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A survey, novel approach to detect Alzheimer's disease at an early stage

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ABSTRACT

Alzheimer's disease is one of the most common neurodegenerative disorders that predominantly affect memory. This happens when neurons lose their structure and function over time. Since there is currently no cure for Alzheimer's disease, it is important to identify the disease early and to slow its development as much as possible. Various computational approaches have been used in various studies to diagnose Alzheimer's disease. The main purpose of this paper is to analyse feature extraction and classification algorithms in order to determine the best method for diagnosing Alzheimer's disease. The following sections make up this paper: (i) a brief overview of the disease and the case; and (ii) a study of feature extraction and classification algorithms.

Keywords: OASIS, ADNI, MRI, SVM, Neural Network

1. INTRODUCTION

In the human body, the brain is the most complicated organ. Cells and neurons make up the brain. As cells begin to deteriorate, the entire body's functionalities begin to crumble. Alzheimer's disease may be caused by such a brain abnormality. Alzheimer's disease is a neurodegenerative condition that affects memory. It occurs when neurons lose structure or function in a gradual manner, meaning it worsens over time. When a person is diagnosed with Alzheimer's disease, his or her brain cells are killed. Signals are not being transmitted between the neurons. Disease is not a common part of ageing, even though it mostly affects the elderly. Dementia affects approximately 50 million people globally, with almost ten million new cases diagnosed each year. Alzheimer's disease is the most prevalent form of dementia and is believed to be responsible for 60–70% of all cases. [1].

Even in high-income countries, people living with dementia have minimal access to adequate healthcare, with just about half of those diagnosed seeking medication. Less than ten percent of cases are diagnosed in low and middle income

countries. The number of people with dementia is growing as populations age as a result of raising life expectancy. According to a recent survey, nearly 47 million people worldwide suffer from dementia, with 4.1 million of them living in India. By 2050, Asia will account for nearly half of all dementia sufferers. [2,3].

The global Alzheimer's Drugs Market is projected to rise at a steady 7.5 percent Compound Annual Growth Rate (CAGR) from 2017 to 2025, according to Transparency Market Research (TMR). In 2017, the market's revenue was more than US\$3.6 billion, and by 2025, it's expected to hit US\$6.4 billion. [4].

Alzheimer's disease is a chronic disease in which dementia symptoms worsen over time. Memory loss is mild in the early stages of Alzheimer's, but people with late-stage Alzheimer's lose their ability to converse and adapt to their surroundings. In the United States, Alzheimer's disease is the sixth leading cause of death. Alzheimer's patients live an average of eight years after their signs are detected by others, but longevity can vary from four to twenty years based on age and other health issues. [5].

People with Alzheimer's disease and other dementias are often marginalized or mistreated. Friends and family may be intimidated by prejudices or misinformation. Some people believe there is little that can be done, or they ignore symptoms as "just part of growing older". Alzheimer's disease and other dementias are often portrayed in a derogatory way. The terminology emphasizes the illness and reduces people with it to a set of names, signs, or medical words. It's vital to understand that negative responses from friends, family, and clinicians can have a negative effect on a person's well-being and ability to cope with the disease's changes. [6]

A biomarker is a biological element that can be calculated to assess the presence or absence of disease, as well as the likelihood of developing disease. Blood glucose levels, for

example, are a biomarker for diabetes, and cholesterol levels are a biomarker for the risk of heart disease. Two increasing proteins, beta-amyloid in the brain, which forms amyloid plaques, and tau in the cerebrospinal fluid, which forms tangles in brain cells (CSF Biomarkers), Blood Biomarkers, and Imaging Biomarkers, are among the factors being examined as potential biomarkers for Alzheimer's disease. The brain volume is decreased, resulting in deformation of the cerebral cortex, hippocampus shape changes, cortical thickness, grey matter voxel changes, and grossly enlarged sulci (space between the folds of the brain). [7].

To diagnose Alzheimer's disease, brain function images such as fMRI (functional magnetic resonance imaging), PET (positron emission tomography), and SPECT (single photon emission computed tomography) are used. A manual interpretation by a person is necessary to make a diagnosis. Because of the large volume of data, manual methods are expensive and time consuming. Physicians may use automated methods to diagnose diseases based on images. A computer researcher may perform a whole-brain investigation after a physician assists in marking the input data. The whole-brain examination, which includes feature extraction and classification, marks the whole brain as a ROI. [8, 9].

The discrete wavelet transforms (DWT), fast fourier transforms, and time frequency distribution are used to extract features. For non-stationary signals, fast fourier transforms aren't very accurate. Windowing must be done in the preprocessing stage for a proper result in time frequency distribution. The wavelet transform is not appropriate for stationary signals, and the appropriate decomposition level must be chosen. The DWT has better directional selectivity, image representation, and multiresolution analysis for a given brain image than the Fourier transform. Wavelet analysis is consistent with the abundance of texture features in various brain regions, but it has many disadvantages, including poor directionality, sensitivity to shifts (a small change in the image degrades performance), and a lack of phase information. The dual-tree complex wavelet transform (DTCWT), a version of the DWT, has appealing image processing properties such as shift invariance and high directionality. [8,9,10].As a consequence, by using variance, entropy, or capacity, variants and advanced variants of DWT can be used.

Extracting features from various image modalities may be used to conduct the analysis. These characteristics are given to classifiers in order for them to perform the required classification. Many different classifiers are available like kernel support vector machine (k-SVM), deep learning methods such as convolution neural network (CNN), radial basis function neural network (RBFNN), random forest, decision trees, and linear discriminative analysis [13]. The classifier's performance is measured in terms of accuracy, sensitivity and specificity of classification.

Deep-learning (DL) has shown tremendous potential for clinical decision support for Alzheimer's disease (for imaging analysis). The ability of DL to learn the most predictive features directly from the raw data provided a dataset of labelled examples. Machine learning is seen as a possible pattern recognition technique.

2. LITERATURE SURVEY

The majority of Alzheimer's disease research has used a number of methods to diagnose the disease. Discrete wavelet

analysis was used for feature extraction. As it has poor directionality and it is sensitive to shifts so variants of discrete wavelet transform were used. It has high directionality and properties of shift variance. The methodology was tested using data from OASIS databases, which contains information related to MMSE (mini mental state examination) and CDR (clinical dementia rating).An entire voxel of the brain was analysed using a whole brain analysis process. T1-weighted image scans were used, and multiple centre slices were chosen from them. Principal Component Analysis was used to decrease the dimensionality. For the pattern classification deep learning methods such as feed forward neural network is employed. This "DTCWT+PCA+FNN" achieved an accuracy of 90.06% [8].

For identification, a three-dimensional image obtained by scanning the entire brain was used. From all sub bands of variant of DWT, variance and entropy was measured. For the classification support vector machine was used. Since these were considered non-declarative memories, they were unable to have physical meanings for the diseases. [9]. The three-dimensional structural images are pre-processed, normalised, and translated to a one-dimensional format. These were analyzed using voxel based morphometry. Features were extracted using discrete transform techniques and the MFCC technique. Better performance was achieved with increased processing time [10].

The classification accuracy of voxel-based and cortical thickness-based methods was comparable. The sulci were considered as neurological biomarker for AD. The tissue segmented functional and structural brain images were used from ADNI (Alzheimer's disease Neuroimaging Initiative) dataset. The depth, volume, mean curvature, and surface area of the sulcal medial features were extracted. The classification was performed using SVM with a linear kernel providing a accuracy around 90% [11].

The feature extraction was performed using different discrete techniques. Different metric parameter values performances were evaluated with small number of extracted features [12]. EEG wavelet algorithms that slow down were thought to be more suitable than Fourier transform techniques because of the reduced complexity of EEG. Different brain imaging techniques were used. FMRI helps to classify hippocampus regions of the brain by detecting brain structure and analyzing blood supply and oxygen within the brain. Also hemodynamic imaging FNIRS was limited to spatial and temporal resolution. Thus it's essential to have neuroimaging techniques such as MEG,SQUID.But these neurophysiological imaging were considered to lead to fatigue . As a result, a comparison of proper dataset selection, preprocessing algorithms, and classifier was performed. [13]. Morphometric and texture characteristics were derived from structural MR images. Texture analysis was used to extract texture features and VBM analysis was used to extract morphometric features. SVM-RFE is combined with covariance matrix was used for feature selection and extraction. More features were not defined due to the lack of a longitudinal and multimodal dataset. [14].

The features were extracted from images from two different databases and compared using different optimization algorithms. The classifier used is SVM.The accuracy was tabulated [16].A methodology for early AD diagnosis using tissue-segmented brain images was presented. The aim is to differentiate between Alzheimer's disease (AD), moderate cognitive impairment (MCI), and elderly stable controls (NC).

The feature extraction methods used were partial least squares (PLS) which uses score vectors as features and principal component analysis (PCA). 188AD patients, 401 MCI patients and 229 control subjects from the Alzheimer's Disease Neuroimaging Initiative(ADNI) database are studied. The classifier used was support vector machines. The classification result obtained in white matter is better than in gray matter [16].

The ventricles, hippocampus, cortical thickness, and brain volume were all calculated. A 3D convolutional auto-encoder was used to create a deep 3D convolutional neural network. ADNI dataset without using skull stripping was used in the classification. The accuracies were compared with other classifiers [17]. The segmentation of Alzheimer disease in PET scan dataset was presented. The clustering algorithms were used based on less distance and high membership value in FCM. These segmented images were seen to provide a better picture of the affected sections. [19, 20].

A new classification technique was presented using a classifier called as TANNN. This data mining technique was applied on real Alzheimer dataset. The content-based image retrieval algorithm is used to segment the images. Threshold was used to extract characteristics, and edge detection was used for classification. [22].

Using various techniques to isolate the ventricle's region, image segmentation and classification were performed on 3D MRI Neuroimaging brain data. The voxel based morphometry technique was used to compare the gray matter of AD patients. The features were ranked using statistical dependency, information gain, and mutual information. The SVM classifier was used [23].

The researchers used a holistic description of brain anatomy approach that provided shape details for an ensemble of cortical and subcortical structures. The Brain print improves ROI-based research by incorporating shape information to volume and thickness measurements. Using this approach linear models are generalized for classification [25].

The method of diffusion tensor imaging was introduced, which offers a wealth of knowledge about nerve fibres by studying the diffusion of water molecules. SVM classifier was used, which uses probabilistic tractography and TBSS analysis of DTI data. It was concluded that fiber pathways tracked by FSL are distributed over a wider range in Alzheimer patients than in normal people. Thus volume of fiber pathways was used as an effective feature [28].

Table 1: Summary of literature survey

Paper & Data Base	Features and classifier	Performance																
[8] OASIS consisting of MRI images 416 subjects 126 samples including 28 ADs and 98 HCs)	DTCWT+PCA FNN	<p>Average sensitivity (%)</p> <table border="1"> <tr> <td>DTCWT+PCA</td> <td>FNN 92.00 ± 0.04%</td> </tr> </table> <p>Average accuracy (%)</p> <table border="1"> <tr> <td>DTCWT+PCA</td> <td>FNN 90.06 ± 0.01%,</td> </tr> </table> <p>Average specificity (%)</p> <table border="1"> <tr> <td>DTCWT+PCA</td> <td>FNN 87.78 ± 0.04%,</td> </tr> </table>	DTCWT+PCA	FNN 92.00 ± 0.04%	DTCWT+PCA	FNN 90.06 ± 0.01%,	DTCWT+PCA	FNN 87.78 ± 0.04%,										
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[9] Dataset66, Dataset160, and Dataset255 consisting of MRI images 20 subjects (5 healthy and 15 pathological)	DTCWT + VE + SVM DTCWT + VE + GEPSVM DTCWT + VE + TSVM	<p>Average accuracy(%)</p> <p>98.43%</p> <p>99.25%</p> <p>99.57%</p>																
[10] OASIS database 416 subjects no disease CDR of 0 very mild AD (CDR=0.5), mild AD (CDR=1) moderate AD (CDR=2)	MFCC DCT DWT DST DCT & DWT DST & DWT SVM	<table border="1"> <thead> <tr> <th>Algorithms/features</th> <th>Accuracy</th> <th>Sensitivity</th> <th>Specificity</th> </tr> </thead> <tbody> <tr> <td>MFCC/50</td> <td>98.3</td> <td>100</td> <td>97.5</td> </tr> <tr> <td>DCT</td> <td>92.5</td> <td>92.4</td> <td>94.5</td> </tr> <tr> <td>DWT</td> <td>91.</td> <td>86.</td> <td>97.5</td> </tr> </tbody> </table>	Algorithms/features	Accuracy	Sensitivity	Specificity	MFCC/50	98.3	100	97.5	DCT	92.5	92.4	94.5	DWT	91.	86.	97.5
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<p>[11] Alzheimer’s Disease Neuroimaging Initiative (ADNI) database</p> <p>Cortical sulci extracted by BrainVISA</p> <p>100 cognitively normal subjects (CN) and 110 Alzheimer’s disease subjects (AD)</p>	Medial surface extraction	Sensitivity 85.11%, Specificity 91.27% and Accuracy 88.49%,																
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<p>[18] Alzheimer and normal Dataset has been collected from four patients at different times</p> <p>first consists of 24 Alzheimer’s EEG signals, of which 12 are the Alzheimer’s EEG and the next 12 are the synthetic Alzheimer’s EEG data</p>	<p>complex wavelet transform SE and TE</p> <p>feed forward neural network (FFNN)</p>	<p>Method Classification rate (%) Noisy signal 35 Denoised signal (DWT with SE) 75 Denoised signal (CWT with SE) 90 Proposed method (CWT with TE) 95 Denoised signal (CWT with Bayes shrink) 55 Denoised signal (CWT with Visu shrink) 35.5</p>																

<p>[19] ADNI database Pet scan images</p>	<p>K-Means algorithm and FCM.</p>	<table border="1"> <thead> <tr> <th>parameter</th> <th>K-Means</th> <th>FCM</th> </tr> </thead> <tbody> <tr> <td>Average voxel intensity</td> <td>86.0916</td> <td>76.409</td> </tr> <tr> <td>Standard Deviation</td> <td>92.0758</td> <td>42.873</td> </tr> <tr> <td>Coefficient of variance</td> <td>106.951</td> <td>56.109</td> </tr> </tbody> </table>	parameter	K-Means	FCM	Average voxel intensity	86.0916	76.409	Standard Deviation	92.0758	42.873	Coefficient of variance	106.951	56.109
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<p>[25] ADNI DATASET multi-center data from hospitals in the Netherlands, including 30 subjects for validation and 354 subjects for testing</p>	<p>PCA Brain Print</p>	<p>ADNI 751 (213/364/174) 437(58%) 314(42%) (71.1/75.3/79.8) Challenge-Validation 30 (12/9/9) 17(57%) 13(43%) (59.3/65.0/68.0) Challenge-Test 354 213(60%) 141(40%) (59.0/64.0/71.0)</p>												
<p>[26] EEGs were recorded from the 19 scalp loci of the international 10-20 configuration using a digital electroencephalograph in “Hospital de São João - Porto”, Portugal. A set of 37 subjects participated in this study (11 as Controls, 8 with MCI, 10 with AD in Mild/Moderate stages and 8 in Advanced stage).</p>	<p>Wavelet Biorthogonal (Bior) 3.5 DWT leave-one-out-cross-validation (LCV) and 10- fold-cross-validation (10FCV)</p>	<p>86.19% of sensitivity, 99.35% of specificity and 94.88% of accuracy</p>												
<p>[27] ADNI database 130 participants, with ages ranging from 56 to 88 years (mean 74.49 ± 6.13 years)</p>	<p>VBM analysis feature ranking SVM</p>	<p>92.48% accuracy</p>												
<p>[28] LONI Image Data Forty data (20 MCI, 20 NC) out of the 84 DTI data were used for cross validation</p>	<p>method for predicting MCI using probabilistic tractography and tract-based spatial statistics (TBSS) analysis of the DTI data SVM</p>	<p>Our prediction model showed and accuracy of 100%, a specificity of 100% and a sensitivity of 100% in a10-fold cross validation on the DTI data of 40 subjects selecting 4500 features</p>												

3. METHODOLOGY

The proposed algorithm employs MRI images to diagnose Alzheimer's disease early. The algorithm will be written in Python to make it easier to construct a CNN with Tensor flow and Keras.[29].The features like texture analysis and statistical features are extracted by writing Mat lab code .These features are then fed to SVM classifier[15] .

When we use CNN, engineering is with transforming characteristics (Mapping Raw Data to Features). Here categorical and non-continuous results are considered to turn the model into one-hot encodings. Preprocessing categorical features for machine learning models is done using One Hot Encoding [30]. This encoding generates a new binary feature for each possible category and assigns a value of 1 to each feature. The tf.one hot operation outputs a One Hot Encoded Tensor from a list of category indices and a depth (for our purposes, basically a number of specific categories).

Construct the ML Model (with reference to Deep Learning for detecting pneumonia from an X-Ray image). Using Keras, create the CNN layers (convolution neural network). AUC (Space Under the ROC Curve) is a metric that calculates the entire 2D area under the entire ROC curve. The AUC value varies from 0 to 1. A model whose predictions are 100% wrong has an AUC of 0.0; one whose predictions are 100% correct has an AUC of 1.0.It measures how well predictions are ranked, rather than their absolute values. Training the model (A scalar used to train a model via gradient descent algorithm).[31]

Change the learning rate and stop the model until it converges to train it more effectively. In the model, the learning rate is a critical hyper-parameter. The model will not be able to converge if the LR is too large. The process will take too long if the LR is too slow. One mechanism for avoiding over-fitting is to stop our model early. Finally visualize the model metric and evaluate the model.

The classifier output from SVM and output from convolution neural network is analyzed for better accuracy.

4. CONCLUSION

In this paper, Existing work done by various researchers is explained; methodology is proposed using machine learning. And using neural networks. Since there is no cure for this disease, the necessity of identifying and controlling this disease has become essential according to many researches as stated in this paper.

The classification algorithms were also compared and briefly discussed based on their characteristics.

Also as a summary, a proper selection of dataset, preprocessing algorithm and classifier can aid to predict Alzheimer's disease in advance and delay the symptoms of the disease with proper medications.

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