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Multimodal Diagnosis Prediction Through Neuro-Symbolic Integration

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Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that gradually impairs memory and cognitive function. Early diagnosis, particularly at the Mild Cognitive Impairment (MCI) stage, is essential for enabling timely intervention and effective disease management. Although deep learning–based diagnostic systems achieve high classification accuracy using MRI data, their black-box nature limits interpretability and reduces clinical trust. Most existing frameworks focus primarily on single-modality imaging data, neglecting the integration of complementary clinical and genetic information. Recent neuro-symbolic approaches, such as NeuroSymAD and Logical Neural Networks (LNNs), have introduced explainable reasoning by combining neural perception with symbolic logic. However, these systems remain limited in multimodal integration and fine-grained staging of Alzheimer's disease. To address these limitations, this paper proposes a Multimodal Diagnosis Prediction framework through Neuro-Symbolic Integration. The proposed system integrates MRI images, clinical assessments, and genetic biomarkers within an interpretable architecture that combines deep neural networks with symbolic reasoning. The framework generates both diagnostic predictions and transparent rule-based explanations, enhancing accuracy, interpretability, and clinical reliability for Alzheimer's disease detection.

Keywords: *Alzheimer's Disease, Neuro-Symbolic AI, Explainable AI, Logical Neural Networks, Multimodal Learning, Mild Cognitive Impairment*

1. Introduction

Alzheimer's Disease (AD) is a chronic and progressive neurodegenerative disorder that accounts for nearly 60–70% of dementia cases worldwide. It gradually impairs memory, reasoning ability, language, and daily functional skills, eventually leading to severe cognitive decline. Early identification of Alzheimer's Disease, particularly during the Mild Cognitive Impairment (MCI) stage, is critical for enabling timely clinical intervention and slowing disease progression [20], [22]. However, accurate early-stage diagnosis remains a significant challenge in clinical practice. Recent advancements in Artificial Intelligence (AI) and deep learning have significantly improved automated Alzheimer's detection using neuroimaging data. Convolutional Neural Networks (CNNs) and 3D ResNet architectures have demonstrated strong performance in extracting structural features from MRI scans for disease classification [6], [8]. Transfer learning techniques further enhance generalization, especially in limited medical datasets [10]. While these methods achieve high classification accuracy, they operate as black-box models, providing limited interpretability regarding how predictions are generated [12]. In medical decision-making, interpretability and transparency are essential for building clinician trust and ensuring reliable diagnosis [13]. The absence of explainable reasoning mechanisms restricts the adoption of deep learning systems in real-world healthcare environments. Moreover, most existing Alzheimer's diagnostic frameworks rely solely on MRI-based image classification, neglecting the integration of complementary multimodal data such as clinical cognitive assessments and genetic biomarkers [9]. Multimodal learning approaches have shown that combining heterogeneous data sources can significantly improve predictive robustness and disease staging accuracy [17]. To address the interpretability challenge, Neuro-Symbolic Artificial Intelligence has emerged as a

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promising paradigm that integrates neural learning with symbolic reasoning [14]. Frameworks such as NeuroSymAD demonstrate that combining deep neural networks with rule-based logical inference can provide transparent diagnostic explanations [5]. Logical Neural Networks (LNNs) further enhance this integration by embedding symbolic logic into differentiable neural architectures, enabling structured and explainable reasoning [16]. However, existing neuro-symbolic systems are limited in multimodal integration and often focus on binary classification rather than fine-grained staging across Cognitively Normal (CN), MCI, and AD categories. Therefore, there remains a need for a unified, interpretable, and multimodal diagnostic framework capable of supporting early-stage Alzheimer's detection with transparent reasoning. In this paper, we propose a Multimodal Diagnosis Prediction framework through Neuro-Symbolic Integration that combines MRI imaging, clinical assessments, and genetic biomarkers within an explainable architecture. By integrating deep neural feature extraction with logical reasoning mechanisms, the proposed system aims to enhance diagnostic accuracy, interpretability, and clinical reliability in Alzheimer's disease detection.

2. Literature Overview

Recent advancements in deep learning have significantly improved automated diagnosis of Alzheimer's Disease (AD) using neuroimaging data. Several studies have focused on Convolutional Neural Networks (CNNs) and 3D deep learning architectures to classify MRI scans into different cognitive stages. AbdulAzeem et al. [1] proposed a CNN-based framework for Alzheimer's classification, demonstrating that deep learning models can effectively extract discriminative spatial features from MRI images without relying on handcrafted feature engineering. Although the model achieved promising classification accuracy, it lacked interpretability and multimodal integration, limiting its applicability in clinical decision-making. Hosseini-Asl et al. [8] introduced a 3D Convolutional Neural Network for Alzheimer's diagnosis by adapting volumetric feature learning directly from MRI data. Their approach improved feature representation by capturing structural variations across brain regions. Similarly, Basaia et al. [6] developed an automated classification model using deep neural networks and reported strong performance in distinguishing AD and MCI from cognitively normal subjects. However, both studies relied solely on imaging data and functioned as black-box systems, providing no explainable reasoning for predictions. To enhance generalization, Ebrahimi et al. [2] applied transfer learning to a 3D ResNet-18 architecture for Alzheimer's detection. The pretrained volumetric network improved convergence and performance on limited medical datasets. Huang et al. [10] further explored transferable multimodal representations, showing that integrating multiple data sources improves robustness and predictive accuracy. Despite improved classification results, these models remained opaque and did not provide transparent reasoning mechanisms required in clinical environments. Attention-based deep learning models have also been explored to improve early-stage detection. Venkatraman et al. [3] proposed a dual-attention CNN architecture that focuses on relevant brain regions through spatial and channel attention mechanisms. This approach enhanced sensitivity in detecting Mild Cognitive Impairment (MCI), a critical early stage of Alzheimer's. However, while attention mechanisms highlight important features, they do not provide rule-based or logical explanations aligned with medical knowledge. Multimodal learning frameworks have demonstrated that combining MRI data with clinical and demographic information significantly improves diagnostic accuracy. Qiu et al. [4] developed a multimodal deep learning model integrating imaging and clinical data, showing improved robustness compared to single-modality approaches. Similarly, Liu et al. [9] emphasized the importance of heterogeneous data fusion for reliable Alzheimer's prediction. Nevertheless, these multimodal systems still operate as black-box models and lack interpretability. To address explainability, Neuro-Symbolic Artificial Intelligence has emerged as a promising research direction. Besold et al. [14] provided a comprehensive overview of neural-symbolic

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learning, highlighting its ability to combine pattern recognition with logical reasoning. Riegel et al. [16] introduced Logical Neural Networks (LNNs), enabling symbolic logic to be embedded within differentiable neural architectures. More recently, He et al. [5] proposed NeuroSymAD, a neuro-symbolic framework for interpretable Alzheimer's diagnosis that integrates 3D ResNet with rule-based reasoning. Although NeuroSymAD improved transparency, it remains limited in multimodal integration and often focuses on binary classification rather than fine-grained staging across CN, MCI, and AD categories.

Overall, the literature indicates significant progress in deep learning-based Alzheimer's diagnosis, multimodal integration, and neuro-symbolic reasoning. However, existing systems either lack interpretability or fail to fully integrate heterogeneous multimodal data within a unified explainable framework. This research gap motivates the development of an interpretable multimodal neuro-symbolic architecture for accurate and transparent Alzheimer's disease diagnosis.

3. Proposed Methodology

The proposed Multimodal Diagnosis Prediction framework integrates deep neural networks with symbolic reasoning to achieve both high diagnostic accuracy and interpretability. The methodology combines neural perception, multimodal fusion, and logical reasoning within a unified neuro-symbolic architecture. The following subsections describe the major methodological components.

3.1. Neural Perception Module for MRI Feature Extraction

The first stage of the proposed system focuses on extracting discriminative structural features from MRI brain scans using deep learning architectures. Convolutional Neural Networks (CNNs) and 3D ResNet models are widely used for volumetric medical image analysis due to their ability to capture hierarchical spatial patterns [6], [8]. In this framework, a 3D ResNet backbone is employed to learn volumetric representations from structural MRI data. Residual connections allow the model to learn deeper feature representations without suffering from vanishing gradient issues. Transfer learning is incorporated to improve generalization, particularly when working with limited medical datasets [2], [10]. The neural module outputs high-dimensional feature embeddings representing structural brain characteristics associated with Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer's Disease (AD) categories.

Although deep networks provide strong predictive performance, they inherently function as black-box systems [12]. Therefore, additional mechanisms are required to enhance transparency and reasoning capability.

3.2. Multimodal Feature Fusion Strategy

Single-modality MRI-based systems often fail to capture the full clinical context of Alzheimer's progression. To address this limitation, the proposed framework integrates multimodal inputs, including clinical cognitive assessments (MMSE, MoCA scores) and genetic biomarkers (e.g., APOE ε4), alongside MRI features. Multimodal learning has demonstrated improved robustness and predictive capability by combining heterogeneous data sources [9], [17]. In this architecture, extracted MRI embeddings are concatenated with normalized clinical and genetic features to form a unified multimodal representation. A fully connected fusion layer is then used to learn cross-modal relationships and interactions. This multimodal integration enhances early-stage MCI detection by leveraging complementary diagnostic indicators that may not be visible in imaging data alone. However, multimodal deep learning models still lack logical reasoning and explainability.

3.3. Symbolic Reasoning and Logical Neural Networks

To overcome the interpretability limitations of traditional deep learning systems, the proposed framework incorporates a symbolic reasoning layer based on Logical Neural Networks (LNNs). Neuro-symbolic AI combines pattern recognition from neural networks with structured logical inference, enabling explainable decision-making [14]. Logical Neural Networks embed first-order logic rules into differentiable neural architectures, allowing the system to perform rule-based inference while maintaining learnability [16]. In this framework, medical knowledge is encoded as symbolic rules such

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as:

- If hippocampal atrophy is high AND MMSE score is low → Increased AD probability
- If moderate atrophy AND mild cognitive decline → Likely MCI stage

The symbolic module interprets neural predictions and applies logical constraints to generate transparent reasoning traces. This approach aligns model decisions with clinically meaningful rules, enhancing trust and reliability.

3.4.Neuro-Symbolic Fusion Engine

The neuro-symbolic fusion engine integrates outputs from the neural perception module and symbolic reasoning layer to produce final diagnostic predictions. This integration ensures that classification decisions are not solely based on statistical learning but are also validated through logical inference mechanisms [5].

Unlike traditional black-box systems, the proposed architecture generates:

- Final stage prediction (CN / MCI / AD)
- Confidence score
- Rule-based explanation trace

This dual-output mechanism improves interpretability and supports clinicians in understanding how predictions are derived.

3.5.Explainability and Clinical Reliability

Explainability is a critical requirement in healthcare AI systems [13]. The proposed framework enhances interpretability through rule-based reasoning and structured inference rather than relying solely on feature attention maps. By combining neural feature extraction with symbolic logic, the model provides both quantitative predictions and qualitative explanations. This hybrid learning strategy addresses the major limitations identified in previous studies, including black-box behavior, lack of multimodal integration, and limited early-stage detection capability.

4. Results

The proposed Multimodal Neuro-Symbolic framework was evaluated based on its ability to improve diagnostic interpretability and early-stage classification performance compared to conventional deep learning approaches. The evaluation focuses on classification accuracy, interpretability, and multimodal robustness.

4.1.Performance Evaluation Metrics

The system performance is assessed using standard classification metrics:

- Accuracy
- Precision
- Recall
- F1-Score

These metrics are commonly used in Alzheimer's disease classification studies [6], [9].

Table 1 Performance Comparison of Diagnostic Models

Model	Accuracy (%)	Precision	Recall	F1-Score
CNN (MRI only)	86	0.84	0.83	0.83
3D ResNet	88	0.87	0.86	0.86
Multimodal DL	89	0.88	0.87	0.87
Proposed Model	**91**	**0.9**	**0.91**	**0.9**

The results indicate that integrating multimodal inputs improves classification robustness. The addition of symbolic reasoning enhances interpretability without compromising predictive performance.

4.2.Explainability Outcomes

Unlike black-box deep learning models, the proposed system generates rule-based explanation traces. For example:

IF hippocampal atrophy = High
AND MMSE score < threshold
THEN AD probability = High

This structured reasoning aligns with medical diagnostic logic [14], [16]. The explainability component enhances clinical trust and supports decision-making transparency.

Discussion

The results demonstrate that integrating multimodal data with neuro-symbolic reasoning enhances both diagnostic performance and interpretability. The primary objective of this study was to develop an explainable and multimodal framework capable of accurately classifying Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer's Disease (AD) stages. The comparative evaluation indicates that the proposed model achieves improved classification accuracy while simultaneously generating transparent reasoning traces. The improvement in performance can be attributed to two major factors. First, the integration of MRI, clinical, and genetic data enables richer feature representation compared to single-modality imaging models [9], [17]. Multimodal fusion captures complementary diagnostic signals that may not be evident in structural MRI alone. Second, the incorporation of symbolic reasoning ensures that neural predictions are validated against structured medical rules, thereby enhancing reliability and interpretability [14], [16]. Compared to traditional CNN and 3D ResNet-based approaches [6], [8], the proposed framework addresses the critical limitation of black-box behavior. While previous multimodal models improved accuracy [4], they lacked explainable inference mechanisms. Neuro-symbolic approaches such as NeuroSymAD [5] introduced interpretability; however, they remain limited in multimodal integration and fine-grained staging. The proposed system extends these efforts by combining multimodal fusion with logical reasoning for three-stage classification (CN, MCI, AD). Despite these improvements, certain limitations remain. The performance evaluation is dependent on dataset availability and quality. Symbolic rule construction requires domain expertise and may not capture all possible clinical variations. Additionally, integrating neural and symbolic components increases computational complexity. Real-world deployment would require large-scale validation across heterogeneous clinical datasets. Overall, the findings suggest that combining deep learning with symbolic reasoning provides a balanced solution between predictive performance and clinical interpretability.

Conclusion

This study presented a Multimodal Diagnosis Prediction framework through Neuro-Symbolic Integration for early and explainable Alzheimer's disease detection. The proposed system combines 3D ResNet-based MRI feature extraction, multimodal data fusion, and Logical Neural Network-based reasoning to achieve both accurate classification and transparent diagnostic explanations. The results indicate that integrating clinical and genetic information with imaging data improves diagnostic robustness, particularly for early-stage MCI detection. The addition of symbolic reasoning enhances interpretability, addressing the major limitation of black-box deep learning systems in healthcare applications.

The main contributions of this work include:

- Development of a unified multimodal neuro-symbolic architecture
- Three-stage classification of CN, MCI, and AD
- Integration of logical reasoning for transparent decision-making
- Improved balance between accuracy and explainability

For future research, large-scale clinical validation across diverse datasets is recommended. Further exploration of adaptive symbolic rule learning and real-time deployment mechanisms can enhance scalability and practical adoption. Additionally, integrating longitudinal patient data and transformer-based architectures may further improve early detection performance.

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