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Alzheimer Disease Detection Techniques: A Review

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Abstract – *Alzheimer's disease (AD) is a progressive neurological illness that impairs thought processes, behaviour, and memory. Longitudinal studies are crucial in understanding the disease's natural history, identifying risk factors, and developing effective treatments. The Longitudinal Analysis of Alzheimer's Disease using diverse machine learning and deep learning models is a rapidly developing field with significant potential for improving our understanding of this complex disease. However, there are also several significant drawbacks to current approaches, and there is a need for innovative techniques that can overcome these limitations. Here is a review of some of the key findings from longitudinal studies on Alzheimer's disease.*

Keywords*- Alzheimer's disease, longitudinal study.*

INTRODUCTION

As the world's population ages, dementia- the loss of mental abilities including remembering, thinking, and reasoning-is on the rise. Each of these impairments is severe enough to interfere with a person's day-to-day activities [1]. Alzheimer's Disease (AD) is the most common cause of dementia among all the different types, and it accounts for a growing percentage of deaths among the elderly (Alzheimer's Association 2012) [2]. Moreover, Mild Cognitive Impairment (MCI), a condition that is a precursor to dementia in AD, is said to develop to AD at a rate of 10% per year on average [3].

Despite the fact that there is presently no pharmacological treatment to restore AD/MCI to Cognitive Normal (CN), it is still critical to identify the diseases early in order to receive prompt treatment that may halt the progression [4]. As a result, it is crucial for the diagnosis or prognosis of AD/MCI in the clinic [5]. Researchers have been working hard to understand the underlying biological or neurological mechanisms of AD/MCI as well as to find biomarkers for the diagnosis or prognosis of the condition since the development of neuroimaging technologies like MRI, PET, and functional MRI [6].

The early deposition of aberrant neuropathological proteins results in the formation of amyloid plaques, which is one of the hallmarks of Alzheimer's dementia [7]. Consequently, amyloid biomarkers are employed as a key diagnostic tool for the clinical diagnosis and prognosis of Alzheimer's dementia and are utilised to identify the accumulation of amyloid plaques in the brain [8]. But the precise aetiology of Alzheimer's dementia is extremely complicated, and it can occur even in the absence of protein deposition [9]. In order to make up for this, Alzheimer's dementia is confirmed by the 18F-Fluorodeoxyglucose (FDG) test, which measures blood flow to the brain [10]. Unfortunately,

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doing several of these tests comes with a financial and physical expense to the patient, and having several tests makes patients anxious and delays therapy [11]. As a result, a lot of work has been done in clinical settings to discover a means to reliably identify Alzheimer's dementia at an early stage without the need for numerous testing [12].

Using the amyloid PET (amyloid PET) biomarker as the early-phase amyloid PET picture is one attempt to use it as a dual-phase biomarker. The early-phase amyloid PET image can substitute the FDG biomarker image since it is identical to it, according to numerous prior studies [13]. Nevertheless, it is unable to do so with clarity, and because of the noise, readers with limited expertise may find it challenging to interpret [14]. Due to their inability to make visual judgments that primarily rely on prior knowledge, inexperienced readers are more susceptible to subjectivity and higher inter-rater variability [15].

Algorithms based on artificial intelligence have recently significantly improved medical diagnostics. The past ten years have seen a great deal of progress in the classification of Alzheimer's disease thanks to the application of machine learning algorithms, which have reduced physical labor for researchers and physicians and eliminated the issue of inter-rater variability. Numerous techniques, including support vector machines, naïve Bayes, artificial neural networks, and deep learning, have been employed in earlier research [16]. To increase the efficacy of AD diagnosis and prognosis, some researchers have employed ensemble techniques [17]. Predictive models based on unimodal or multimodal data, such as computed tomography, positron emission tomography, or magnetic resonance imaging, were often proposed in these investigations. This multimodal strategy may contribute to the solution of the puzzle of how to explain the diverse physiological features of AD.

LITERATURE REVIEW

In 2022, Ferreira et al. [18] have started employing structural MRI and machine learning to diagnose AD and mild cognitive impairment (MCI) in a multi-diagnostic and broadly applicable manner. Subjects from the Open Access Series of Imaging Studies (OASIS) project database (n = 531) and the AD Neuroimaging Initiative (ADNI) database (n = 570) were used to train and test classifiers. Voting was used to compare and aggregate multiple classifiers in order to reach a conclusion. The impact of applying graph theory measures on diagnostic classification performance, the relative importance of various brain regions on classification for better interpretability, tests of generalizability across datasets and protocols (IR-SPGR and MPRAGE), and an assessment of the classifier's potential for clinical applicability were also reported.

In 2022, Yoon et al. [19] have developed an 18F-Florbetaben Dual-Phase Image Classified by Machine Learning and Feature Selection Based on Rank. To improve classification performance, this model analyses the frontal and temporal lobes efficiently. It decreases the ambiguity and subjectivity. It does not provide efficient classification results over multi-modal data.

For the classification problem, Zeng and Peng [20] created a multi-task learning method based on Deep Belief Networks (DBNs) in 2021. Specifically, the zero-masking approach and dropout technology were utilized to overcome the overfitting issue and improve the model's durability and capacity for generalization. Then, a novel framework for precise AD diagnosis was developed, based on DBN-based multi-task learning. Following MRI preprocessing, a multi-task feature selection approach was implemented to select the feature set related to all tasks by taking into account the internal relevancy among multiple related tasks. Principal component analysis was also used to reduce the feature dimension. The DBN-based MTL algorithm created in this work proved to be an efficient, superior, and useful technique of diagnosing AD based on the findings of experiments.

In 2020, Frangi et al. [21] have presented a new model that combines low-rank self-calibrated functional brain networks and structural brain networks for joint multi-task learning to automatically diagnose MCI (early MCI, late MCI, and SMC), as well as its earlier phases. They specifically created a novel functional brain network estimate technique initially. They performed correlation analysis in conjunction with low-rank structure and offered data quality indicators for self-calibration, which might enhance data quality while completing brain network estimation. Second, to choose relevant and discriminative characteristics for fine MCI analysis, functional and structural linked neuroimaging patterns were incorporated into this multi-task learning model. The best way to accomplish different classification tasks was to use different modalities, and the most effective way to identify the similarities and differences between various tasks was to use joint learning to identify the

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most discriminative characteristics. The non-convex regularizer, which roughly approximates the original rank minimization problem and successfully minimized the penalty bias of the trace norm, finished the learning process. Ultimately, a Support Vector Machine (SVM) was used to classify the most pertinent illness features in order to identify MCI. According to experimental data, this technique demonstrated promising performance with high classification accuracy and the ability to discriminate between various MCI sub-stages with effectiveness.

In 2018, Adeli et al. [22] have presented a Deep Multi-Task Multichannel Learning (DM2L) framework for concurrent clinical score and illness classification of brain diseases regression, utilizing patient demographic data and MR imaging data. To be more precise, they isolated many image patches surrounding these landmarks after initially using data-driven methods to identify the discriminative anatomical landmarks from MR images. Next, suggest a deep convolutional neural network with several tasks and channels for simultaneous regression and classification. This DM2L system might directly include the participants' demographic data into the learning process in addition to automatically learning discriminative features for MR images. The suggested approach was assessed using four sizable multi-center cohorts including 1, 984 participants. The outcomes of the experiment showed that DM2L outperformed other cutting-edge joint learning techniques in the tasks of clinical score regression and disease categorization.

In 2018, Wang et al. [23] have put out a novel multi-task learning formulation for precisely forecasting the disease's cognitive scores and determining the most predictive biomarkers. This formulation took into account a correlation-aware sparse and low-rank limited regularization. Furthermore, the suggested non-smooth convex objective formulation was optimized by the development of an effective iterative algorithm. Additionally, they have conducted tests to assess the suggested optimization formulation using information from the Alzheimer's disease Neuroimaging Initiative (ADNI) dataset. In particular, they use the baseline MRI features to predict the cognitive scores at various time points. In addition to demonstrating the validity and accuracy of the suggested approach for forecasting the course of the disease, the outcome also revealed a few significant and stable MRI characteristics that agreed with earlier studies.

In order to recursively eliminate uninformative features; Lee et al. [24] introduced a unique deep architecture in 2016 that uses hierarchical sparse multi-task learning. They also postulated that the relative significance of characteristics in describing the target response variables is reflected in the ideal regression coefficients. In order to achieve this, they developed a weighted sparse multi-task learning technique and utilised the best regression coefficients discovered in one hierarchy as feature weighting factors in the subsequent hierarchy. Finally, they used clustering-induced subclass label vectors as target response values in our sparse regression model, taking into consideration the distributional properties of data within each class. The proposed method was found to be superior to state-of-the-art methods in the experiments conducted on the ADNI cohort. The trials involved both binary and multi-class classification tasks in the diagnosis of AD/MCI.

In 2013, Cheng et al. [25] have introduced a framework for joint feature selection from multi-modality data using manifold regularized multi-task learning. To be more precise, they developed a multi-task learning framework around the multi-modality classification, with each task concentrating on the classification according to each modality. To capture the intrinsic relatedness across various tasks, or modalities, they used a group sparsity regularizer, which guaranteed that only a limited set of features would be jointly selected. To maintain the geometric distribution of the original data from each job, they also added a new manifold-based Laplacian regularization term, which may help choose more discriminative features. Additionally, they expand this approach to the semi-supervised context, which was crucial because it was typically more difficult and costly to obtain a sizable amount of labelled data—that is disease diagnosis—than it was to obtain unlabeled data. They have thoroughly examined the baseline Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) and Magnetic Resonance Imaging (MRI) data from the Alzheimer's disease Neuroimaging Initiative (ADNI) database in order to validate this strategy.

Table 1: Features and challenges of existing multi-task learning-based AD detection model

Author [citation]	Methodology	Features	Challenges
Ferreira *et.al* [18]	SVM	• Early manifestations can be detected with high precision rate. • MRI is non-invasive and does not give any harmful radiation and hence, it does not provide any effects for patients.	• It does not provide proper interpretability and it struggles to take proper classification decision. • This model makes the patient uncomfortable.
Yoon *et.al* [19]	SVM, Naïve Bayes, RF and logistic regression	• In this model, the frontal and temporal lobes are effectively analyzed to provide better classification results.	• It decreases the ambiguity and subjectivity. • It does not provide efficient classification results over multi-modal data.
Zeng and Peng [20]	DBN	• The utilization of hidden layers was useful in DBN and the performance got gained by adding extra layers. • It has high robustness in terms of size, position and color.	• Since the network is unsupervised there is no requirement for labelled data. • It needs further improvement to support different neuroimaging modalities.
Frangi *et.al* [21]	Functional Brain Network Estimation Method	• Choosing the most distinctive characteristics from the structural and functional data is helpful. • Low rank constraints are used to encode the brain modular structure, and it automatically calibrates the data quality to eliminate noise and low quality data points.	• It does not support different modalities of data. • The reliability of the system is slightly low.
Adeli *et.al* [22]	CNN	• The learning performance can be promoted using this regression framework. • It helps to predict the feature progressions more accurately.	• It needs adaptation strategy for reducing the negative influence on the difference of distribution values.
Wang *et.al* [23]	Neural network	• In order to enhance the generated model's classification performance, the relationship between the cognitive scores and the imaging marker is investigated.	• Multi-modal data are not supported in the developed model. • Large dimensional data are not effectively processed by using this approach.
Lee *et.al* [24]	Binary And Multi-Class Classification	• For feature selection, parse regression techniques have been extensively used to lower the dimensionality. • With this strategy, uninformative features are filtered out in a hierarchical fashion iteratively.	• The availability of the system is very low. • It takes more time to execute the process.
Cheng *et.al* [25]	Manifold Regularized Multi-Task Feature Selection	• It effectively detects the disease over the multi-modal data. • It achieved with higher classification accuracy.	• It is usually time consuming and expensive.

CONCLUSION

Alzheimer's disease is now considered a threat to world health. Many criteria, such as body fluids, imaging investigations, and clinical biomarkers, have been put forth for a more precise diagnosis of AD. Longitudinal studies have provided valuable insights into the natural history of AD, identifying risk factors, and identifying potential treatments and prevention strategies. Continuous longitudinal Research is essential to improving our comprehension of AD and creating successful treatments. The field of analysing Alzheimer's disease using various deep learning and machine learning models is one that is quickly expanding and has the potential to greatly advance our comprehension of this complicated illness. While longitudinal investigation of Alzheimer's disease has demonstrated considerable potential for machine learning and deep learning models, there are still a number of issues that need to be resolved. Innovative techniques that improve the performance and interpretability of these models can help to overcome these challenges and facilitate the development of effective interventions for this debilitating disease.

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