






Article

MRI-Driven Alzheimer's Disease Diagnosis Using Deep Network Fusion and Optimal Selection of Feature

Muhammad Umair Ali ^{1,†} , Shaik Javeed Hussain ^{2,*,†} , Majdi Khalid ³ , Majed Farrash ³, Hassan Fareed M. Lahza ⁴  and Amad Zafar ^{1,*} 

¹ Department of Artificial Intelligence and Robotics, Sejong University, Seoul 05006, Republic of Korea; umair@sejong.ac.kr

² Department of Electrical and Electronics, Global College of Engineering and Technology, Muscat 112, Oman

³ Department of Computer Science and Artificial Intelligence, College of Computing, Umm Al-Qura University, Makkah 24382, Saudi Arabia; mknfiai@uqu.edu.sa (M.K.); mmfarrash@uqu.edu.sa (M.F.)

⁴ Department of Cybersecurity, College of Computing Umm Al-Qura University, Makkah 24382, Saudi Arabia; hflahza@uqu.edu.sa

* Correspondence: s.javeedhussain@gcet.edu.om (S.J.H.); amad@sejong.ac.kr (A.Z.)

† These authors contributed equally to this work.

Abstract: Alzheimer's disease (AD) is a degenerative neurological condition characterized by cognitive decline, memory loss, and reduced everyday function, which eventually causes dementia. Symptoms develop years after the disease begins, making early detection difficult. While AD remains incurable, timely detection and prompt treatment can substantially slow its progression. This study presented a framework for automated AD detection using brain MRIs. Firstly, the deep network information (i.e., features) were extracted using various deep-learning networks. The information extracted from the best deep networks (EfficientNet-b0 and MobileNet-v2) were merged using the canonical correlation approach (CCA). The CCA-based fused features resulted in an enhanced classification performance of 94.7% with a large feature vector size (i.e., 2532). To remove the redundant features from the CCA-based fused feature vector, the binary-enhanced WOA was utilized for optimal feature selection, which yielded an average accuracy of 98.12 ± 0.52 (mean \pm standard deviation) with only 953 features. The results were compared with other optimal feature selection techniques, showing that the binary-enhanced WOA results are statistically significant ($p < 0.01$). The ablation study was also performed to show the significance of each step of the proposed methodology. Furthermore, the comparison shows the superiority and high classification performance of the proposed automated AD detection approach, suggesting that the hybrid approach may help doctors with dementia detection and staging.

Keywords: Alzheimer disease; dementia; deep features; feature fusion; feature selection; canonical correlation analysis; optimization; machine learning



Citation: Ali, M.U.; Hussain, S.J.; Khalid, M.; Farrash, M.; Lahza, H.F.M.; Zafar, A. MRI-Driven Alzheimer's Disease Diagnosis Using Deep Network Fusion and Optimal Selection of Feature. *Bioengineering* **2024**, *11*, 1076. <https://doi.org/10.3390/bioengineering11111076>

Academic Editor: Andrea Cataldo

Received: 19 September 2024

Revised: 20 October 2024

Accepted: 26 October 2024

Published: 28 October 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative condition characterized by irreversible cognitive decline, memory loss, and a gradual deterioration of brain function, which eventually causes dementia [1]. AD primarily targets brain regions related to cognition, memory, and communication, ultimately leading to an inability to perform daily tasks independently. As the most common form of dementia, AD necessitates specialized medical care. The global burden of AD is substantial and projected to grow significantly, with a projected 152 million people affected by 2050. This presents immense economic, healthcare, and societal challenges [2]. Dementia is a rapidly growing global health crisis, affecting approximately one person worldwide every three seconds. AD constitutes the majority of dementia cases, representing around 60% of all diagnoses [3].

AD is linked to several stages of dementia: severe dementia, moderate dementia, mild dementia, and mild cognitive impairment (MCI). MCI often manifests as memory lapses associated with aging but may progress to dementia in some individuals. Mild dementia is marked by cognitive difficulties impacting daily life, including disorientation, memory loss, mood changes, and trouble with routine tasks. Moderate dementia presents more severe symptoms, requiring increased support for daily activities. Individuals may experience significant personality changes, sleep disturbances, and challenges with basic self-care. In the advanced stage of severe dementia, individuals exhibit profound cognitive decline, loss of communication abilities, and dependence on others for all aspects of care.

Currently, no effective treatments exist to cease or slow the progression of AD, and the underlying causes remain largely unknown. MCI represents a transitional phase between normal aging and AD, with individuals experiencing MCI at a higher risk of developing the disease [4]. The early detection of AD is crucial for developing preventive strategies and improving treatment and care approaches.

Diagnosing AD involves a comprehensive evaluation, including the patient's medical history, a physical examination, and a neurological assessment. Imaging techniques such as MRI, CT, and PET scans are essential for confirming the diagnosis [5]. MRI, in particular, offers detailed brain images, aiding in detecting structural changes associated with AD [6]. Developing advanced computer-aided systems to analyze MRI images could significantly improve the accuracy and efficiency of an AD diagnosis [7,8].

Machine-learning techniques, particularly deep learning, have shown promise in enhancing the accuracy of identifying different dementia subtypes through neuroimaging analysis [9]. Traditional machine-learning methods, such as boosting algorithms, random forests, and support vector machines, have been applied to MRI data for AD detection [10–12]. However, these approaches often rely on manually selected brain regions, which can be subjective and limited. The pre-selected regions probably do not have all the information needed to comprehend the intricacies of AD because definite MRI biomarkers for AD are still poorly understood. Manual selection is not only time-consuming and labor-intensive, but it also has the risk of subjective errors.

Deep learning, especially convolutional neural networks (CNNs), has emerged as a powerful tool for automatically extracting features from MRI images [13–15]. CNNs have demonstrated superior performance in classifying AD compared to conventional methods [16–18]. Many advantages contribute to its popularity, such as using spatial information from nearby pixels, taking image data directly, and effectively lowering model parameters through weight sharing, subsampling, etc. A CNN model trained with MRI slices retrieved features automatically; it is no longer necessary to manually choose features during the learning phase [19].

Various AD diagnostic CNN models have been reported in the literature [20]. In a study [21], an MRI-and-PET-image-based CNN model has been developed. This multimodality-based CNN achieved 82.4% accuracy for MCI patients later exposed to AD. For the non-demented class, it yielded a classification rate of 86.3%. Ahmed et al. [22] achieved accuracies of 90.05% and 85.55% for healthy and AD, respectively. A pre-trained network, such as VGG-16, was also trained for brain MRI slices for AD detection [23]. It yielded a high classification rate of 95.73% for various stages. Similarly, in another study [24], the authors fused the CNN and ensemble-learning models for AD identification. In a recent study, the authors developed a DEMNET to identify and detect several phases of dementia [25]. The DEMNET demonstrated a high classification rate of 95.23% for various stages of dementia. In another study [26], a pre-trained model, such as AlexNet, was utilized to extract the deep features, and various linear machine-learning classifiers were used to identify various stages of dementia. The strategy showed some promising results compared to CNN and handcrafted models. While various CNN architectures have achieved promising results, challenges remain regarding the model complexity, training time, and high classification performance.

In this study, a hybrid deep feature fusion and optimal feature selection approach is presented for detecting and staging dementia using brain MRIs. Deep features were extracted using various pre-trained deep-learning models. The extracted features were merged to form a new feature vector using a canonical correlation analysis (CCA) feature fusion approach to enhance the classification performance. Furthermore, the wrapper-based approach, a binary-enhanced whale optimization algorithm (WOA), is utilized for optimal feature selection and the removal of redundant features. An online brain MRI dataset is used to validate the proposed approach. A comparison of the proposed approach with various wrapper-based approaches was also conducted. The results are also compared with other SOTA approaches.

2. Materials and Methods

2.1. Proposed AD Detection and Staging Framework

AD is a degenerative brain condition characterized by progressive memory loss and cognitive decline. As the most prevalent form of dementia, it currently lacks a cure. MRI imaging plays a crucial role in diagnosis by visualizing structural brain abnormalities linked to the disease. Therefore, this study presented an automatic detection and staging machine-learning framework for dementia diagnosis. After acquiring the MRIs, the deep features were extracted using various pre-trained deep-learning models. In the next step, the extracted deep features with a classification accuracy above 91% were merged using a CCA feature fusion approach. The wrapper-based optimal feature selection method further enhances the classification rate. The flowchart of the proposed dementia detection and staging approach is shown in Figure 1.

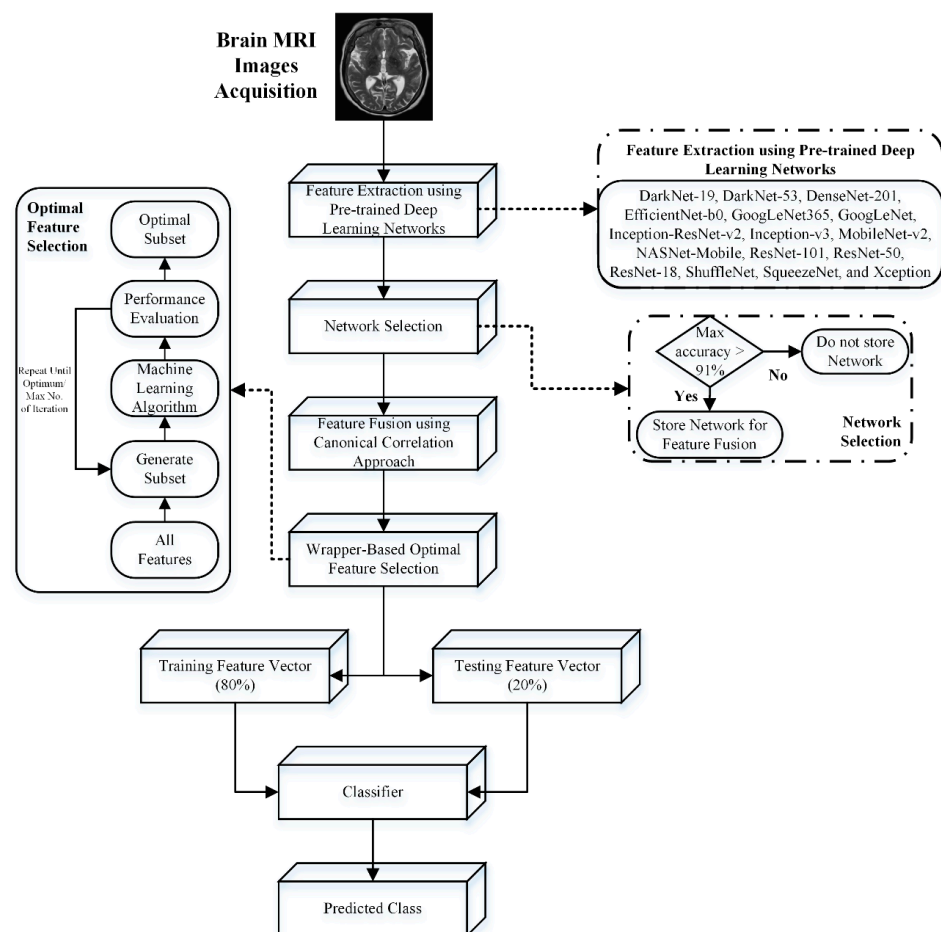
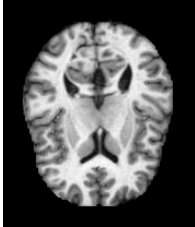
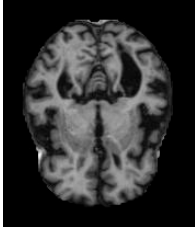
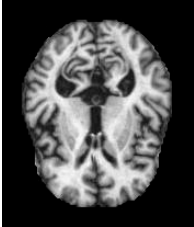
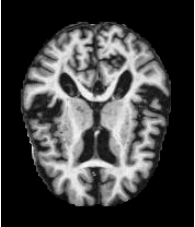


Figure 1. AD detection and staging using deep feature fusion and optimal feature selection approach.

2.2. Datasets

In this study, an online dataset (Alzheimer’s Dataset (4 classes of Images)) is used to validate the AD detection and staging approach. The dataset is publicly available (<https://www.kaggle.com/datasets/tourist55/alzheimers-dataset-4-class-of-images>, accessed on 13 November 2023). The details of this dataset are listed in Table 1.

Table 1. Details about online AD dataset.

Parameters	Classes			
	Non-Demented (ND)	Mild Demented (MID)	Moderate Demented (MOD)	Very Mild Demented (VMD)
Brain MRI images				
No. of Samples	2560	717	52	1792

2.3. Deep Feature Extraction

2.3.1. Convolutional Neural Networks (CNNs)

CNN, or ConvNET, handles data in a grid-like layout and is a subclass of artificial neural networks. CNN excels at identifying various features in an image, such as corners and edges, and effectively eliminates the need for specific handicraft feature extraction approaches by including these in their architecture. Various layers, such as input convolutional, ReLU, and pooling, are used for the image’s feature/information extraction. In the end, a fully connected layer retrieved features for image classification [27,28]. The other fundamental elements of a CNN are weights, neurons, bias factors, and activation functions.

2.3.2. Deep Feature Extraction Using CNNs

The CNN’s performance improved by using a larger training dataset. In this regard, transfer learning allows knowledge to be transferred from one domain to another. In this process, a model is trained for one issue and re-used to transfer the knowledge to another related problem. Assume a domain with two components [29,30]:

$$d^m = A + prob(a) \quad (1)$$

where A and $prob(a)$ denote the feature space and marginal probability. Assume that a task has the following elements:

$$t^r = B + \omega \quad (2)$$

where B and ω are the space label and the objective function. d_s^m and t_s^r denote the source domain and task, whereas d_t^m and t_t^r are the target domain and task. The transfer learning used source information to learn the conditional probability for the target domain. The use of several pre-trained models has been reported in the literature for various medical-imaging applications [31,32]. Figure 2 shows an example of the basic transfer-learning concept using ImageNet.

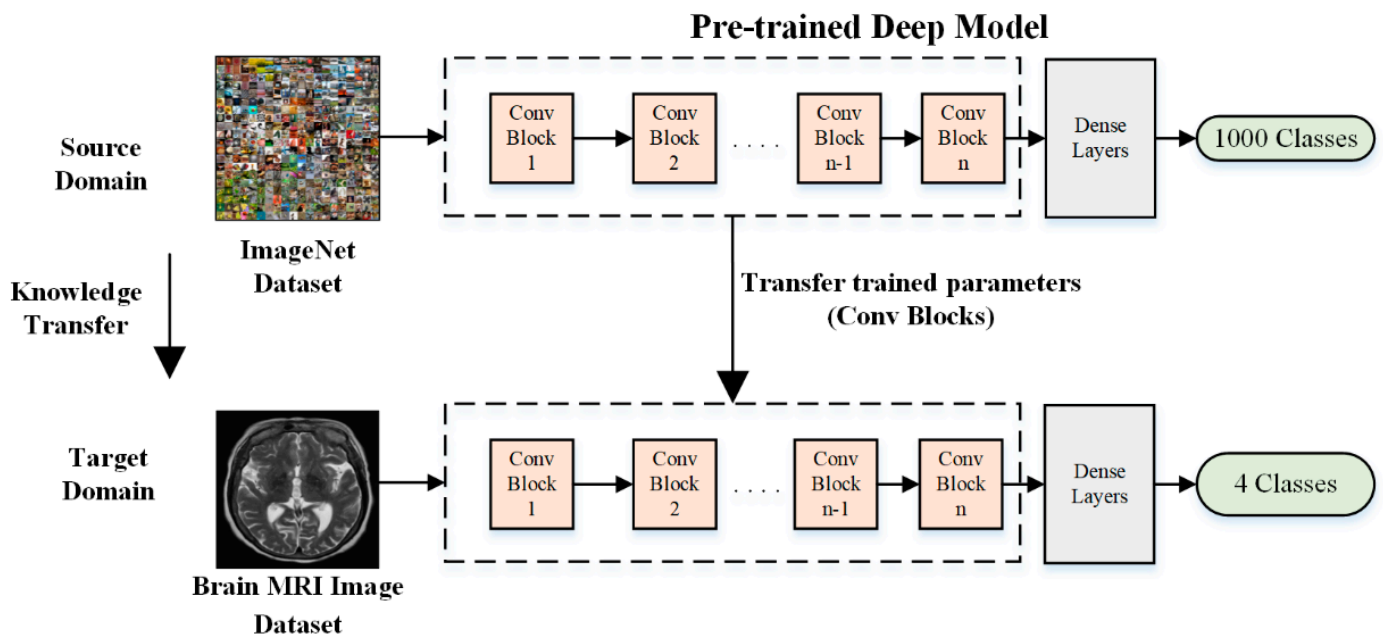


Figure 2. Deep feature extraction using modified AlexNet using transfer learning.

In this study, the frozen weights of various pre-trained networks are fine-tuned using AD MRI images, and features are extracted from the dense layer. Sixteen pre-trained models, such as Xception, SqueezeNet, ShuffleNet, ResNet-18, ResNet-50, ResNet-101, NASNet-Mobile, MobileNet-v2, Inception-v3, Inception-ResNet-v2, GoogLeNet, GoogLeNet365, EfficientNet-b0, DenseNet-201, DarkNet-53, and DarkNet-19, were used.

2.3.3. Canonical Correlation Analysis (CCA) for Feature Fusion

This work uses the CCA for deep feature fusion of MRI. The objective is to maximize the correlation between feature subsets. Assume two feature sets ($f_x \in R_{p_1 \times b}$ and $f_y \in R_{p_2 \times b}$) with n feature sets, with p_1 and p_2 as dimensions of the features, which can be defined as follows:

$$\left. \begin{aligned} f_x &= [f_x^1, f_x^1, \dots, f_x^n] \\ f_y &= [f_y^1, f_y^1, \dots, f_y^n] \end{aligned} \right\} \quad (3)$$

The function may be defined as follows:

$$\sigma = \max(W_x, W_y) \left(\frac{W_x^T C_{xy} W_y}{(W_x^T C_{xx} W_x)(W_y^T C_{yy} W_y)} \right) \quad (4)$$

The within-covariance matrices may be defined as $C_{xx} \in R^{p_1 \times p_1}$ and $C_{xy} \in R^{p_1 \times p_2}$. The final correlation function can be expressed as follows:

$$\left. \begin{aligned} C_{xx}^{-1} C_{xy} C_{yy}^{-1} C_{yx} W_x &= \sigma W_x \\ C_{yy}^{-1} C_{yx} C_{xx}^{-1} C_{xy} W_y &= \sigma W_y \end{aligned} \right\} \quad (5)$$

The final transformed vector can be obtained using Equation (6):

$$\tilde{Z} = W_x^T \sigma_{x,i} + W_y^T \sigma_{y,i} = W_x^T W_y^T \begin{bmatrix} \sigma_{x,i} \\ \sigma_{y,i} \end{bmatrix} \quad (6)$$

CCA enables the integration of multiple characteristics/networks into a unified representation, capturing complementary information and maximizing the correlation between projected features. Furthermore, it reduces dimensionality while preserving the relevant information. Overall, it enhanced the representation of the fused features.

2.3.4. Enhanced Whale Optimization Algorithm (WOA)

The WOA, developed by Mirjalili and Lewis [33], is a population-based meta-heuristic algorithm that has been effectively used to address global optimization problems in various areas. It uses humpback whale's natural hunting behavior to solve global optimization challenges. They create a bubble-net in a spiral pattern to capture their prey and swim up to the water's surface. The WOA utilizes three phases, (i) encircling, (ii) searching, and (iii) spiral bubble-net attacking, to capture the prey in humpback whale's natural hunting behavior.

Let $Y_j(k) = (y_{j,1}(k), y_{j,2}(k), \dots, y_{j,D}(k))$ represent the position of j th whale at iteration k , where $j = 1, 2, \dots, N$ is the population of whales in a D -dimension search space. $Y(1)$ is randomly initialized for the first and $k > 1$ iterations and $Y(k)$ is updated using three phases: (i) encircling, (ii) searching, and (iii) spiral bubble-net attacking. During optimization, WOA takes into account the probability rate (σ) for each $Y_j(k)$ for switching among the three phases, while it also considers coefficient vector $W_j(k)$ for each whale to select encircling and searching for prey, as Equation (7) shows:

$$Y_j(k+1) = \begin{cases} \text{Encircling prey } (\sigma_j(k) < 0.5) \text{ and } (|W_j(k)| < 1) \\ \text{Search for prey } (\sigma_j(k) < 0.5) \text{ and } (|W_j(k)| \geq 1), 0 < \sigma_j(k) < 1 \\ \text{Spiral bubble-net attacking } (\sigma_j(k) \geq 0.5) \end{cases} \quad (7)$$

$$W_j(k) = 2 \times w_j(k) \times rand - w_j(k) \quad (8)$$

where $w_j(k)$ is the linearly decreased variable computed using Equation (9):

$$w_j(k) = 2 - k \times \left(\frac{2}{MaxIt} \right) \quad (9)$$

Equation (10) gives the encircling prey phase:

$$\left. \begin{aligned} Y_j(k+1) &= Y_{best}(k) - W_i(k) \times S(k) \\ S(k) &= |C_j(k) \times Y_{best}(k) - Y_j(k)| \\ U_j(k) &= 2 \times rand \end{aligned} \right\} \quad (10)$$

where $S(k)$ denotes the distance between the current and the optimal whale position and $C_j(k)$ is the coefficient vector at iteration k . The search for prey phase is given in Equation (11):

$$\left. \begin{aligned} Y_j(k+1) &= Y_{rnd}(k) - W_j(k) \times S(k) \\ S(k) &= |C_j(k) \times Y_{rnd}(k) - Y_j(k)| \end{aligned} \right\} \quad (11)$$

Finally, the third phase (i.e., the spiral bubble-net attacking) is given as Equation (12), where c is the logarithmic spiral shape:

$$\left. \begin{aligned} Y_j(k+1) &= S'(k) \times \exp^{cl} \times \cos(2\pi l) + Y_{best}(k) \\ S'(k) &= |Y_{best}(k) - Y_j(k)| \end{aligned} \right\}, -1 \leq l \leq 1 \quad (12)$$

Despite being a widely used optimization technique, the WOA still suffers from early convergence, poor population diversity causing insufficient solutions, and a mismatch of local and global search strategies further addressed in its enhanced WOA and binary E-WOA variants for feature selection.

To further enhance the performance of conventional WOA, Nadimi-Shahraki and coworkers introduced a pooling mechanism and three efficient search techniques (i.e., migrating, preferential selection, and enriched surrounding prey). Furthermore, advanced search techniques were also incorporated.

In pooling mechanism, at the end of each iteration, the pool matrix $(P(1), P(2), \dots, P(m))$ having members $P_j = P_j(1), P_j(2), \dots, P_i(m)$ are computed using Equation (13):

$$P_j(k) = B_j(k) \times Y_{brnd}(k) \times \bar{B}_j(k) + Y_{worst}(k) \quad (13)$$

where $Y_{brnd}(k)$ are randomly computed to generate random positions around $Y_{best}(k)$. $Y_{worst}(k)$ represents the worst whale at the current iteration, whereas $B_j(k)$ and $\bar{B}_j(k)$ are the random binary vectors and their reverse binary vector. In order to foster population diversity, the pooling mechanism uses a crossover operator to combine the worst solution with the best one. When the pool's size is reached, a new solution is replaced by an existing pool member.

The migrating search method divides a group of whales at random using Equation (14) to allow them to explore previously unexplored places and increase their exploration. Furthermore, this separation is projected to improve population diversity, lowering the risk of becoming locked in local optima:

$$\left. \begin{aligned} Y_j(k+1) &= Y_{rnd}(k) - Y_{brnd}(k) \\ Y_{rnd}(k) &= rand \times (\delta_{\max} - \delta_{\min}) + \delta_{\min} \\ Y_{brnd}(k) &= rand(\delta_{best_max} - \delta_{best_min}) + \delta_{best_min} \end{aligned} \right\} \quad (14)$$

where δ_{best_max} and δ_{best_min} are the upper and lower bounds of $Y_{best}(k)$.

Finally, the preferential selection strategy computed using Equation (15) further enhances the search-for-prey approach:

$$Y_j(k+1) = Y_j(k) + W_j(k) \times (U_k(k) \times P_{rnd1}(t) - P_{rnd2}(t)) \quad (15)$$

where $P_{rnd1}(t)$ and $P_{rnd2}(t)$ are randomly selected from pool matrix.

The encircling prey method is further enhanced using the following equation:

$$\left. \begin{aligned} Y_j(k+1) &= Y_{best}(k) - W_j(k) \times S'(k) \\ S'(k) &= |C_j(k) \times Y_{best}(k) - P_{rnd3}(k)| \end{aligned} \right\} \quad (16)$$

where $P_{rnd3}(t)$ can be randomly selected from the pool matrix.

Furthermore, for the effective selection of features, Nadimi-Shahraki et al. [34] also proposed the binary version of the enhanced variant of WOA (Algorithm 1). The binary version is especially useful for determining the most important or optimal features associated with specific medical disorders. These binary optimization feature selection methods are useful in medical applications because they improve diagnostic accuracy and efficiency by focusing on the most important characteristics or variables.

To evaluate the selected feature, the k-nearest neighbor (kNN)-based fitness function is given below:

$$F(X) = 0.99 \left(1 - \frac{\text{Images which are correctly classified}}{\text{Total images}} \right) + (0.01) \left(\frac{f_{SL}}{f_{FL}} \right) \quad (17)$$

where f_{FL} and f_{SL} are the total number of features and the selected number of features [35]. Finally, the results of the classifier were analyzed using the confusion matrix, which included the true positive rate (TPR), false negative rate (FNR), positive predictive value (PPV), and false discovery rate (FDR).

Algorithm 1: Pseudo-code of binary-enhanced WOA [34].

```

1. Generate a random population of  $N$  whales using

$$b_{j,i}^k = \begin{cases} 1 & \text{rand} \geq 0.5 \\ 0 & \text{rand} < 0.5 \end{cases}, j = 1, 2, \dots, N \text{ and } i = 1, 2, \dots, D$$

2. Initialize  $K$  (maximum iterations)
3. Evaluate the solution of the population using the fitness function
4. Determine  $Y_{best}$ 
5. Set  $k = 1$ 
6. while ( $k < K$ ) do
7. Randomly select a portion  $P$  of the  $N$  population
8. Determine  $Y_{j \in P}^{k+1}$  (mitigating search strategy)
9. if  $k$  is not in  $P$  then
10. Compute  $\sigma_j^k$  and  $W_j^k$ 
11. if ( $\sigma_j^k < 0.5$ ) then
12. if  $W_j^k < 0.5$  then
13. Compute  $Y_j^{k+1}$  using (10) for enriched encircling prey strategy
14. else if  $A_i^t > 0.5$  then
15. Compute  $Y_j^{k+1}$  using (9) for a preferential selection strategy
16. end if
17. else if ( $\sigma_j^k > 0.5$ ) then
18. Compute  $Y_j^{k+1}$  using (6) for the spiral bubble-net attacking strategy
19. end if
20. Transform continuous search space to binary using  $b_{i,j}^t = \begin{cases} 1 & U(y_{ij}^k) \geq \text{rand}(0, 1) \\ 0 & U(y_{ij}^k) < \text{rand}(0, 1) \end{cases}$ 
21. Evaluate the fitness value for each solution
22. Update  $Y_j^{k+1}$  using the position with lower fitness value from  $\{Y_j^k, Y_j^{k+1}\}$ 
23. end if
24. Update  $Y_{best}$ 
25.  $k = k + 1$ 
26. end while

```

3. Results

In this study, all the simulation and analysis are performed on MATLAB 2023a running on a 64-bit Windows 11 personal computer with the following specifications: 12th Generation, Core i7, 1 TB SSD, NVIDIA GeForce RTX 3050, and 32 GB RAM. The dataset was randomly divided into a 80:20 ratio for model training and testing. Augmentation was also carried out to balance the dataset at 1000 samples per class.

To check the performance of various commonly used pre-trained models, such as DenseNet-201, EfficientNet-b0, GoogleNet, Inception-v3, and ResNet50, they were trained to classify the brain MRIs into subclasses. The findings are listed in Table 2.

Table 2. Results of various pre-trained models for Alzheimer’s Dataset.

CNNs	Training Accuracy (%)	Training Loss	Validation Accuracy (%)	Validation Loss	Training Time
DenseNet-201	100	1.4×10^{-04}	93.93	0.2152	1062 min 20 s
EfficientNet-b0	100	2.8×10^{-03}	90.32	0.3030	329 min 45 s
GoogleNet	100	3.6×10^{-04}	92.57	0.3584	40 min 30 s
Inception-v3	100	4.3×10^{-04}	84.84	0.5598	435 min 47 s
ResNet50	100	1.9×10^{-04}	88.95	0.3938	299 min 40 s
MobileNet-v2	100	3.2×10^{-04}	91.02	0.3818	195 min 55 s

The results presented in Table 2 show that DenseNet-201 has the best classification accuracy of 93.93% for AD detection, but the model took almost 17 h to train. In contrast, GoogleNet shows a reasonable classification performance (92.57%) with minimal training time (almost 41 min). To reduce the training time, the deep features were extracted for various pre-trained models, and a conventional/linear classifier was used for classification. The results are presented in Figure 3, which shows that the accuracy achieved using the deep features is similar to that of pre-trained networks shown in Table 2 but with a reduced computational time.

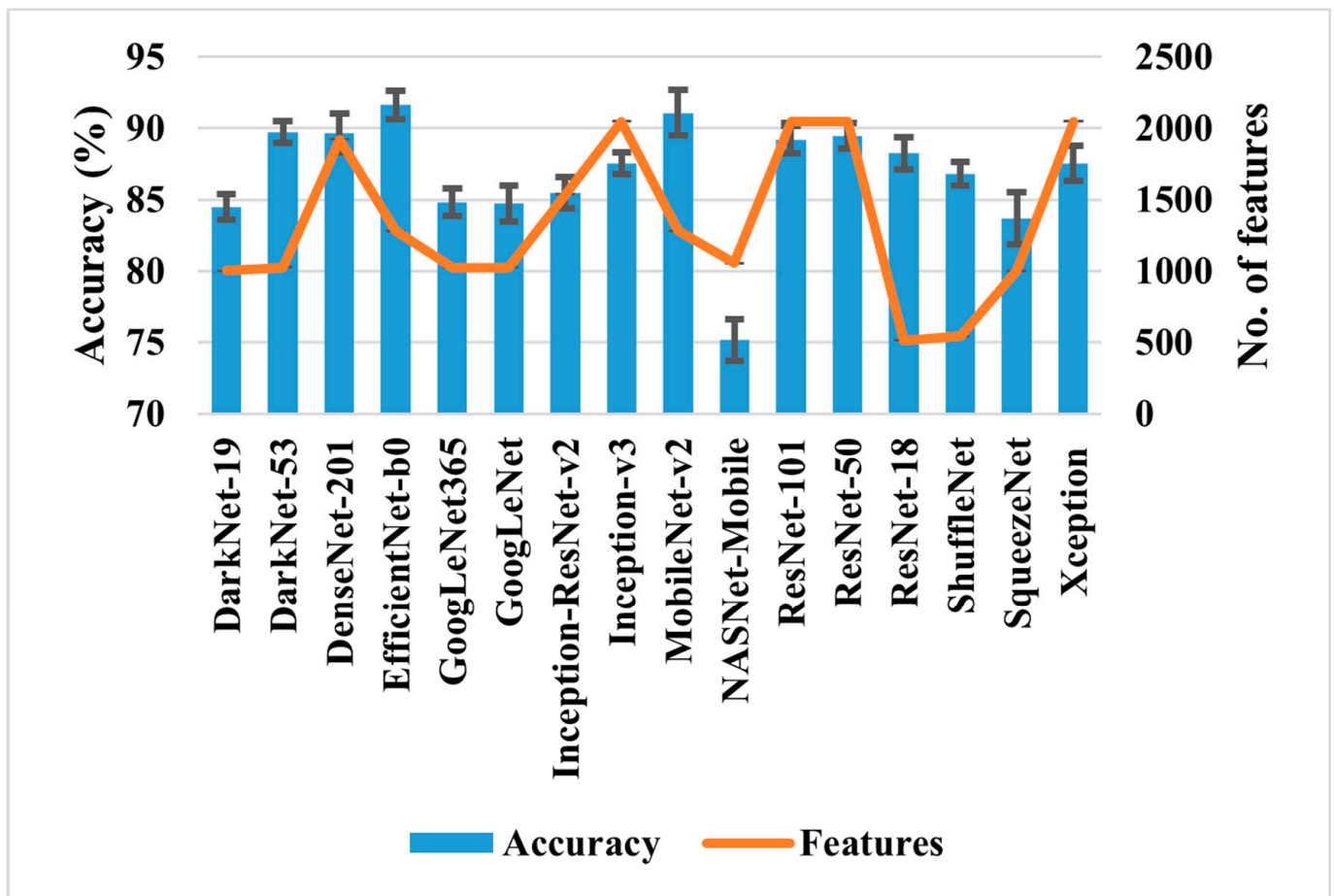
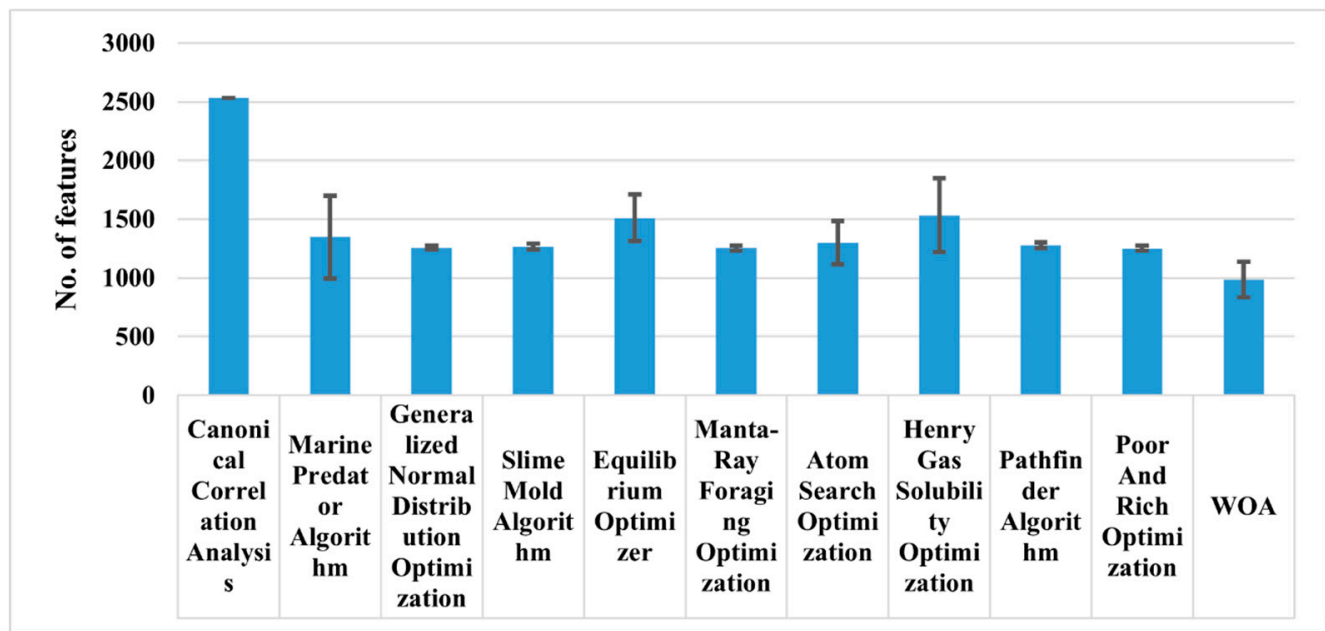


Figure 3. Classification performance comparison of various deep features for AD detection.

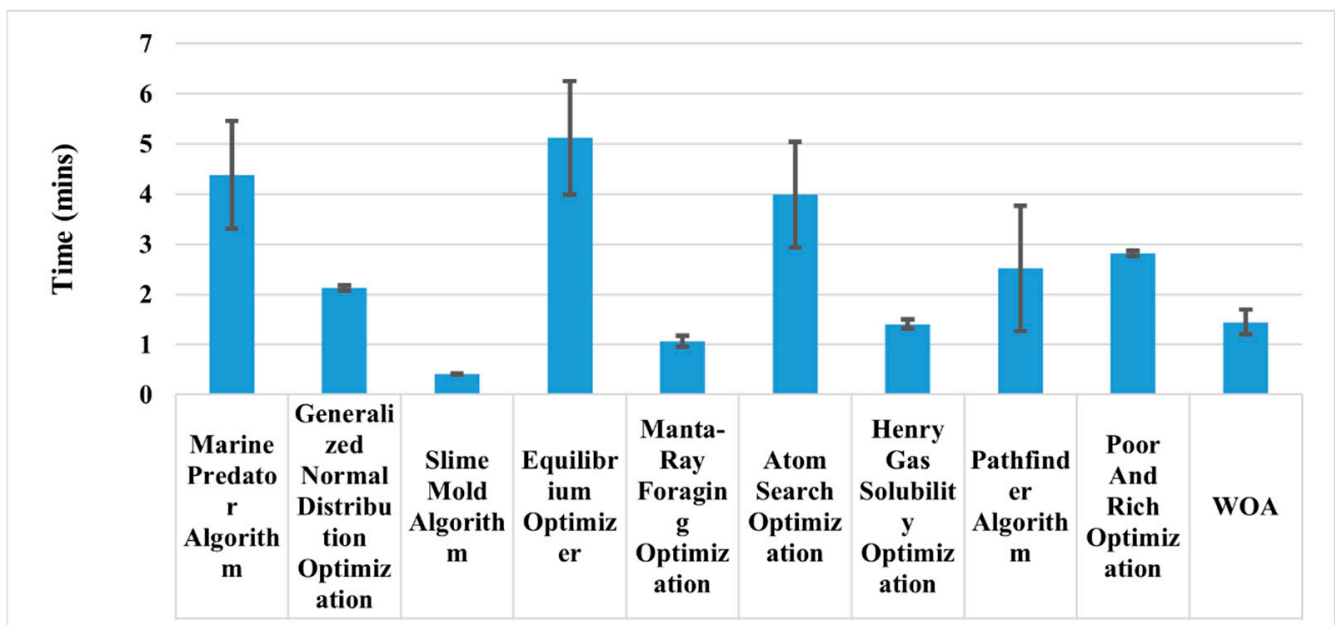
After analyzing the results shown in Figure 3, it can be concluded that the models trained on EfficientNet-b0 and MobileNet-v2 deep features (1280 for each) show the highest classification accuracy of $91.64 \pm 0.99\%$ and $91.08 \pm 1.62\%$ for ten runs. To enhance classification, the CCA feature fusion approach was applied to merge the deep features of both models. After that, various feature selection approaches were used to reduce the feature size of the CCA-based fused feature vector, and the results are presented in Table 3 and Figure 4.

Table 3. Classification accuracy of approaches to subclassify the brain MRI images for AD detection (10 runs).

No. of Runs	CCA-Based Fused Features	CCA + Feature Selection Approaches									
		Marine Predator Algorithm	Generalized Normal Distribution Optimization	Slime Mold Algorithm	Equilibrium Optimizer	Manta-Ray Foraging Optimization	Atom Search Optimization	Henry Gas Solubility Optimization	Pathfinder Algorithm	Poor And Rich Optimization	WOA
1	95.21	97.17	97.17	96.00	97.17	97.17	96.09	95.80	96.68	97.46	98.05
2	95.12	97.17	96.88	95.61	97.36	96.68	96.78	95.70	96.00	96.88	97.95
3	95.51	96.88	96.39	94.92	96.09	96.58	96.29	95.41	96.09	96.58	96.97
4	93.75	95.70	95.61	93.95	95.21	95.90	94.92	94.53	94.92	95.70	96.68
5	94.04	96.29	96.00	94.63	95.90	96.29	95.02	94.63	95.12	95.70	96.68
6	95.90	97.46	96.88	96.19	96.97	97.36	96.97	96.39	97.07	97.36	98.24
7	94.14	96.39	95.90	94.63	96.29	95.80	95.61	95.02	95.41	95.90	97.17
8	94.43	96.78	96.00	94.82	96.19	96.29	96.09	95.41	96.00	96.29	96.97
9	93.65	96.58	95.41	94.43	95.70	95.90	94.82	94.73	95.12	95.70	96.78
10	95.21	96.78	96.78	95.02	96.29	96.88	96.00	95.41	96.19	96.39	97.27
mean ± std	94.7 ± 0.79	96.72 ± 0.51	96.3 ± 0.6	95.02 ± 0.71	96.32 ± 0.67	96.48 ± 0.54	95.86 ± 0.75	95.3 ± 0.58	95.86 ± 0.71	96.4 ± 0.67	97.28 ± 0.59



(a)



(b)

Figure 4. (a) Number of features used to subclassify brain MRI images; (b) processing time taken by each approach.

Compared to all, the WOA has shown the highest classification performance of $97.28 \pm 0.59\%$ with an average of 985 features. It also took less than one and a half minutes to find the optimal feature and train the model, as shown in Figure 4b. Therefore, the binary-enhanced variant of WOA is applied to increase the classification performance further, and the results are presented in Figure 5. Finally, the results of the ablation study are presented in Figure 6.

True Class	MID	198	1	1		99.0%	1.0%
	MOD		200			100.0%	
	ND		1	198	1	99.0%	1.0%
	VMD	3	2	5	190	95.0%	5.0%

98.5%	98.0%	97.1%	99.5%
1.5%	2.0%	2.9%	0.5%
MID	MOD	ND	VMD
Predicted Class			

Figure 5. Result for dementia identification and staging using a hybrid deep feature fusion and optimal feature selection approach.

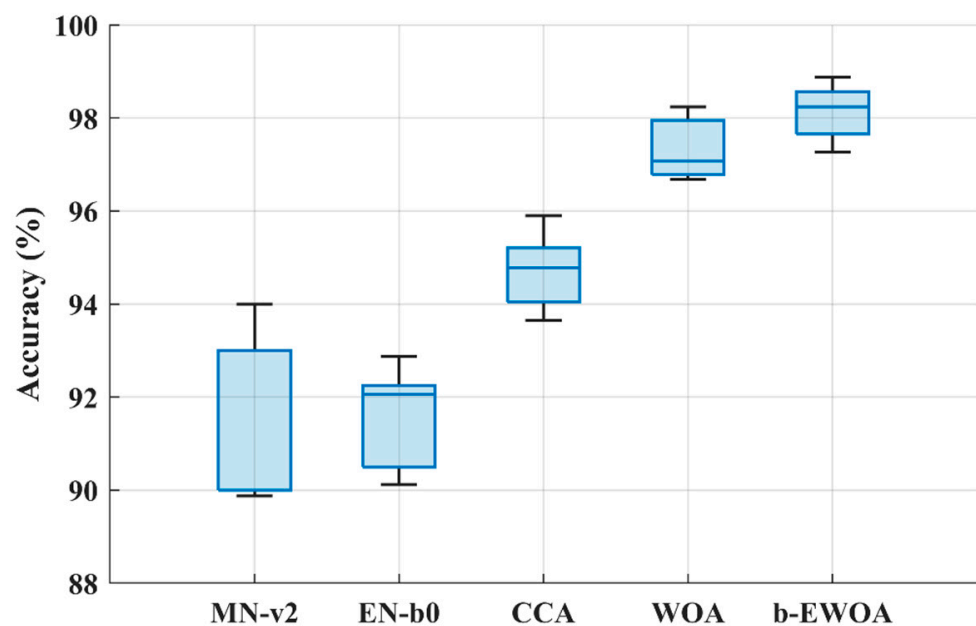


Figure 6. Ablation study results for AD detection (for ten runs). MN-v2, MobileNet-v2; EN-b0, EfficientNet-b0; CCA, canonical correlation analysis; WOA, whale optimization algorithm; b-EWOA, binary-enhanced whale optimization algorithm.

4. Discussion

Diagnosing AD involves a multifaceted approach. A detailed examination of neuroimaging data, particularly brain MRIs, plays a vital role in understanding the disease progression and determining appropriate treatment strategies. However, distinguishing between healthy and diseased brain tissue requires specialized knowledge and expertise. The manual analysis process can be time-consuming, potentially hindering prompt diagnosis and care. Therefore, automated AD detection techniques are urgently needed to streamline

diagnosis, improve accuracy, and enhance patient care. This research investigates a hybrid framework combining deep features, canonical correlation analysis, and optimal feature selection to improve the accuracy of automated AD detection using brain MRIs. This study aims to contribute to accurate early AD detection by computer-aided systems.

Initially, sixteen pre-trained deep-learning models ranging from simple to complex were selected for deep feature extraction. In our study, the accuracy-driven selection provides a straightforward and effective way to identify pre-trained networks' suitable deep features. EfficientNet-b0's and MobileNet-v2's deep features were chosen (Figure 3), and feature fusion was carried out using CCA. CCA reduces dimensionality while preserving the relevant information. Overall, it enhanced the representation of the fused features. It is evident from Table 3 that the classification accuracy of subclassifying the dementia class is increased by almost 3% compared to simple single-model deep features. However, it also increases the feature vector size to 2532, as shown in Figure 4a. Therefore, various wrapper-based methods were applied to further reduce the feature vector size and enhance the classification performance. All the approaches performed better with small feature vector sizes than the fused feature vectors (see Table 3 and Figure 4a). Compared to all, the WOA has shown the highest classification performance with the least features. Therefore, the binary-enhanced WOA was further implemented, increasing the classification performance to 98.25% and reducing the misclassification rate compared to the conventional WOA. It also reduces the feature vector size to 953 features with only an 87 s average processing time. The binary-enhanced WOA demonstrates superior feature detection and selection capabilities owing to its effective search methodology. Conventional WOA relies solely on objective functions, which may overlook complexities in the AD dataset, potentially selecting suboptimal features. This limitation can compromise classification accuracy. In contrast, the binary-enhanced WOA employs a multifaceted feature selection approach, combining objective functions with three advanced search techniques. This hybrid strategy enables an exhaustive exploration of the feature space, uncovering a diverse array of optimal features. As discussed in Section 2.3.4, this enhanced search capability allows the binary-enhanced WOA to outperform the conventional WOA, yielding improved classification results.

The ablation study was also performed to see the effect of each phase of the proposed methodology (Figure 6). The *t*-test was performed to check the statistical significance of each step, and it was observed that each step of the proposed approach statistically enhanced the classification accuracy with $p < 0.01$. This shows that the addition of each step is statistically significant, and the results are reliable. Table 4 compares the outcomes of the presented hybrid approach with other SOTA methods.

Table 4. Performance comparison of various SOTA approaches with a proposed hybrid approach.

Study	Alzheimer's Dataset
Shukla et al. [36]	94
Mohammed et al. [37]	94.8
Murugan et al. [25]	95.23
Acharya et al. [38]	95.70
El-Latif et al. [39]	95.93
Loddo et al. [40]	97.71
Proposed hybrid approach	98.25 (maximum) 98.12 ± 0.52 (mean ± standard deviation)

Table 4 demonstrates that the presented hybrid approach has the best classification performance compared to other SOTA approaches. These results emphasize the effectiveness of the presented hybridized approach in accurately and efficiently handling dementia detection and staging, highlighting its potential as a strong solution for AD detection.

This study's findings are based on a single dataset, and future work will focus on assessing the methodology's broader applicability across varied datasets. Furthermore, this study focuses exclusively on MRI data, whereas future investigations will explore the potential of multimodal data integration to enhance AD detection. Finally, this manuscript considered a simple accuracy-based network selection strategy. Future research should consider incorporating diverse evaluation metrics and dynamic strategies to further improve the network selection process and support real-time/online implementations.

5. Conclusions

AD is a widespread and debilitating neurological condition. It significantly diminishes the quality of life for those affected, impacting not only the patients themselves but also their families and society at large. A timely diagnosis is crucial for effectively managing AD and minimizing its socioeconomic impact. This study presented an automated dementia detection and staging approach using brain MRIs. First, various pre-trained networks were utilized to compute the deep features. The models trained with EfficientNet-b0 and MobileNet-v2 deep features (1280 for each) show accuracies of 91.64% and 91.08%, respectively. After that, canonical correlation analysis was performed for feature concatenation. An accuracy of 94.7% was obtained with 2532 features. Furthermore, the binary-enhanced WOA was utilized for the optimal selection of features, resulting in a 98.25% classification rate with optimal features (i.e., 953). The results obtained were compared with other feature selection techniques, showing that the binary-enhanced WOA results are statistically significant ($p < 0.01$). These results demonstrate the superior performance of the proposed hybrid approach in dementia detection and staging, showcasing its potential as a reliable tool for Alzheimer's disease detection.

Author Contributions: Conceptualization, M.U.A. and S.J.H.; formal analysis, M.F.; methodology, M.U.A. and S.J.H.; project administration, A.Z.; software, H.F.M.L.; supervision, A.Z.; validation, M.K.; visualization, A.Z.; writing—original draft, M.U.A. and S.J.H.; writing—review and editing, M.K., M.F., H.F.M.L. and A.Z. All authors have read and agreed to the published version of the manuscript.

Funding: We acknowledge the Global college of Engineering and Technology, Muscat for funding this research under an internal funding grant.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The original data presented in the study are openly available in Kaggle at <https://www.kaggle.com/datasets/tourist55/alzheimers-dataset-4-class-of-images> (accessed on 13 November 2023).

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Ulep, M.G.; Saraon, S.K.; McLea, S. Alzheimer disease. *J. Nurse Pract.* **2018**, *14*, 129–135. [CrossRef]
2. Salvatore, C.; Cerasa, A.; Battista, P.; Gilardi, M.C.; Quattrone, A.; Castiglioni, I. Magnetic resonance imaging biomarkers for the early diagnosis of Alzheimer's disease: A machine learning approach. *Front. Neurosci.* **2015**, *9*, 307. [CrossRef]
3. Patterson, C. World Alzheimer Report 2018. 2018. Available online: <https://www.alzint.org/resource/world-alzheimer-report-2018/> (accessed on 4 February 2024).
4. Liu, S.; Liu, S.; Cai, W.; Pujol, S.; Kikinis, R.; Feng, D. Early diagnosis of Alzheimer's disease with deep learning. In Proceedings of the 2014 IEEE 11th International Symposium on Biomedical Imaging (ISBI), Beijing, China, 29 April–2 May 2014; pp. 1015–1018.
5. Sabbagh, M.N.; Lue, L.-F.; Fayard, D.; Shi, J. Increasing Precision of Clinical Diagnosis of Alzheimer's Disease Using a Combined Algorithm Incorporating Clinical and Novel Biomarker Data. *Neurol. Ther.* **2017**, *6*, 83–95. [CrossRef] [PubMed]
6. Moser, E.; Stadlbauer, A.; Windischberger, C.; Quick, H.H.; Ladd, M.E. Magnetic resonance imaging methodology. *Eur. J. Nucl. Med. Mol. Imaging* **2009**, *36*, 30–41. [CrossRef] [PubMed]
7. Noor, M.B.T.; Zenia, N.Z.; Kaiser, M.S.; Mamun, S.A.; Mahmud, M. Application of deep learning in detecting neurological disorders from magnetic resonance images: A survey on the detection of Alzheimer's disease, Parkinson's disease and schizophrenia. *Brain Inform.* **2020**, *7*, 11. [CrossRef] [PubMed]

8. Baratti, C.; Barkhof, F.; Hoogenraad, F.; Valk, J. Partially saturated fluid attenuated inversion recovery (FLAIR) sequences in multiple sclerosis: Comparison with fully relaxed FLAIR and conventional spin-echo. *Magn. Reson. Imaging* **1995**, *13*, 513–521. [\[CrossRef\]](#)
9. Mateos-Pérez, J.M.; Dadar, M.; Lacalle-Aurioles, M.; Iturria-Medina, Y.; Zeighami, Y.; Evans, A.C. Structural neuroimaging as clinical predictor: A review of machine learning applications. *NeuroImage Clin.* **2018**, *20*, 506–522. [\[CrossRef\]](#)
10. Rabeh, A.B.; Benzarti, F.; Amiri, H. Diagnosis of Alzheimer Diseases in Early Step Using SVM (Support Vector Machine). In Proceedings of the 2016 13th International Conference on Computer Graphics, Imaging and Visualization (CGiV), Beni Mellal, Morocco, 29 March–1 April 2016; pp. 364–367.
11. Tripoliti, E.E.; Fotiadis, D.I.; Argyropoulou, M. A supervised method to assist the diagnosis and monitor progression of Alzheimer’s disease using data from an fMRI experiment. *Artif. Intell. Med.* **2011**, *53*, 35–45. [\[CrossRef\]](#)
12. Hinrichs, C.; Singh, V.; Mukherjee, L.; Xu, G.; Chung, M.K.; Johnson, S.C. Spatially augmented LPboosting for AD classification with evaluations on the ADNI dataset. *NeuroImage* **2009**, *48*, 138–149. [\[CrossRef\]](#)
13. Hinton, G.E. Deep belief networks. *Scholarpedia* **2009**, *4*, 5947. [\[CrossRef\]](#)
14. Vincent, P.; Larochelle, H.; Lajoie, I.; Bengio, Y.; Manzagol, P.-A.; Bottou, L. Stacked denoising autoencoders: Learning useful representations in a deep network with a local denoising criterion. *J. Mach. Learn. Res.* **2010**, *11*, 3371–3408.
15. Rawat, W.; Wang, Z. Deep Convolutional Neural Networks for Image Classification: A Comprehensive Review. *Neural Comput.* **2017**, *29*, 2352–2449. [\[CrossRef\]](#)
16. Ali, M.U.; Kallu, K.D.; Masood, H.; Tahir, U.; Gopi, C.V.V.M.; Zafar, A.; Lee, S.W. A CNN-Based Chest Infection Diagnostic Model: A Multistage Multiclass Isolated and Developed Transfer Learning Framework. *Int. J. Intell. Syst.* **2023**, *2023*, 6850772. [\[CrossRef\]](#)
17. Alanazi, M.F.; Ali, M.U.; Hussain, S.J.; Zafar, A.; Mohatram, M.; Irfan, M.; AlRuwaili, R.; Alruwaili, M.; Ali, N.H.; Albarrak, A.M. Brain Tumor/Mass Classification Framework Using Magnetic-Resonance-Imaging-Based Isolated and Developed Transfer Deep-Learning Model. *Sensors* **2022**, *22*, 372. [\[CrossRef\]](#)
18. Almalki, Y.E.; Ali, M.U.; Kallu, K.D.; Masud, M.; Zafar, A.; Alduraibi, S.K.; Irfan, M.; Basha, M.A.A.; Alshamrani, H.A.; Alduraibi, A.K.; et al. Isolated Convolutional-Neural-Network-Based Deep-Feature Extraction for Brain Tumor Classification Using Shallow Classifier. *Diagnostics* **2022**, *12*, 1793. [\[CrossRef\]](#) [\[PubMed\]](#)
19. Lin, W.; Tong, T.; Gao, Q.; Guo, D.; Du, X.; Yang, Y.; Guo, G.; Xiao, M.; Du, M.; Qu, X.; et al. Convolutional Neural Networks-Based MRI Image Analysis for the Alzheimer’s Disease Prediction From Mild Cognitive Impairment. *Front. Neurosci.* **2018**, *12*, 777. [\[CrossRef\]](#)
20. Wen, J.; Thibeau-Sutre, E.; Diaz-Melo, M.; Samper-González, J.; Routier, A.; Bottani, S.; Dormont, D.; Durrleman, S.; Burgos, N.; Colliot, O. Convolutional neural networks for classification of Alzheimer’s disease: Overview and reproducible evaluation. *Med. Image Anal.* **2020**, *63*, 101694. [\[CrossRef\]](#)
21. Lu, D.; Popuri, K.; Ding, G.W.; Balachandar, R.; Beg, M.F.; Weiner, M.; Aisen, P.; Petersen, R.; Jack, C.; Jagust, W.; et al. Multimodal and Multiscale Deep Neural Networks for the Early Diagnosis of Alzheimer’s Disease using structural MR and FDG-PET images. *Sci. Rep.* **2018**, *8*, 5697. [\[CrossRef\]](#)
22. Ahmed, S.; Choi, K.Y.; Lee, J.J.; Kim, B.C.; Kwon, G.R.; Lee, K.H.; Jung, H.Y. Ensembles of Patch-Based Classifiers for Diagnosis of Alzheimer Diseases. *IEEE Access* **2019**, *7*, 73373–73383. [\[CrossRef\]](#)
23. Jain, R.; Jain, N.; Aggarwal, A.; Hemant, D.J. Convolutional neural network based Alzheimer’s disease classification from magnetic resonance brain images. *Cogn. Syst. Res.* **2019**, *57*, 147–159. [\[CrossRef\]](#)
24. Pan, D.; Zeng, A.; Jia, L.; Huang, Y.; Frizzell, T.; Song, X. Early Detection of Alzheimer’s Disease Using Magnetic Resonance Imaging: A Novel Approach Combining Convolutional Neural Networks and Ensemble Learning. *Front. Neurosci.* **2020**, *14*, 259. [\[CrossRef\]](#) [\[PubMed\]](#)
25. Murugan, S.; Venkatesan, C.; Sumithra, M.G.; Gao, X.Z.; Elakkiya, B.; Akila, M.; Manoharan, S. DEMNET: A Deep Learning Model for Early Diagnosis of Alzheimer Diseases and Dementia From MR Images. *IEEE Access* **2021**, *9*, 90319–90329. [\[CrossRef\]](#)
26. Nawaz, H.; Maqsood, M.; Afzal, S.; Aadil, F.; Mehmood, I.; Rho, S. A deep feature-based real-time system for Alzheimer disease stage detection. *Multimed. Tools Appl.* **2021**, *80*, 35789–35807. [\[CrossRef\]](#)
27. Akram, M.W.; Li, G.; Jin, Y.; Chen, X.; Zhu, C.; Ahmad, A. Automatic detection of photovoltaic module defects in infrared images with isolated and develop-model transfer deep learning. *Sol. Energy* **2020**, *198*, 175–186. [\[CrossRef\]](#)
28. Oyetade, I.S.; Ayeeni, J.O.; Ogunde, A.O.; Oguntunde, B.O.; Olowookere, T.A. Hybridized deep convolutional neural network and fuzzy support vector machines for breast cancer detection. *SN Comput. Sci.* **2022**, *3*, 58. [\[CrossRef\]](#)
29. Fatima, M.; Khan, M.A.; Shaheen, S.; Almujaally, N.A.; Wang, S.-H. B2C3NetF2: Breast cancer classification using an end-to-end deep learning feature fusion and satin bowerbird optimization controlled Newton Raphson feature selection. *CAAI Trans. Intell. Technol.* **2023**, *8*, 1374–1390. [\[CrossRef\]](#)
30. Zahoor, S.; Shoaib, U.; Lali, I.U. Breast Cancer Mammograms Classification Using Deep Neural Network and Entropy-Controlled Whale Optimization Algorithm. *Diagnostics* **2022**, *12*, 557. [\[CrossRef\]](#)
31. Baltruschat, I.M.; Nickisch, H.; Grass, M.; Knopp, T.; Saalbach, A. Comparison of Deep Learning Approaches for Multi-Label Chest X-Ray Classification. *Sci. Rep.* **2019**, *9*, 6381. [\[CrossRef\]](#)
32. Kang, J.; Gwak, J. Ensemble of Instance Segmentation Models for Polyp Segmentation in Colonoscopy Images. *IEEE Access* **2019**, *7*, 26440–26447. [\[CrossRef\]](#)
33. Mirjalili, S.; Lewis, A. The Whale Optimization Algorithm. *Adv. Eng. Softw.* **2016**, *95*, 51–67. [\[CrossRef\]](#)

34. Nadimi-Shahraki, M.H.; Zamani, H.; Mirjalili, S. Enhanced whale optimization algorithm for medical feature selection: A COVID-19 case study. *Comput. Biol. Med.* **2022**, *148*, 105858. [[CrossRef](#)] [[PubMed](#)]
35. Agrawal, P.; Abutarboush, H.F.; Ganesh, T.; Mohamed, A.W. Metaheuristic Algorithms on Feature Selection: A Survey of One Decade of Research (2009–2019). *IEEE Access* **2021**, *9*, 26766–26791. [[CrossRef](#)]
36. Shukla, A.; Tiwari, R.; Tiwari, S. Alz-ConvNets for classification of Alzheimer disease using transfer learning approach. *SN Comput. Sci.* **2023**, *4*, 404. [[CrossRef](#)]
37. Mohammed, B.A.; Senan, E.M.; Rassem, T.H.; Makbol, N.M.; Alanazi, A.A.; Al-Mekhlafi, Z.G.; Almurayziq, T.S.; Ghaleb, F.A. Multi-Method Analysis of Medical Records and MRI Images for Early Diagnosis of Dementia and Alzheimer’s Disease Based on Deep Learning and Hybrid Methods. *Electronics* **2021**, *10*, 2860. [[CrossRef](#)]
38. Acharya, H.; Mehta, R.; Singh, D.K. Alzheimer Disease Classification Using Transfer Learning. In Proceedings of the 2021 5th International Conference on Computing Methodologies and Communication (ICCMC), Erode, India, 8–10 April 2021; pp. 1503–1508.
39. El-Latif, A.A.A.; Chelloug, S.A.; Alabdulhafith, M.; Hammad, M. Accurate detection of Alzheimer’s disease using lightweight deep learning model on MRI data. *Diagnostics* **2023**, *13*, 1216. [[CrossRef](#)]
40. Loddo, A.; Buttau, S.; Di Ruberto, C. Deep learning based pipelines for Alzheimer’s disease diagnosis: A comparative study and a novel deep-ensemble method. *Comput. Biol. Med.* **2022**, *141*, 105032. [[CrossRef](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.