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Research Paper: Analysis and Neural Modeling of MRI Scans in Alzheimer's Disease

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ABSTRACT

This study is aimed to demonstrate how analysis and neural modeling of the MRI scans of patients with Alzheimer's disease can help in its diagnosis at an early stage. This can guide an early prediction and if applied with instant medications then it can help diminish the deterioration rate of the brain cells of the patients. The dataset of the MRI scans of patients was analyzed with the help of machine learning algorithms including ANN (Artificial Neural Network), K Nearest Neighbour(KNN), Linear Regression, Support Vector Machine(SVM), RESNET50 (Residual Network), and Exploratory Data Analysis (EDA) which resulted with KNN having the highest precision rate for group classification.

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1. Background

Alzheimer's disease (AD) is an age-related neurodegenerative disorder that results in progressive loss of cognitive function. AD is characterized by the accumulation of the amyloid-beta (Aβ) peptide into amyloid plaques in the extracellular brain parenchyma and by intraneuronal neurofibrillary tangles caused by the abnormal phosphorylation of the tau protein [1]. Amyloid deposits and tangles are necessary for the post mortem diagnosis of AD [2].

The hallmark pathologies of Alzheimer's disease are the accumulation of the protein fragment beta-amyloid (plaques) outside neurons in the brain and twisted strands of the protein tau (tangles) inside neurons. These changes are accompanied by the damage and death of neurons. Alzheimer's is a slowly progressive brain disease that begins many years before symptoms emerge [3].

Several methods have been proposed to diagnose AD while each has its advantages and drawbacks. Current diagnostic approaches for AD mainly depend on neurocognitive tests, brain imaging, and cerebrospinal fluid (CSF) assays. Deposition of amyloid plaques, neurofibrillary tangles, and significant synapse loss is noted in brain pathology in patients with AD. Diagnostic guidelines have included cerebrospinal fluid (CSF) levels of amyloid-β1-42 (Aβ42), total tau protein, and hyperphosphorylated tau (p-tau). CSF biomarkers like Aβ42 and p-tau have been used for research purposes. However, these methods are expensive and relatively invasive. Besides, the sensitivity and specificity of CSF Aβ42 and p-tau biomarkers have raised concerns about their clinical implication. The sensitivity of CSF Aβ42 ranges from 0.69 to 0.81 and specificity ranges from 0.44 to 0.89.

Moreover, patients with AD are generally diagnosed late. If AD can be detected in the early stages before major brain damage develops, patients may benefit more from treatment. Therefore, identifying biomarkers that can assist in detecting AD early or at onset is critical. Biomarkers can improve diagnostics and enable treatment initiation at the earliest possible stage.

The approach used in this paper can be one of the possible solutions that can be used effectively. For that, performing computations and deriving results focused on analytics and neural modeling of MRI scans for Alzheimer's Disease can be proved a good fit for it.

Literature Review

No.	Name of Paper	Author Names	Key Takeaways
1.	Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria.	Dubois B, Feldman HH, Jacova C, Hampel H, Molinuevo JL, Blennow K, DeKosky ST, Gauthier S, Selkoe D, Bateman R, Cappa S, Crutch S, Engelborghs S, Frisoni GB, Fox NC, Galasko D, Habert MO, Jicha GA, Nordberg A, Pasquier F, Rabinovici G, Robert P, Rowe C, Salloway S, Sarazin M, Epelbaum S, de Souza LC, Vellas B, Visser PJ, Schneider L, Stern Y, Scheltens P, Cummings JL	The PET imaging with amyloid tracers provides important information about the neuritic plaque burden which is present in the brain which can be useful for earlier detection and can be a hallmark of Alzheimer's detection. The harmony between florbetapir amyloid PET images and post mortem increases the accuracy to a huge extent making it almost 96 percent.
2.	Application of Artificial Neural Networks to Identify Alzheimer's Disease Using Cerebral Perfusion SPECT Data.	Świetlik D, Białowąs J	The family history of Alzheimer's and higher age groups indicated an increased risk of Alzheimer's disease. The ANN leveraging the Cerebral Perfusion SPECT data concluded to have a precise and efficient screening of Alzheimer's disease at low cost.
3.	Application of artificial neural network model in diagnosis of Alzheimer's disease.	Wang, N., Chen, J., Xiao, H. et al	For early diagnosis, Urinary AD7c-NTP was found useful and the higher age group in urban communities were associated to have a higher risk of getting Alzheimer's disease.
4.	Family members' attitudes toward telling the patient with Alzheimer's disease their diagnosis.	Maguire CP, Kirby M, Coen R, Coakley D, Lawlor BA, O'Neill D	After the assessment done by the physicians, the majority of the relatives associated with the patients did not want the patient to have the awareness of the diagnosis but would themselves wish to know about if they developed, so the clinicians must evaluate each situation individually.

2. Methods:

For this research, we used the Open Access Series of Imaging Studies (OASIS) data set. The data set includes longitudinal MRI data from 150 individuals age 60 to 96 years, including 64 individuals with very mild to moderate AD as diagnosed clinically and characterized using the Clinical Dementia Rating (CDR) scale (Morris et al., 2001; Morris, 1993) at their initial visit. Another 14 of the individuals were characterized as nondemented at the time of one or more scans and then clinically determined to have an AD at the time of a subsequent scan. All data were acquired on the same scanner using identical procedures. Subjects were screened to eliminate individuals with psychiatric and neurological conditions that might contribute to dementia but, where possible, variation typical of advanced aging was included. Thus, many of the older adults had age-related increases in blood pressure, and a small percentage treated diabetes. Sample characteristics were similar between the individuals with and without AD. This set consists of a longitudinal collection of 150 subjects aged 60 to 96. Each subject was scanned on two or more visits, separated by at least one year for a total of 373 imaging sessions. For each subject, 3 or 4 individual T1-weighted MRI scans obtained in single scan sessions are included. The subjects are all right-handed and include both men and women. 72 of the subjects were characterized as nondemented throughout the study. 64 of the included subjects were characterized as demented at the time of their initial visits and remained so for subsequent scans, including 51 individuals with mild to moderate Alzheimer's disease. Another 14 subjects were characterized as nondemented at the time of their initial visit and were subsequently characterized as demented at a later visit.

Age	Age at time of image acquisition (years)
Sex	Sex (M or F)
Education	Years of education
SES	Socioeconomic status as assessed by the Hollingshead Index of Social Position and classified from 1 (highest status) to 5 (lowest status) (Hollingshead, 1957)
MMSE	Mini-Mental State Examination score (range is from 0 = worst to 30 = best) (Folstein, Folstein, & McHugh, 1975)
CDR	Clinical Dementia Rating (0 = no dementia, 0.5 = very mild AD, 1 = mild AD, 2 = moderate AD) (Morris, 1993)
ASF	Atlas scaling factor (unitless). A computed scaling factor that transforms native-space brain and skull to the atlas target (i.e., the determinant of the transform matrix) (Buckner et al., 2004)
eTIV	Estimated total intracranial volume (cm3) (Buckner et al., 2004)
nWBV	Normalized whole-brain volume, expressed as a percent of all voxels in the atlas-masked image that are labeled as gray or white matter by the automated tissue segmentation process (Fotenos et al., 2005)

Approaches

For classification, we used: K-nearest neighbor (KNN) and SVM along with Linear Regression, while for Neural Networks we used: Artificial neural network (ANN), and ResNet50 and for correlation, we created a heat map.

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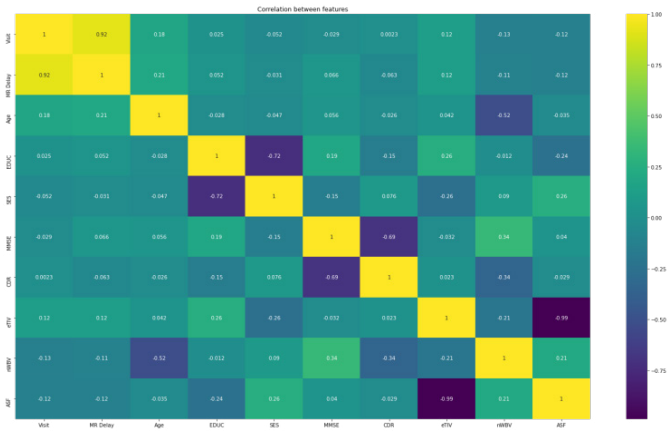

Figure 1. Heatmap for Correlation

A simple way to understand the correlation between different features is to visualize it with a heatmap as shown above. Color-coded heatmaps make it easier to understand the underlying relationship in the data. The features with a relationship closer to one are coded with yellow shade and the ones very far from it are colored in darker shades. One could also make a reference to this map and remove the features with negative correlation to not skew the study.

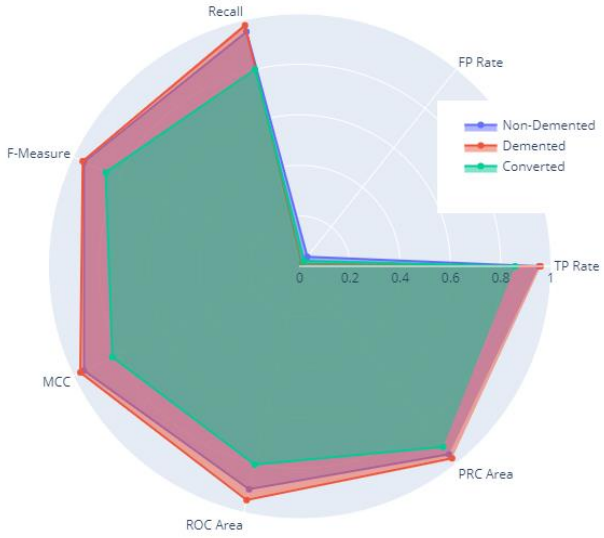

Figure 2. KNN for Groups

The above graph is a good representation of the recalling capability of the model as the recall values are very close to one for the demented cases and remain relatively similar in the case of the non-Demented and converted cases. One major observation can also be made that the model has a nearly 0 FP rate, which states that it does not classify incorrectly.

The above radar graph is to understand the basic attributes of Cognitive Brain Tests when run on the LR model and what results they generate. SES, eTIV, MMSE values cannot be used to train our model as they generate higher Root mean squared error and mean absolute error which may cause deviation when included in the study.

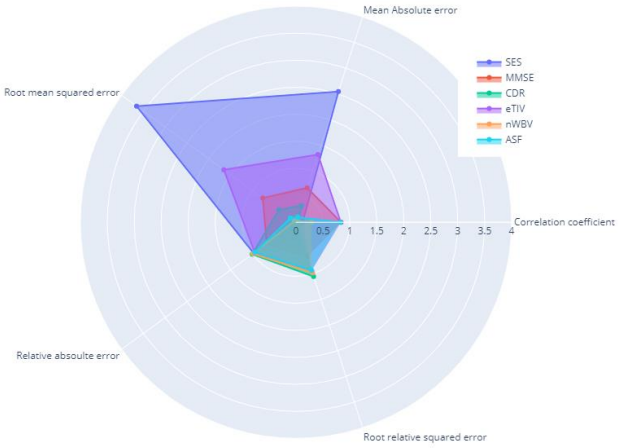

Figure 3. Linear Regression

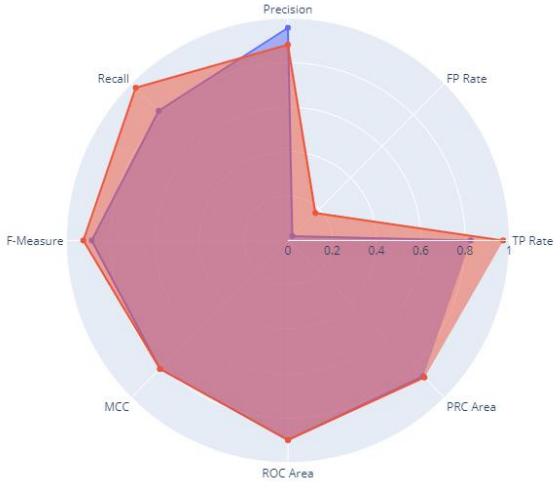

Figure 4. SVM for Gender

In the above figure, red indicates females, while blue indicates males. We found the precision rate for males was slightly higher compared to females while the TP rate for females was higher compared to males.

Figure 5. SVM for Groupss

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Here, the Blue color indicates Demented cases, the red color indicates non-Demented cases and the color green color indicates converted cases. As there are relatively more cases of Demented, we see a better Recall and TP rate. It can also be noted that less data for non-demented and converted cases have affected our study by not generating desired results.

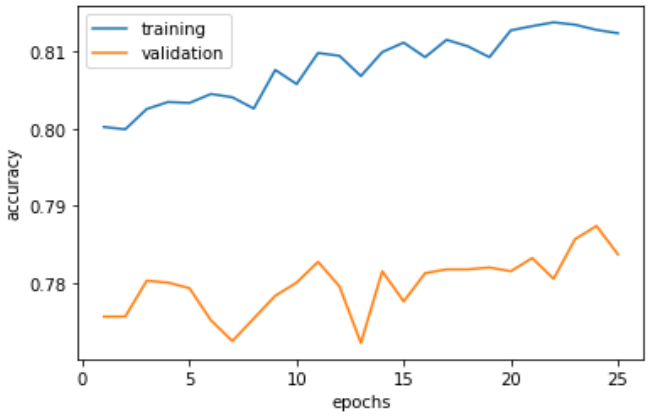

Figure 6. ANN Validation and Training

The above figure helps us understand that having sufficient computing power that can support more epochs to be run can help us yield better accuracy with the ANN model. Although the accuracy increases gradually with the number of epochs, these minor improvements are very crucial when it comes to dealing with Color-coded life at risk.

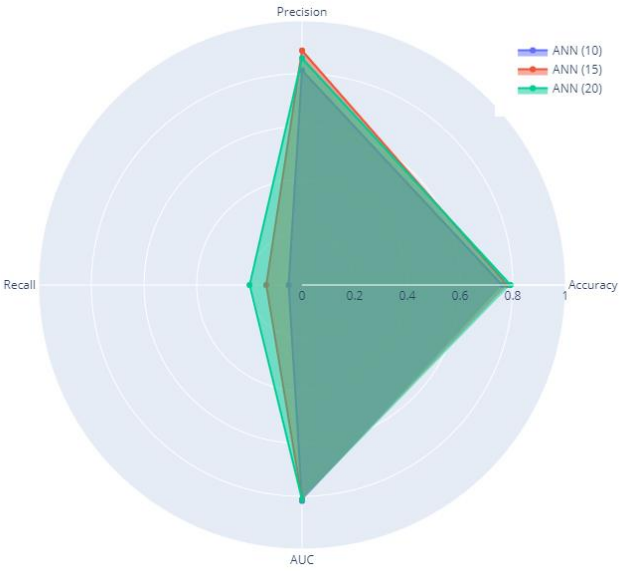

Figure 7. ANN

With ANN, observations were made that although the Precision, Accuracy, and AUC remained relatively unchanged with the increase in the epochs run, recall values showed better results with more epochs. So, the model had achieved its ideal accuracy and precision values in the least number of epochs but to obtain better Recall values it became directly proportional to the number of epochs run.

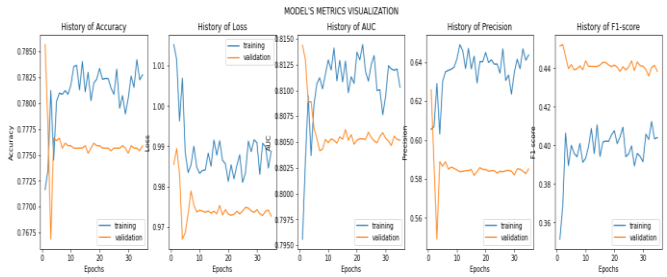

Figure 8. ResNet50

These metric visualizations are useful in identifying the trend that Accuracy and Precision increase relatively as the epochs are increased. Also, with more epochs the results we obtain on the validation set become consistent and reliable. The number of epochs are also inversely proportional to the Loss obtained, which is a very good indicator of a precisely trained model.

3. Results

From our trial and error , we found:

- KNN (Group): Precision = 0.989 and F-measure = 0.989.

- Linear Regression: mWBV got the least mean root error= 0.0302 out of all parameters.

- SVM (Group): Precision = 0.558 and F- measure = 0.639
- SVM (Gender): Precision = 0.913 and F-measure = 0.908

- ANN : Precision = 0.8586 and Accuracy = 0.7916 (after 25 epochs)
- ResNet50: Precision = 0.7137 and Accuracy = 0.7731 (after 35 epochs)

4. Discussion and Concluding Remarks

a. Classification

According to the amyloid PET scans, we can make out that the PET scans were considered as a surrogate marker of brain fibrillar amyloid pathology. PET ligands have also shown good predictability of progression to AD dementia in heterogeneous groups of patients with MCI. Also, in post-mortem analysis of AD, a positive amyloid PET can be considered, by extension, as a good marker of Alzeheimer's pathology. Other physical factors like age, lower education, monthly family income, family history of dementia, or physical inactivity may lead to the development of AD. Urinary AD7c-NTP is clinically valuable for early diagnosis.

b. Neural Networks:

It can also be noted that the Artificial neural network (ANN) with all the information including epidemiological parameters, neuropsychological functions, and biomarker obtained a high diagnostic precision and efficiency. This model could also be used as a low-cost practicable tool for the screening and diagnosis of AD for citizens.

RESTNET50 does not have comparable precision and recall values when operated on low epochs. Hence on powerful systems and more epochs, we can compare and obtain a clear analysis of the two Neural networks.

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