

EXPLAINABLE AI IN THE CATEGORIZATION OF ALZHEIMER'S DISEASE

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Abstract: Recent years have seen an unparalleled expansion in computing power, which has made it possible to create Artificial Intelligence (AI) models for medical applications with impressive outcomes. The usual blackbox nature of many AI models, however, has hindered the acceptability and implementation of many AI-powered Computer Aided Diagnosis (CAD) techniques in the medical field. Thus, in order to encourage medical professionals to use these AI models, the algorithms' predictions need to be comprehensible and interpretable. The goal of the new discipline of explainable AI (XAI) is to demonstrate why the predictions made by these models are reliable. The literature on Alzheimer's disease (AD) detection with XAI that has been published in the past ten years is systematically reviewed in this paper. In order to classify AI models into various conceptual approaches (such as Post-hoc, Ante-hoc, Model-Agnostic, Model-Specific, Global, Local, etc.) and frameworks (such as Layer-wise Relevance Propagation, or LRP, Gradient-weighted Class Activation Mapping, or GradCAM, the Local Interpretable Model-Agnostic Explanation, or LIME, and SHapley Additive exPlanations, or SHAP), research questions were carefully formulated. This classification offers a wide range of interpretations, from intrinsic to global, by extending local explanations. Additionally, many interpretations that offer a thorough understanding of the elements supporting the clinical diagnosis of AD are also covered. Finally, XAI research's needs, limitations, and unresolved issues are described, along with potential applications in AD detection.

Keywords Explainable Artificial Intelligence, Black Box Models, Alzheimer Disease Classification, Interpretable Machine Learning

I. INTRODUCTION

Elderly people are susceptible to Alzheimer's Disease (AD), a neurological condition that is incurable and can change a person's life [1]. About 55 million people worldwide have been clinically diagnosed with AD, and by 2050, that number is expected to climb to 139 million, according to the most recent World Alzheimer Report [2]. According to the report, a startling 75 of problems remain misdiagnosed for a variety of reasons. AD sufferers will experience a variety of challenges, including cognitive decline, behavioral abnormalities, vision problems, and mobility issues that disrupt everyday activities [3] [4].

A person's capacity to conduct an independent personal and social life will be hindered by these sufferings, which will also cause a great deal of hardship for the family members offering care [5]. In recent times, a variety of application domains have benefited from Artificial Intelligence (AI) techniques involving machine learning (ML) and deep learning (DL) algorithms. These include anomaly detection, biosignal and image analysis, neurodevelopmental disorder assessment and classification with an emphasis on autism, neurological disorder detection and management, elderly monitoring and care, various disease diagnosis, smart healthcare service delivery, personalized learning, so on [6]- [16].

Using compound medical data, several of these techniques have greatly improved the clinical diagnosis of AD in a very precise, quick, and effective way [16] [17]. This achievement is due to many different kinds of things, including the development of some algorithms and the availability of powerful GPUs that are already loaded with a variety of open-source computing tools [16]. In order to make the best decisions with the least amount of human involvement, AI-driven AD prediction is predicated on the idea that systems can recognize dementia phases by identifying patterns in the input data. Modern ML and DL algorithms for AD identification have produced incredibly impressive outcomes across a range of criteria [17] [21].

Nonetheless, medical professionals primarily view these AI models as "blackbox" models since they are unable to provide valid explanations (explainability) for the predictions they make, which results in uncertainty [22] [23]. Even highly qualified medical professionals frequently find it difficult to understand the answers due to the high level of opacity of these contemporary AI techniques. Because of this, decision-makers will have to choose accuracy over reliability [24]. Because of this, stakeholders and policymakers frequently favor trustworthy and accountable decision-making over precise decision-making. Even though AI-driven computer-aided diagnosis (CAD) has been shown to be accurate in recent research, the medical community is still hesitant to use it because of this lack of explainability [25].

Over the past ten years, a number of machine learning and deep learning algorithms have produced groundbreaking outcomes in a variety of AI-based decisionmaking fields, including machine fault analysis , drug discovery and development , solid-state material research, and disease prognosis and prediction. Additionally, DL is used in biology, biomedicine, and audio processing, voice recognition, and synthesis [26]-[31]. These performances occasionally outperformed humans in precision.

Uncertain situations like "Why didn't you classify that as class Y, as you had predicted?" "When will you be successful or unsuccessful?" "How can an incorrect feature selection be fixed?" "To train the model, which prominent feature are you looking for?" and "Can I trust the forecast you provided?" are frequently the result of using such blackbox models [22]. Conversely, Explainable AI (XAI) models can provide users with comforting results like "I know that the wrong feature selection needs to be fixed," "I understand why you are putting that in class x and not class y," "I can trust your prediction," and similar statements. Therefore, XAI is essential to the reliable deployment of AI-based CAD.

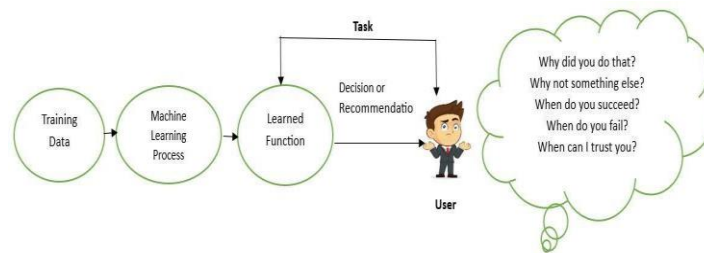


Fig. 1. AI.

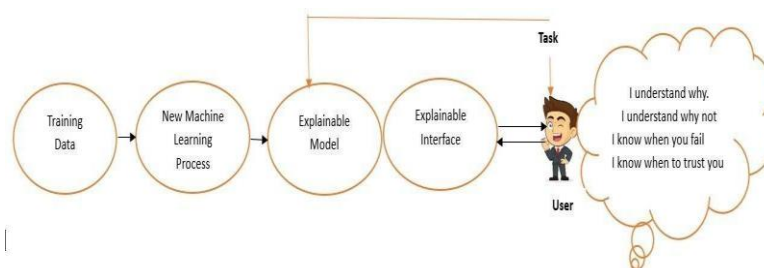


Fig. 2. Explainable AI.

The phrases "XAI" and "interpretable AI" can be used inter-changeably to describe a new area of artificial intelligence. A set of capabilities known as XAI can interpret the construction of a blackbox model, make

predictions, and win people's trust so they may effectively use the system [32] - [34]. A model must be explainable in order to support its output, make the operation of blackbox models clear, acquire new information for more informed decision-making to enhance model performance, and boost user confidence in the model's output [33]. It seeks to develop techniques and resources that help decision-makers comprehend the choices, advice, or direction made by AI systems. For clinical applications to be accurate, trustworthy, and usable, the model must be interpreted and explained. To fully utilize modern AI solutions, the trust of all stakeholders is required, and XAI is the only way to achieve this. Apart from offering sophisticated insights into AI solutions, XAI has the potential to present novel prospects. AI solutions and human knowledge work together to address difficult issues when neither can produce a suitable solution, and including a human in the decision-making process is a common medical scenario [35]. Fig. 3 provides a broad perspective on converting the blackbox concept into an explainable model.

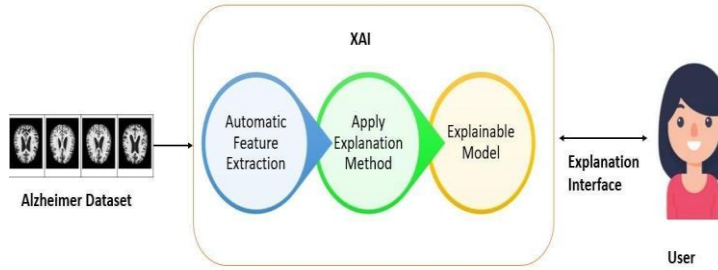


Fig. 3. Explainable AI Outlook

There is a frequent trade-off among model accuracy and its associated explainability. Decision tree (DT) or linear regression models are intuitive, naturally interpretable, and simple for even a non-expert in AI to validate and comprehend [36]. This makes such models more trustworthy. However, machine learning algorithms may provide a non-linear model to handle a complex problem, which might produce good results but compromise explainability. Convolutional Neural Networks (CNNs), for example, frequently exhibit the best performance but are the least explicable [37].

XAI has been increasingly significant in the AI world in recent years, not only because it is utilized in high-stakes decisions but also because regulators hold businesses responsible for the choices their AI models make. The explainable aspect of AI has been adopted by a number of various fields, which place a higher value on reliability than accuracy. XAI has been used in recommender systems, neurological illnesses, industrial applications, gaming, and drug development. In recent years, the healthcare industry has seen a number of XAI-based papers as a result of this amazing rise [38] - [43]. This paper aims to create a collection of fundamental research questions (RQ) that encompass the full range of XAI for the classification of AD, GitHub links to a collection of various XAI methods for deciphering blackbox models used for AD detection, An examination of XAI techniques for AD classification that has been published in the past 10 years, together with a critical evaluation of the results, discoveries, capabilities, and limits, determining the XAI models' strengths for AD detection in order to guarantee their dependability and credibility for clinician adoption and a thorough examination of the advantages, drawbacks, difficulties, and potential future paths of present XAI research. These important discoveries will close a number of research gaps and spur the development of new models that help physicians better understand how an AI system is perceived.

II. CONCEPT AND CONTEXT

A brief overview of the various XAI techniques in general is given in this section (XAI Methods). Additionally, it offers a succinct synopsis of the most widely used XAI frameworks for AD prediction. This section's main goal is to give a thorough background that will be useful for discussions in subsequent sections.

A. XAI Methods

As seen in Fig. 4, the XAI techniques can be roughly divided into four groups [44] according to: i) explanation scope, ii) implementation stages, iii) model applicability, and iv) explanation formats. The range of explanations produced by the XAI approach is known as the explainability scope. Depending on the input test data, it can interpret a single instance of the model or the complete model. As a result, a model's explainability can be

classified as either local or global. A global approach takes into account the full set of inferential data in order to explain the entire model. It provides a broad overview of how the model interacts with each input instance. Since the decision-making process for every instance of input data can be clearly explained by visualizing in tree form, the well-known DT algorithm may be inherently global in nature. However, a local technique aims to provide the user with an explanation of only a few examples of test data. In particular cases, local explanations can boost user confidence and provide insight into the reasoning behind particular decisions. For DTs, a single branch in the tree may represent a local explanation. It is noteworthy that the model can gain global insights by integrating local inferences from several input cases. A concept in XAI known as "applicability of models" describes how explainable techniques can be applied to any model as a post-process or limited to certain models. The former is referred to as model-specific, whereas the latter is known as model-agnostic, which is a post-hoc method. Explainability is incorporated into the model architecture in a model-specific method, which is intrinsic and cannot be applied to other model architectures. Interpreting the weight or activation values of a neural network model, for example, is unique to that neural network learning methodology. Deep neural network model-specific methods emphasize particular areas of the input image that significantly influenced the choice by following the CNN's route in reverse order. Two examples of model-specific techniques are LRP [45] and guided backpropagation [46].

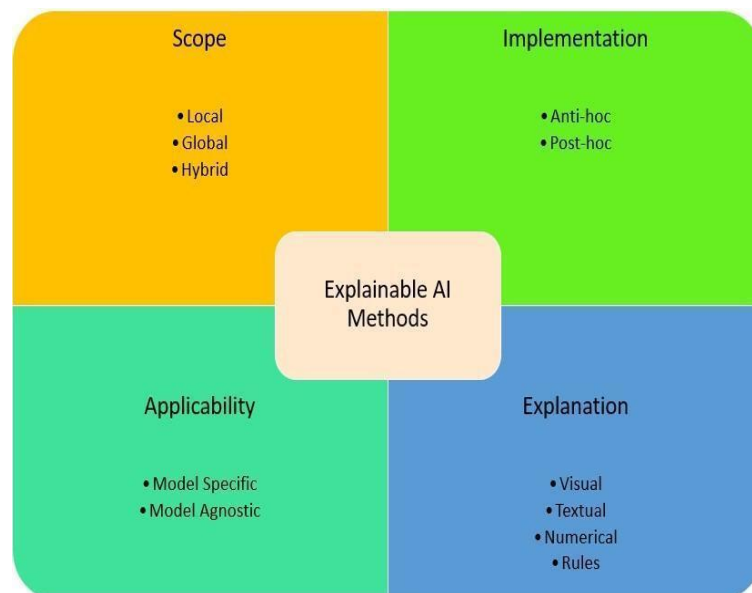


Fig. 4. XAI Methods

In XAI, the term "applicability of models" refers to the idea that explainable techniques can be applied to any model as a post-process or limited to certain models. The second technique is referred to as model-agnostic, while the former is known as model-specific. When explainability is incorporated into the model architecture and cannot be transferred to another model architecture, this is known as a model-specific method. Interpreting the weight or activation values of a neural network model, for example, is unique to that neural network learning methodology. Deep neural network model-specific techniques highlight particular areas of the input image that significantly influenced the choice by navigating the CNN's path in reverse order. Two examples of model-specific techniques are LRP [45] and guided backpropagation [46].

While model agnostic approaches can be applied to any learning strategy, they do not take into account internal factors such as weight or activation values. They do this by altering and perturbing the input data, then comparing the performance's sensitivity to the original data to uncover reasons. To put it another way, we can gauge the extent to which changing the input or weights of significant features has affected the model's performance. This will offer important information about a specific area of the input data that experienced disturbance. Other techniques include Feature Importance, GradCAM, and Occlusion Sensitivity analysis. LIME and SHapley Additive exPlanations (SHAP) are two well-liked model-agnostic techniques [47] - [50].

Images can be classified using a very different approach than those that use text, categories, or temporal data, like voice. For this reason, a model's input formats—numerical, visual, textual, or temporal—can be crucial in

defining several ways to explain XAI techniques. The interpretations of predictions can be in many forms and depend on the end users' needs and concerns. There are four forms of explanations commonly used to interpret a prediction: numerical, visual, rule-based, and textual. Depending on the needs and concerns of the end users, forecasts might be interpreted in a variety of ways. Four types of explanations are frequently used to interpret a prediction: textual, rule-based, visual, and numerical [44]. Models typically produce numerical explanations that are a measure of the input variables that influence the model's output. They depict numerical representations such as matrices, values, or vectors of numbers. A neural network layer's probability measure can also serve as a numerical explanation. Graphical descriptions of a model's operation are most frequently provided using visual aids. Novice AI model end users can quickly understand a visual explanation. For individual predictions, textual explanations are typically used because they are accurate and detailed. The significant computational cost of this explanation method, which requires natural language processing (NLP), makes it uncommon. Nonetheless, they are mostly created for a local audience and are readily comprehensible to humans. Compared to textual and visual explanations, rule-based explanations are more ordered and straightforward. They are easy for people to understand and can be used to explain how models with IF-THEN rules or trees with AND/OR operators anticipate outcomes [44].

Table 1: XAI FRAMEWORKS IN THE AD CLASSIFICATION

XAI	Local	Global	Ante-hoc	Post-hoc	Model Specific	Model Agnostic	Forms
SHAP	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Numeric, Textual
SM	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Visual
GradCAM	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Visual
LIME	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Visual, Textual
LRP	Yes	Yes	Crossmark	Yes	Yes	Crossmark	Visual
XGNN	Yes	Yes	Crossmark	Yes	Yes	Crossmark	Visual
Sensitivity	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Visual
Occlusion	Yes	Yes	Crossmark	Yes	Crossmark	Yes	Visual

B. XAI Frameworks

Table II categorizes XAI frameworks based on scope, application, implementation, and interpretable forms for various popular XAI tools in the literature.

Table 2: AN OVERVIEW OF AI FOR AD RESEARCH THAT USES XAI

	Objective
G LOVELEEN Et. Al	<i>Developing an Explanation-Driven HCI Framework for medical research</i>
Moritz Böhle Et. Al.	<i>Explaining deep neural networks using Layer-Wise Relevance Propagation</i>
Shaker El-Sappagh Et. Al.	<i>To develop an accurate and interpretable model for both AD diagnosis and MCI to AD progression detection</i>
Bloch L Et. Al.	<i>Analyzing a fair and automated data visualization</i>
Angela Lombardi Et. Al.	<i>Methodically categorizing and explaining AD and MCI</i>
Ruengchaijatuporn Et. Al.	<i>Use clock drawings and other drawing tasks as input to categorize MCI and healthy control.</i>
Monica Hernandez Et. Al.	<i>Assess pure ML contribution to diagnosis accuracy, focusing on interpretability.</i>
Lai Et. Al.	<i>Stress-related gene prediction for AD based on interpretable</i>
Bojan Et. Al.	<i>Investigates AD using explainable machine learning</i>
Min Young Chun Et. Al.	<i>Interpretable machine learning for predicting MCI to AD</i>
E Khodabandehloo	<i>Early cognitive disease diagnosis using the HealthXAI system</i>

Lu Yu Et. Al.	<i>Diagnosis with the use of PCR (Prediction basis Creation and Retrieval Module), HAM (High Resolution Activation Mapping), and</i>
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SHapley Additive exPlanations SHAP is a XAI technique that applies a weight, or Shapley value, to each feature in a trained model. All potential weighted input combinations are observed to have these qualities with a given weight. Each Shapley value-added feature's contribution is evaluated for all conceivable weighed input combinations based on efficiency, symmetry, features with no zero contributions, and cumulative contribution of a feature with sub-parts. SHAP consistently performs well and predicts accurately within its small scope [53].

Saliency Map (SM) Another key idea in deep learning is the SM, which Simonyan et al. initially proposed [51]. In SM, every pixel of an AD-classified image is eliminated and then processed, in contrast to an occlusion map, which hides parts of the input image with a black patch and produces a heatmap. The resulting heatmap is examined for differences in probability; a low probability suggests that the deleted pixel is crucial to the classification of AD [52].

Gradient-weighted Class Activation Mapping GradCAM is an approach for increasing the transparency of CNN models by selecting the most essential portions of an input image for prediction. GradCAM uses gradient information from the CNN model's output layer to create a localization map that highlights key places in an image. This is accomplished by providing an important value to each neuron for making certain decisions. GradCAM produces a heatmap that identifies key zones for prediction and explanation [54].

Local Interpretable Model-Agnostic Explanations LIME is a freebie that generates explanations for a single instance rather than the complete dataset, thus the word local. LIME gives explanations by manipulating the model's input data, building a surrogate model, analyzing the changes in pre-diction, and picking the most significant aspects. The LIME model is agnostic and may be applied to any black box model after prediction training. LIME can analyze picture classifications and explain text-based models and tabular datasets in textual, numeric, or visual formats for blackbox explanations [55].

Layer-wise Relevance Propagation (LRP) LRP, like GradCAM, provides a heatmap with highlighted sections of an image. LRP is utilized in CNN, where the inputs might be photos or videos. LRP assigns relevance scores to all neurons of a certain output in the last layer of a CNN. LRP generates a heat map based on the final relevance score to indicate influential places for prediction [56].

Occlusion Sensitivity Analysis To accurately forecast Alzheimer's disease, it's important to pinpoint portions of the image that contribute to the classification. Zeiler and Fergus first proposed the OSA approach [57]. This approach creates a heatmap by obscuring or hiding areas of the input image with a gray or black patch. Variations

in the output likelihood of an obscured image are detected [58]. If the most crucial region is occluded, it will have a significant impact with a low chance. As a result, an occlusion sensitivity map is utilized to identify key areas of the image that are responsible for AD.

III. SEARCH APPROACH

The following section describes the general stages required in doing a systematic review, including searching for and finding relevant papers. Fig. 5 shows the approach considered for the study. This summary will look into research articles that employ XAI in diagnosis/early detection and interpret the reasons for classification. To uncover contributions and summarize the findings, published articles on artificial intel-ligence and related disciplines are reviewed. This study aims to highlight research gaps and encourage XAI-based research for AD detection.

Research Question: The primary objective of formulating research questions is to establish a clear strategy for obtaining papers only from the targeted areas of study. In this manner, the reader will be able to comprehend the information more thoroughly.

- Which XAI-incorporating AI systems are available for AD research?
- For blackbox interpretability, which XAI techniques are employed to identify AD?
- Which XAI frameworks are available in the literature for the detection of AD in healthcare as a whole?
- What are the established advantages of applying XAI to AD?
- What are the constraints, difficulties, requirements, and future potential of XAI in the detection of AD and healthcare in general?

Choosing the right search terms is one of the difficult aspects for an inclusive and thorough systematic review. The search terms used for this study were chosen with care to ensure that they are neither too general to weed out irrelevant publications nor too specific to miss pertinent articles [59]. Articles were chosen from the popular databases IEEE Explore, ACM Digi-tal Library, SpringerLink, ScienceDirect, and PubMed. Below is the inclusion and exclusion criteria used in this article - **Inclusion Criteria:** Research on the use of AI methods for AD diagnosis, Explainable AI research for AD prediction and research on the performance outcomes of ML/DL models for AD.

Exclusion Criteria: Magazines, proceedings, editorials, and pilot papers, Articles unrelated to the diagnosis of AD and AI-based AD and Detecting AD are not covered in the article.

IV. OUTCOMES AND DISCUSSIONS

This section presents the results of our thorough review of the articles using the RQs set.



Fig. 5. Research Strategy

AI Systems for AD Research Using XAI "Which XAI-incorporating AI systems are available for AD research?" is the first research question that this section attempts to answer. The use of AI in the diagnosis, treatment, and prognosis of disease began in the early 1970s and has grown significantly over time. XAI was not used in research on AI-based AD prediction until the last ten years [60]. A growing desire for explainability and openness in healthcare and medical practice has led to the recent integration of XAI into AI-based AD prediction, even though the time has not yet come for computers to replace doctors. Numerous research that use XAI in AI-based AD detections have been found. Numerical datasets have been utilized in numerous studies to train AI models, with results that can be explained. Sappagh El et al [61]. AD and mild cognitive impairment (MCI), and use XAI techniques to interpret the predictions. A trustworthy multi-class classification model backed by XAI techniques is put out by Xu and Yan to precisely explain the predictions [62]. Sha et al. suggest a computer method called Systems Metabolomics utilizing Interpretable Learning and Evolution (SMILE) [63]. In order to comprehend and diagnose the onset and progression of disease, this paper employs supervised metabolomics data analysis and the XAI approach to learn and identify the most informative compounds. In order to classify AD, Hammond et al. examine beta-amyloid, tau, and neurodegenerative biomarkers. The author also employs XAI techniques to determine which biomarker has the greatest impact on AD detection [64]. According to Bloch and Friedrich, the various causes of AD can result in inconsistent disease patterns, protocols for obtaining scans, and MRI scan preprocessing problems that contribute to incorrect machine learning classification [65]. This study examines whether employing an automated and equitable data valuation strategy based on XAI techniques can improve ML classification by choosing the most informative people from the ADNI and Australian Imaging Biomarker and Lifestyle (AIBL) cohorts. The top three models from "The Alzheimer's Disease Prediction of Longitudinal Evolution" (TADPOLE) competition are compared by Hernandez et al. in terms of prediction and interpretability using a common XAI framework [66]. Using an interpretable machine learning approach, Chun et al. [126] attempt to increase the predicting power of the development from amnesic MCI to AD [48]. Numerical input values from neuropsychological and apolipoprotein test datasets are used in this investigation. In order to give an early diagnosis of AD, Sidulova et al. suggest a unique method for categorizing Electroencephalogram (EEG) data. Using EEG recordings from people with probable AD, MCI, and HC, the study's XAI technique offers quantitative elements that aid in making the prediction [67].

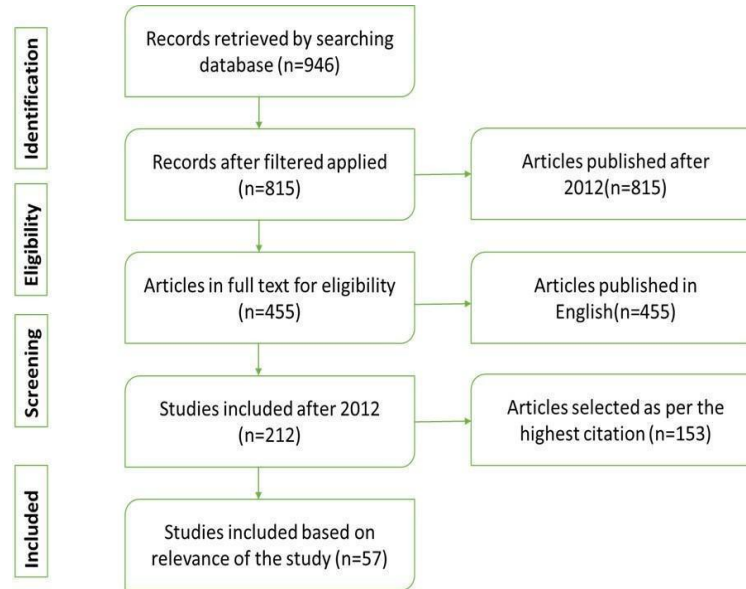


Fig. 6. PRISMA Chart

In order to train AI-based AD detection models using MRI as input data, numerous research articles have used datasets such as ADNI, OASIS, and Kaggle data. The following table suggests deep neural network classifiers for HC, MCI, and AD prediction and classification. Each of these articles selects MRI as the input and uses ADNI datasets. To identify and classify dementia into many categories, Jain et al. provide a DCGAN-based Augmentation and Classification (D-BAC) model technique based on the prevalence and severity of dementia in the available MRI [68].

The datasets of MRI scans used for this purpose are gathered from Kaggle.

XAI Techniques for Deciphering Blackbox Models to Dis-cover AD: This section discusses the research question, For blackbox interpretability, which XAI techniques are employed to identify AD?

Finding the quantity and kind of XAI techniques now accessible for the blackbox interpretability in AD detection is the goal of this research inquiry. In the XAI context of AD detection research, it offers crucial information such as comprehending the main actions made to be local/global, posthoc/ante-hoc, and model agnostic/model-specific.

- Why do certain explanations have a local AND global scope, a local limit, or a global limit?
- Why do certain blackbox models—like Random Forest (RF)—appear in many XAI approach categories?
- What makes CNN a model-specific as well as model-agnostic?
- What makes a XAI approach both posthoc and model-agnostic at the same time?
- For what reason would a XAI technique be regarded as both Antehoc and Model-Specific at the same time?

In order to address the research question with greater clarity, we respond to these questions.

Certain XAI techniques exhibit either global or locally interpretable behavior. However, by combining the local explanations, the researcher has the right to utilize those methodologies to interpret internationally. Consequently, there is no hard and fast rule stating that a model can either be local or global. For example, local interpretation is the main application for the XAI framework SHAP. But a global population can also be interpreted using SHAP. Likewise, by combining local explanations, the LIME approach, a local explainer, may also be applied to global understanding.

Blackbox models Both XGBoost and LGBM are tree-based models; XGBoost classifies data level-wise, whereas LGBM classifies data branch-wise. As a branch-wise classifier, LGBM's explainability can therefore be local. Global explanations can then be established by aggregating local results. The ultimate path to the last level can be seen as a global explanation, and XGBoost can achieve a local description at each tree level due to its level-wise classification. Therefore, while being blackbox models, LGBM and XGBoost can be aggregated

both locally and internationally. A CNN model's prediction can be explained using a model-agnostic method that doesn't alter the internal layers (like kernel SHAP).

These blackbox models, in which the inner workings of the model are left unaltered, are the major applications for post-hoc models. The resulting prediction needs to be subjected to a XAI process in order to generate explainability. This idea might be referred to as model-agnostic or post-hoc. Table II focuses on an overview of AI for AD Research that uses XAI.

The key components of a training model are naturally available in the ante-hoc model. One can use either a model-specific or model-agnostic XAI approach to extract explainability from an ante-hoc model. An ante-hoc model's training requires explainability to be included, while a model-specific XAI approach requires the inner working details.

Frameworks for AD Detection with XAI: This section answers the third research question: Which XAI frameworks are accessible in the literature and are applied to the detection of AD?

Finding the XAI frameworks and methods employed in the research to unravel AI-based AD categorization is the goal of this Research Question. Researchers, developers, and subject matter experts will be inspired to understand the inner workings of a machine-learning model by the discussions in this section. Explainable embedded machines, especially in healthcare, can significantly minimize the time medical personnel spend on repeated patient examinations and spend time concentrating on deciphering disease diagnoses. To address the issue of blackbox models—predictions that are extremely accurate but the inner workings are concealed—there are numerous XAI frameworks available. Among the numerous well-known XAI frameworks that are widely utilized in AD and relevant to RQ3 are LIME, SHAP, and GradCAM. A well-liked technique for straightforward human readings of predictive models is LIME. The research employ a variety of ML/DL classifiers, such as CNN, SpinalNet, kNN, XG-Boost, SVM, and transfer-based model BERT, to interpret the predictions using LIME. These kinds of datasets, including as MRI, gene expressions, EEG signals, and linguistic or textual data, have been used by the classifiers in the investigations. Kamal et. al [77] suggested a study that uses MRI scans and gene expression to classify people into four categories: mild dementia, moderate dementia, no dementia, and very mild dementia. Using MRI with CNN and gene expressions with kNN and XGBoost, the author employs LIME to provide local explanations for AD classifications. LIME was helpful in determining and prioritizing the important feature sets associated with an AD patient based on likelihood values. Users can learn which features have a good and negative impact on the prediction thanks to LIME. The probability values can be used to describe trust, even though trust cannot be defined. In order to distinguish between control and dementia patients, Ilias and Askounis [78] perform a comprehensive linguistic analysis using a dataset of medical transcripts using the transfer learning model, BERT, with the co-attention mechanism using the co-attention mechanism to distinguish between people with dementia and those in control.

Game theory is used by SHAP, which is model-agnostic, to explain the results of any machine learning model. The SHAP framework is another popular XAI framework, according to this review. MRI and PET scan volumetric measurements, Apolipoprotein measurements, Mini-Mental state tests, Clinical Dementia scores, and demographic data are among the types of datasets used in the majority of studies. Finding the Shapley values for each sample characteristic that requires comprehension is the basic idea behind SHAP.

ADVANTAGES OF DETECTING AD USING XAI TECHNIQUES

The fourth research question, "What are the established advantages of applying XAI to AD?" is addressed in this section. According to the review, there are a number of advantages to using the idea of XAI to AI-based AD detection. The majority of research has attempted to report model transparency, fairness, and correctness. When employing AI models for prediction, they have emphasized the value of XAI in building trust and confidence, especially in the medical sector. Benefits from independent research have indicated a responsible approach to XAI's AI development. The advantages of the chosen research are categorized in this section according to the four types of explanation: textual, rule-based, visual, and numerical. Researchers will find this classification useful in determining which theories, given the available data modalities, should be pursued.

Textual: Promising classification findings are obtained in the field of dementia detection using transcripts and the transformer-based network, BERT, developed by Ilias et al. [78]. The authors use LIME to demonstrate how transcripts clarify the distinction between people with dementia and those without. Different colors are applied to

the textual forms or tokens in transcripts to denote which ones belong to a control group. The significance of these markers for the final transcript classification is shown by the tokens' color intensity.

Rule-based: In our review, we discovered two articles that provide rules as explanations. One project uses AI agents and the Internet of Things (IoT) to remotely check on the health of senior citizens. In order to help with the early detection of cognitive decline, Khodabandehloo et al. [75] provide a novel HealthXAI system that uses a DT regression algorithm. The system also provides caregivers with high-level numerical scores for reporting inappropriate behaviors and natural language explanations of the forecasts. The decision rule forecasts the target variable's value and describes it in natural language as either HC or AD. The diagnostic tool presented by Garc'ia-Gutierrez et al. [79] uses a DT that gives doctors a clear and straightforward set of choice rules to help them understand the pathophysiology of AD and behavioral frontotemporal dementia (bvFTD).

Visual: CNN and 3D CNN are data models used in studies that employ LRP as an AI explanation. When recognizing brain atrophy, LRP offers visual explanations in the form of heat maps of important brain regions. The amygdala, entorhinal cortex, and hippocampal regions are among the important elements identified by LRP for interpretation. The use of LRP with guided backpropagation to find heat maps with pertinent, important features is covered by Bo'hle et al. [80]. Similar noteworthy features have been found by Pohl et al. [81] utilizing composite LRP with several propagation rules. According to the author, verbal semantic memory and visual memory issues are caused by injury to the left and right temporal lobes, respectively. A DL model's predictions are visually explained in a number of experiments using the GradCAM XAI tool. A VGG16 deep learning model's predictions are visually explained by Ruengchaijatuporn et al. [72] using GradCAM.

Numeric: By selecting the appropriate XAI approach, classifier, and available data, Salih et al. [82] attempt to create a proxy that will verify the explanation's stability. By quantifying the informative predictors, the authors have employed Principal Component Analysis (PCA) to confirm the stability of the identified predictors with the selected parameters. The method used in this study to associate predictors with SHAP and the proxy PCA yields uncorrelated variables that provide stable ranking for the majority of classifiers. The results are useful to the medical community because XAI is widely used in sensitive areas, such as the prognosis of long-term mortality, admission to critical care units, and ejection failure.

V. CHALLENGES, LIMITS, REQUIREMENTS, AND FUTURE OF XAI IN AD DETECTION

This part tackles research question "What are the constraints, difficulties, requirements, and future potential of XAI in the detection of AD and healthcare in general?"

The XAI idea has been developed in a number of research in recent years to better explain the decisions made by AI systems. The advent of high-performance computers and easy access to a number of XAI frameworks with easily accessible source code have made it possible to integrate these explainers into stand-alone AI systems with ease. Despite the encouraging findings of independent research, it should come as no surprise that these efforts have a number of limitations. In order to stimulate more study in this area, we have listed a number of XAI-based AD detection limitations and research gaps.

Without consulting a medical expert, XAI researchers frequently rely on their own instincts to evaluate what constitutes a sound explanation [83]. In order to maximize the benefits to stakeholders, medical and AI professionals must work together to determine the interpretability developed by the XAI framework.

The lack of ground truth data is one of the major problems with XAI-based AD diagnosis [84]. There are a number of clinical biomarker and neuroimaging datasets for AD, but none offer ground truth to support the explainability that XAI models elicit.

Additionally, when given to individuals with different degrees of topic competence, the effects of XAI explanations differ significantly [80]. People become confused and start to doubt the XAI systems' paradoxical relationship when they see explanations that go against their own intuition.

In computer-aided diagnosis, where an incorrect prediction is nearly always fatal, confidence measures are essential. If the system is unable to provide a reliable prediction, a manual intervention must be justified in order to reach a suitable conclusion. Therefore, before offering explanations, XAI techniques must additionally include a confidence score to detect instances in which the classifier is wrong. If not, the end user could instill erroneous

confidence in the system [85].

Several XAI frameworks were utilized in some articles to improve explainability. From an intellectual perspective, it might be beneficial, but in practice, it adds to the already existing ambiguity. For example, one study combined the use of the SHAP and LIME frameworks [69].

The sparse use of medical datasets or the absence of a thorough benchmark dataset with variations that reflect real-world situations is another serious flaw in practically all of the research we looked at [86].

Even while some research used multimodal data to pre-dict AD [66] [77], only one modality's explanations were drawn.

MRI volumetry, cortical thickness, and other disease indicators that are highly correlated with dementia were not taken into account by certain research, despite the fact that they employed XAI methods to predict AD [72] [47].

The majority of research has not identified variables that impact model performance and the resulting explainability, such as hyperparameter settings, the split percentage of train-test data, data preparation, etc. [74].

Medical professionals' hesitation to trust AI solutions is further exacerbated by the technology's incapacity to take into account the history of abnormalities that led to cognitive deterioration. A fundamental drawback for any medical area, not alone AI-based AD diagnosis, is the absence of real-world labelled data sets of people gathered over an extended period of time [75].

The AI forecast and the related brain region did not always correlate, despite the fact that researchers used one or more XAI frameworks in the AD prediction [67].

VI. CONCLUSION

Over the past few years, explainable AI has become increasingly important due to scientific needs and regulatory compliance. Different XAI frameworks that describe the model's accuracy, rationality, and clarity in AI-assisted decision-making—all of which are crucial in the healthcare industry—are being investigated by researchers. Extubation failures and long-term mortality are two examples of expectations that XAI helps to solve effectively by fostering synergistic ecosystems. Therefore, it is essential to encourage a broader distribution of XAI concepts, backgrounds, and approaches across the research community.

This paper provides a thorough overview of the use of XAI models and frameworks on multimodal AD data in order to achieve this goal and act as a reference. Over the past ten years, we have examined papers that use XAI to diagnose AD. Re-search publications that were carefully examined using well-crafted research questions were included in the study. Several ML and DL models that have incorporated XAI frameworks to integrate transparency and integrity in AI predictions were revealed by the RQs, which also highlighted numerous XAI-based studies used for AD diagnosis. In addition, the study identifies a number of advantages, drawbacks, and potential directions for clinical diagnosis. We acknowledge that it is too soon to make any comments about closing the gap between the medical and AI domains to zero. However, these assessments will highlight the advantages and drawbacks for the research community, allowing the trade-off between explainability and accuracy in AI solutions to be resolved with a satisfactory degree of precision. In order to fully utilize AI's potential in promoting accuracy in clinical decision support systems, this review will assist in investigating numerous healthcare domains.

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