A Deep Learning Model in the Detection of Alzheimer Disease

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Abstract: Precise detection of Alzheimer's disease (AD) plays an important role in health treatment, particularly at an early stage, since understanding of the likelihood of incidence and development helps patients to take preventive steps before permanent brain damage is induced. While several experiments have recently used machine learning approaches for the computer-aided diagnosis of AD, a bottleneck in diagnostic performance has been found in most of the previous studies, mainly due to the congenital defects of the selected learning models. In this research paper, to resolve the bottleneck and help diagnose AD and its prodromal level, Mild Cognitive Impairment (MCI), with stacked auto-encoders and a softmax output layer, we have created a deep learning architecture. Compared to previous workflows, our approach is capable of evaluating a variety of groups in a single setting that involve fewer labeled training samples and limited prior domain awareness. A substantial improvement in efficiency was achieved in the description of all diagnostic classes in this research paper.

Keywords: Alzheimer's Disease, Deep Learning, Machine Learning, Mild Cognitive Impairment, Dementia, Computer-Aided Diagnostic.

1. Introduction

The global occurrence of dementia has a huge impact on the global economy, with millions of persons suffering from dementia worldwide. Also, its occurrence has a detrimental effect on the lives of patients and the physical and mental conditions of their caregivers. As a consequence of certain risk factors, Dementia may be formed as well as it have several manifestations whose symptoms are often identical. Although there is currently no treatment for dementia, in treating it, successful early diagnosis is key. Early diagnosis allows patients to identify effective interventions that minimize or even avoid more cognitive dysfunction, and to gain charge of their situation and prepare for the future. In addition, it also makes scientific attempts to understand the causes and symptoms of dementia simpler. Early diagnosis is based on the classification of characteristics drawn from three-dimensional images of the brain. The characteristics must precisely capture important anatomical differences in brain structures related to dementia, such as hippocampus size, volumes of gray and white matter tissues, and brain volume [1].

Many researchers [30-37] have been working to develop new or enhanced Computer-Aided Diagnostic (CAD) technology to reliably diagnose of dementia in recent years. The purpose of the CAD methods is to help radiologists improve the accuracy of the diagnosis and decrease false positives. There are, however, a variety of restrictions and unsolved challenges in the state-of-the-art that need to be tackled. Such drawbacks are that, to date, research has focused on differentiating the nature of Alzheimer's Disease (AD) multi-stage, excluding other forms of dementia that may be as debilitating or even more [3]. In addition, the high dimensionality of neuroimages, as well as the sophistication of biomarkers of dementia, can impede the performance of classification. In addition, owing to the inconsistencies and anomalies of the different types of evidence, the augmentation of neuroimaging research with contextual knowledge has received little attention to date. This work focuses on resolving the need in the early stages to distinguish between various forms of dementia including AD.

AD is a form of dementia. It is a type of progressive and neurodegenerative disease. The early diagnosis of the disease can help the disease from worsening even though it is incurable. Currently the method that is being currently utilized for AD is analysing the Magnetic Resonance Images (MRIs), to arrive at a conclusion regarding the disease. Analysing MRIs can help distinguish between an AD and Normal Control (NC) due to its high resolution characteristics. However, the method is time-consuming, and since the symptoms vary from person to person it may lead to misdiagnosis. Early diagnosis of AD is primarily correlated with the identification of AD prodromal level, Mild Cognitive Impairment (MCI). While memory complaints and MCI deficiencies may not have a major effect on patients' day-to-day operations, MCI has been reported to have a strong likelihood of advancement to AD or other forms of dementia. Precise early detection of AD, in particular the recognition of the possibility of development from MCI to AD, increases consciousness of the severity of AD patients and encourages them to take proactive measures, such as dietary adjustments and drugs [2].

Deep learning is an artificial intelligence method. Deep learning basically works like a human brain. Deep learning has the capability to learn from data that is unstructured or unlabelled. The artificial network used in deep learning has several levels. At the initial level certain information is gained by network [12]. The information thus gained by the initial level is send to the higher level of the network. This continues as information gained at each level

gets transcended to its next higher level and as it gets transcended a higher complex data is also evolved from the data obtained. An example for identifying an object, the first level of a deep learning network identifies the edges and lines at a preliminary stage. This may be done by identifying the differently lighted areas. As mentioned before the information gained about the edges and lines in the first level gets transferred to the next higher level where further identification takes place. The next level puts together all the lines and edges identified to get an idea of the shapes present. The next higher level then uses the information generated by the previous lower level to get an abstract idea of what the object actually is with the Avid features finally it's in the final level that the object gets identified. The deep learning has a higher complexity. The main problem that we face when it comes to using deep learning is the availability of data. A large dataset is required in order to obtain an accurate result. So in short only large dataset can provide us with best result while classifying a patient as AD, MCI and NC. In order to obtain the result accurately and to avoid any kind of misdiagnosis, we made sure to include all kinds of images while training such as different ages, gender etc [13].

Targeting the shortcomings of previous studies [30-37], we investigate how existing workflows may be streamlined efficiently. Based on a deep learning architecture, consisting of stacked sparse auto-encoders and a softmax regression layer, we suggested a novel early diagnosis method for AD in this research paper. The suggested solution is multi-class in nature which may minimize the reliance on prior knowledge. In addition, our method is semi-supervised, and can be extended to make it easier and cheaper to procure unmarked training samples [2].

2. Literature Review

Several machine learning methods have been proposed to support diagnose AD based on high-dimensional features acquired from different subclasses of neuroimaging biomarkers [4], i.e. It's MRI. In addition to the automated isolation of AD subjects from NC subjects, these machine learning models often need to anticipate the likelihood of MCI subjects switching to AD, so MCI instances can be classified as MCI non-converters (N-MCI) or MCI converters (C-MCI) depending on the probability of progression. As a consequence, early detection of AD will naturally be modeled as a multi-class classification problem [2].

The problem has been simplified by some earlier studies [30-37] in the binary classification method. The workflow incorporates features from a broad variety of biomedical modalities utilizing a multi-kernel Support Vector Machine (SVM) classifier. However, SVM considers it difficult to distinguish subjects in more than two groups in one setting. A variety of techniques have incorporated prior expertise in the design of the network. An algorithm i.e. optimized graph cut was proposed and implemented in the training data set with changed parameters corresponding to the distribution of specific groups. Dependence on previous knowledge can often be vulnerable and challenging to customize for dataset adjustments [2].

Authors [14] in the paper proposes the idea of Region of Interest (ROI) to be inculcated to detect whether a person has the AD or not .The grey matter and white matter of the brain were utilized for the same. The major steps involved are i.e. Pre-processing, Image Segmentation, ROI, Classification. The images were taken from Alzheimer's Disease Neuroimaging Initiative (ADNI) database [15]. Image Pre-processing involves grey scale conversion and noise removal using median filters. Segmentation of the image is done to highlight the areas of interest. The segmentation changes the image representation by processing label to each pixel of the input image. ROI is obtained from the segmented image by carrying out a binary mask operation on the segmented image. Prior to training feature extraction was carried which was done using wavelet transforms. Binary and multiclass classification was done, by taking into consideration the volumetric features and then this feature are considered for the calculation of the amount of the grey matter distribution in each image. The dimensionality reduction was done using Principal component analysis (PCA). Several classifiers were used and the three of them SVM, Import Vector Machines (IVM) and Rough Extreme Learning Machine (RELM) were found to be effective; Thus SVM was used for pattern recognition. The main idea behind using grey matter and white matter was to observe that the ratio of grey matter and white matter will be more for person having the diseases. So based on the ratio obtained, it is concluded whether the person has AD or not.

Authors [17] in the paper propose a deep neural network for the AD detection. The proposed network has several layers that perform each of their specific operations. The dataset used was Open Access Series of Imaging Studies (OASIS) [16], which has about 416 data samples. The layers are convolution, batch normalization, Relu and pooling. The SoftMax layer is used in the final output end with four classes as non demented, very mild, mild and moderate. The MRIs are not fed such to the proposed network; they are converted to several patches which are then fed into the proposed network. Sensitive training was incorporated to handle any imbalance in the dataset and a cost matrix is used at the final end, to modify or make any changes to the output. The weight is assigned based on the number of samples present in the class [4]. The network actually utilizes only a small set of data. The data was divided into training and validation set [4]. The validation was prepared using 10 percent of the training dataset. The performance was analysed and since this uses only a small set of data, it was found that this method can be improvised by incorporating more data. The model due to less data, suffered overfitting as well.

Authors [18] In this paper proposes Random Forest (RF) as the method that can be used to eliminate some of the features which were not required. ADNI dataset was used for the studies. Data cleaning was performed as ADNI

data included 12749 data from 1737 patients. The follow up of some of the patients up to 10 years was collected while some were collected only up to 2 years. This was repeated in every 6 months and some of data was found missing by them later. The study was conducted as solution at find the similarities when AD and MCI changes occurs. During data cleaning, healthy patients and patients without disease at present were deleted. RF is used after data cleaning and Gini feature selection was used for taking the features into consideration. Using the features that were selected by RF the Neural Networks were created.

Authors [19] in the paper provide an overview of Prediction of AD using different machine learning methods. The major steps involved are Pre-processing, Feature Extraction and selection, Training and testing and Classification [3]. The image Segmentation is the step involved in Pre-processing and it is performed using Fuzzy logic based segmentation algorithm. It is implemented using Fuzzy rule base and FIS targeted at detecting strong and weak edges of brain MRI images. Feature extraction involves extraction of specific features from the images .It is mainly used to decrease size of original data. Then SVM classifier is used for classification of disease.

Authors [20] in the paper mainly uses a Convolutional Autoencoder based unsupervised learning for AD and NC classification. The most important biomarkers are detected using gradient based visualization method which approximates the spatial influence of the Convolutional Neural Network (CNN) model. Autoencoders serve to provide dimensionality reduction as well. Moreover the advantage is that it does not require labelled data. The input data are transformed into lower dimensional feature space during encoding phase and the data which has been encoded is then reconstructed to obtain the data in original space. Fine tuning was performed for task specific binary applications and transfer learning was used for MCI classification.

Authors [21] propose a three-dimensional CNN (3D-CNN) to be built using the Tensor flow framework. This model built could facilitate end-to-end classification. Apart from being able to provide the best classification performance when compared to other models it also helps identify biomarkers that are considered to be relevant. It was noted by the experimenters that the hippocampus region of the brain is very crucial when it come to the detection of the AD .An extensive hyper parameter tuning is made use of and a best architecture model is being made of to the fullest. The MCI layer is fine-tuned as well. In the long run they also found that the simple architectures provide better results compared to the other more complex architecture as the chance of overfitting might be less.

Authors [5] proposed a multi-modal deep learning approach to predict MCI to AD conversion using longitudinal cognitive performance and Cerebrospinal Fluid (CSF) biomarkers. Cross Sectional neuroimaging and demographic data was also used. Multiple Graphics Processing units (GPUs) were applied by them to make use of the longitudinal multi-domain data .The Results gained confirms that it achieved the better prediction accuracy of MCI to AD conversion only being used the longitudinal multi domain data. This approach will be able to identify persons who are at the risk of developing AD and thus be able to provide adequate treatment.

Authors [6] proposes the need for proper selection of effective and better biomarkers (features) of brain MRI scans for AD, which would facilitate better prediction The multistage classification model for AD detection and image retrieval, were investigated. The Particle Swarm Optimization (PSO) technique for feature selection was the method employed by the experimenters and it was performed to get an adequate amount of information regarding the brain structural change, which is concerned with to the clinical detection of AD. The feature selection examines were cortical thickness features, volume features, as well as a combination of thickness and volume. The multistage classifier which was utilized showing a good performance for AD detection when compared to other machine learning approaches and the image retrieval scheme followed by the method also portrayed appropriate results. The accuracy was high and performance was good.

A new automatic approach based on SVM classification of whole-brain anatomical MRI is introduced and tested by the authors [7] to differentiate between AD patients and elderly control subjects. The investigators analyzed 16 AD patients (mean age ± standard deviation (SD) = 74.1 ± 5.2 years, MMSE = 23.1 ± 2.9) and 22 elderly controls (72.3 ± 5.0 years, MMSE = 28.5 ± 1.3). Three-dimensional T1-weighted MRIs were automatically converted into ROIs for each subject. SVM algorithm used to identify the subjects and statistical techniques based on bootstrap re-sampling to ensure the robustness of the results, based on the characteristics of gray matter derived from each ROI. For AD and control subjects, proposed system gained 94.5 percent average accurate classification (mean specificity, 96.6 percent; mean sensitivity, 91.5 percent). A tool that can automatically distinguish patients with early AD from control subjects. This approach has the potential for early AD diagnosis. In MCI patients and other neurodegenerative disorders, the procedure will be tested and its robustness will be evaluated in patients with images acquired from multiple MRI scanners with varying acquisition parameters.

In order to improve diagnostic methods and to better understand the neurodegenerative process, precise recognition of the most important brain regions involved with AD is crucial. Statistical grouping is ideal for this purpose. Authors [22] proposed to apply a novel approach based on SVM recursive feature elimination (SVM-RFE) to segmented brain MRI to detect the most discriminating AD with ROIs. Both gray and white matter tissues are analyzed, obtaining up to 100 percent accuracy after classification and outperforming the findings obtained by the typical set of t-test features. This approach, applied to various subject sets, allows high-resolution areas surrounding the hippocampal region to be automatically determined without the brain images having to be

separated according to any standard blueprint. By way of an SVM based wrapper approach applied to structural pictures, that is, MRI, the major area of brain concern involved in AD has been delimited. In terms of precision, the proposed approach, which recursively eliminates the least important features from the initial collection (SVM-RFE), has proved to outperform t-test range, achieving almost 100 percent. For both gray and white segmented problems, the high-resolution ROIs were computed, matching recent literature that recognizes the hippocampal area as one of the most significant in the development of AD. In addition, to help explain the anatomical morphology connected to AD, 3-D drawings of the regions have been given. In addition, this procedure, previously unexplored for MRI, may provide useful knowledge for aging research on brain structures in other clinical applications.

AD is typically recognized by multiple behavioural signs that are frequently erroneously attributed to age related problems or stress [23]. However, there are additional services needed for proper diagnosis and control of the disease. Authors [8] provide a novel approach to identify AD from patient support MRI. A wide database of over one thousand patients has been used. Two separate problems are addressed: one where a classification system is created to identify MRIs as either normal or with AD, and the other where normal subjects, MCI patients, and AD patients are categorized and graded. It is interesting that it may provide a method to promote the early diagnosis of dementia. The technique overview includes wavelet function extraction from the MRIs, reduction of dimensionality, subdivision of training-test and classification using SVMs. Any issues related to performance measurement and reductions in dimensionality are addressed. It tackles the considerable problem of AD recognition and the MCI disorder prior to dementia, creating intelligent classifiers that can successfully identify various patients according to their disorder using MRI knowledge. For feature extraction, Discrete Wavelet Transform (DWT), PCA for feature reduction, and various methodologies have been used, such as the Normalized Shared Knowledge Feature Selection algorithm, as a choice of features. Research has shown that the use of dimensionality reduction in this problem resulted in a worse accuracy of classification, using both PCA and feature selection algorithms, thereby highlighting the importance of using all available classification information and the complexity of choosing appropriate classification problem information. In the training of the classifiers, this leads to a greater computational cost, but that is worth the cost in certain situations, according to the results obtained for the NAD problem. As a classification method, SVM was used and the results obtained proved to be promising. The research on the best slices to perform the classification, the use of other dimensionality reduction algorithms that could achieve a reduction in time complexity for the problem, and the study on other databases of the same algorithm suggested here remain as potential work at this stage.

Using cerebral image characteristics obtained from MRI, numerous studies [30-37] have distinguished AD. Authors [3] were interested in integrating volumes of hippocampus and amygdala and entorhinal cortex thickness to enhance the distinction efficiency of AD. The aim of the research was therefore to analyze the useful features obtained from MRI for the classification of AD patients using the help of SVM [3]. In order to measure hippocampus and amygdala volumes and entorhinal cortex thicknesses in both brain hemispheres, T1 weighted MR brain images of 100 AD patients and 100 average subjects were analyzed using FreeSurfer tools [3]. To correct the difference in the human head size, proportional volumes of the hippocampus and amygdala were measured. With five feature variations, SVM was used with (H: hippocampus relative volumes, A: amygdala relative volumes, E: entorhinal cortex thicknesses, HA: hippocampus and amygdala relative volumes and ALL: all features). To test the system, Receiver Operating Characteristic (ROC) analysis was used. The Area Under the Curve (AUC) values were 0.8575 (H), 0.8374 (A), 0.8422 (E), 0.8631 (HA) and 0.89066 (A) for the five variations (ALL) [3]. Although "ALL" had the highest AUC, except for the "A" feature, there were no statistically significant differences between them. Research has shown that for computer-aided classification of AD patients, all proposed features could be feasible. A computer-aided method for classification of AD patients and normal subjects based on SVM with cerebral image characteristics derived from T1-weighted brain MRI, including proportional volumes of hippocampus and amygdala and entorhinal cortex thicknesses, was suggested. Preliminary findings showed that strong separation of AD was given using "ALL" characteristics [9].

A variety of experiments have been performed in recent years on automatic detection and diagnosis of AD using various methods. Several of these studies [30-37] centered on the detection of AD from neuroimaging evidence. However, it is important to recognize symptoms as early as possible as the condition-altering drug will be more effective before the advent of irreversible brain damage if administered early in the disease phase [24]. Therefore, the usage of sophisticated methods to diagnose AD symptoms from such data is of high value. To assess the right AD pre-detection method, the authors [10] report an experimental approach. Studies were made up of laboratory studies. These two experiments were used utilizing the DNA dataset. This study related to an assumption prior to the first experiment, which is that there is a good method of AD detection that will also be effective in the pre-detection of AD. Various data sets and various methods of diagnosis have been utilized by different scholars. The SVMs was validated as the first trial, the latest and most powerful form of detection. The sensitivity is 95.3 percent, the precision is 71.4 percent and the accuracy is 84.4 percent with the usage of SVM, according to the results of the initial experiment. The proposed CNN model was tested using a number of image segmentation techniques and datasets. At the end of the day, a strong precision of around 96 percent (sensitivity-96 percent, accuracy-98

percent) was obtained by the best image segmentation solution and the CNN model stayed dataset neutral. The results of this study suggest a major function in early detection of AD utilizing imaging and deep learning techniques. In this research work, The two research concerns are what is acceptable for the methods used in previous studies [30-37] to diagnose AD, such as SVM, in the function of early diagnosis and how feasible it is to integrate deep learning strategies such as CNNs to identify Alzheimer's symptoms from neuroimaging outcomes. It is evident from the first experiment that the SVM strategy previously used is not appropriate for the detection of symptoms in moderate to extreme cases of AD. Early AD diagnosis requires sorting the images into three categories (AD, MCI and NC). However, SVM does not perform well in multiclass classifications. Therefore, SVM cannot be used for early diagnosis of AD. The precision of the description may also be further improved with the usage of a deep learning approach. In addition, the usage of deep learning approaches is applicable since it functions well in multi-class classifications. A second research issue was posed in the second experiment. The utility of the different imaging segmentation strategies was tested in the first sub-experiment. The reason for this is that the full picture is too complicated and contains non-brain regions that are not related to the AD as compared to other pictures. Subsequently, certain non-brain areas were omitted from all images and the output was measured. The best outcome of the six evaluation processes without detecting any extended ROI edges (Sensitivity 96 percent, Specificity 98 percent, and Accuracy 96 percent). The goal of edge detection is to illustrate the amount of cortex, hippocampus and ventricles. However, as the canny edge detection algorithm excludes both white matter and gray matter details from the brain picture, the improved ROI performance decreases significantly when the edges are identified. However, there is a lot of evidence that show that white matter and gray matter have helped to establish the number of these three characteristics rather than to recognize boundaries. Small ROI without edge detection has a precision of 89 percent (Sensitivity 89 percent, Specificity 95 percent) based on findings and is roughly 92 percent with edge detection (Sensitivity 92 percent, Specificity 96 percent). Restricted ROI should have the best precision relative to the predictions produced during deployment, since it is focused more on three common features than other segmentation approaches. When considering the results, there was a contradiction in the hypothesis. The main drawback of the tiny ROI is that some of the common features inside the ROI are not connected. Two databases were evaluated for the second sub-experiment. There is no substantial variation between the findings obtained from different datasets. There is plenty of documentation to prove that the dataset was not based on the CNN standard. Accordingly, the CNN model stays neutral to the dataset.

3. Research Methodology

Machine learning models' output is highly dependent on the level of representation of the original training samples. The other algorithms are challenged by representative learning models through the ability to disentangle dynamic and structural dependencies in high-dimensional feature spaces. The representation of the function will take advantage of the depth of the learning structure, which learns deeper representations from the multiples derived by the previous hidden layers [2].

Two primary components will illustrate our learning structure: stacked sparse auto-encoders and a layer of softmax regression. Deep representations of the original input are obtained by the auto-encoders. By choosing the highest predicted probabilities of each mark, the softmax regression layer classifies instances [2].

The sparse auto-encoder is an encoding structure which, as shown in Figure 1, consists of a neural network with several hidden layers. The input layer's neurons interpret the initial input vector. Each hidden layer can be seen as a reflection of the previous layer at a higher level, while determining the exact meaning of each layer is typically non-trivial. A sparse representation of the input layer with the same dimensionality as the input is the output layer [2].
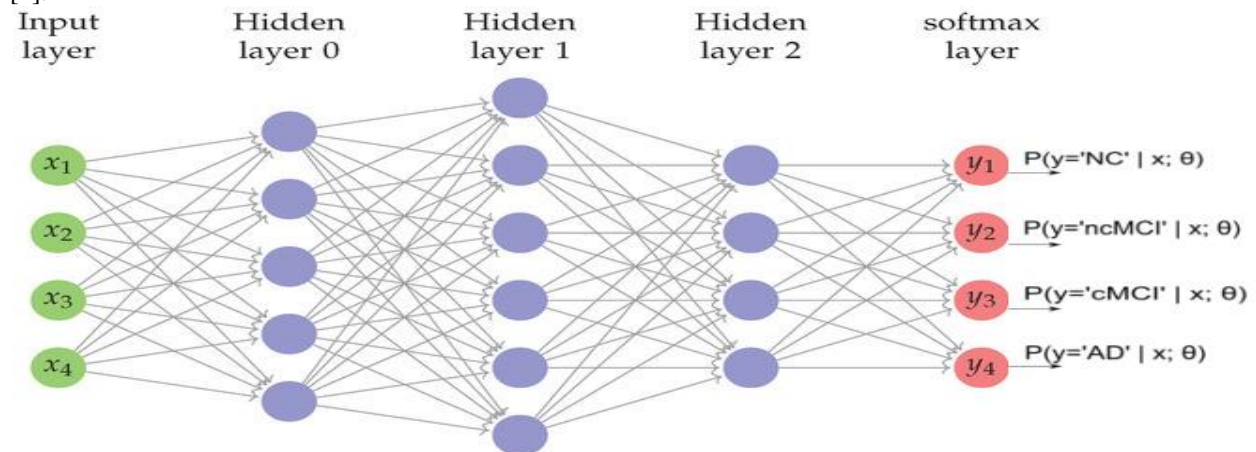

Figure 1: Deep Learning Network With The Softmax Layer

Figure 1 shows the illustration of the structure for deep learning with a multilayered neural network. The input layer feeds pre-computed features to the hidden layers, from MRI data [11]. Nonlinear transformations from the previous layer are obtained by each hidden layer and optimized to reconstruct the original case. The softmax layer takes the activations as inputs of the last hidden layer and gives the likelihood of each AD level [2].

Using Equation 1 as defined in previous research [2], the activation signals are iteratively propagated forward through the network until the output layer is reached. The following formulas will measure the neuron activation a of each layer [2].

$$
\begin{cases}
a_{(l)}^{(i)} = x^{(i)}, l = 1 \\
a_{(l)}^{(i)} = \sigma(W^l a + b), l > 1 \\
\quad h(W, b, x) = a^{(N)},
\end{cases}
$$

(1)

(2)

Where x is the unlabeled data $\{x^{(i)}\}_{i=1}^m$; W is the weight matrix that controls the activation effect on neighboring layers between neurons; b is the bias term; σ is the activation function that can be set to sigmoid or hyperbolic tangent function to add non-linearity to model complex relationships for the network; and $h(W, b, x)$ is the representation of the input data and the activations at the output [11] as shown in Equation 2 as defined in previous research [2].

By altering the number of neurons on each hidden layer, we are able to reduce or over-complete the dimensionality of the function. Characteristics of various views or modalities may also be merged by concatenating features into one input vector. In data fusion, the sparse auto-encoder is shown to function well, capturing the synergy between various modalities [2].

As in Equation 3 as defined in previous research [2], representation loss is used as the objective function for optimization in order to train this unsupervised model [11].

$$
L(W, b, x, z) = \min_{W,b} E(W, b, x, z) + \gamma \|W\|_2^2 + \beta K(W, b, x),
$$

(3)

Where $E(W, b, x, z) = \|h(W, b, x) - z\|_2^2$ is the squared error representation loss [11]; the second term is the weight decay that results in small weights; the third term is the regularized sparsity penalty of β with a target activation of ρ close to 0, which enforces a sparse representation by penalizing the objective function through n training samples using Kullback-Leibler divergence [26] as defined in equation 3 as defined in previous research [2].

$$
K(W, b, x) = \sum_j^n ID_{KL}\left(\rho \| \frac{1}{m} \sum_{i=1}^m h_j(x^{(i)}; W, b)\right)
$$

(4)

By applying the back-propagation algorithm [11], the gradients of the objective function can be precisely computed; thus, the cost function in Equation 3 can be optimized by algorithms based on gradient descent. In this research paper, we applied Limited-Memory Broyden-Fletcher-Goldfarb-Shanno Algorithm [25] as defined in previous research [2] for better output in view of the restriction on the amount of biomedical data as shown in equation 4.

By removing the temporary output layer, we train the hidden layers of the sparse auto-encoder one at a time and stack them to form a full neural network. The first and last few hidden layers have been shown to be more beneficial than propagating the entire network [2].

A Softmax output layer is attached to the top of the qualified auto-encoder stack for AD classification, containing only previous hidden layers. A new activation function, which may have nonlinearity, is used by the softmax layer, different from the one applied in previous layers. The activation function of softmax is defined as follows as shown in equation 5 (as defined in previous research [2]):

$$
h_i^l = \frac{e^{W_i^l h^{l-1} + b_i^l}}{\sum_j e^{W_j^l h^{l-1} + b_j^l}},
$$

(5)

Where W_l^i is the ith row of W^l, and b_i^i is the last layer's i^{th} bias term [11]. As an estimator of $P(Y = i|x)$, we can use h_l^i, where Y is the corresponding input data vector mark as x. In our case, it is possible to interpret four output neurons on the softmax layer as the probabilities of diagnosing an example like NC, N-MCI, C-MCI or AD [2]. Similar to the Deep Belief Net (DBN) training technique, by unfolding all the auto-encoders and applying the backpropagation algorithm on the whole network, we can further fine-tune all the parameters in the network with respect to the overall classification loss [2].

Hidden neurons are equipped to capture various patterns of the input data on the first layer of our network. It is possible to analyze the features acquired from the first hidden layer to classify Region of Interests (ROIs) that are responsive to the progression of AD [2].

We can derive the input pattern x_j^* based on Equation 1, which activates the hidden neuron a_i maximally as shown in equation 6 as defined in previous research [2].

$$x_{ij}^* = \frac{W_{ij}^{(1)}}{\|W\|_2} \qquad (6)$$

We are able to map x_{ij}^* to the ROI where this function was extracted in our case. We measure the variance $D_j^{(m)}$ of all x_j^m of the same ROI by splitting the pattern x into m function views, calculating how various hidden neurons are triggered by the ROI. When $D_j^{(m)}$ is low, we consider that the characteristics derived from region j are more stable than the high-variance regions for AD diagnosis. The overall stability of the jth ROI as a function s_j can be determined as follows and shown in Equation 7 as defined in previous research [2]:

$$S_j = \sum_m \frac{\Sigma_j D_j^{(m)}}{D_j^{(m)}} \qquad (7)$$

To exaggerate the differences between each ROI, S can be convoluted with a Gaussian filter as shown in Equation 7 as defined in previous research [2].

SIMULATION

The neuroimaging information collected from the Alzheimer's disease Neuroimaging Initiative (ADNI) database [15] was used in our experiment. From the ADNI baseline cohort, we recruited the MRI images of 2500 subjects, including 480 AD subjects, 490 C-MCI subjects, 880 N-MCI subjects and 650 NC subjects. All MRI images are nonlinearly recorded and further segmented into 70 functional regions. We extracted the volumes of grey matter from MRI and Cerebral metabolic rate of glucose consumption patterns. Before each classification, the features were further selected using Elastic Net as defined in previous research [2]. All the characteristics are normalized to zero mean and between 0 and 1 to support the sigmoidal decoder.

Via Python [27], we have applied the deep learning framework outlined in this research article. Random search in a log-domain was extended to select the hyper-parameters that could be sensitive to the effects while training sets are small as defined in previous research [2].

The widely used single-kernel SVM (S-SVM) and multi-kernel SVM (M-SVM) were chosen in contrast to our proposed method. Both SVM-based experiments were conducted with the implementation of the Radial Basis Function (RBF) kernel using the LibSVM [28] packages for Python. We implemented the one against all method to allow SVM to perform the four-class classification task. Grid search was used to adjust the SVM parameters. With the same functionality, all the measurements were performed as defined in previous research [2].

The framework was tested by using 5-fold cross validation on the softmax layer. In order to maximally prevent the fortunate trails, we randomly sampled the training and testing instances from each class to ensure that they had the same distributions as the initial dataset [2]. Approximately 85% of subjects, including pre-training of deep neural networks, were used for preparation for all approaches in each cross-validation fold, and the remaining subjects were used for testing.

4. Results And Perforance Analysis

Figure 2 is a mapping of stability of features on a masked 3D MRI image to ROIs (70 ROIs). For various ROIs, the variations were clearly visualized. As features originating from these ROIs tend to similarly benefit all hidden neurons, the darker regions tend to be more vulnerable than the lighter ROIs to the development of AD and MCI. We merged the image with a Gaussian filter for better distinctions. It is not understood that the dark regions are totally negligible, but they contain fewer predictive results [2].
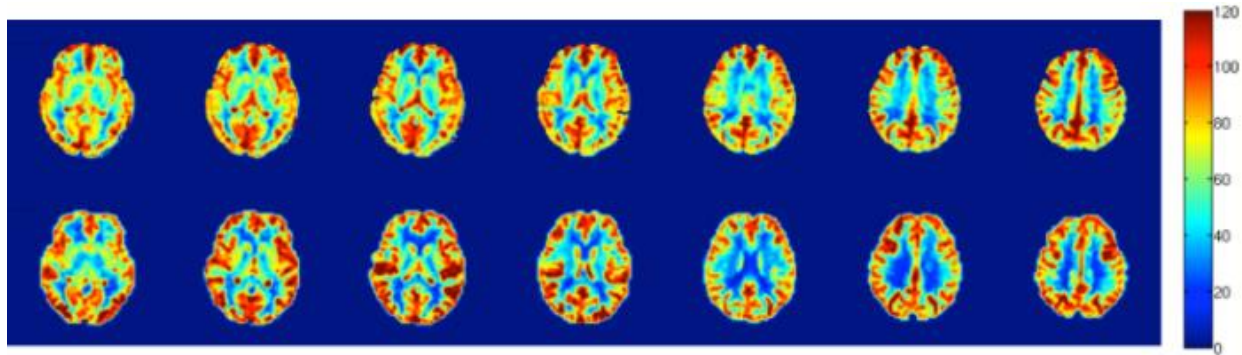
Figure 2: The Variance Map [29]

For example, the variance map suggests that AD progression tends to be more affected by brighter ROIs.
Output contrasts between the proposed approach and the SVM-based approaches are shown in Table 1 and Table 2.

Table 1: Performance Analysis

Models	AD vs. NC			MCI vs. NC		
	Accuracy	**Sensitivity**	**Specificity**	**Accuracy**	**Sensitivity**	**Specificity**
Single-kernel SVM (S-SVM) Model	91.26	91.32	90.56	89.23	79.82	93.59
Multi-kernel SVM (M-SVM) Model	93.57	92.71	94.29	90.36	77.24	94.23
Proposed Model	95.21	96.26	94.01	88.34	86.13	89.46

Mean values of binary classification results (percent) for pre-computed MRI features as seen in Table 1.

Table 2: 4-Class Classification Performance Analysis

Models	NC	N-MCI	C-MCI	AD	Accuracy	Sensitivity	Specificity
S-SVM Model	51.86	50.31	52.23	61.07	60.16	85.04	82.68
M-SVM Model	57.12	49.02	64.87	60.91	63.07	91.61	85.15
Proposed Model	67.28	54.56	42.26	64.03	68.36	88.04	92.01

The mean output values for the 4-class classification (percent) with pre-computed MRI features as seen in Table 2.

All the figures shown in both Table 1 and Table 2 were mean values obtained from the optimized settings experiments. As shown in Table 1, the deep learning approach in the binary classification of AD provided a better overall accuracy (95.21 percent). The proposed approach showed almost even accuracy when classifying NC and MCI as SVM, since the training set for this task has an unbalanced proportion of each class (650 NC subjects and 1370 MCI subjects), which is more difficult for parametric model training. Higher sensitivity values (96.26 percent and 86.13 percent) were observed, in addition to classification accuracy. It is also understood that the higher sensitivity is useful for diagnosis, since the cost of misclassification typically differs between different classes, e.g. diagnosing AD or MCI patients with NC can cause more serious effects than the reverse. The previous 4 columns in Table 2 reflect the average classification accuracy achieved for each class and the overall performance is reflected by the latter 3 columns. In three classes, better accuracies were observed (67.28 percent on NC, 54.56 percent on N-MCI, and 64.03 percent on AD), with the exception of C-MCI, which includes far fewer subjects than its N-MCI sibling class. The overall accuracy and overall precision (68.36 percent and 92.01 percent) compared to SVMs have achieved a performance benefit.

5. Conclusion

For the early detection of AD and MCI, we suggested a novel method focused on deep learning in this research paper. Compared to conventional binary classification methods, such as SVM, our approach performs AD diagnosis as a multi-class classification task, with limited prior knowledge dependency in model optimization. The proposed solution also conducts dimensionality reduction and data fusion simultaneously in order to reserve

synergy between data modalities. A gain in performance was achieved in both binary and four-class classifications. We have also shown that it is possible to apply a multi-layered parametric learning model for extracting high-level biomarkers to smaller medical datasets. This research paper may help researchers and forwarded about the tremendous potential for computer-aided diagnosis and lead to a new insight in other medical fields.

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