Survey of the use of AI models and techniques in the analysis and prediction of neuro-degenerative diseases

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Abstract. Neurodegenerative diseases are caused by the gradual breakdown of the nerve connections. The detection and prediction of these diseases has been attempted with a variety of different artificial intelligence techniques, using the wide range of modalities available resulting in variations in accuracy and other metrics. This paper aims to offer a methodical as well as quantitative comparison among the various predictive methodologies that have been conducted for three neurodegenerative diseases, namely Alzheimer's, Schizophrenia and Dementia. Lastly this paper focuses on the variation in occurrences of these diseases with changing demographics such as age, sex and location.

1. Introduction

The term "neurodegenerative diseases" refers to a broad spectrum of illnesses caused by the progressive breakdown of neurons and neural pathways and the cells that are necessary for mobility, strength, coordination, sensibility, and cognition.

The objectives of this paper are as follows:

- Analysis of the clarification accuracy of various models and techniques for detecting neuro-degenerative diseases.
- Analysis of the occurrences of these neuro-degenerative across various populations and demographics.
- Thorough analysis of the different features/modality used by these models for the purpose of prediction.

2. Methodology

To conduct our research, we first looked for publications on conference, journal and review papers using key terms like "Neurodegenerative Diseases," "Artificial Intelligence," "Machine Learning," "Deep Learning," "Mental Health," "Detection," and "Diagnosis" and its variations. We gather information on several neuro-degenerative disorders, such as Alzheimer's disease, dementia, and schizophrenia, using the range of works that are now available. By contrasting their research sample sizes, accuracy levels, and classification techniques, we combine the current literature.

Furthermore, we investigated the classification accuracy of several Machine Learning and Deep Learning Models, namely, but not exhaustive: Random Forests, CNNs, Neural Networks, and SVMs, while considering the de-facto accepted techniques of diagnosing these disorders in clinical practice. The frequency of these neuro-degenerative conditions globally as well as their severity among a range of people of different ages and ethnicities were also taken into consideration by combining other demographic data.

3. Comparison of Various ML and DL models for Analysis of Different Neurodegenerative diseases

3.1. Alzheimer's

Alzheimer's Disease (AD), accounts for more than 60% of the Dementia cases. AD is characterized by the death of brain cells. At its onset, Alzheimer's is signalled by Mild Cognitive Impairment (MCI): a decline in thinking ability. As it progresses it can leader more severe stages of Dementia.
Over the past decade, Artificial Intelligence Techniques are being used extensively, along-side with the conventional diagnostic techniques. This is because Artificial Intelligence can effectively use the correlation among the various features and modalities to reach a conclusion for individual subjects.
There are a wide variety of options utilized to detect AD using AI methodologies. The extraction and categorization of features can be carried out using a variety of different methods.

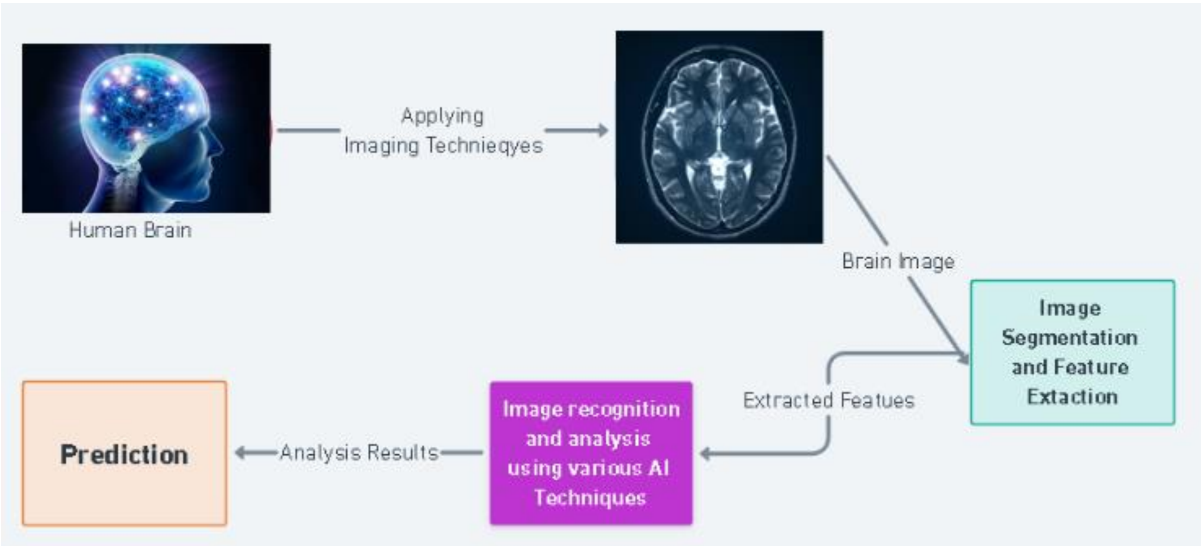

Figure 1: Steps followed for the detection of Alzheimer's using AI techniques.

These AI techniques help not only to detect the disease as discussed above but also to understand the current stage of progression of the disease in an individual. Some of the AI techniques that can be employed to detect Alzheimer's are:

3.1.1 K Nearest Neighbours: k-NN is a technique that classifies the data by comparing the give test data-point to its closest training data points. Each data point exists in an n-dimensional space (n being the number of features under consideration), and the Euclidean distance of that point is calculated from that of its *k* nearest training data points and its label is calculated based on the labels of these points.
In [1] a three-step algorithm is proposed for disease detection using MRIs where LDA (linear discriminant analysis) and PCA (Principal component Analysis) are applied to the figures and lastly the extracted features then serve as inputs to k-NN classifiers as well as SVM (which we will be analysing below).

3.1.2 Support Vector Machines (SVMs): SVM is a supervised machine learning algorithm that aims to separate the n-dimensional space into classes or regions, which is then used to classify test data points into classes depending on the region in which they lie. The decision boundary used to separate the n-

dimensional space in the most optimum way possible is known as the hyperplane. In many previous works, SVMs have been used to detect AD using Support Vector Machines.
For example, in [2] an Alzheimer's detection method is proposed, based on features extracted from structural MRIs. A voxel-based morphometry process is utilised to separate the global from the local changes in the grey matter (GM) of AD patients with HCs. Following which a SVM is utilized for classification. Operating on the ADNI dataset, this methodology achieved an accuracy of 92.48% for classification.
Furthermore, in [3] 3D SPECT (single-photon emission computerized tomography) images were used build a CAD system, improving the detection and classification of AD patients. Following feature extraction from these images, a CAD system for AD detection was the end result of using component based SVM Classifiers The proposed framework resulted in an accuracy of 96.91%.

3.1.3 Random Forests: A random forest classifier is a ML classification model that consists of many individual decision trees, with each individual tree giving a particular prediction of the class based on a subset of parameters. The predictions of individual decision trees are compiled and the class in majority, would become the output prediction from the random forest classifier.
[4] discusses a framework that works to pre-process MRI images, extract features from the images and subsequently employ the use of Random Forrest Classifiers to differentiate among MCI, cMCI, AD and HC, obtaining the final output with the help of majority voting in ensemble classification.

3.1.4 Deep Neural Networks: A Neural Network was developed with the aim of imitating the behaviour of a human brain. For each neural network the number of nodes can be decided along with the weights to be allocated to each of the nodes. These are then varied to improve the accuracy of prediction of the model. A Deep Neural Network refers to a neural network with multiple internal hidden layers, with each layer processing the output data of the previous layer. Hence each layer works to learn more complex data.
Deep learning frameworks have become increasingly popular in the field of medical imaging. In [5] the deep learning framework proposed works to differentiate among the various progression stages of Alzheimer's patients by using their MRI's as well as their PET scans. The dropout technique is used to ensure that overfitting of the parameters does not occur. The method proposed in this paper proves to be 5.9% more accurate than the average for classification.

3.1.5 Convolutional Neural Networks: A CNN is a Deep Learning technique that operates on images. Taking in the 2-Dimensional format of an image as an input it performs pre-processing on it with the use of filters. To produce the final output, all filter activation maps obtained are then added together. The end goal is to reduce the size of each feature map while keeping the relevant data. The pooling layer resizes the input spatially and operates on each feature map individually.
As there is great resemblance among AD, MCI, and NC, it is difficult yet imperative to distinguish among them at the early stage to ensure proper care can be provided for the same. In [6] a deep learning framework has been implemented that accomplishes efficient diagnosis of AD. This architecture is called 3D fine-tuning convolutional neural network (3D-FCNN). When this architecture was implemented on the ADNI MRI dataset, its performance it terms of accuracy as well as robustness was superior to that of traditional methods, as evident from Table 1.

Table 1: Variations in prediction accuracy of Alzheimer's using different modalities and classifiers.

Classifier	**Modalities**	**ACC**	**AUC**
SVM	MRI, PET, CEF, APOE	83.6%	-

ELM	MRI, PET, CEF, APOE	84.7%	88.8%
ELM	MRI, PET, CEF, APOE, neurophysical scores	85.1%	92.6%
CNN	MRIs	92.6%	94%
3D FCNN	ADNI MRI Dataset	AD/MCI: 88.43 AD/NC:96.81 MCI/NC: 92.62	AD/MCI:0.91 AD/NC:0.98 MCI/NC:0.94

ACC: Accuracy, APOE: Apolipoprotein, AUC: Area under ROC Curve, CSF: Cerebrospinal Fluid, CNN: Convolutional Neural Network, ELM: Extreme Learning Machines, SVM: Support Vector Machines, MRI: Magnetic Resonance Imaging

3.2 Schizophrenia

Schizophrenia is a serious mental condition in which victims have odd perceptions of reality. Hallucinations, delusions, disorganised speech, and other symptoms that affect cognition, attention, and memory and cause problems in social or professional settings are characteristics of SZ. Only when organic causes like dementia or delirium, which may present similarly, have been ruled out can it be identified.

3.2.1 Discriminant function analysis (DFA): SZ. Leonard et al. [7] successfully classified the subjects from the structural MRIs with a 77% accuracy rate using discriminant function analysis (DFA). In this study, hemisphere and third ventricle volume as well as the normalised (Talairach) location of three association cortex sulcal landmarks were measured using high-resolution MRI scans of 37 male patients with schizophrenia and 33 male control subjects who were matched for age, handedness, and parental socioeconomic status.

3.2.2 SVMs, or support vector machines: A popular method for classifying SZ is to use support vector machine (SVM) classifiers, particularly non-linear SVM and its derivatives. SVM is used for most of the analysis from structural MRI image detection. In most studies, the SVM models were created using just one set of subjects (the training set), and then they were tested on a new set of subjects (the test set) to make sure they were still accurate. Numerous researchers also used SVM to contrast the at-risk mental state (ARMS) SZ subjects with the healthy controls (HC).

The use of SVM through the combining of various features is the subject of another study. In comparison to single-modal characteristics, the classifier with integrated features of structural and functional MRI data performed better (accuracy 77.91% vs 72.09%). Furthermore, 10% of the features chosen by feature selection accurately identified 74 (86%) of the 86 participants, indicating that a significant amount of functional connectivity features was redundant to categorization.

3.2.3 Random Forest: In [8], 74 anatomic brain MRI subregions and Random Forest (RF) were utilised to classify 99 age, sex, and ethnicity-matched healthy controls and 98 people with childhood onset schizophrenia (COS). Using RF, it was also calculated how likely it was that a person would receive a diagnosis of schizophrenia based on MRI results. With a combined accuracy of 73.7%, brain areas categorised the COS and control groups, demonstrating that worse functioning and fewer developmental delays were associated with higher brain-based illness risk. The region's most important in group classification were the left medial parietal lobe, bilateral dorsolateral prefrontal regions, and left temporal lobe.

3.2.4 Deep Neural Networks: Most DL research is concerned with categorising SZ patients and healthy controls in binary terms (pattern recognition). The most often used data in these investigations include fMRI, MRI, genomics, and EEG.
With extremely good findings (accuracy 90%), DNNs have been employed for SZ diagnosis (classification) on neuroimaging data. For instance, fMRI single-frame data (90.8% accuracy) [9] and EEG time-frequency (95% accuracy) [10].

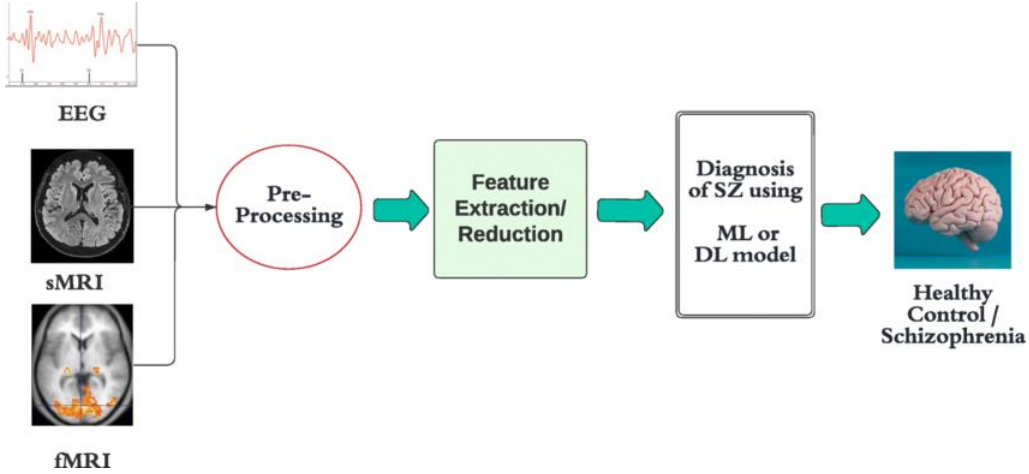

Figure 2: Methodology to detect SZ using AI Techniques

Table 2: Variations in prediction accuracy of Schizophrenia using different models.

Model Name	**Discriminant Function Analysis**	**SVM's**	**Random Forests**	**Deep Neural Networks**
Best. Avg. Accuracy	77%	90.34% (second trials) *	73.7%	95%

3.3 Dementia – Vascular Dementia, Lewy Body Dementia and Frontotemporal Dementia

Vascular Dementia is the second most frequently occurring type of dementia, after Alzheimer, affecting around 15-20% of dementia cases in the American continent, and around 30% of dementia cases in the Asia Pacific region. It is caused by a reduced blood flow to the brain and the chances of being diagnosed with his diseases increases exponentially after the age of 65. Symptoms are like that of Alzheimer, with various aspects overlapping. Another type of dementia is Lewy Body Dementia (LBD) is caused by abnormal deposits of a protein called alpha-synuclein in the brain. These deposits are called Lewy bodies. Frontotemporal dementia is another type which affects the temporal and frontal lobes of the brain.

We have discussed the various ML and DL models created for the differentiation of dementia from each other below.

3.3.1 ML Algorithms - The various features taken into consideration by ML models were age, sex, first-visit MMSE, haemoglobin, Mean Corpuscular Volume, platelets, creatinine, TSH, parathyroid hormone (PTH), vitamin B12, vitamin D, folic acid, cholesterol. The implementation in [11] evaluates the model based on metrics like F1 score, Accuracy and Recall. Bagging method gives 85.29% accuracy, 82.14% F1-Score and 85.19% Recall. The other methods are Stacking and Boosting with accuracies, F1-Score and Recall as 85.29, 80.77, 77.78 and 86.26%, 83.64%, 85.19% respectively. Folate, MCV, PTH, creatinine, vitamin B12, TSH, and haemoglobin were the best predictive parameters individuated by the best ML model: Random Forest. Another ensemble model achieved 89.74% accuracy, 93.75% sensitivity and 85.73% specificity [12].

3.3.2 Multi-layer-perceptron – This model [13] combined with Adaptive Neuro-Fuzzy Inference System (ANFIS) [30] (Castellazzi et al) discriminated between Alzheimer and VD the best, areas like the hippocampus, precenues, cingulum are key areas, giving a accuracy of 77.3%, including clinical tests.

3.3.4 KNN's: Methods such as the KNN's had an accuracy of 91.2%, with a sensitivity and specificity of 96.42% and 91% respectively, in this implementation by Bougea A[12].

3.3.5 Convolutional Neural Networks: The process of artificially deriving fresh data from previously collected training data is known as data augmentation. Techniques include cropping, flipping, rotating, and resizing. It strengthens the model's performance and addresses problems like overfitting and a lack of data. Features are extracted from the ADNI dataset, processes using SPM8. Jingjing Hu et.al [14] has found out studies for discriminating Frontotemporal and Lewy Bodies Dementia, as AD and dementia have overlapping symptoms [14]. Some differences are extrapyramidal symptoms, hallucinations, apathy, REM sleep, and a few others described in their paper. They trained CNN models on raw-T1 images, and proposed a model with accuracy of 91.83%, using the ReLU loss function.

Akihiko Wada etl.al [15], used CNN's as well to distinguish Lewy Body Dementia with Alzheimer, using the brain connectome. The brain connectome is a 3D model of the interactions happening in the brain with different neurons, using a MRI scan. They used the standard 4 metrics: Precision, Accuracy, Recall and F1 score to make predictions. Their CNN model has six layers, with three convolutional layers and three fully connected layers. Adam was their optimizer, and 4-fold cross-validation was leveraged. It achieved an average accuracy of 73%, precision of 78% and recall of 73%. The F1 score was similar for all AD classification, LBD classification and Healthy control, around 73%.

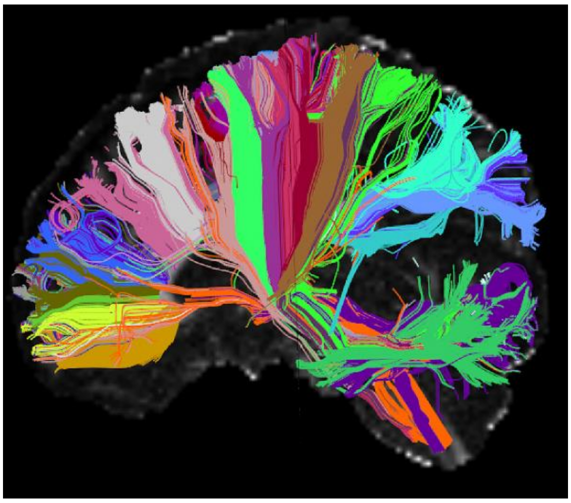

Figure 3: Human Brain Connectome

3.3.6 Regression: Methods like binomial logistic regression [12] averaged accuracies over 90%, for vascular dementia. Penalized regression methods like Ridge Regression, Elastic Net methods were also implemented in [16], using mRNA expression data from clinical samples, and other phenotypes. Even in their paper, Gradient Boosted Decision Trees have the highest accuracy of 82.9%, for Lewy Bodies Dementia. Jun Pyo Kim et.al [28] researched about the hierarchical classification of dementia, and the various subclasses associated with Frontal Temporal Dementia.

3.3.6 Support Vector Machines and Naïve Bayes: Daichi Shigemizu [16] applied Support Vector Machines with a radial function, tinkering with parameters gamma and C. Anastasia Bougea et.al[12], proposed an accuracy of 84.6%, on 15 features, achieving 90.62% sensitivity and 78.58% specificity. They further put forward a Naïve Bayes model having accuracy of 82.05%, 93.10% sensitivity and 74.41% specificity.

Table 3: Variations in prediction metrics of Dementia using different ML models.

Model Name	Accuracy	Precision	Recall	F1-Score	Specificity	Sensitivity
Random Forests	85.14%	-	85.19	82.14%	-	-
KNN's	91.2%	-	-	-	96.42%	81%
CNNs	91.83%	78%	73%	-	-	-
SVM's	84.6%	-	-	-	78.58%	90.62%
Naive Bayes	82.05%	-	-	-	74.41%	93.10%
Ensemble Models	89.74%	-	-	-	85.73%	93.75%

However, despite all of this, medical standards such as MRI biomarker scans, CT scans, cerebrospinal fluids, electroencephalograms(EEG), positron emission tomography (PET), Fluorodeoxyglucose positron emission tracer (FDG-PET) scans, and other cutting-edge techniques are more commonly used than AI models because these standards are understandable, doctors can dive deep in the voxels of the brain connectome, identify borders, and detect areas of low metabolism in the brain, whereas deep learning is a black-box and cannot be extrapolated by professionals, even though they offer incredible accuracies. Various research has been done in the detection of the former strategies. [17]

4. Comparison of variations in Demographics for different neurodegenerative diseases

Globally, more women are affected by dementia than men. In 2019, women with dementia outnumbered men with dementia 100 to 69. This has often been attributed to the fact that women live longer than men on average. Also, animal trial data infers that oestrogen can have some sort of neuroprotective effect, so this assumption is not entirely true or 100% backed by science. Early-onset dementia affects age groups less than 65 years of age, with around 5%-6% people affected by it.

One popular methodology used for the analysis and prediction of neurodegenerative diseases is a population-based approach where demographic characteristics such as gender, age, location, and other factors are taken into account and the occurrence and variation of these diseases, among the variety of populations, is noted. One such example is the Cognitive Function and Aging Studies (CFAS) that worked on examining the changes in occurrence of dementia from 1991 to 2011 in the UK. [18]

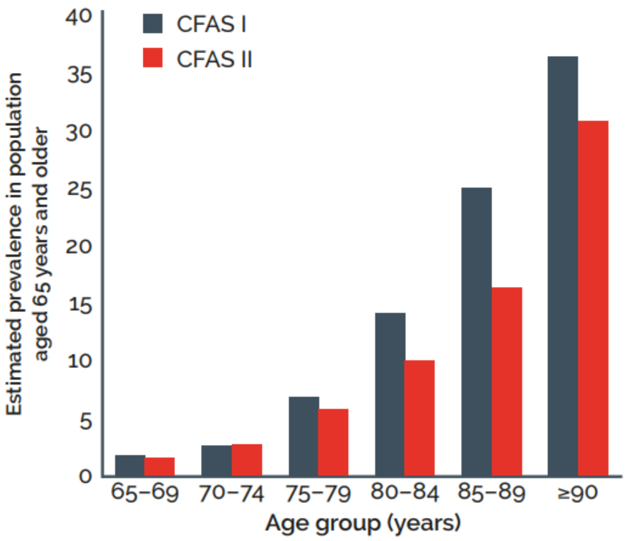

Figure 4: Age Specific Prevalence of Dementia in CFAS I and II

The following tables depict the variation in the population groups affected by dementia in a variety of demographics.

Table 4: Variation by location of prevalence of dementia in older aged population (India)

Location	Mishriwala (Rural)	Suttur (Rural)	Chennai (Urban)	Pune (Urban)	Mumbai (Urban)	Kolkata (Urban)	Vellore (Rural)
Percentages (>= 60 years)	6.5%	10%	11.1%	4.1%	2.44%	2.55%	11.4%

Table 5: Variation by age of prevalence of dementia in older aged population (European Union) [19]

Disease	<60	**60-75**	**75-85**	**85+**
Overall Percentages	<1.5%	~5.4%	~20.1%	62.7%

Table 6: Variation by Country based on death rate due to Alzheimer's and Dementia (/100000) [20]

Country	Finland	U. K	Slovakia	Albania	Iceland	Brunei	Netherlands	**USA**	Ireland	Sweden
Death Rate	54.65	42.70	38.15	36.92	35.59	33.87	33.78	33.26	32.23	30.96

5. Shortcomings:

While this paper centres around the various Artificial Intelligence techniques that can be utilized for the analysis, detection, and prediction of a variety of widespread neurodegenerative diseases, however some shortcomings of our work would be as follows:

- It focuses on primarily three diseases, namely Alzheimer's, Schizophrenia, and Dementia, disregarding some of the other widely prevalent diseases such as Parkinson's, Huntington's, and Amyotrophic Lateral Sclerosis.
- Our survey mainly includes work on Computer Vision, however, Natural Language Processing can also be leveraged, for the detection and classification of dementia in various ways, some of them includes: analysing the speech of the diagnosed patients, and investigating their way of speaking, extracting features like the amount of slur, vocabulary, number and duration of pauses and more; or the variation of brain signals in diagnosed patients vs control subjects and so on.

6. Future Works:

To build upon our work done in this paper, the comparison drawn among the various AI techniques for AD, SZ and dementia needs to be extended to include other common neurodegenerative disorders such as Parkinson's disease. Furthermore the demographics comparisons done above based primarily on the location and age of the individuals can also be expanded to include factors such as sex, mental disposition, nutrition, financial status, to draw a more complete comparison.

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