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Performance Enhancement of Alzheimer's Disease Diagnosis Using Generative Adversarial Network

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ABSTRACT

Insufficient medical images have always been a challenge for deep learning-based Alzheimer's disease classification and detection tasks. The availability of Magnetic Resonance Imaging (MRI) data is limited due to patients' privacy issues. Access to individual medical records is strongly protected by the law, and appropriate consent is needed to utilize them for research purposes. Besides that, publicly available databases often experience imbalanced classes, further contributing to the issue of insufficient data. Thus, the performance of deep learning models used to diagnose Alzheimer's disease is often hindered by this issue. Basic data augmentation methods such as geometrical augmentation techniques also had limited applications to medical data. Hence, this study proposes a deep learning technique of Generative Adversarial Network (GAN) to expand the MRI dataset and improve the classification model performance. MRI images from the Open Access Series of Imaging Studies (OASIS) database are used in this study to perform experiments and validate hypotheses. After applying GAN to expand the dataset, a pre-trained Convolutional Neural Network (CNN) model is used to classify the data into multiple classes of Alzheimer's and the model's performance is measured. As a result, an improvement in accuracy for the classification task can be observed, indicating that the GAN is a solution for overcoming the challenge of insufficient data for Alzheimer's diagnosis.

1. Introduction

Being known as an irreversible disease that has no cure yet to date, Alzheimer's disease (AD) is a type of chronic neurodegenerative disease that often affects older adults. According to the World Health Organization (WHO), AD is ranked as the seventh leading cause of death, while World Alzheimer's Disease estimates that approximately 50 million individuals worldwide are affected by this illness [1,2]. This number is expected to double every 20 years, demonstrating the severity of AD. Thus, early detection and diagnosis of AD has been a significant step that is strongly recommended

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by professional doctors so that the worsening of the disease can be slowed down using appropriate treatments [3].

In diagnosing AD, medical imaging techniques such as magnetic resonance imaging (MRI) allow radiologists to effectively examine the brain's internal components and gain more information about the patient's condition [4]. MRI is a type of scan that uses radio waves and magnetic fields to capture the image of the brain, providing detailed information on brain regions affected by AD [5]. Through the analysis of MRI brain images, radiologists can identify the presence of AD in a patient for diagnosis and develop suitable treatment plans. However, the abundance and intricacy of images resulting from the MRI scan have posed a difficulty in diagnosing AD [6]. Moreover, the diagnosis task is also hindered by a prodromal stage of AD, known as mild cognitive impairment (MCI), in which its features are hard to distinguish from AD [7].

Thus, recent medical advancements include applying deep learning (DL) to analyze medical images and diagnose diseases due to its ability to learn directly from raw datasets and produce excellent results [8-10]. Venugopalan *et al.,* [11], Maqsood *et al.,* [12], Mehmood *et al.,* [13], Jain *et al.,* [14], Shanmugam *et al.,* [15], and Asgharzadeh-Bonab *et al.,* [16] have applied DL in their research to diagnose AD, and they showed promising results. Despite the excellent performance of DL models in diagnosing AD, limitations still exist, which is the issue of insufficient medical data [17]. Generally, the training of DL models requires a large amount of data to ensure its smooth learning process [18]. On the contrary, the availability of medical images like brain MRI images is very limited due to the privacy concerns of patients. AD patients' medical records are subject to stringent legal protection, and researchers must acquire consent to utilize this data for research purposes. Hence, this has caused a problem in most DL-based AD diagnosis studies.

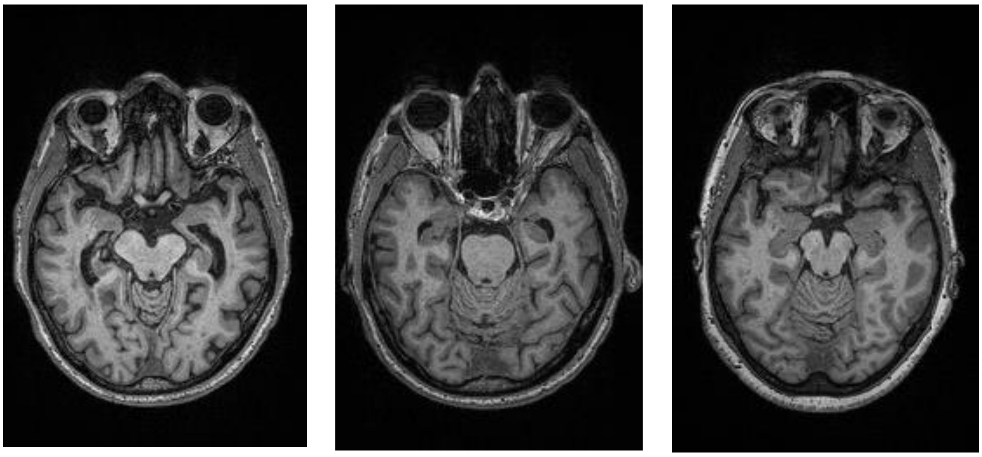
In order to solve this issue of insufficient medical data for the application of DL in AD diagnosis, this research proposes an unsupervised DL model known as the Generative adversarial network (GAN) to expand the MRI dataset and eventually improve the classification performance of DL models. GAN is a generative DL model usually used for data augmentation tasks to replace basic data augmentation techniques such as rotating, flipping, and cropping [19]. These techniques are part of geometrical transformations; hence, applying them to medical images such as MRI might damage the local position information inside [20]. Instead of using these data augmentation techniques, GAN is gaining popularity as it can generate realistic samples based on input images by learning the image features [19]. Thus, this research will be applied to generate realistic MRI samples of high similarities to expand the dataset and improve the classification performance. This work's main contribution lies in performing a multi-stage AD classification task using the proposed GAN method and DL classification model, which presents a greater challenge than the binary classification task typically addressed in this field.

2. Methodology

2.1 Dataset

This study uses MRI brain images from the Open Access Series of Imaging Studies (OASIS) to train the GAN and Convolutional neural network (CNN) models for diagnosing AD. OASIS is an open-access database commonly used by researchers in the scientific community for studies related to dementia and ageing [21]. The OASIS database was established in 2007, and its data have been collected from ongoing projects at Washington University Knight Alzheimer Disease Research Centre for 15 years. In the latest release, the OASIS-3 dataset comprises 2000 MR sessions collected from 1098 participants ranging from 42 to 95 years old. Among these individuals, there are 605 cognitively normal subjects and 493 subjects with different stages of Alzheimer's. It can be seen that the distribution of MRI data in this database is imbalanced, where normal subjects are in a larger quantity than Alzheimer-affected subjects [22]. Thus, this is another factor contributing to insufficient data when diagnosing AD using DL approaches.

For conducting the experiments in this study, MRI data from three (3) classes of Alzheimer's are collected from the OASIS database to perform multi-stage classification of AD using DL models. Despite the imbalanced distribution in OASIS, a balanced dataset is obtained in this study to maintain the quality of training and avoid bias in the results. 100 subjects from each of the 3 different classes: (normal control (NC), MCI, and AD) are collected from OASIS, where the MRI images are selected based on the clinical dementia rating (CDR) score. Figure 1 shows the MRI slices according to each class of Alzheimer's, while Table 1 shows the demographic and clinical characteristics of the MRI subjects selected for this study. Table 2 shows the dataset distribution of MRI images obtained from OASIS that will be used for training and validation in this study. From the 300 subjects, 1920 MRI slices will be allocated for training, while the remaining 1080 will be for validation.



(a) (b) (c)

Fig. 1. MRI image slices for different classes obtained from OASIS: (a) AD (b) MCI (c) NC [21]

Table 1
Demographic and clinical characteristics of MRI subjects

Classes	AD	MCI	NC
Number of subjects	100	100	100
Gender	Males and females		
Age	65 years old < Age < 74 years old		
CDR score	CDR > 2	0.5 < CDR < 1	CDR = 0

Table 2
Dataset distribution of MRI subjects

Dataset	AD	MCI	NC	Total
Training	640	640	640	1920
Validation	360	360	360	1080

2.2 Proposed Methodology

In this study, there are generally 2 phases that will be carried out through the experiments. The training phase refers to the training of DL models, where in this study, two DL models need to be trained, as shown in the flowchart in Figure 2. Firstly, the GAN model will be trained after receiving input from the MRI dataset for generating sample MRI images to expand the dataset. Secondly, the data will be passed to the pre-trained CNN model for the multi-stage classification task into three different classes of Alzheimer's.

Subsequently, the trained DL model will be validated using an unknown set of MRI data to evaluate its performance and generalizability. The GAN model will be benchmarked with the ability of the CNN model to accurately classify MRI images into multiple classes.

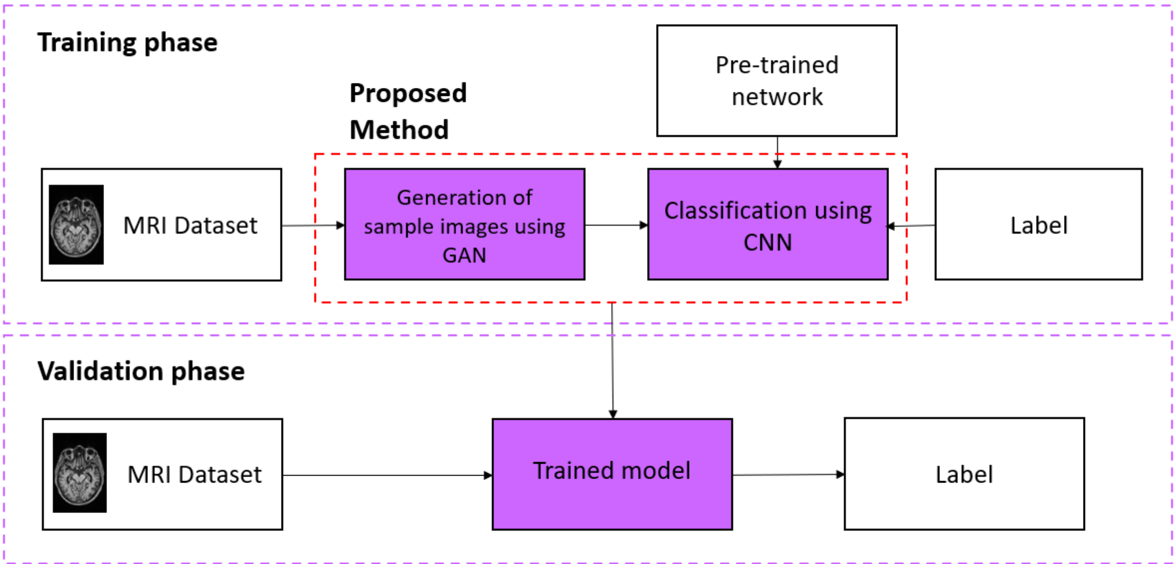


Fig. 2. Framework overview of proposed methodology

2.2.1 Generative Adversarial Network (GAN)

According to Goodfellow *et al.,* [23], GAN is an unsupervised DL network commonly used for data augmentation tasks due to its generative nature. It can generate realistic and high-quality samples by learning the features of the inputs. GAN was first applied for natural language processing (NLP) applications, and due to its excellent contributions, it is gradually being applied in various domains, including medical applications. Unlike basic augmentation techniques that might damage the local position information of medical images, GAN provides an efficient and input-friendly approach to these images, as no geometrical transformation is done to alter the information inside the images. Through the multiple hidden layers inside the network, it gradually learns the image features and creates similar-looking samples based on its knowledge.

As shown in the model structure in Figure 3, there are generally 2 network models in a GAN: the generator and discriminator models. These two models work concurrently in a game-like situation to ensure the accuracy of the output sample image generated. Firstly, the generator receives the input MRI images and starts to learn their features. Playing as a "thief" in this game, the generator tries to generate sample images that look similar to the input images by hiding any flaws or imperfections in the generated MRI images. On the other hand, the discriminator plays a "police" in this game and is responsible for identifying and catching any fake images by comparing them to the real MRI images it receives from the input. After identifying and classifying the fake images from the real ones, the output will be backpropagated to both models to update and improve them to generate better sample images in the next round. Eq. (1) shows the loss function of the GAN that is continuously learnt by both the generator (G) and discriminator (D) models to achieve the goal of generating realistic-looking samples. This process will be looped continuously until an equilibrium is reached, indicating that the generated MRI images are perfect, as the discriminator can no longer distinguish any fake samples.

$$\min_{G} \max_{D} V(D, G) = \mathbb{E}x{\sim}p_{\text{data}}(x) \log D(x) + \mathbb{E}z{\sim}p_z(z) \log (1 - D(G(z))) \quad (1)$$

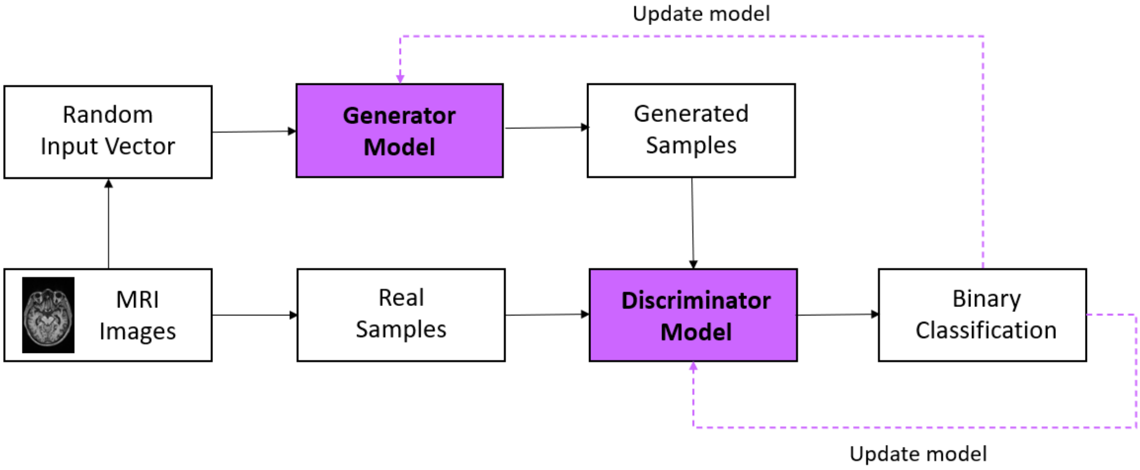


Fig. 3. GAN model structure [23]

2.2.2 Pre-trained CNN classification model

According to the flowchart in Figure 2, the expanded MRI dataset will be inputted into a CNN model for the multi-stage classification of AD. CNN is a DL model popularly used for image analysis tasks such as pattern recognition, identification, and classification due to its ability to capture rich feature representations directly from raw images [10]. Lately, pre-trained CNN models using transfer learning have been gaining attention in artificial intelligence (AI) due to their excellent performance compared to the basic models. Transfer learning entails repurposing a DL model for another task through minor adjustments or fine-tuning [15]. The transfer of knowledge provides the DL model with a higher slope and asymptote, thereby a better training start value [24]. Pre-trained CNN models are previously trained on large datasets, such as the ImageNet dataset that consists of millions of images from different classes. Therefore, these models already have the best parameters that can produce accurate results for training. Moreover, transfer learning saves time by eliminating the need to create a new model from scratch.

In this study, a pre-trained CNN model known as the EfficientNet model will be utilized for the multi-stage classification task after the MRI dataset is expanded using the GAN model. By efficiently adjusting the network's size and resolutions, the EfficientNet model can achieve better accuracy with fewer computational resources than other models [25]. As shown in Figure 4, its model structure is mainly built from convolutional blocks, especially mobile inverted bottleneck convolutional units (MBConv), which leads to its improved efficiency, thus explaining why the EfficientNet is chosen to be used as the classification model in this study [26].

Fig. 4. EfficientNet model structure [26]

2.3 Experiment Setup

According to the flowchart shown in Figure 2, two experiments will be conducted in this study to achieve the objective proposed. Experiment I will utilize GAN to generate sample MRI images for expanding the dataset, while experiment II will perform a multi-stage classification task using the EfficientNet model to classify the different stages of AD. In both experiments, the DL models will be developed using PyTorch's Python-based deep learning framework, while the training processes will utilize a graphics processing unit (GPU).

2.3.1 Experiment I: Generation of sample images using GAN

In this experiment, the GAN is used to generate sample MRI images to grow and expand the dataset. Table 3 shows the hyperparameters used in the training of the GAN model. Around 3000 MRI images obtained from the OASIS database are used as input images for training the GAN model, where they are equally distributed among the three classes of AD. Before inputting into the model, the MRI images are first resized into a dimension of 64 by 64 pixels to suit the model requirement. Then, based on the other parameters, such as the size of the latent vector, batch size, and learning rate, as shown in Table 3, the GAN is trained accordingly for 100 epochs. The performance of the GAN will be validated by observing its losses and the quality of the sample MRI images produced.

Table 3
Summary of hyperparameters used for training the GAN model

Hyperparameters	Values
MRI image size	64 x 64 x 3
Number of training images	AD: 1040 MCI: 1050 NC: 1035
Latent vector size, z	100
Number of epochs	100
Batch size	64
Learning rate	0.0002
Optimizer	Adam optimizer
Loss function	Binary cross entropy

2.3.2 Experiment II: Multi-stage classification using EfficientNet

After expanding the MRI dataset using GAN, the data is inputted into the EfficientNet model for a multi-stage classification task. In this study, the hypothesis states that incorporating GAN will help increase the classification performance of the EfficientNet model. Thus, this experiment is set up in a way that can test the validity of the hypothesis. As shown in Table 4, different amounts and ratios of GAN-generated MRI images will be added to the basic MRI dataset, and their changes in performance will be observed accordingly. In order to compare its performance with other GAN-incorporated sets, the EfficientNet model is initially trained on a basic dataset that exclusively consists of original MRI data from OASIS and does not incorporate any additional data from GAN. A total of 1920 MRI data only are obtained from OASIS for this experiment, and different proportions of GAN-generated data will be added for each different set of data, as shown in Table 4. In order to observe the changes in the performance of the model, a gradual increment of GAN data is added to the basic dataset in the proportion of 20%, 50%, 70%, and 100%, and the resulting dataset size after the increment are tabulated in Table 4. The EfficientNet model will be trained and validated using these five datasets, and the model's classification performance will be observed accordingly.

Table 4
MRI dataset distribution for Experiment II

No.	Amount of data used	Proportion of GAN-generated data used	Dataset size
1	Original amount of data	-	AD: 640; MCI: 640; NC: 640
2	Add 20% data from GAN	128 GAN-generated images	AD: 768; MCI: 768; NC: 768
3	Add 50% data from GAN	320 GAN-generated images	AD: 960; MCI: 960; NC: 960
4	Add 70% data from GAN	448 GAN-generated images	AD: 1088; MCI: 1088; NC: 1088
5	Add 100% data from GAN	640 GAN-generated images	AD: 1280; MCI: 1280; NC: 1280

3. Results and Discussion

3.1 Experiment I: Generation of Sample Images Using GAN

The GAN expands the MRI dataset in this experiment by generating realistic MRI image samples. It receives the real MRI images as input, learns their features using DL, and creates similar-looking fake MRI images based on the knowledge learnt. Results from this experiment are shown in Figure 5 and Figure 6. Figure 5 illustrates how the generator (G) and discriminator (D) losses changed during the training of the GAN. Based on Eq. (1), the generator's goal is to generate better and more realistic fake images, while the discriminator is trained to classify each input image as real or fake data correctly. Both G and D models are trained simultaneously to improve each other's accuracy and produce better sample MRI images. Ideally, the G and D losses will gradually converge to a fixed value when the equilibrium point is reached. However, training a GAN model is always susceptible to mode collapse or non-convergence issues. Thus, GAN models that converge to a stable value instead of reaching the equilibrium point are considered sufficient to produce good results. As shown in Figure 5, the loss graph shows that both the generator and discriminator model losses gradually converged to a stable value as the number of iterations increased.

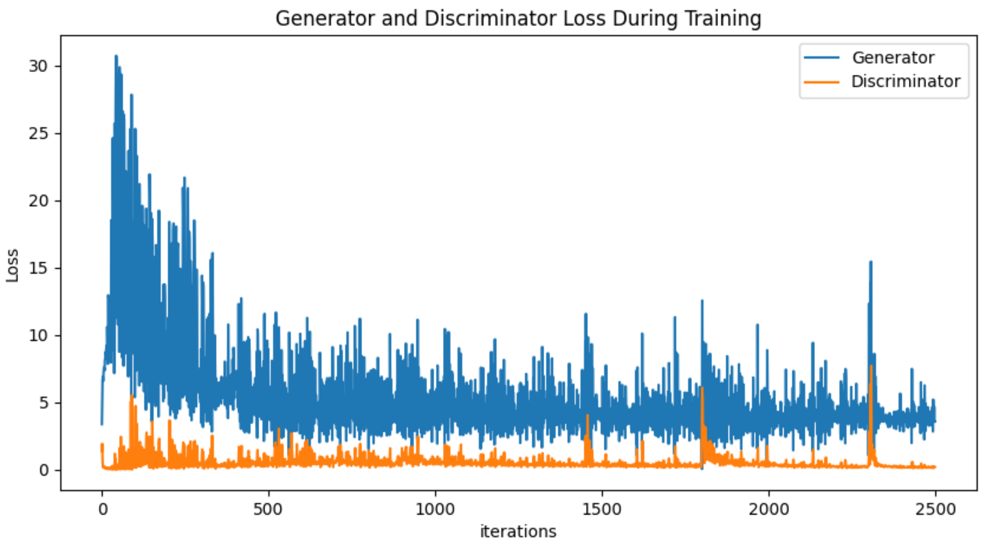


Fig. 5. Loss graph of the GAN model during training

Moreover, in Figure 6, a batch of real MRI images is compared with a batch of fake MRI images generated by the GAN to visualize the quality of samples produced. The imitation MRI images generated closely resemble the actual images, as the GAN has managed to replicate a significant portion of the image features. It can be perceived that the GAN has successfully generated synthetic MRI images to expand the MRI dataset in this study.

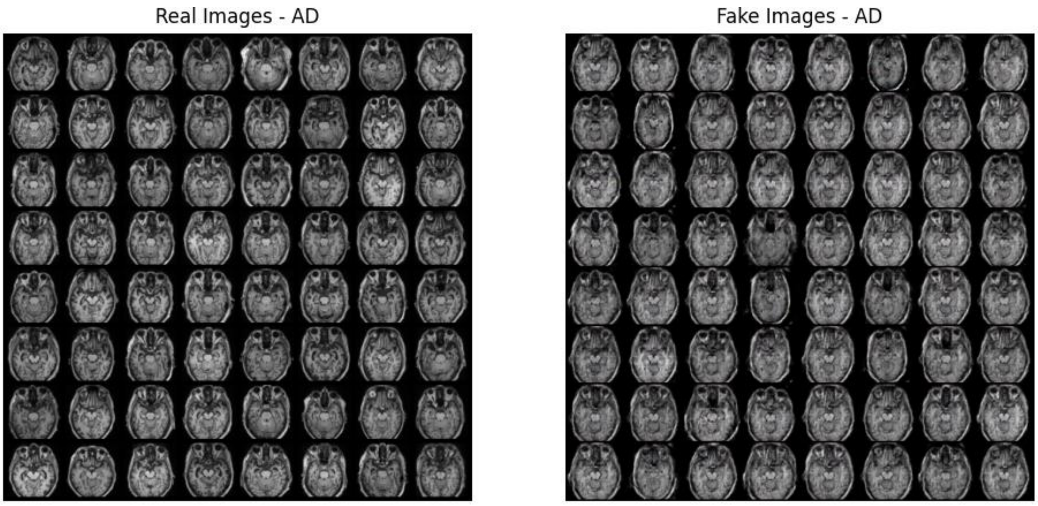


Fig. 6. Side-by-side comparison between real and fake MRI images generated

3.2 Experiment II: Multi-stage Classification Using EfficientNet

This experiment was carried out after the completion of the MRI dataset expansion by GAN in the previous experiment. This experiment uses a pre-trained CNN model, EfficientNet, to classify the MRI images into their respective classes: AD, MCI, and NC. Five (5) datasets with different amounts of MRI images are used to train the classification model, as shown in Table 5. The first dataset has the least amount of MRI data as it only consists of original OASIS images, without any additional data from GAN. Training this dataset is a benchmark compared to the other datasets containing additional GAN-generated data. In this benchmark dataset, the training accuracy achieved is 90.157% for classifying the MRI images into three classes. An accuracy of 78.477% was obtained in the classification task when the EfficientNet model was tested on an unknown data set.

Following this, the generated images by GAN are gradually added to the MRI dataset based on the proportions shown in Table 5 to expand the dataset and observe their respective classification accuracies. A steady increment of generated images is performed and tested on the EfficientNet model to visualize how the model's performance changes in response to the growth of the dataset. As shown in Table 5, it can be seen that both the training and validation accuracies gradually increase as the size of the MRI dataset increases. When 20% of GAN-generated images are added, the EfficientNet model increased accuracy to 92.789% for training and 79.620% for testing. When more generated data are added in the 50%, 70%, and 100% percentages, the training accuracy increases to 95.199%, 97.150%, and 98.683%, respectively. Besides, the validation accuracy of the model also increases in the same manner to as high as 85.107% in the largest dataset with the most generated MRI data added. Thus, this pattern of changes in the accuracies of the EfficientNet model has proven that the classification performance improves as the dataset size improves, as suggested by the hypothesis of this study.

Table 5
Performance of EfficientNet model corresponding to dataset size

No.	Amount of data used	Training Accuracy (%)	Validation Accuracy (%)
1	Original amount of data	90 .157	78.477
2	Add 20% data from GAN	92.789	79.620
3	Add 50% data from GAN	95.199	80.207
4	Add 70% data from GAN	97.150	82.887
5	Add 100% data from GAN	98.683	85.107

Table 6 shows a comparison made between the proposed approach in this study with other existing works. They are all related works that performed AD classification using CNN models and MRI images but with different classification types and usage of GAN for data augmentation. Thus, their accuracy is compared with the current study to validate our results. In previous studies, only multi-stage classification using different CNN models is performed without utilizing GAN [18,27]. On the other hand, studies by Konidaris *et al.,* [28] and Zhou *et al.,* [29] performed data augmentation using GAN and classified MRI images using ResNet and a fully convolutional network (FCN). By comparing the performance of four existing works with the current study, it can be seen that the accuracy of this EfficientNet with the GAN model is relatively higher. Moreover, despite the more challenging multi-stage classification task, our suggested model has demonstrated a higher accuracy level than existing works that only conducted binary classification into AD and NC classes [28,29].

Table 6
Comparison with other related works

Reference	Model	Modality	Classification type	Data augmentation using GAN	Accuracy (%)
Yildirim and Cinar [27]	VGG	MRI	Multi-stage	No	78.00
Islam and Zhang [18]	ResNet	MRI	Multi-stage	No	82.50
Konidaris *et al.,* [28]	ResNet + GAN	MRI	Binary	Yes	83.49
Zhou *et al.,* [29]	FCN + GAN	MRI	Binary	Yes	83.98
This paper	EfficientNet + GAN	MRI	Multi-stage	Yes	85.11

4. Conclusions

From the findings obtained from the experiments conducted in this study, it can be concluded that the experimental results successfully answered the proposed research objective. In this study, an unsupervised DL model, GAN, is used to expand the MRI dataset, where this expansion aims to improve the classification performance of the CNN model. From the experiments done, it is observed that the GAN model has successfully produced realistic MRI sample images. Then, by gradually increasing the dataset size using the generated sample images, the EfficientNet model is trained on five different MRI dataset sizes. As per the experimental results, it can be observed that the model's classification performance increases gradually with the increase in dataset size. Moreover, with improved accuracy, the model can successfully classify MRI images into their respective classes - AD, MCI, and NC. However, some limitations of this study include the difficulty in training the GAN model and the presence of some overfitting in the classification model. Thus, improvisations such as improving the GAN model stability and fine-tuning the CNN model parameters can be done to improve the performances further. Besides, future works and scopes include exploring the usage of different types of GAN models for MRI data augmentation and incorporating various enhancement modules for AD classification.

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