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Early Alzheimer's Disease Detection Using Deep-Ensemble Learning and MRI-Image Analysis

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Abstract

Early detection of Alzheimer's disease (AD) is crucial to slowing cognitive decline and enabling timely clinical interventions. Traditional diagnostic methods, including cognitive tests and single-model classifiers, have limited sensitivity during early stages of the disease. This paper presents a deep ensemble learning approach that integrates multiple convolutional neural networks (CNNs) for accurate Alzheimer's disease detection using structural Magnetic Resonance Imaging (MRI) data. The proposed framework utilizes ResNet50, VGG16, and DenseNet121 as base learners and a meta-learner based on gradient boosting for final classification. Preprocessing includes skull stripping, normalization, and spatial smoothing. Data augmentation enhances generalization, and feature fusion at the decision level improves robustness. We evaluate our approach on the ADNI dataset using five-fold cross-validation. The ensemble model outperforms individual CNNs, achieving 94.3% accuracy, 95% precision, 93.5% recall, and 94.2% F1-score. SHAP-based interpretability further enables visualization of brain regions influencing predictions. The study concludes that deep ensemble learning provides a powerful, scalable framework for early-stage AD prediction and has strong potential for integration into clinical decision support systems.

Keywords: Alzheimer's disease, CNN, Deep Learning, Ensemble Learning, MRI

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that primarily affects memory, cognitive function, and behavior. It accounts for 60–70% of dementia cases globally and is one of the leading causes of disability among the elderly. The societal and economic burden of Alzheimer's is immense, impacting not only the affected individuals but also caregivers and healthcare systems [1]. Despite decades of research, early, and accurate diagnosis of AD remains a significant challenge, primarily due to its insidious onset and overlapping symptoms with other neurodegenerative conditions.

Early detection is critical in managing Alzheimer's disease. Intervening during the prodromal or mild cognitive impairment (MCI) stage can slow disease progression, enhance quality of life, and provide valuable time for planning and care. Traditional diagnostic tools, such as cognitive screening tests (e.g., MMSE, MoCA), biochemical biomarkers, and structural neuroimaging, although useful, suffer from limitations including subjectivity, variability, and limited sensitivity to early structural changes in the brain [2–4].

Magnetic Resonance Imaging (MRI) has emerged as a non-invasive, highly informative tool for detecting subtle anatomical changes in the brain associated with AD. MRI scans can reveal hippocampal atrophy, ventricular enlargement, and cortical thinning – hallmarks of early Alzheimer's pathology [5–7]. However, manual interpretation of MRI scans is time-consuming and requires expert radiological skills, which limits scalability in

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clinical settings. As a result, there is a pressing need for automated, robust, and accurate diagnostic tools that can leverage MRI data for early Alzheimer's detection [8].

Machine Learning (ML) and Deep Learning (DL) techniques have shown promising results in medical image analysis. Convolutional Neural Networks (CNNs), in particular, have demonstrated high efficacy in recognizing spatial hierarchies in imaging data. Despite this, single CNN models often struggle with overfitting, bias toward dominant features, and sensitivity to noise, especially when dealing with complex neuroimaging data with high inter-subject variability [9–14].

To address these challenges, ensemble learning offers a compelling solution. Ensemble methods aggregate predictions from multiple base learners to reduce generalization errors and improve model robustness. By combining diverse architectures, like ResNet, VGG, and DenseNet, the ensemble approach captures a wider range of spatial features, balances bias-variance tradeoffs and mitigates individual model weaknesses [15].

In this research, we propose a deep ensemble framework for early Alzheimer's detection using structural MRI images [16]. Our methodology integrates multiple pre-trained CNN models – ResNet50, VGG16, and DenseNet121 – and utilizes a gradient boosting-based meta-learner to synthesize predictions. Preprocessing steps, such as skull stripping, normalization, and spatial smoothing, ensure clean and standardized input data. Data augmentation further enhances model generalization. Evaluation is performed on the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset using five-fold cross-validation and standard metrics such as accuracy, precision, recall, and F1-score [17–20].

Furthermore, we incorporate SHapley Additive exPlanations (SHAP) to visualize and interpret the model's predictions, enhancing trust and transparency in clinical applications [21–26]. This research aims to contribute a scalable, interpretable, and clinically relevant tool for early AD detection, paving the way for better patient outcomes through timely intervention.

LITERATURE SURVEY

The use of machine learning and deep learning for Alzheimer's disease (AD) detection has significantly evolved over the past decade, particularly with the availability of neuroimaging datasets like the Alzheimer's Disease Neuroimaging Initiative (ADNI) [27–30]. MRI-based approaches have gained attention due to their non-invasive nature and ability to capture fine-grained structural changes in brain tissue [31]. This literature review highlights major contributions in this field, with a focus on deep convolutional neural networks (CNNs), ensemble methods, interpretability, and the integration of multimodal data.

Traditional Machine Learning Approaches

Early efforts in automated AD diagnosis relied on conventional machine learning classifiers like Support Vector Machines (SVM), Decision Trees, and k-Nearest Neighbors (kNN). Kloppel et al. (2008) used SVMs on voxel-based morphometry data from MRI scans and reported reasonable classification accuracy [32–36]. However, these approaches required extensive handcrafted feature extraction, were prone to overfitting, and struggled to generalize to heterogeneous populations. Feature engineering was typically domain-specific and lacked scalability, which limited real-world applicability.

Emergence of Deep Learning in AD Diagnosis

The advent of deep learning, particularly CNNs, revolutionized medical image analysis by automating feature extraction and classification. Sarraf and Tofighi (2016) introduced one of the first applications of CNNs on MRI data for AD detection using axial 2D slices, achieving around 85% accuracy [37–41]. However, their approach did not leverage the full 3D structure of brain scans, potentially missing spatial context important for AD-related atrophy.

To overcome this limitation, Liu et al. (2018) proposed a 3D CNN architecture to capture volumetric information, resulting in improved performance (accuracy ~89%) [42–49]. Islam and Zhang (2022) extended this by applying DenseNet121 to 3D MRI volumes. Their approach benefited from dense skip connections that allowed deeper feature extraction and better gradient flow, leading to enhanced generalization on unseen data.

Multi-View and Multi-Modal Models

Cheng et al. (2021) addressed spatial redundancy and improved feature extraction by designing a multi-view CNN framework that processed sagittal, axial, and coronal slices simultaneously [50–54]. This technique improved model robustness by integrating complementary spatial perspectives. Likewise, Gupta et al. (2020) emphasized the fusion of multimodal data such as PET, CSF biomarkers, and MRI for AD diagnosis. By combining imaging and non-imaging features, their ensemble approach achieved an F1-score exceeding 0.90 [55].

However, multimodal models require access to multiple clinical data sources, which may not always be feasible. Additionally, they face challenges in harmonizing input formats and handling missing modalities, which necessitates complex preprocessing pipelines.

Deep Ensembles in Alzheimer's Prediction

Ensemble learning methods offer a practical solution to improve prediction robustness especially when dealing with noisy medical data [56–59]. Suk et al. (2017) combined multiple classifiers including autoencoders, SVMs, and logistic regression in a hybrid ensemble framework to classify Mild Cognitive Impairment (MCI) and AD. Their model demonstrated significant improvement in sensitivity and generalization [60–65].

Hosseini-Asl et al. (2018) developed a novel 3D-CNN-RNN hybrid ensemble model that not only captured spatial features from MRI but also temporal progression through recurrent layers [66–70]. Their model outperformed standalone 3D CNNs, with an accuracy of 92.1% on the ADNI dataset. The use of multiple architectures allowed the model to learn different aspects of disease manifestation such as brain shrinkage and ventricle expansion.

In another notable study, Basaia et al. (2019) proposed an ensemble of ResNet-based CNNs trained on 3D patches of the brain. Their model used attention mechanisms to highlight regions most indicative of AD. Results showed a 94% accuracy in distinguishing AD from healthy controls and MCI subjects. Such work underscores the power of model diversity and feature fusion in improving classification performance [71–76].

Explainable AI and Model Interpretability

Interpretability remains a key concern in medical AI applications. Clinicians are often reluctant to rely on "black-box" predictions without insight into the reasoning behind them. To address this, Lundervold, and Lundervold (2019) employed gradient-based class activation maps (Grad-CAM) and Layer-wise Relevance Propagation (LRP) to highlight areas in MRI scans that influenced CNN decisions. Their findings aligned with known neuropathological markers like hippocampal and cortical atrophy [77–81].

More recently, SHAP (SHapley Additive exPlanations) values have been used to attribute model outputs to specific input features [82, 83]. Pereira et al. (2021) applied SHAP to CNN predictions for AD diagnosis and validated that features contributing to predictions corresponded to medically plausible brain structures. This integration of explainable AI (XAI) with diagnostic models enhances trust, particularly for deployment in clinical decision support systems (CDSS) [84].

Challenges in Deep Learning Models for AD

Despite notable success, several challenges persist. First, MRI datasets often have limited size, which constrains the training of deep models. Data augmentation techniques help but cannot fully replicate the diversity of real-world data [85–89]. Second, class imbalance – especially the underrepresentation of early-stage AD or MCI – skews model predictions and reduces sensitivity for minority classes [90–94]. Researchers have applied techniques, such as SMOTE and focal loss functions, to address this, though with mixed results.

Third, overfitting remains a major issue, particularly when using deep architectures on relatively small datasets. Regularization strategies, such as dropout, weight decay, and early stopping, are commonly applied, but ensemble models have proven more effective in mitigating these risks.

Fourth, standardization across imaging protocols, scanners, and sites is limited, which affects model transferability. Harmonization techniques, such as ComBat or cycle-GANs, are being explored to align multi-center data, though further validation is needed.

Gaps and Future Directions

Several areas remain underexplored. For example, few studies have integrated longitudinal imaging data to model disease progression over time. Temporal models, like LSTMs or transformers, have potential to capture evolving biomarkers that precede cognitive decline.

Furthermore, most deep learning studies focus on binary classification (AD vs. CN), neglecting the more clinically relevant problem of predicting MCI conversion. Forecasting MCI-to-AD transition is crucial for early intervention but requires more complex temporal and probabilistic models [95].

Finally, model deployment remains a hurdle. Most models are tested in experimental setups with ideal data. Real-world hospital systems require models that are explainable, efficient, and capable of handling noise, missing data, and distribution shifts. Lightweight architectures, edge AI deployment, and federated learning may help bridge this translational gap.

METHODOLOGY

Our proposed deep ensemble framework for Alzheimer's disease detection from MRI images follows a structured multi-phase approach

Dataset Selection

We utilized the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, comprising structural T1-weighted MRI scans of patients categorized as Cognitively Normal (CN), Mild Cognitive Impairment (MCI), and Alzheimer's Disease (AD). A total of 3,000 MRI scans were selected and equally distributed across the three classes.

Preprocessing

- *Skull Stripping:* To remove non-brain tissues using the Brain Extraction Tool (BET).
- *Normalization:* Intensity normalization was applied using z-score scaling.
- *Resampling:* All volumes were resampled to a uniform dimension of 128 × 128 × 128 voxels.
- *Smoothing:* Gaussian smoothing with $\sigma = 1.0$ was applied to reduce noise.
- *Augmentation:* Rotations, flips, zoom, and contrast variations to improve generalization.

Base Learners (CNN Models)

- *ResNet50:* Deep residual learning with skip connections for robust feature extraction.
- *VGG16:* Sequential convolution layers known for their simplicity and depth.
- *DenseNet121:* Densely connected layers promoting feature reuse and efficient gradient flow.

Each CNN was trained on 70% of the dataset with categorical cross-entropy loss and the Adam optimizer (learning rate = 0.0001). Batch size was 32, and training was conducted for 50 epochs with early stopping.

Meta-Learner

Predictions from each base model on the validation set were passed as input to a Gradient Boosting Classifier that acted as the meta-learner. This stacking ensemble leveraged the strengths of each CNN for improved final classification.

Interpretability Engine

To enhance clinical trust, SHAP (SHapley Additive exPlanations) was applied to the meta-learner's output to visualize feature contributions and important brain regions associated with AD diagnosis.

We evaluated our ensemble framework on the ADNI dataset using five-fold stratified cross-validation. The dataset was split into 70% training, 15% validation, and 15% test sets. Performance metrics included Accuracy, Precision, Recall, and F1-score.

Performance Metrics Table

Table 1 shows performance analysis of different algorithms.

Table 1. Performance metrics of individual models vs. ensemble.

Model	Accuracy	Precision	Recall	F1-score
ResNet50	89.7%	90.1%	88.3%	89.2%
VGG16	87.2%	88.4%	85.9%	87.1%
DenseNet121	91.0%	91.6%	89.8%	90.7%
Ensemble	94.3%	95.0%	93.5%	94.2%

DISCUSSION

- The ensemble model outperformed all individual CNNs across all metrics.
- DenseNet121 performed the best among base learners due to dense connectivity.
- SHAP visualizations revealed hippocampal atrophy and parietal cortex shrinkage as dominant predictive features – consistent with known AD pathology.
- Model training time increased with stacking but yielded substantial gains in accuracy.

CONCLUSION

This study demonstrates the potential of deep ensemble learning for early detection of Alzheimer's disease using MRI imaging. By combining ResNet50, VGG16, and DenseNet121 with a gradient boosting meta-learner, our model achieved a notable classification accuracy of 94.3%. The integration of SHAP improved interpretability, enabling transparent decision-making in clinical settings.

The ensemble approach proved effective in capturing diverse spatial patterns and reducing bias-variance trade-offs. It also showcased robustness against MRI noise and anatomical variability. These results suggest that deep ensemble models are viable tools for computer-aided diagnosis of Alzheimer's disease, especially at the early stages where intervention is most beneficial.

Future Scope

Several enhancements can be pursued in future work:

- *Longitudinal Data Integration:* Incorporate time-series scans to track progression.
- *Multimodal Fusion:* Combine MRI with PET, EEG, or genomic biomarkers.
- *Lightweight Deployment:* Optimize models for real-time edge computing on hospital systems.
- *Clinical Trials:* Validate model effectiveness on larger and diverse population datasets.
- *Transfer Learning and AutoML:* Employ meta-optimization for hyperparameters and architecture tuning.

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