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Role of Computational Intelligence Techniques in Diagnosing Alzheimer's disease at Early Stages: A Systematic Literature Review

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***Abstract*— Computer aided disease diagnosis with computational intelligence research has shown that several intelligent models have been developed to assess medical data and make assumptions about illness severity and early diagnosis. Many researchers find it difficult to anticipate and diagnose the deadly neurodegenerative disorders that fall under the category of dementia using medical image data. Alzhiemers is now the most common dementia, affecting around a third of all people. Many machine learning models have been developed, but there is still a lot of room for further improvement in the field of Alzheimer's disease detection and prevention. This article includes a thorough literature evaluation of machine learning approaches that have been developed to detect Alzheimer's disease at an earlier stage. As a result of these studies, budding Alzheimer's disease researchers will be able to better understand the extent of study in forecasting the illness via the use of artificial neural networks, support vector machines, and deep learning-based ensemble models.**

Keywords*— *Dementia, Alzheimer's, Computational intelligence, soft computing , Image analytics, Machine learning, Deep Image analytics

I. INTRODUCTION

One of the most common symptoms of dementia is an inability to comprehend information and perform regular activities. Alzheimer's disease (AD), a kind of dementia, is characterised by memory loss and cognitive impairment. Indicators such as neurotic plaques and the slow loss of brain cells are indicative of this condition. In this circumstance, the disease's consequences on daily life are the most noticeable as it advances. Even though Alzheimer's disease is more common among the elderly, it is not a disease of old age... Early Alzheimer's disease memory loss may have a long-term effect on daily activities. Although the progression of Alzheimer's disease (AD) cannot be slowed down with the present treatments, early treatment may help people age better and live longer. It is predicted that one in five persons would suffer from Alzheimer's disease by the year 2050. Precision treatment is essential in the early stages of Alzheimer's disease (AD). Alzheimer's disease accounts for 70% of all occurrences of dementia, and it is wreaking havoc on public health systems across the world, whether developed or developing. Cognitive and executive failure, psychiatric problems, and behavioural disorders are all signs of Alzheimer's disease-induced dementia. This complicates ordinary life, and as a result, people die. Postmortem examination of the brain has only lately been viable for Alzheimer's disease diagnosis.

Alzheimer's disease patients have been using cholinesterase inhibitors licenced by FDA since the end of the 20th century. There is no cure for dementia, but frequent and persistent medical treatment might help alleviate some of its symptoms. Alzheimer's disease biomarkers have made remarkable progress during the last decade. A common study approach is to look for these markers if amyloid eta (A) plaques are found in the brain or CSF. With the use of biomarkers, we were able to tell the difference between Alzheimer's disease and dementia. Alzheimer's disease biomarkers may be used to identify persons at an early stage, even if there are no medical symptoms of the illness. Since the earlier tests failed, there has been no medical intervention.

Treatments that don't work in the early stages of a disease might lead to deterioration and even death. At this point, the Alzheimer's disease development may be readily seen. Another way to express it is to describe this move toward secondary prevention from the early indicators of sickness as stepping in between pre-symptomatic at risk individuals and preventing or accelerating disease progression. We can now treat Alzheimer's patients in their early stages as a prophylactic step due to technological developments. It is essential that you have a fundamental understanding of machine learning before applying it to Alzheimer's disease prediction. Machine learning is a component of artificial intelligence, which offers a wide range of capabilities. New occurrences are divided into groups depending on how they performed in the past. Machine learning requires a thorough understanding of the approaches used in order to provide correct results. The possibility of successful results is increased when the process is correctly implemented and all observations are meticulously recorded. With regards to machine learning, for example, each approach is somewhat different from the others. One such example is built on information and software that has no relevance to the wide range of data types it is intended to handle.

There are a number of ways to analyse training data. Learning algorithms may be broken down into the following three categories: supervising training Learning without supervision [3] Reinforcement-based learning." There are many different ways to learn, and each has its own advantages and disadvantages. Pre-labeled or otherwise organised data

may be used in unsupervised learning to provide insight. In Alzheimer's research, all of the algorithms that have been used so far have been supervised learning algorithms.

Computer-based research on Alzheimer's disease suggests that machine learning may be used to identify and forecast the condition. Alzheimer's disease has been widely studied using artificial neural networks (ANNs), support vector machines (SVMs), and deep learning. There are two major differences between ANN and SVM when it comes to optimising the final output: Both the local and global optimality of the SVM solution may be achieved. A lot of research have shown that merging autonomous and intelligent agents with neural networks may considerably enhance the diagnosis of medical imaging. When dealing with huge datasets, deep learning may be able to improve prediction since it combines feature extraction as its core step. Ensemble techniques were used in just a small number of research to improve their forecasts, as well. Now is the time to conduct a comprehensive review of a wide range of research publications on the use of machine and deep learning in the early detection of Alzheimer's disease.

Methods for conducting a systematic literature review in the diagnosis of Alzheimer's disease are presented in Section 2 of this paper, which uses a pragmatic research strategy [5]. Section 3 focuses on the detection of Alzheimer's disease and the classification of several routes. Numerous diagnostic devices and techniques are also examined in depth in this book. Section 4 focuses on unanswered research concerns and research gaps that have yet to be addressed.

II. RESEARCH METHODOLOGY

The systematic review (SLR) described in [6] is an example of pragmatic research approach used in this paper. IEEE, Springer, and other well-known scientific databases were searched for publications with strong connections to each other. The use of databases such as Science Direct, ACM, and Scopus to find the most frequently cited publications is an important part of doing a literature analysis. In this case, systematic research aids in the identification of articles most important to the prediction of Alzheimer's disease. Researchers may use the results of this comprehensive investigation to confirm, verify, and synthesise the experimental findings of other experts in the field of Alzheimer's disease prognosis. In the SLR procedure, the research protocol is as follows:

- For this purpose, we have designed a technique for reviewing all the SLR processes that are involved in diagnosing and predicting Alzheimer's disease at an early stage.
- The PICO method has been shown to be a useful tool for identifying research articles that are based on reliable evidence.
- Alzheimer's disease prediction research papers that have received the greatest attention.
- In order to reply to the research questionnaire, compile a synthesis of relevant research results from a number of sources.
- There are still a number of questions that need to be answered in the field of medical imaging data and Alzheimer's disease research.

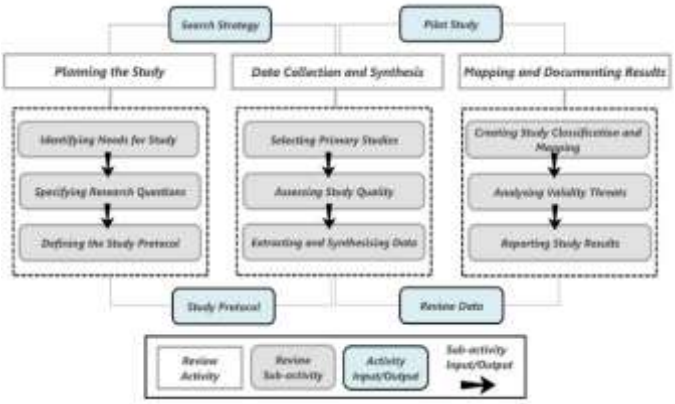

Figure 1: Research Methodology

2.1 Research Questions

Setting a research topic is the most critical step in the SLR process, since it essentially outlines the goal of the literature review. Defining a clear research topic helps to focus the investigation on the most important aspects. With the use of this article's PICO technique [7], researchers may improve the quality of their research questionnaire. The Alzheimer's disease research questionnaire is as follows:

RQ1	How machine learning and deep learning affect the accuracy of early detection of Alzheimer's illness
RQ2	List the current methods for predicting Alzheimer's disease accurately
RQ3	What kinds of datasets and technologies are used in current research projects for analysing experimental results?
RQ4	What is the present state of research and what are the unanswered research questions in the area of early detection of Alzheimer's disease symptoms?

2.2 Search Strategy

According to the principles of evidence-based research outlined in [8], this study's primary goal is to find, assess, and collect significant research works connected to the prediction of Alzheimer's disease in medical picture data. We'll use a variety of scientific databases and indexed articles to gather and extract data in this procedure. As indicated in Table 1, the search phrases may be combined in a variety of ways.

Table 1: Key Words utilized while mining relevant studies from Scientific Databases

Alzheimer's disease**OR**Dementia**OR**thinking impairment
AND
Prediction **OR** multi-objective analysis **OR** multivariate analysis **OR** Optimization Or Diagnosis
AND
Classification **OR** Clustering
AND
Artificial intelligence **OR** ArtificialNeural networks **OR** Time series prediction models
AND
Hybrid Models **OR** Deep learning Models **OR** Machine learning Models **OR** Fuzzy Models
AND
Systematic Study **OR** SLR **OR** Mapping Study **OR** Review

We found 172 research publications focusing on the diagnosis of dementia and Alzheimer's disease symptoms in

medical picture data using the previously mentioned combination of search strings from scientific databases such as Springer, IEEE, Science Direct, ACM, and Scopus that were indexed with high citations. The number of publications in scientific databases is shown in Table 2.

Table 2: No. of Research articles obtained from various scientific databases

Database	No. of Papers
IEEE	34
ACM	22
SPRINGER	36
SCIENCE DIRECT	35
GOOGLE SCHOLAR	45
Total	**172**

2.3 Selection of the relevant research articles

According to the interpreted search strings, about 172 relevant research publications were retrieved from scientific databases in the first phase of data gathering. For this reason, a data filtering method that examines relevant research papers based on their relevance rate to the issue statement is required. In addition, the publications will be screened in the early stages based on the inclusion and exclusion criteria in Table 3. Finally, 32 of the most relevant studies are included in the systematic review.

Table 3: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
As ANN, AI, Fuzzy models and any other hybrid prediction techniques are included in these articles.	Articles that don't indicate how the suggested procedures will be implemented, or articles that are just theoretical.
Comprehensive implementation details and tools, datasets and test beds in research publications based on solid evidence	notes, publications, and conference presentations relating to Alzheimer's disease prediction
Electronics and computer engineering-focused articles	Written in languages other than English are articles.
Articles that are written in English.	

III. REVIEW OF VARIOUS MACHINE LEARNING TECHNIQUE FOR DIAGNOSING ALZHEIMER'S DISEASE

4.1 Analysis of SVM based Techniques:

Support vector machines (SVMs) are a well-known and widely used technology for classifying and predicting data. Due to the Structural Risk Minimization concept, SVM performs well. It employs the notion of greatest margin to distinguish data points. Non-linear data may be categorised using kernel functions. Variants are introduced in connection to generalisation ability and training duration in order to boost production. Twin support vector machines and Least squares based twin support vector machines are two computationally efficient variations.

a. Image modality using SVM:

Image modality is critical to differentiating MRI pictures. When comparing T1 and T2 scans, T1 images are more often used for structural imaging. T1-weighted pictures clearly show atrophy-induced delineation in the ventricular surface of the brain. Researchers favour T1 pictures because of this.

b. Feature selection and extraction with SVM

According to Fan et al [9], positron emission tomography (PET) scans offer new resources to MRI scans in order to increase the classification accuracy of the CN vs MCI using SVM. According to Dukart et al. [10], the characteristics of fluorodeoxyglucose-PET (FDG-PET) differ from those of MRI. PET scans (100%) are connected with more optimism in cancer patients than in Alzheimer's disease (AD) patients (97.5 percent). The results of CN vs AD [12] are consistent, however PET images (96.67 percent) are more precise than SPECT images (94.5 percent). Kamathe et al. [13] separated the data into two groups using T1, T2, and proton density (PD) scans. Hojjati et al. [14] and Sheng et al. [15] employed rs-fMRI and fMRI data to categorise MCIc and MCInc in the brain, respectively.

An enhanced parcellation technique for the identification of tiny grey matter changes is presented in [16]. (GM). Magnin and colleagues [17] developed a characteristic selection strategy for CN vs. AD using histograms of regions of interest (ROIs). Gerardin et al. [18] were able to discriminate between CN, MCI, and AD using hippocampus-related shape data, indicating that shape deformation characteristics are more essential than volumetric features. The NMSE traits of CN and early AD may be separated [19]. The clustering-based approach was provided for a group of neighbouring voxels in the divisions of CN, MCI, and AD [20].

Fisher's discrimination ratio may be used to identify useful voxels in SPECT images (VAFs) (FDR). [22] compares CN with AD using a Gaussian mixture model (GMM). GMM-based features The goal is to segregate the data in a logical order. To discover the optimum technique to separate the contents of PET and sMRI data, Ortiz et al. [23] combine a sparse inverse covariance estimation (SICE) approach with SVM. Based on its contents, a non-negative matrix factorization (NMF) classification of CN vs. AD is superior than either PCA or SVM.

Abdulkadir et al. [24] looked at how hardware heterogeneity affects SVM classification accuracy. –> They identified a high level of classification accuracy using large datasets. For CN, MCIc, and MCInc, Cuingnet et alDARTEL .'s approach outperforms SPM features. When applied to sMRI images, the introduction of hyperparameters affects the accuracy of feature selection algorithms. In addition, Schmitter et al. [26] found that volume-based morphometry is superior than voxel-based morphometry (VBM). Long et al. used shape differences in brains to categorise CN, AD, sMCI, and pMCI. Plocharsky et al. employed morphological characteristics of brain regions to differentiate CN from AD, whereas Long et al.

used shape differences in brains to categorise CN, AD, sMCI, and pMCI.

For a large number of studies, wavelet-based features are used. Chaplot et al. [28] used different aspects of wavelet transform (DWT), while Zhang et al. [29] showed that 3-D DWT and SVM are effective in differentiating CN, MCI, and AD individuals. According to Segovia and colleagues [30], FDR was found to be higher in CN PCA than AD using SPECT images with sub-square (PLS) images. Ortiz et al. use unsupervised separation of sMRI images using self-aligning maps (SOMs) [31] to distinguish between CN and AD. According to Chaplot et al. [28], SVM beats SOM when it comes to seeing Alzheimer's patients using T2-weighted images. Methods such as SVM-RFE [32, 33] use a selective factor in [34] discrimination between CN and AD. Using independent component analysis, SVM may be used to differentiate between CN and AD (ICA). Using EEG data, SVM can be used to identify between CN and AD. Mazaheriet al. [37] used EEG recordings from word-based individuals to differentiate MCIc from MCInc and CN.

4.2 Analysis of ANN based Mechanisms

Machine learning algorithms for extremely nonlinear patterns of data are offered in the form of artificial neural networks (ANN). Here, we look into the approaches that use ANNs and other techniques.

a. Transfer Learning

If the number of samples is small, it is a common practice in typewriter machine models to analyze only data from a single domain. Samples from both target and auxiliary domains are analyzed in the transfer learning process. According to Cheng and colleagues [38], multidisciplinary transmission modification (M2TL) may transfer learning from additional domain (CN) to target domain (AD). Comparison (MCIc versus MCInc), In their recent study, Cheng et al. [39] developed a novel multi-domain learning (MDTL) learning model[60].

[40] An in-depth study of transmission using Hon et al. [40] by modifying two pre-trained neural networks (VGG16 and Inception) for the purpose of recognizing people with AD and CN. The TrAdaBoost algorithm is seen as a means of transmitting information by Zhou et al. [41]. If confusing is ignored during the transmission of information, the result will be degrading and improper labeling of the class. Cheng et al. [41] introduced rMLTFL, a strong study of multi-label transfer, to address this problem. Multi-bit vector code created by changing labels. As shown by Li et al. [43], a sub-field management approach may be used to transfer information from ADNI samples to local samples[61].

b. Feature Selection Techniques

There are a number of strategies for improving feature selection (FS) in neuroimaging data. A non-linear feature that Ahmadlou et al. [44] may have discovered may assist differentiate the two groups (CN and AD) within EEG band-limits. Visibility graphs are used to derive features from EEG data (VG). The short time Fourier transform (STFT) and WT features of Rodrigues et al. [45] were used to classify using an ANN. One of the most common symptoms of Alzheimer's disease (AD) is the gradual decrease in the volume of various parts of the brain's grey matter and white matter (WM). The ventricles become bigger, and there's more CSF in there. Yang et colleagues [46] have grouped GM and WM into one classification scheme. Using ventricular 2D and 3D form characteristics, the volumetric parameters of cerebrospinal fluid (CSF) are shown. Surface-based morphometry is another method for extracting cortical features from MR images. The thickness of the cortex may be used as an indicator of the quality of the meat. [47] Cho et al. developed a strong incremental categorization strategy. Using a manifold harmonic transform, spatial frequency may be calculated. In addition to genetic, neuropsychological, and physiological tests, socioeconomic and demographic data may also be analysed.

The usage of ANNs is permissible in this context. Using data from neuropsychological tests, age, and education, Quintana et al. [48] were able to discriminate between MCI and Alzheimer's disease. Chyzyk et al. [49] have developed a novel feature selection approach that combines GA with an extreme learning machine. [(ELM). In their continuing work, Yang et al. [50] analysed volumetric and form factors as a team. To overcome the limitations of prior knowledge and high dimensionality, Ortiz and colleagues have used SOM to build a new method for pinpointing brain ROIs that are particularly important. Artificial Bee Colony (ABC) optimization was integrated with a neural network by Wang and colleagues [52]. (FFNN). A well-known method for dealing with the high dimensionality of whole brain research is to extract characteristics from separate ROIs of the brain. It's a disadvantage since it requires prior knowledge[59]. Table 4 summarises the most significant findings from the preceding three years.

Table 4 in Summary of Significant studies in past three years

Year	Authors	Target	Modality	Feature extraction	Machine learning	Dataset	Validation	Performance		
								Acc (%)	Sens (%)	Spec (%)
2016	Moller et al.	CN vs AD	sMRI (T1)	VBM	SVM (Linear)	178 (94 CN, 84 AD)	LOOCV	85	83	87
2016	Plocharsky et al.	CN vs AD	sMRI (T1)	Morpholgical features (length, area, depth)	SVM (Linear)	210 (100 CN, 110 AD)	10-fold	87.9	90	86.7
2017	Alam et al.	CN vs AD	sMRI (T1)	VolBM+KPCA	SVM (Multiple kernel)	293 (102 CN, 102 MCI, 89 AD)	10-fold	93.85	92.1	94.45
		CN vs MCI						86.54	84.85	87.74
		MCI vs AD						75.12	73.92	77.24
2017	Khedher et al.	CN vs AD	sMRI (T1)	ICA	SVM (RBF)	818 (229 CN, 401 MCI, 188 AD)	k-fold	89	92	86
		CN vs MCI						79	82	76
		MCI vs AD						85	85	86
2017	Beheshti et al.	CN vs AD	sMRI (T1)	VBM+GA	SVM (Linear)	458 (162 CN, 65 sMCI, 71 pMCI, 160 AD)	10-fold	93.01	89.13	96.8
		pMCI vs sMCI						75	76.92	73.23
2017	Long et al.	CN vs AD	sMRI (T1)	MDS+PCA	SVM (Linear)	427 (135 CN, 132 sMCI, 95 pMCI, 65 AD)	10-fold	96.5	93.85	97.78
		CN vs pMCI						97.1	87.37	94.82
		sMCI vs pMCI						88.99	86.32	90.91
2017	Tangaro et al.	CN vs AD	sMRI (T1)	VolBM	SVM (Linear)	372 (117 CN, 86 MCIc, 71 MCInc, 98 AD)	10-fold	100	-	-
		MCIc vs MCInc						83.4	-	-
2017	Lu et al.	CN vs MCI	FDG-PET	VBM	RF-RSVM	272 (152 CN, 120 MCI)	3-fold	90.53	90.63	93.33
2017	Alam et al.	CN vs AD	sMRI	DTCWT/LDA	TWSVM	237 (130 CN, 137 AD)	10-fold	96.88	97.72	95.61
2017	Hojjati et al.	MCIc-MCInc	rs-fMRI	PCC+F-score	SVM (Linear)	80 (18 MCIc, 62 MCInc)	9-fold	91.4	83.24	90.1
2017	Kulkarni et al.	CN vs AD	EEG	ICA/ Wavelet/ Spectral	SVM	100 (50 CN, 50 AD)	LOOCV	96	-	-
2018	Sun et al.	CN vs AD	sMRI (T1)	VBM+PCC	Group lasso SVM	509 (162 CN, 134 sMCI, 76 pMCI, 137 AD)	5-fold	95.1	93.8	83.8
		CN vs MCI						70.8	72.1	69.1
		sMCI vs pMCI						65.4	67.6	64.2
		MCI vs AD						65.7	63.2	67.3

4.3 Review of Deep Learningtechniques for predicting Alzheimer's disease

According to Suk et al., SAE may improve the accuracy of AD, MCI, and MCIc diagnosis. These links aren't in a straight line. To distinguish between Alzheimer's disease and moderate cognitive impairment (MCI), Suk et al. employed a deep Boltzmann machine (DBM). When SAE and CNN are used to detect AD and MCI from CN, Payan et al3D-CNN .'s performs effectively, according to Payan et al. Suk et al. employed SAE-based classifiers to categorise MCIc, AD, MCI, and CN [56]. Softmax logistic regressions may be used to derive high-level properties. Liu et al. [55] used the SAE-based DL design to treat Alzheimer's disease. There are numerous approaches to distinguish between Alzheimer's disease and MCI (LR). Hosseini et al. [57] developed a highly checked adaptive 3D-CNN using MRI-based 3D convolutional autoencoders (DSA-3DCNN). For example, when it comes to Ortiz and his employees,

The AAL atlas is used to create and train 3D and DBN patches by Ortiz et al. [58]. The DBN (FEDBN-SVM) structure provides very high phase accuracy. According to D. Zhang et al., Alzheimer's disease can be detected using a combination of MRI, PET, and CSF indicators (2011). Of the 51 patients, Alzheimer's disease (AD) was diagnosed, 99 had moderate cognitive impairment (MCI) and 52 had no symptoms at all. In MRI, PET, and CSF, it was tested using a 10-fold contrast confirmation method. 93.2 percent accuracy of the sections and 93.3 percent specificity may be due to the combined use of these methods, with a maximum accuracy of 86.5 percent in the various tests. Over time, the author's method of multimodal differentiation (including MRI, PET, and CSF data from different brain areas) improved and became more powerful. More information on how Zhang and his colleagues could be used in a database of 96 AD patients and 273 healthy controls using just two MRIs and CSF, although this information was not provided. With a combined MRI and CSF combined of 91.8 percent, the Cuingnet R1, 2011 method has achieved the highest points. R. Chaves et al. (2010) believe that differentiation is easier to use than the Single-Modality Approach for initial diagnosis. With the use of affiliate system mining, features of pre-processed data sets can be detected.

IV. CHALLENGING ISSUES AND RESEARCH GAPS

The research discussed in the last part provide a few instances of how machine learning experiments might be conducted, and the results are spectacular. These researches asserted the validity technique and discussed the prognosis and prediction of Alzheimer's disease. However, it is critical to detect any input data concerns that may arise during implementation and validation for diverse investigations. The most typical issues in the analysis of the research reported are the size, qualities, and validity of the input data. Higher accuracy can be achieved by utilising tiny data sets but the techniques involved are straightforward. With limited data sets, overtraining is more likely to occur, but with big data sets, numerous effects like as resilience, accuracy, and reproductivity may be seen.

Pathologically untested data are largely used in research, which introduces uncertainty. The ratio of characteristics to instances has an influence on the findings. The quantity and

general information of qualities has been the focus of previous research.. Machine learning relies heavily on the quality of the data and the selection of the most essential attributes to provide useful results. Unfortunately, the authors did not go into great detail on the procedures they employed to assure the integrity and quality of the data. Data quality is dependent on the selection of a feature. However, the characteristics selected for certain clinical data, such as histological evaluations, may no longer be useful in the future.

As a result, a classifier should keep its feature sets up to date throughout time. Likewise, the specifics of the training and testing data must be provided accurately. The majority of algorithms indicate to the categorization of the main class together with the minor class being disregarded. This form of class imbalance results in a dominating class followed by poor class prediction and a damaged classification with quality.

According to a review of the literature, the current emphasis of research into Alzheimer's disease prediction is on feature extraction rather than clustering and classification. As new algorithms and approaches are developed, this element of Alzheimer's disease research may be regarded a large research subject that merits further study. Furthermore, new machine and deep learning models are needed in order to accurately and early diagnose Alzheimer's disease..

V. CONCLUSION

Most of this article's content is dedicated to giving a detailed review of the many methods and intelligent models that have been developed to diagnose Alzheimer's disease early on. Deep learning ensemble models and artificial neural networks are investigated in detail in this publication by researchers. Additionally, ensemble models and transfer learning are discussed here. Comprehensive literature evaluation indicates that feature extraction rather than clustering and classification may be the future focus of investigation for an accurate diagnosis of Alzheimer's disease.

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