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An Assessment of Algorithms Utilizing Machine Learning to Classify the Various Stages of Alzheimer's Disease

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Abstract: *Alzheimer's disease (AD) is a chronic, irreversible illness that causes shrinking of the brain, impairing memory and causing cognitive impairment. Many medical professions make extensive use of machine learning methods. The proper classification of Alzheimer's disease has been the subject of several investigations. Using a variety of machine learning approaches, we have evaluated several papers written by different researchers to provide readers a more thorough picture of the research being done on Alzheimer's disease. The only purpose of this is to assess more sensible and efficient learning approaches for the categorization of Alzheimer's disease. Deep Learning (DL), Support Vector Machines (SVM), and Artificial Neural Networks (ANN) are the three primary machine learning approaches examined.*

Keywords: Alzheimer's Disease, Support Vector Machine

I. INTRODUCTION

Alzheimer's disease (AD) is a neurological condition that progresses slowly but steadily and causes a gradual but constant deterioration in memory. It is a kind of dementia that occurs often. The brain changes structurally as a result of Alzheimer's disease. The symptoms start off mildly, become worse with time, and get worse more slowly. The patient first exhibits mild cognitive impairment (MCI), which gradually progresses to Alzheimer's disease (AD). MCI is an intermediate stage of AD. But not every MCI patient goes on to develop AD [1]. Even while AD is now incurable, its development may be prevented if caught early [2]. 26.6 million people worldwide suffered from AD in 2006. By 2050, 1 in 85 people globally are expected to develop AD, and 43% of frequent cases would need intensive care[3]. Therefore, the main objective of this research is to predict the shift from MCI to AD.

In the last 10 years, machine learning techniques have been widely used to AD diagnosis [4,5,6]. Support vector machines (SVM), artificial neural networks (ANN), and deep learning (DL) are the most popular algorithms for classification. The main difference between ANN and SVM is the nature of the optimization problem. The solution scope is local in ANN, but global in SVM [7]. The feature extraction stage is the most important one in both SVM and ANN. Deep learning, on the other hand, builds the feature extraction procedure right into the learning model. The benefit of deep learning has been shown by large datasets, including image data[8]. The most widely used databases are the Alzheimer's Disease Neuroimaging Initiative (ADNI) [9] (adni.loni.usc.edu), the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) (aibl.csiro.au), and the Open Access Series of Imaging Studies (OASIS) (www.oasis-brains.org). Magnetic resonance imaging (MRI) images of AD, MCI, and cognitively normal healthy (CN) persons are pooled using ADNI datasets[10]. Diagnosing AD using high-resolution magnetic resonance imaging (MR) greatly improves diagnostic accuracy.

Due to patterns of grey matter (GM) atrophy, MR scans are essential in separating AD patients from CN. Many studies have proposed measuring the spatial distribution of GM atrophy in the brains of AD and MCI patients using Voxel-based Morphometry (VBM) [12,13, 14]. VBM uses Statistical Parametric Mapping (SPM) for the analysis of structural MRI data [15,16]. SPM was developed for public use by the Wellcome Centre for Human Neuroimaging. Another popular open-source application for volume-based morphometry that is used by many academics is FreeSurfer.

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In this study, we provide a comprehensive and impartial analysis of the three main machine learning approaches—SVM, ANN, and DL—on the diagnosis of AD. In Sections 2.1, 2.2, and 2.3, respectively, an analysis of the classification of AD using the SVM, ANN, and DL methods is provided. In addition, a brief comparison of SVM, ANN, and DL is provided in Section 3, along with an explanation of their advantages and disadvantages.

II. CLASSIFICATION ALGORITHMS USED IN ALZHEIMER'S DISEASE

Support Vector Machine (SVM)

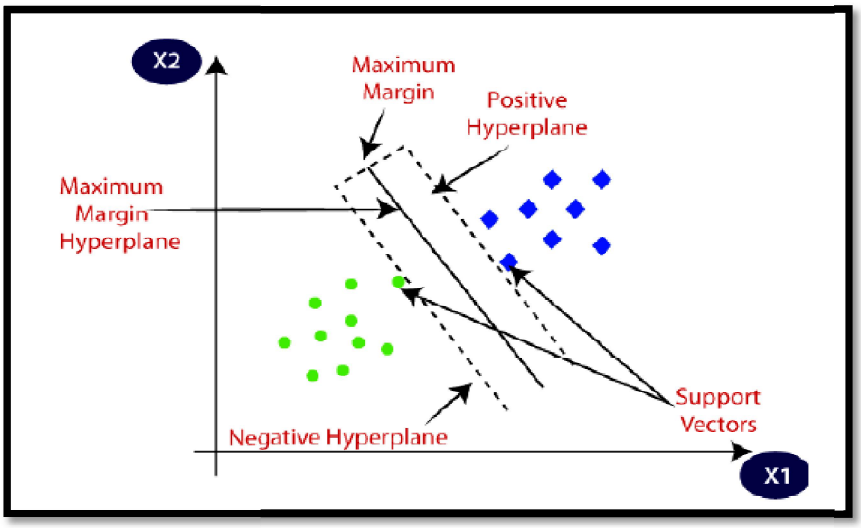

Fig -1: Support Vector Machine

Support Vector Machine is a method for classifying binary machine learning data. It establishes a decision boundary, often called a hyperplane, and is suitable under dire circumstances. To detect AD early, Zhu et al. [17] proposed using a spatial-temporal technique to identify the aberrant structure using a longitudinal MRI sequence. First, they compared the classification performance of the Temporally structured SVM (TS-SVM) early detection technique with that of the conventional SVM-based methodology. Both the TS-SVM early detection method and the standard SVM-based strategy were expanded to include later feature selection. Consequently, the classification performance of SVM, SVM+FS, TS-SVM, and TS-SVM+FS were compared with one another. It was shown that TS-SVM outperformed ordinary SVM in classification accuracy by 10%; this demonstrates the usefulness of temporal and monotonous restrictions. Feature selection has a major role in the accuracy of AD detection; 3.8% and 2.9% more accuracy is predicted for SVM+FS and TS-SVM+FS over SVM and TS-SVM, respectively. Temporal consistency and early detection are the two main benefits of using TS-SVM over traditional SVM in early diagnosis and high accuracy AD detection. Consequently, TS-SVM was used to early-stage AD prediction and to distinguish between MCI converters and non-converters on longitudinal MRI. After 10-fold cross-validation on 151 patients—70 MCI-C individuals and 81 MCI-NC subjects—an accuracy of 82.5% was obtained. For exceptional classification accuracy, Sheng et al. [18] examined many classification techniques using the Matlab machine learning toolkit. A variety of kernel functions were used to train classifiers utilizing features. The two fundamental methods for doing appropriate feature selection are filter and wrapper feature selection. Rather than being dependent on the particular classification technique, the selection criteria for filter features are often used to estimate statistical characteristics. The six most generally used criteria are the Kruskal-Wallis test, Chi-square score, relief feature score, Gini score, and multivariate minimal redundancy maximum relevance (MRMR). An examination of these six filter alternatives using Matlab revealed that the relief feature score performed the best. The introduction of wrapper feature selection aimed to reduce the number of features. After processing over three thousand features using filter and wrapper feature selection, thirty features were selected in the end. The following classifiers were put to the test: Support Vector Machine (SVM: Linear, Quadratic, Cubic, Fine Gaussian, Medium Gaussian, Coarse Gaussian), KNN (fine, medium, coarse, cosine, cubic, weighted), Tree (fine, medium, coarse), Discriminant (Linear, Quadratic, Logistic), and Ensemble (boosted trees, bagged trees, subspace

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discriminant, subspace KNN, RUS boosted trees). Out of all the classifiers previously discussed, the SVM classifier yielded very accurate results. They achieved classification accuracies of 93.8% for EMCI vs. CN, 95.8% for LMCI vs. CN, 95.8% for AD vs. CN, and 91.7% for LMCI vs. AD by using 5-fold cross-validation. They achieved this by applying the field mapping technique to a functional MRI dataset including 24 AD, 24 CN, 24 EMCI, and 24 LMCI subjects. Peng et al. [19] integrated genetic and high-dimensional multi-modality imaging data, such as single nucleotide polymorphism (SNP) genome data of 189 individuals (47 CN, 93 MCI, 49 AD), as well as MRI sequence and PET data. Each feature was assigned a distinct feature mapping. Multiple kernel SVM accuracies of 80.3% for CN vs. MCI, 76.9% for MCI vs. AD, and 96.1% for CN vs. AD were discovered using 10 fold cross-validation. Utilizing Fludeoxyglucose (18F-FDG) data, Positron Emission Tomography (PET) data, and segmented Magnetic Resonance imaging (MRI) multi-modality datasets, Ortiz et al. [20] used Sparse Inverse Covariance Estimation (SICE) methods. SICE evaluates the undirected graphs to identify the functional and structural link patterns between CN, MCI, and AD. In circumstances when the sample size is close to or less than the total number of brain regions, one may still accurately estimate the inverse covariance using SICE. Linear SVM was applied to 249 individuals (68 CN, 111 MCI, and 70 AD). The accuracy ratings for CN vs AD, CN versus MCI, and MCI versus AD were 92%, 86%, and 84%, respectively. The approach of cross-validation was tenfold. For the purpose of classifying CN, MCI, and AD patients, Zhang et al. [21] divided the MCI patient group into early MCI (EMCI) and late MCI (LMCI). To assess the categorization ability of classifiers, the MCI group was split apart. Using the Diffusion Tensor Imaging (DTI) data, the White Matter (WM) regions of the brain were calculated in terms of location, orientation, and anisotropy. Patients with AD have patterns of atrophy in both their white matter (WM) and gray matter (GM). It is thought that GM atrophy precedes WM atrophy. Mean diffusivity (MD) and fractional anisotropy (FA) are the two DTI measurements that are most often used [42]. Whereas MD measures the gross voxel diffusion, FA assesses the directionality of the water diffusion in the tissue. Conversely, the diffusion coefficients that are parallel and vertical to the direction of the WM area are shown by the axial and radial diffusivities, respectively. Local diffusion homogeneity (LDH) uses the Kendall's coefficient concordance (LDHk) and the Spearman's rank correlation coefficient (LDHs) to quantify the diffusivity series' overall consistency. These diffusion metrics separate WM's microstructural characteristics. Preprocessed DTI data gave an idea of the WM diffusion parameters. Next, the SVM and Logistic Regression (LR) techniques are used to the four categories (CN, EMCI, LMCI, AD). Leave-one-out cross-validation (LOOCV) is used to evaluate classification performance even with small sample numbers. A trustworthy estimate is generated by LOOCV when the classifiers are generalized. SVM was used with the Recursive Feature Elimination (RFE) method to get the final feature dimension. Accuracy values of 89.9%, 88.1%, 100%, and 92.98% were obtained for CN against AD, CN versus eMCI, 84.55% for eMCI versus AD, and 97.7% for lMCI versus AD using DTI scans of 213 subjects (51 CN, 75 eMCI, 39 lMCI, and 48 AD) from the ADNI dataset.

Artificial Neural Networks (ANN)

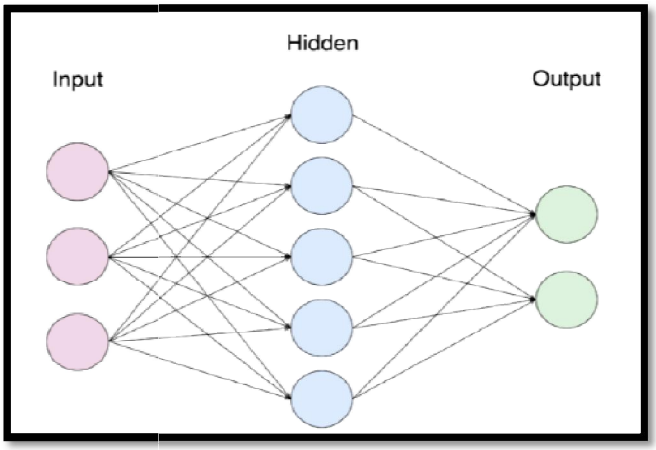

Fig -2: Artificial Neural Network

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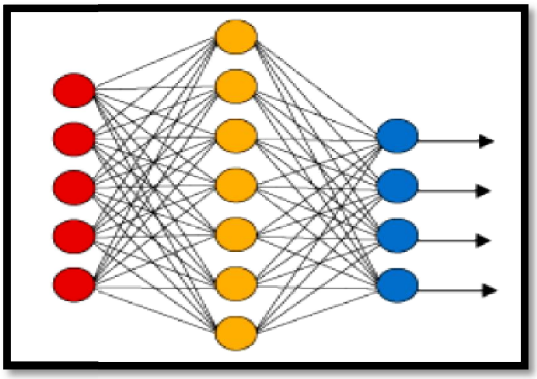
An artificial neural network is a computer system that simulates how the human brain functions, including how it evaluates and processes data. ANNs are capable of self-learning, which enables them to generate output layers with input, hidden, and output layers for improved performance. Efficient pseudo Zernike moments (PZMs) were suggested by Gorji et al. [22] for the diagnosis of MCI and AD from CN. From structured MRI (T1), PZM is utilized to extract any discriminating information. 500 MRI datasets (148 CN, 172 MCI, and 180 AD) were classified using two types of neural networks: feed-forward Pattern Recognition Neural Network (PRNN) and supervised Learning Vector Quantization Neural Network (LVQNN). Using 10-fold cross-validation, accuracy of 97.27% for CN versus AD, 94.88% for MCI vs AD, and 95.59% for CN vs MCI were found. By integrating with several distinct kernel functions, several Kernel Learning (MKL) represents a potential class of machine learning algorithms for complex data mining applications.[23]. MKBoost is an MKL method for classification issues that improves the multiple kernel learning classifier. The fundamental idea of MK boost is to use boosting to teach a series of multiple base kernel classifiers, each of which is taught from a single kernel. Liu et al. [24] classified 710 individuals (200 AD, 120 MCIc, 160 MCInc, and 230 NC) using SVM with MKBoost. The accuracy rates with a 10-fold validation were as follows: 95.37% for CN vs AD, 90.41% for MCI versus AD, 86.56% for CN versus MCI, and 73.95% for MCIc versus MCInc. Transfer Learning, which applies the information acquired from addressing one issue to another, may be used to tackle a variety of distinct but related problems. Samples from a single domain are used by conventional machine learning algorithms, and it has been shown that using fewer samples has an impact on the algorithms' performance. Important observations may be made using correlation data from several fields. In their publication, Cheng et al. [25] introduced a Multi-Domain Transfer Learning (MDTL) framework that may help with early AD detection. It comprises of a multi-domain transfer feature selection (MDTFS) model and a multi-domain transfer classification (MDTC) model. Additionally, they contrasted the standard SVM with least absolute shrinkage and selection operator (LASSO) [31], Multitask Feature Selection (MTFS) [32], Manifold regularized MTFS (M2TFS) [33], and their own MDTFS. They discovered that, due to the fact that all of the other methods—aside from Lasso—are multi-auxiliary domains, MTFS, M2TFS, and MDTFS achieve better classification performance than Lasso method. MDTFS performs better than M2TFS and MTFS. Accuracy rates of 94.7% for CN versus AD, 81.5% for CN vs MCI, and 73.8% for progressive MCI (pMCI) vs stable MCI (sMCI) were obtained using 10 fold validation and MRI of a total of 807 patients (186 AD, 167 pMCI (progressive MCI), 228 sMCI (stable MCI), and 226 NC). In order to mitigate the adverse impacts of unconnected source domains, Cheng et al. [26] improved their techniques even further by creating a reliable multi-label transfer feature learning (rMLTFL). Three components make up the framework: (1) pre-processing and feature extraction of the picture; (2) rMLTFL; and (3) classification using baseline SVM. rMLTFL helps distinguish unrelated domains and can concurrently find and extract similar characteristics from a multi-source domain. Accuracy rates of 95.2% for CN versus AD, 82.4% for CN vs MCI, 76.3% for pMCI vs sMCI, and 76.7% for MCI vs AD were attained by classifying 406 individuals (112 CN, 86 pMCI, 106 sMCI, and 102 AD). Thus, using rMLTFL resulted in a significant improvement in accuracy.

Deep Learning (DL)

Simple neural network



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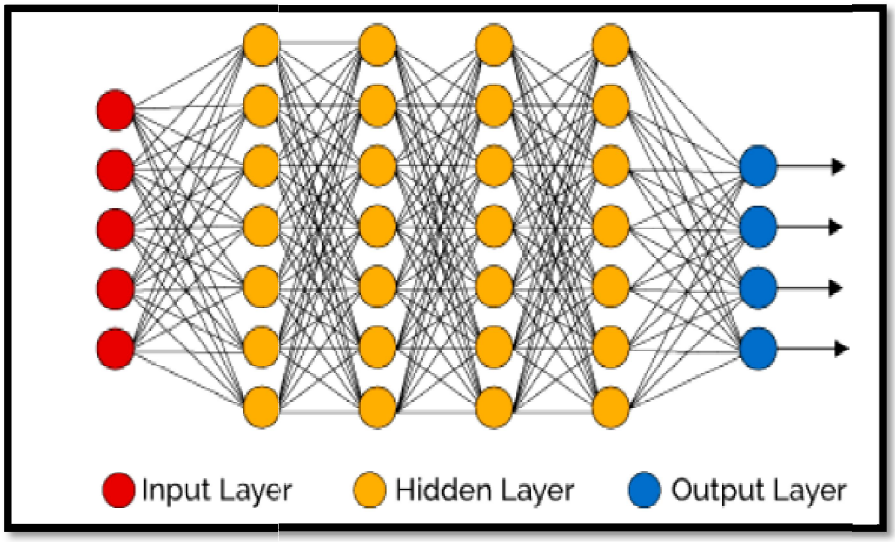

Fig. 3. Deep Learning Network

Deep learning is a subfield of machine learning that uses artificial neural networks to simulate the structure and functions of the human brain. Suk et al. [27] proposed a deep learning-based latent feature representation called stacked auto-encoder (SAE). The concept that demonstrates how deep designs perform better than shallow structures in terms of the computational components and parameters required to identify unknown functions forms the basis of deep learning [34]. One of the main ideas of deep learning is that low-level properties are defined by the low-layer and extracted by the high-layer. The latent representations from the original neuroimaging and biological features are made visible using the stacking auto-encoder (SAE). Their investigation included 52 CN participants, 51 AD patients, 99 MCI patients (43 of whom were MCI converters, or patients who proceeded to AD), and 56 MCI non-converters, or patients whose transition to AD did not occur in 18 months. The neuroimaging data included biological information such CSF data, as well as baseline MRI and 18-fluorodeoxyglucose (FDG) PET image data. Deep architecture may be utilized to uncover latent or buried representation that is present in the low-level features from modalities and eventually increase classification accuracy when it comes to neuroimaging and biological data. They used GM for classification because it has a higher connection with AD and MCI patients than WM and CSF [35]. The GM tissue volume from MRI and the mean intensity from FDG-PET were utilized as characteristics for each ROI. 93 features were obtained from MR scans, and the same dimensional characteristics were obtained from FDG-PET images. They arrived at a conclusion and confirmed the effectiveness of the proposed method by figuring out that the accuracy of the classification of AD vs. CN, MCI vs. CN, AD vs. MCI, and MCI-C vs. MCI-NC was 98.8%, 90.7%, 83.7%, and 83.3%, respectively, using tenfold validation. In relation to the AD prediction Hosseini et al. [28] introduced a 3D convolutional neural network (3D-CNN) that is pre-trained using 3D Convolutional Autoencoder (3D-CAE) in order to identify general chosen AD characteristics in the lower layers. A typical unsupervised autoencoder is used to obtain a few co-oriented scalar feature maps from input 3D image sets including scalar or vector voxel-wise signals via the integration of data encoding and decoding. Back-propagation, which limits the feature space characteristics to lower the reconstruction error, is used in the autoencoder training process to extract features that represent distinct patterns of changes in the input data. Using previously trained 3D-CAE, the Deeply Supervised Adaptive 3D-CNN (DSA-3D-CNN) was updated and refined using adadelta gradient descent [36]. Five groups were classified using structural MRI (sMRI) scans from the ADNI database, 210 individuals (70 AD, 70 CN, and 70 MCI): There are one ternary (AD vs. MCI vs. NC) and four binary (AD vs. MCI, MCI vs. NC, AD vs. MCI, and AD+MCI vs. NC). The DSA-3D-CNN was pre-trained using a source domain of thirty individuals with CADDementia. Then, the recovered features were used to find AD biomarkers in the bottom layers of the 3D CNN network. The accuracy of the group's AD vs. NC, MCI vs. NC, AD vs. MCI, AD+MCI vs. NC, and AD vs. MCI vs. NC classifications was determined to be 99.3%, 94.2%, 100%, 95.7%, and 94.8%. They arrived at a conclusion and confirmed the efficacy of the recommended approach by

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differentiating between AD, MCI, and NC. Seven classification measures were obtained using ten-fold cross-validation: F1-score, accuracy (ACC), precision (PPV), sensitivity (SEN), balanced accuracy (BAC), specificity (SPE), and sensitivity (SEN). Zheng et al. proposed a stacked Deep polynomial network (S-DPN) [29]. The S-DPN technique aims to enhance feature representation, while the DPN method efficiently determines feature representation from fewer samples. They used neuroimaging data from the ADNI database, including MR and PET. Their proposal was to combine multi-modality neuroimaging data and use a multi-modality S-DPN (MM-S-DPN) approach to create a more powerful and distinctive feature representation for AD classification. For S-DPN, a deep hierarchy is produced by successively stacking several 2-level basic DPNs. Every DPN is built using a three-layer network, with the output from one basic DPN level being used as the input for the next basic DPN level. A two-stage S-DPN is used in the MM-S-DPN algorithm. In the first step, the high-level feature representation from MRI and PET is extracted using two S-DPN, respectively. Since each of these modalities contains attributes unique to AD, in the second step these extracted high-level characteristics are fed to another S-DPN to connect the modalities. We used the same MRI data from 51 AD patients and 52 CN patients. The sMRI was segmented using the following procedures: cerebellar excision, anterior commisure (PC) correction, posterior commisure (AC) correction, grey matter, white matter, and cerebrospinal fluid. Each MR image was divided into 93 regions of interest (ROIs) using atlas warping. Furthermore, the grey matter volumes of all 93 ROIs were considered as a feature. Each PET image is inflexibly registered with the corresponding magnetic resonance image of the same subject. When developing features for PET imaging, the average intensities of the 93 ROIs were taken into account. As a result, 93 traits in all were obtained across all modalities. An embedded classifier and a linear SVM classifier were the two classifiers used to do the classification. We investigated the accuracy of the MM-S-DPN method using these two classifiers. When using the SVM classifier, the MM-S-DPN approach successfully combines MRI and PET data, producing a 97.27% classification accuracy. The AD vs. CN classification using MM-S-DPN with embedded classifier was 97.27% accurate. Zheng et al. [30] developed a multi feature-based network (MFN) employing sparse linear regression (LASSO) applied to six distinct types of morphological data in order to give structure-based auto diagnostic. They examined baseline magnetic resonance imaging (MRI) data for 528 individuals, 165 CN, 142 AD patients, and 221 MCI patients, of whom 126 had progressive MCI (pMCI) and 95 had stable MCI (sMCI) from the ADNI database. These images were prepared using the following techniques: gray matter (GM) segmentation, motion correction, coordinate transformation, non-brain tissue removal, GM/white matter border reconstruction, and FreeSurfer [37, 38, 39]. The cross-validation process was used to evaluate the morphological characteristics, network connections, network properties, and their combinations. In every interaction, layered feature selection, parameter optimization, and classifier training were used to perform cross-validation. They employed a two-step feature selection strategy to isolate the dominant subgroup and reduce the risk of overfitting. The feature selection algorithms used were SVM-based recursive feature elimination (SVM-RFE), minimum redundancy and maximum relevance, and SVM. Although SVM-RFE is an iterative backward feature elimination strategy, minimum redundancy and maximum relevance choose features that are highly distinguishable and have low redundancy [40], while computing the ranking weights for all the features and eliminating the features with the lowest weight [41]. Because MFN is sparse, 75% of less discriminative or non-discriminative characteristics were eliminated; SVM-RFE was then used to evaluate the remaining features. In the MFN classification performance, CN vs AD achieved an accuracy of 96.42%, CN against MCI of 96.37%, MCI vs AD of 70.52%, and sMCI vs pMCI of 65.61%. The classification performance increased with the inclusion of morphological features and network properties; the corresponding accuracies for CN against AD, CN vs MCI, MCI vs AD, and sMCI vs pMCI were 98.70%, 97.93%, 73.82%, and 67.42%.

III. DISCUSSION

We discussed the SVM, ANN, and DL approaches to AD classification. Table 1 provides a synopsis of every article we have read. The primary categories that were identified were CN against AD, CN vs MCI, MCI vs AD, CN vs eMCI, CN vs lMCI, and so on. The main objective of this comparison is to assess various algorithms. The accuracy of classification is contingent upon the used modality, dataset, and feature extraction methodologies. Cross-validation was often done using ten fold validation. Table 2 lists the advantages and disadvantages of every algorithm. For deep learning, huge datasets are optimal, for ANN, small and large datasets are optimal, and for SVM, tiny datasets are

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optimal.SVM works well with both linear and non-linear data, while ANN and DL do well with non-linear data. The implementations of ANN and DL algorithms are more complex than those of SVM. In contrast to ANN and DL, SVM requires more training time.

IV. CONCLUSION

As machine learning has become more and more popular, corresponding advancements have made it possible for it to play a significant role in healthcare, including the identification and diagnosis of several illnesses as well as the creation of novel techniques that support medical treatment. In this work, three machine learning methods are compared: The methods Support Vector Machine (SVM), Artificial Neural Networks (ANN), and Deep Learning (DL) were all utilized to categorize Alzheimer's disease into different phases. It is noted that more study is needed to classify eMCI versus lMCI and sMCI vs pMCI. It is noted that there is a wealth of studies on the distinctions between CN and AD and CN and MCI. In our next study, we want to evaluate several machine learning methods for Alzheimer's disease detection and diagnosis.

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