It uses cascade chains of different processing units for feature extraction and transformation. Each of the successive layers utilizes the output from the previous layer as inputs. The algorithms used may be supervised for pattern analysis applications and unsupervised for applications include classifications.

2. EXISTING METHOD

Various biomarkers are used to evaluate the biological changes carried due to Alzheimer’s disease. The different biomarkers like cerebrospinal fluid (CSF) biomarker in MRI brain images was utilized to detect Alzheimer’s disease and to track the progression of the disease. Here variations in the level of biomarkers are used for the diagnosis of AD. A set of serum markers have been discovered which may occur due to inflammatory actions in the central nervous system during the early course of AD [4]. This technique is the most acceptable method to diagnose AD with high specificity and sensitivity. But Biomarkers are not useful for early diagnosis of the disease. Moreover, it must use an intra cerebral ventricular injection. To collect the CSF the clinical employees have to take utmost care without damage brain tissues and spinal card. This is one among the foremost important mechanism to estimate the Alzheimer’s where they estimate the tangle and plague of the brain tissues for Alzheimer’s analysis.

Recently volumetric analysis is used for analyzing manually or semi-automatic techniques using SPM-5 in MATLAB Environment [5]. There the neurologist need to calculate the total volume of the different regions such as white matter, gray matter, CSF and sum together come to conclusion about the stage of the disease.

3. PROPOSED METHOD – PREDICTIVE K-NEAREST NEIGHBOR INSTANCE BASED APPROACH

Different powerful machine learning algorithms that extract low-to high-level features from MRI images for detection of Alzheimer disease have been developed by Scientists. Here KNN instance based method is used to detect and find the severity of Alzheimer’s disease (AD) [6, 7]. The k- Nearest Neighbor (KNN) algorithm is one of the simplest and most elegant classification methods. The KNN classifier distinguishes the ailment by examination of components that determines the data vectors by considering the classes. This method increases the efficiency and the performance in data mining. The time taken for classification is also reduced.

In the proposed method, Input Datasets having more number of data’s which contains all type of information’s including the Normal, Mild cognitive Impairment (MCI), and the Alzheimer’s disease (AD) are created. At first the MRI input image is fed to a pre-processing unit. Pre-processing guarantees effective operation of disease analysis. The main purpose of data pre-processing is to reduce the amount of features used for classification method [8]. Data pre-processing techniques involves data collections and processing the information. Feature extraction is a common method that contains all measured data are as both informative and non-redundant for the disease analyzing purpose [9]. The T-test method is used for Feature Selection. This method is used to assess whether the means of two classes are statistically different from each other by calculating the ratio between the difference of two class means and the variability of two classes [10]. We map the original feature into the target space to identify the informative and predictive features by k-Nearest Neighbor classifier. k-Nearest Neighbor learning algorithm assumes all instances correspond to points in the n-dimensional space R^n. The nearest neighbors of an instance are defined in terms of Euclidean distance. Euclidean distance between the instances Xi = <Xi1,…,Xin>and Xj = <Xj1,…,Xjn> is given by

$$d(Xi,Xj)=\sqrt{\sum_{r=1}^{n}(Xi-Xj)^2} \qquad (1)$$

For a given query instance Xq, f(Xq) is calculated the function values of k-Nearest Neighbor of Xq. The learning is carried out as follows:

- Store all training examples<Xi,f(Xi)>
- Calculate f(Xq) for a given query instance Xq using k-Nearest Neighbor
- Nearest neighbor: (k=1)
  – Locate the nearest training sample Xn, and estimate f(Xq) as
  f(Xq) ←f(Xn)
- k-Nearest Neighbor:
  – Locate k nearest training examples, and estimate f(Xq) as
  – If the target function is real-valued, take mean of f-values of k-Nearest Neighbor.
  – If the target function is discrete-valued, take a vote among f-values of k-Nearest Neighbor.

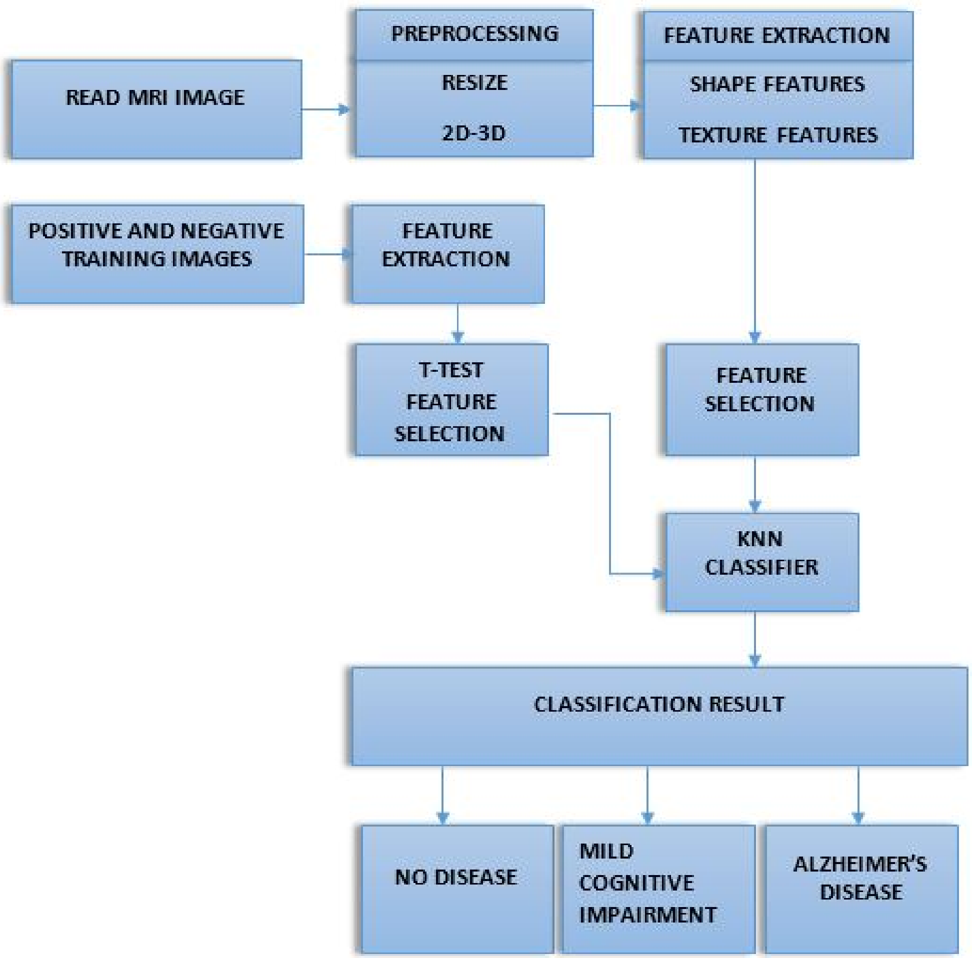


Figure 1: Work Flow of Proposed System – Instance Based k-NN Approach

The Figure 1 represents different stages in detection of Alzheimer Disease (AD) from the datasets by using instance based KNN Classification algorithm

4. PERFORMANCE ANALYSIS

In this work, three classes are separated for the analysis

- Class 1-Alzheimer's Disease (AD)
- Class 2- Mild Cognitive Impairment (MCI)
- Class 3- No Disease

The four parameters deliberate such as TP (True Positive), TN (True Negative), FP (False Positive), and FN (False Negative) is used to classify the normal, MCI and AD images present in the Datasets.

4.1 Classification Accuracy

The closeness of a measured value to the standard or known value is termed as accuracy.

$$\text{Classification Accuracy} = \frac{TP+TN}{P+N} \quad (2)$$

Or

$$\text{Classification Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (3)$$

4.2 Time Consumption

Time taken to obtain the result is available from MATLAB results viewer.

5. RESULTS AND DISCUSSIONS

The input images used for the research is taken from Alzheimer's Disease Neuroimaging Initiative (ADNI) database that consists of 140 samples those between ages 18 to 87.The parameter metrics such as Accuracy and Time Consumption is analysed.

Table 1: Parameters measurements of different classes

Parameters	Class 1	Class 2	Class 3
TP	81	44	52
TN	66	15	44
FP	0	0	6
FN	6	3	0

Table 1 shows the parameters such as TP, TN, FP and FN having measures of different classes which indicates the disease in database.

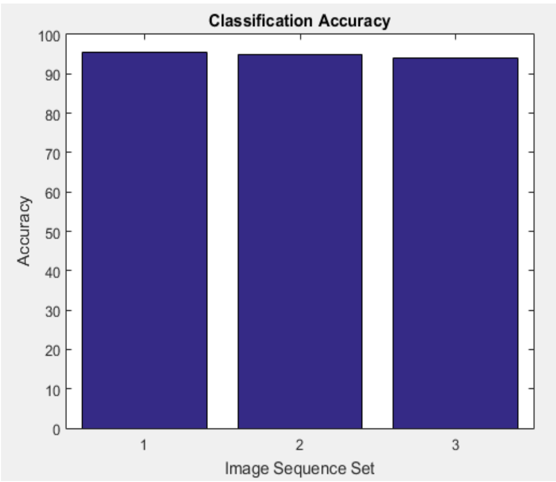


Figure 2: Accuracy

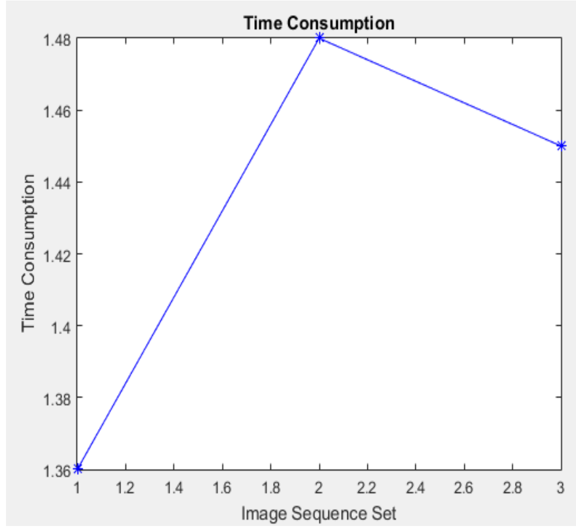
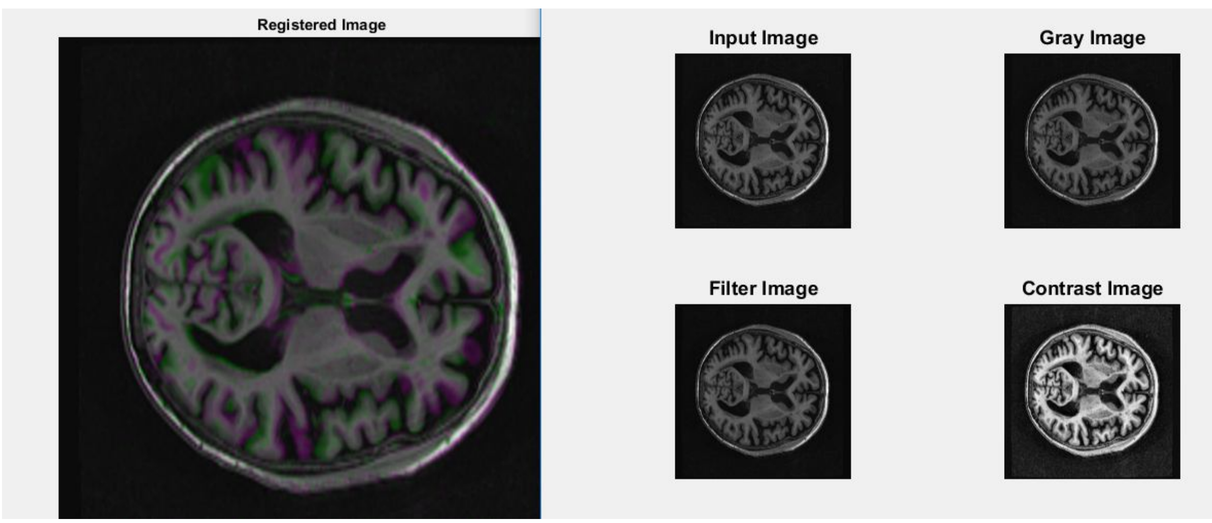
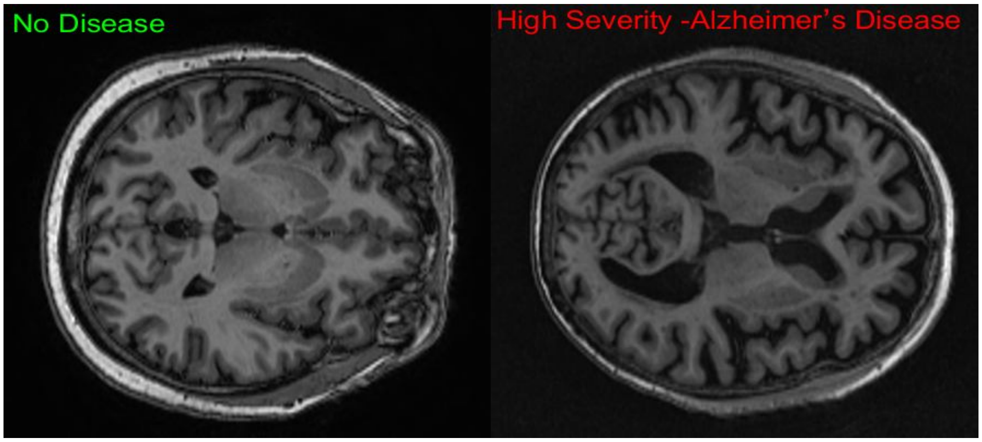


Figure 3: Time Consumption

The Figure 2 indicates the Accuracy and Figure 3 indicates Time Consumption during the prediction of Alzheimer's disease using instance based k-Nearest Neighbor algorithm. From the analysis, the accuracy rate is found to be 96% and the rate can be further increased by adding more training images. The below images in Figure 4 shows the output from MATLAB.



(a)



(b)

Figure 4: Results: (a) Image registration process (b) MRI of Alzheimer's patient after classification

6. COMPARISON OF PROPOSED METHOD WITH OTHER EXISTING METHODS

The recent neural network techniques used for the automatic diagnosis of Alzheimer's disease is briefly described below.

A Probabilistic Neural Network

The Probabilistic Neural Network for classification of AD extracts the features using coherence discriminates [11].This method yields a classification rate of 95%.

B Discriminative sparse learning method with relational regularization

Baiying Lei introduced a novel discriminative sparse learning method with relational regularization to predict the clinical score and classify AD disease stages using various multimodal features [12]. A discriminative learning technique is applied to expand the class specific difference and include geometric information for effective feature selection. The classification accuracy of the proposed method is 94.68%.

C SVM and combination of the Discrete Wavelet Transform and the Principal Component Analysis

Jesia Mathew and LasithaMekkayil developed a Robust Algorithm for Early Detection of Alzheimer's Disease using Multiple Feature Extractions. A combination of the Discrete Wavelet Transform (DWT) and the Principal Component Analysis (PCA) is used for the feature extraction and classification is carried out using the Support Vector Machine (SVM) [13]. The multiple feature extractions with both the DWT and the PCA together give an accuracy of 91%.

D SVM and Wavelet Transform

Priyanka Thakare developed Alzheimer Disease Detection AI system. In this work, by using wavelet transform feature extraction is carried out and classification is done by support vector machine [14]. It gives an accuracy of 94%.

E Shape-constrained regression-forest algorithm and SVM

Jun Zhang proposed a landmark-based feature extraction method based on a shape-constrained regression-forest algorithm [15]. SVM is used for classification. The AD classification accuracy is 83.7%.

F Grading Biomarker using Sparse representation techniques and SVM

Tong proposed A Novel Grading Biomarker for the Prediction of Conversion from Mild Cognitive Impairment to Alzheimer's disease. The grading biomarker is calculated for each MCI subject using sparse representation techniques [16]. SVM is used for classification in this system. The classification accuracy is 92% when age and cognitive measures are combined with the proposed grading biomarker.

G Voxel-wise GM and LDS

Moradi, A. Pepe, C. Gaser, H. Huttunen, and J. Tohka proposed a machine learning framework for early MRI-based Alzheimer's conversion prediction based on Voxel-wise GM and LDS [17]. Experimental results provide an accuracy of 83%.

H Data-driven ROI GM and SVM ensemble

M. Liu, D. Zhang, and D. Shen introduced a view-centralized multi-atlas classification for Alzheimer's disease diagnosis using Data-driven ROI GM and SVM ensemble as classifier [18]. The experimental results provide an accuracy rate is 92.51%.

I Data-driven ROI GM and SVM

R. Min, G. Wu, J. Cheng, Q. Wang, and D. Shen proposed a multi-atlas based representations for Alzheimer's disease diagnosis using Data-driven ROI GM and SVM classifier [19]. This method provides an accuracy rate of 91%.

J ROI-wise cortical thickness measurements and Linear Discriminant Analysis(LDA)

S. F. Eskildsen, P. Coupé, D. García-Lorenzo, V.Fonov, J.C. Pruessner, and D.L. Collins introduced a method for prediction of Alzheimer's disease with mild cognitive impairment from the ADNI cohort using patterns of cortical thinning [20]. The classification technique used for this method is Linear Discriminant Analysis. Accuracy rate is found to be 84.50%.

K Voxel-wise GM and RVR

C. Gaser proposed a method for early detection of Alzheimer's disease using Voxel-wise GM and Relevant Vector Regression (RVR) classifier [21]. The accuracy rate is found to be 84.6%.

L Ensemble Random forests

K. R. Gray proposed Random forest-based similarity measures for multi-modal classification of Alzheimer’s disease [22]. The accuracy rate obtained is 89%.

M Voxel-Stand-D GM and SVM

R. Cuingnet proposed an automatic classification of patients with Alzheimer's disease from structural MRI [23]. This method uses Voxel-Stand-D GM along with SVM classifier. This method gives an accuracy of 88.58%.

N ROI GM and SVM

D. Zhang, Y. Wang, L. Zhou, H. Yuan, and D. Shen proposed a multimodal classification of Alzheimer's disease and mild cognitive impairment using ROI GM and SVM classifier [24]. Experimental results provide an accuracy of 86.20%.

O Tensor-base Morphometry and Linear regression

J. Koikkalainen introduced a Multi-template tensor-based morphometry for early diagnosis and analysis of Alzheimer's disease [25]. The accuracy rate of this method is obtained as 86%.

TABLE 2: Accuracy values of different Machine Learning Techniques

Machine Learning Techniques	**Accuracy**
Instance Based K-Nearest Neighbour [New proposed method]	96%
Probabilistic Neural Network [11]	95%
Discriminative sparse learning method with relational regularization [12]	94.68%
SVM and combination of the Discrete Wavelet Transform and the Principal Component Analysis [13]	91%
SVM and Wavelet Transform [14]	94%
Shape-constrained regression-forest algorithm and SVM [15]	83.7%
Grading Biomarker using Sparse representation techniques and SVM [16]	92%
Voxel-wise GM,LDS [17]	83%
Data-driven ROI GM, SVM ensemble [18]	92.51%
Data-driven ROI GM,SVM [19]	91%
ROI-wise cortical thickness, LDA [20]	84.50%
Voxel-wise GM, RVR [21]	84.6%
Ensemble Random forests [22]	89.0%
Voxel-Stand-D GM,SVM [23]	88.58%
ROI GM,SVM [24]	86.20%
Tensor-base Morphometry, Linear regression [25]	86%

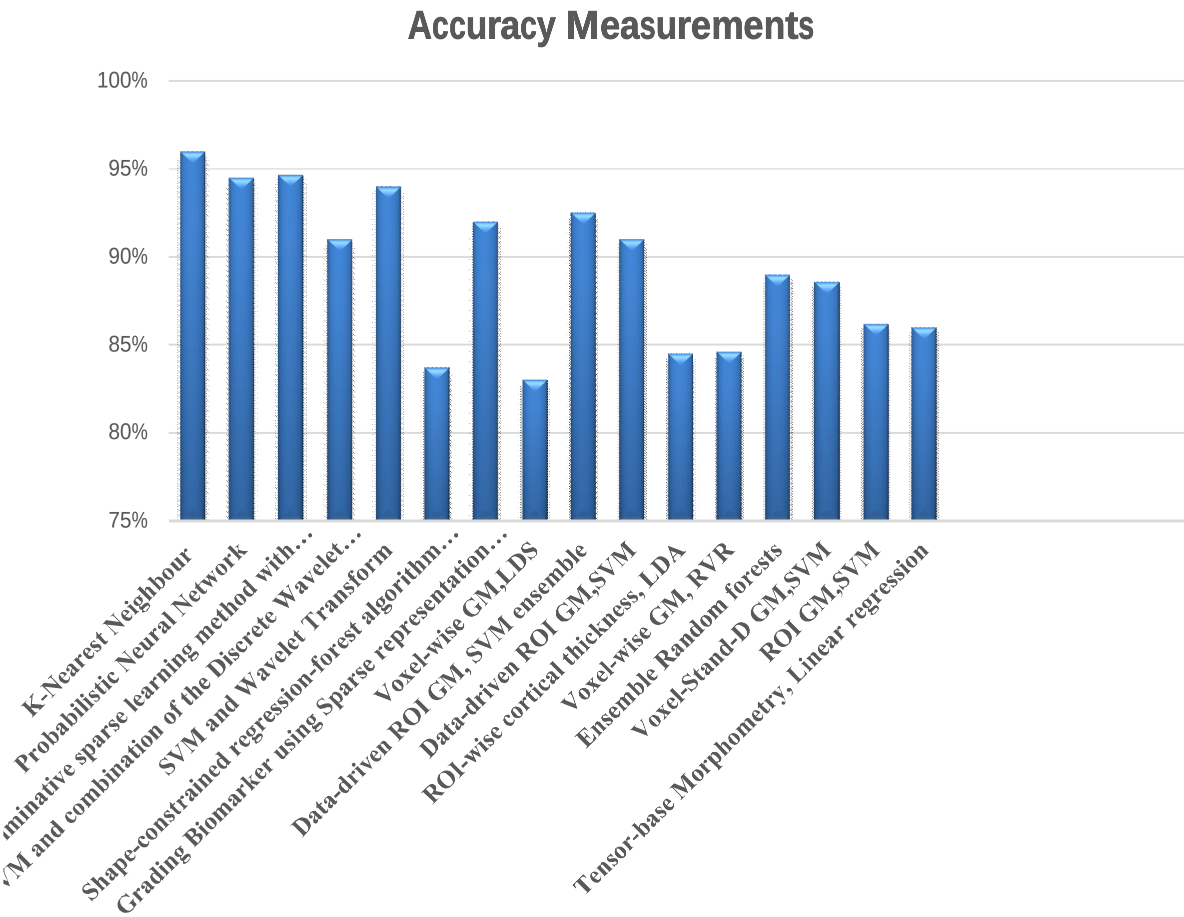


Figure 5: Accuracy of different Neural Networks algorithms

Various recent neural network techniques used in feature extraction and classification accuracy values for early prediction of Alzheimer's disease is shown is Table 2 and the accuracy measures of different existing Neural Networks algorithms is shown in Figure5.

7. CONCLUSION

In this work, an instance based k-Nearest Neighbor classifier using T-Test method for joint regression and classification is proposed for Alzheimer's disease detection. The results have been analyzed in terms of accuracy and time consumption. This paper also provides a high level overview and comparison of classification accuracy of recent neural network classifier algorithms used for early detection of Alzheimer's disease. From the analysis results it is evident that the accuracy measures and performance of the new method is relatively high when compared to existing techniques in early prediction of Alzheimer's disease. The computational complexity of new method is low when compared to other methods. Hence the cost of implementation of the application is also relatively less. The future work intends to combine the different feature extraction methods with the classification algorithm to yield better classification accuracy with optimal time consumption.

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