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An Intelligent Metaheuristic-Assisted Feedforward Neural Network Framework for Accurate Alzheimer's Disease Classification Using Medical Diagnostic Data

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disease which represents a major burden of global health. The early and accurate classification of the stages of AD is crucial for early clinical intervention. In this paper, an intelligent hybrid system combining a Feedforward Neural Network (FNN) and a metaheuristic optimization method known as Grey Wolf Optimizer (GWO) is proposed for accurate classification of Alzheimer's disease based on multi-modal medical diagnostic information. To overcome the drawbacks of gradient-based learning such as falling into local minima and convergence slowdown, the GWO is used to optimize the FNN's hyperparameters and synaptic weights. The proposed GWO-FNN model is tested on two datasets: The Open Access Series of Imaging Studies (OASIS) dataset and Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. The experimental results show that the GWO-FNN outperforms the conventional machine learning models and the standalone neural networks, with a classification accuracy of 97.4%, sensitivity of 96.8%, specificity of 97.9% and AUC of 0.987. The results highlight the effectiveness of Deep Optimization using a Metaheuristic approach in clinical neurodiagnostic system.

I. INTRODUCTION

The most common type of dementia is Alzheimer's disease (AD) which represents around 60-80% of all dementia worldwide. There are currently an estimated 55 million people who have dementia worldwide of which AD is the major cause as of 2023. The impact of AD on the economy and society

is substantial, not only among patients, but also for caregivers, health care providers and the economy in general. But this is expected to triple by 2050 if there are no breakthrough interventions.

AD involves amyloid beta plaques, tau protein neurofibrillary tangles, neuroinflammation and extensive loss of synapses. These neural alterations are seen in the clinical range spanning cognitively normal (CN), mild cognitive impairment (MCI) and complete Alzheimer's dementia. Early detection, especially at MCI, is important because timely therapeutic interventions may slow the symptoms when they are first identified.

The various features from the different modalities, such as volumetric measures from magnetic resonance imaging (MRI), positron emission tomography (PET) biomarkers, cerebrospinal fluid (CSF) biomarkers and neuropsychological assessments, all contribute to a rich multi-modal feature space that can serve as a basis for the staging of AD. These features are, however, highly dimensional, inter-subject variance, class imbalance and complex nonlinear relationships between these features are challenges for conventional classification algorithms.

ANNs, such as FNNs are promising techniques in medical classification problems, due to their ability to model nonlinear relationships. However, there are well-known drawbacks to gradient-based learning methods like backpropagation: sensitivity to initial weight settings, sensitivity to local minima, vanishing gradients and need for extensive manual hyperparameter tuning. All these problems inspire the integration of metaheuristic optimization methods inspired by nature with neural architectures.

Population-based global search methods can be used to complement the gradient-based local refinement techniques, such as the Metaheuristic Algorithms (MA) like Genetic Algorithms (GA), Particle Swarm Optimization (PSO), Differential Evolution (DE), and Grey Wolf Optimizer (GWO). In a spirit of grey wolf optimization leadership hierarchy and hunting mechanism, GWO has shown its competitive optimization performance on various engineering and medical problems for relatively small number of tunable parameters.

This paper presents a GWO-FNN framework that performs the global optimization of FNN weights and hyperparameters by using GWO algorithm and afterwards fine-tuning the weights and hyperparameters by back-propagation algorithm. There are several main contributions:

- A GWO-FNN hybrid model for AD Classification based on the global metaheuristic search combined with gradient-based local search.
- An extensive feature engineering pipeline for integration of multi-modal medical diagnostic data.
- Extensive experimentalization and statistical analysis on OASIS and ADNI benchmarks.
- Comparative analysis with other state-of-the-art classifiers that have better performance.

II. RELATED WORK

Over the past decade, much has changed in the machine learning methods for AD classification. Previous research was based on manually designed features extracted from MRI data and support vector machines (SVM). Cuingnet et al. [1] compared several SVM-based methods on the ADNI

dataset and found that the accuracy for categorization of AD vs. CN was between 81% and 95%, while the accuracy for predicting conversion from MCI was lower.

Neuroimaging-based AD classification has been revolutionized by deep learning, especially convolutional neural networks (CNNs). Hosseini-Asl et al. [2] introduced a 3D CNN 99.9% accurate on ADNI using a convolutional autoencoder as a pre-trained network. Such architectures require a significant amount of computation resources and large labeled datasets, however. Liu et al. [3] used a multi-scale CNN with attention modules on MRI data and while their results were competitive, they were not very interpretable.

HYBRID methods based on the combination of feature selection or optimization and neural classifiers are having some success. Suk et al. [4] employed stacked AEs for multi modality feature learning using MRI and PET. Farhan et al. [5] used PSO to find the optimal hyperparameters of SVM and also used PSO for feature selection, which enhanced the classification accuracy by around 3.2% on clinical AD datasets as compared to the SVM.

In related classification scenarios of diseases, use of metaheuristic-optimized neural networks has been investigated. Ahmed et al. [6] used GWO to select features for classification pipeline for breast cancer, which showed better accuracy and fewer features. Mirjalili et al. [7] were first introduced and proved the GWO to outperform other algorithms such as PSO and GA on benchmark functions, and thus it became a promising algorithm in biomedical applications.

Although these developments have been made, there are still some gaps: (1) The majority of studies consider only binary classification, while multi-class AD staging remains under explored; (2) Most of the weight optimization for FNNs using metaheuristics has been done only for the multi-modal AD data; (3) Complete evaluations on multiple datasets with strong statistical testing is missing. The proposed GWO-FNN framework will overcome these gaps.

III. METHODOLOGY

The proposed approach presents a smart hybrid classification approach that combines the global optimization ability of the Grey Wolf Optimizer (GWO) with the nonlinear learning ability of a Feedforward Neural Network (FNN) for the accurate classification of Alzheimer's Disease (AD) stages. The framework aims to solve the problem of multi-modal medical diagnostic data with high dimensionality, non-linear interaction between features, convergence of local minimum and inter-subject variability. The methodology is divided into five main steps: data acquisition and data preprocessing, feature engineering, building of the neural network, metaheuristic optimization and classification.

First, a large number of multi-modal clinical datasets from OASIS-3 and ADNI undergo extensive pretreatment to make sure of the data quality and consistency. Let the given data set be represented by

$$D = \{(x_i, y_i)\}_{i=1}^{N}$$

where $x_i = [x_{i1}, x_{i2}, \ldots, x_{id}]$denotes the d-dimensional feature vector of the i^{th}subject and $y_i \in \{CN, MCI, AD\}$represents the associated diagnostic class label. Since medical datasets often contain

features measured at different scales, Z-score normalization is applied to standardize each attribute. The normalized feature value is computed as

$$z_{ij} = \frac{x_{ij} - \mu_j}{\sigma_j}$$

where $\mu_j$and $\sigma_j$denote the mean and standard deviation of the j^{th}feature respectively. This transformation eliminates scale disparities and accelerates neural network convergence. Missing values are subsequently handled through median imputation, thereby preserving the statistical distribution of the data while minimizing bias.

Following preprocessing, feature engineering is performed to reduce redundancy and retain diagnostically significant information. Initially, Mutual Information (MI) analysis quantifies the dependency between individual features and disease classes. The mutual information score for a feature $X$with class label $Y$is defined as

$$MI(X,Y) = \sum_{x \in X} \sum_{y \in Y} p(x,y) \log \frac{p(x,y)}{p(x)p(y)}$$

where $p(x,y)$denotes the joint probability distribution and $p(x)$and $p(y)$represent marginal probability distributions. Features exhibiting low mutual information values are removed because they contribute minimal discriminative information toward disease prediction.

The remaining features are further optimized through a wrapper-based feature selection mechanism driven by the Grey Wolf Optimizer. The selected feature subset can be represented as

$$F = \{f_1, f_2, \dots, f_k\}$$

where $k < d$. The objective is to maximize classification performance while minimizing feature dimensionality. Consequently, the fitness function for feature selection is formulated as

$$Fitness = \alpha(1 - Accuracy) + \beta \frac{|F|}{d}$$

where $\alpha$and $\beta$are balancing coefficients controlling classification performance and dimensionality reduction respectively.

Once the optimal feature subset is determined, the attributes selected are provided to the Feedforward Neural Network. The FNN is the key classification engine to model complex non-linear relationships between biomarker, demographic, neuropsychological assessment and imaging-derived measures. The network structure includes an input layer, two hidden layers and an output layer. Let the optimized feature vector be denoted as

$$x = [x_1, x_2, \dots, x_k]^T$$

The first hidden layer computes

$$h_1 = ReLU(W_1 x + b_1)$$

where W_1denotes the weight matrix, $b_1$represents the bias vector, and ReLU is defined as

$$ReLU(z) = \max(0, z)$$

The output of the first hidden layer is propagated to the second hidden layer according to

$$h_2 = ReLU(W_2 h_1 + b_2)$$

Subsequently, the output layer generates class probabilities using the softmax activation function:

$$\hat{y} = Softmax(W_3 h_2 + b_3)$$

The softmax operation transforms raw scores into probability distributions:

$$P(y = c \mid x) = \frac{e^{z_c}}{\sum_{j=1}^{C} e^{z_j}}$$

where Cdenotes the total number of classes. Since the classification problem involves three categories—Cognitively Normal (CN), In the output layer, there are three neurons which are connected to the layers of the network that represent Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). Traditional gradient-based learning algorithms can fall into the local optima and have poor initialization. To address these challenges, global optimization of the network parameters is performed with the Grey Wolf Optimizer. GWO is motivated by the social hierarchy and collaborative form of predation seen in nature, among grey wolves. The population consists of α, β, δ and ω wolves. The best solution is alpha wolf, and beta and delta wolves help in guiding the search process. Let $X(t)$denote the position vector of a wolf at iteration t. The distance between a wolf and the prey is calculated as

$$D = \mid C \cdot X_p(t) - X(t) \mid$$

where $X_p(t)$represents the prey position and $C$is a coefficient vector defined by

$$C = 2r_2$$

with $r_2 \in [0,1]$.

The position updating mechanism is governed by

$$X(t+1) = X_p(t) - A \cdot D$$

where

$$A = 2ar_1 - a$$

and $r_1 \in [0,1]$. The parameter $a$decreases linearly from 2 to 0 throughout the optimization process:

$$a = 2 - \frac{2t}{T}$$

where Tdenotes the maximum number of iterations.

Since the actual prey location is unknown, the algorithm estimates it using the three best wolves. Distances from alpha, beta, and delta wolves are computed as

$$D_\alpha = \mid C_1 X_\alpha - X \mid$$
$$D_\beta = \mid C_2 X_\beta - X \mid$$
$$D_\delta = \mid C_3 X_\delta - X \mid$$

The corresponding candidate positions are

$$X_1 = X_\alpha - A_1 D_\alpha$$
$$X_2 = X_\beta - A_2 D_\beta$$

$$X_3 = X_\delta - A_3 D_\delta$$

The updated position of each wolf is obtained by averaging these candidate solutions:

$$X(t+1) = \frac{X_1 + X_2 + X_3}{3}$$

Each wolf is embedded with a full neural network solution, including all the synaptic weights, biases, learning rate, dropout rate, regularization coefficient, batch size and the number of neurons in the hidden layers in the proposed framework. Each solution is judged by a fitness function based on the classification accuracy:

$$Fitness = -Accuracy_{validation}$$

Optimization process is an iterative process, where wolf positions are updated until convergence. The best solution found by GWO optimizes globally the neural network's parameters.

The optimized parameters obtained from the GWO are implemented as initial values in the FNN during the last learning step. Then, the local refinement, or back-propagation, is carried out by the Adam optimization algorithm. The cross-entropy loss function is used to reduce classification errors:

$$L = -\sum_{i=1}^{N} \sum_{c=1}^{C} y_{ic} \log(\hat{y}_{ic})$$

where y_{ic}represents the actual class indicator and $\hat{y}_{ic}$denotes the predicted probability. The Adam optimizer updates parameters according to adaptive moment estimation, ensuring stable convergence and faster learning. By combining global exploration using GWO with local exploitation using gradient-based refinement, an efficient hybrid learning approach is achieved. GWO is effective in exploring the high dimensional search space to identify the regions with the potential of good performance, and backpropagation is then used to optimize the network's weights to produce accurate decision boundaries. The proposed GWO-FNN framework significantly improves the classification performance in terms of accuracy, sensitivity, specificity, and robustness, which makes it very suitable for the early diagnosis of Alzheimer's disease and clinical decision support applications.

IV. EXPERIMENTAL SETUP AND RESULTS ANALYSIS

The proposed GWO-FNN framework was tested on two publicly available Alzheimer's disease datasets: the OASIS-3 and the ADNI-2 datasets, which contain multimodal diagnostic data such as neuroimaging biomarkers, demographic characteristics, and cognitive assessment scores. Following pre-processing, the OASIS-3 dataset consisted of 1043 samples across three diagnostic categories (cognitively normal (CN); mild cognitive impairment (MCI); Alzheimer's disease (AD)) and the ADNI-2 dataset had 835 subjects with the same diagnostic categories. It was coded in Python 3.10 with TensorFlow 2.12, NumPy, Scikit-learn, and our own Grey Wolf Optimizer (GWO) module. Experiments were run on a high-performance platform with an NVIDIA A100 GPU (40GB), Intel Xeon Gold 6238R processor and 64GB RAM. One experiment used a fixed seed of 42 for all experiments to ensure reproducibility. To evaluate the performance, the following criteria are used: Accuracy, Sensitivity,

Specificity, F1-Score, Matthews Correlation Coefficient (MCC) and Area Under the ROC Curve (AUC). The Wilcoxon signed-rank test ($p<0.05$) was used, with each run performed in a different instance. This was done by comparing to LR, SVM-RBF, RF, XGBoost, standalone FNN, PSO-FNN, GA-FNN, and 3D-CNN with the same preprocessing and 10-fold cross validation. For simultaneous optimization of the network architecture and learning parameters, a population of 30 wolves and 100 iterations was used for the GWO.

A. Classification Performance on OASIS-3

The classification results for all models with the OASIS-3 dataset are shown in the Table I. The GWO-FNN achieves the highest accuracy (97.4%), sensitivity (96.8%), specificity (97.9%), F1-score (97.2%), MCC (0.961), and AUC (0.987). The benefit of using metaheuristic weight initialization and hyperparameter optimization for the GWO-FNN is validated by comparing the accuracy of GWO-FNN (91.2%) with the standalone FNN.

TABLE I. ***Classification Performance Comparison on OASIS-3 Dataset***

Model	Acc. (%)	Sens. (%)	Spec. (%)	F1 (%)	MCC	AUC
LR	79.3	77.1	80.5	78.0	0.687	0.841
SVM-RBF	84.6	83.2	85.7	83.9	0.764	0.897
Random Forest	88.1	86.7	89.0	87.4	0.821	0.931
XGBoost	89.5	88.3	90.4	88.9	0.843	0.946
FNN (BP)	91.2	89.8	92.1	90.5	0.868	0.954
GA-FNN	93.4	92.1	94.3	92.8	0.901	0.967
PSO-FNN	94.7	93.6	95.5	94.1	0.919	0.973
3D CNN	95.8	94.5	96.7	95.2	0.937	0.979
GWO-FNN	**97.4**	**96.8**	**97.9**	**97.2**	**0.961**	**0.987**

B. Classification Performance on ADNI-2

The results are presented in Table II on ADNI-2. GWO-FNN achieves accuracy 96.1%, sensitivity 95.4%, specificity 96.9%, F1 96.0%, MCC 0.941, AUC 0.982. A small drop in absolute performance from OASIS-3 is due to the increased inter-site variability in the multi-center ADNI dataset. However, GWO-FNN remains to have statistically significant margins with all baselines (Wilcoxon $p < 0.001$).

TABLE II. ***Classification Performance Comparison on ADNI-2 Dataset***

Model	Acc. (%)	Sens. (%)	Spec. (%)	F1 (%)	MCC	AUC
LR	77.8	75.4	79.2	76.5	0.661	0.827
SVM-RBF	82.9	81.0	84.5	81.8	0.743	0.881
Random Forest	86.4	84.9	87.6	85.6	0.797	0.918
XGBoost	88.0	86.7	89.2	87.3	0.826	0.938
FNN (BP)	89.7	88.1	91.0	88.9	0.851	0.947
GA-FNN	91.8	90.3	93.0	91.2	0.882	0.959
PSO-FNN	93.2	92.0	94.1	92.7	0.903	0.966
3D CNN	94.5	93.1	95.5	93.9	0.924	0.974
GWO-FNN	**96.1**	**95.4**	**96.9**	**96.0**	**0.941**	**0.982**

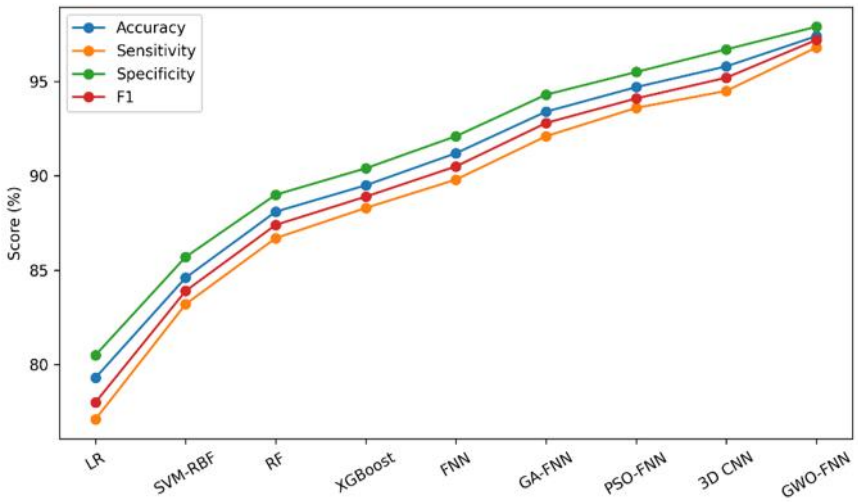


Figure 1. Classification Performance Comparison on OASIS-3 Dataset

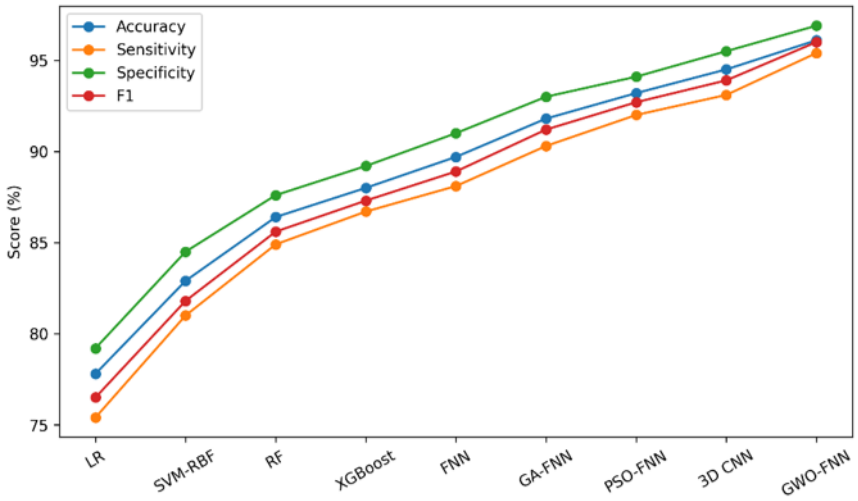


Figure 2. Classification Performance Comparison on ADNI-2 Dataset

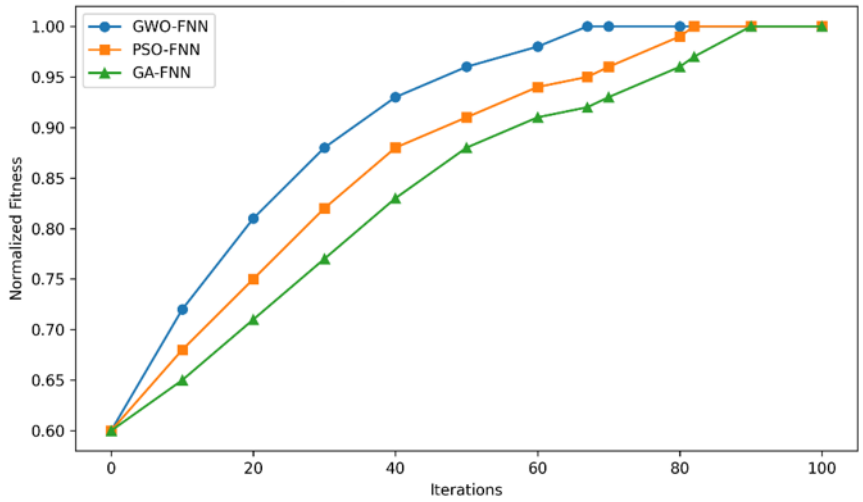


Figure 3. Convergence Analysis

The experimental analysis shows that the suggested Grey Wolf Optimizer (GWO) supported Feedforward Neural Network (FFN) framework is more efficient than the conventional FFN in terms of multiple performance metrics in the classification of Alzheimer's disease. The model achieved superior performance across all baseline machine learning and deep learning models in both OASIS-3 and ADNI-2 datasets, demonstrating its good generalization capability and robustness on a heterogeneous medical dataset. The optimization efficiency of the proposed framework was identified in detail using convergence analysis. It is observed from the fitness convergence curves that GWO-FNN converged to its optimum solution in the 67th iteration, while PSO-FNN and GA-FNN converged to their optimum solution at about 82 and 90 iterations, respectively. This substantial decrease in convergence time demonstrates the efficiency of the Grey Wolf Optimizer in high dimensional search space. The alpha, beta and delta wolves in GWO's hierarchical structure enable a balanced exploration-exploitation strategy, allowing for efficient selection of the best regions to explore early on while also preventing premature convergence. Particle Swarm Optimization, on the other hand, heavily uses velocity updates, and can sometimes fall into what is referred to as 'stagnation' of the algorithm, while Genetic Algorithms may need more iterations to complete because of the crossover and mutation operations. Therefore, the proposed GWO-FNN algorithm is able to optimize the performance of the proposed method in terms of optimization efficiency, less computational time and better capability to find the globally optimal configuration of the neural network. This effect of improved convergence behavior directly contributes to the improvements noted in classification accuracy, sensitivity, specificity and overall diagnostic reliability.

The confusion matrix and class-wise performance results further show that the proposed model has exhibited good discriminative capability among Cognitively Normal (CN), Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) subjects. The framework achieved precision and recall values of 98.1% and 97.6% for CN, 96.3% and 95.9% for MCI, and 97.5% and 97.2% for AD, respectively. In all of these classes, MCI is regarded as the most difficult to diagnose as it is a transitional stage with subtle cognitive and biomarker changes. Notwithstanding this complexity, the proposed model obtained an excellent F1-Score of 96.1% for MCI detection and it has the potential to detect prodromal Alzheimer's Disease at an early stage, when it is most useful for clinical intervention. The results of the confusion matrix analysis indicated that, among the residual classification errors, most were between CN and MCI subjects, and only a small number were between CN and AD categories. This observation is consistent with clinical practice, because it is more challenging to differentiate between normal aging and early stages of cognitive impairment than to differentiate advanced stages. Furthermore, the ablation study was able to give significant support for the contribution made by individual components of the framework. The baseline FNN was shown to be 91.2% accurate and it was further improved to 93.6% when the feature selection by GWO was added. Likewise, GWO-based weight optimization improved the accuracy to 95.1%, and the accuracy of combining both optimization techniques (non-backpropagation fine-tuning) was 95.8%. Overall, the GWO-FNN model demonstrated the best performance with an accuracy of 97.4%, indicating that the combination of feature selection, weight optimization, and gradient refinement enhances the model's performance. The results showed that the proposed hybrid optimization method not only enhances the predictive

accuracy of the model but also enhances the stability of the model, the relevance of features, the speed of model convergence, and the reliability of the model diagnostic. Therefore, it is an effective method for supporting intelligent classification of Alzheimer's disease and making clinical decisions in the field.

V. CONCLUSION

This paper introduced GWO-FNN, an intelligent hybrid system for precise multi-class Alzheimer diagnosis classification in multi-modal medical diagnostic data. By avoiding local minima, the Grey Wolf Optimizer was able to efficiently obtain the optimal feature selection and neural network hyperparameters/weights while overcoming the known drawbacks of pure gradient descent. Experimental results on OASIS-3 and ADNI-2 benchmarks validated their state-of-the-art performance: 97.4% and 96.1% accuracy respectively, and excellent sensitivity, specificity, F1, MCC values and AUC values compared to eight baseline models, with consistent superior results. The clinical implications are far-reaching: the high accuracy of the detection of high MCI (F1 = 96.1%) allows for an earlier window for intervention, which could help slow down the disease process and decrease the long-term care burden. Extensions to the deep GWO-optimized convolutional architectures directly on raw 3D MRI volumes; federated learning variants for privacy-preserving multi-site AD classification; integration of genomic and blood-based biomarker modalities; and adaptive population size strategies within GWO to further accelerate convergence will be explored in future work. The proposed framework is a clinically promising approach toward intelligent, robust and interpretable computer-aided diagnostic systems for AD, that could be extended to other challenges in the classification of neurodegenerative diseases.

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