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AUTOMATED DIAGNOSIS METHOD FOR ALZHEIMER'S DISEASE USING CEREBRAL CATHETER ANGIOGRAM NEUROIMAGING AND ALEXNET ARCHITECTUREIN DEEP LEARNING

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Abstract

Alzheimer's disease (AD) is a neurological disorder that kills brain cells and causes memory loss in the patient. Early detection can protect the patient's brain cells from further damage and prevent irreversible memory loss. Several treatments focus on detecting the condition quickly, accurately, and early to limit the damage to a patient's mental health. Recently, various automated technologies and methods for diagnosing Alzheimer's disease have been introduced. Deep learning is a robust machine learning technique for classifying and extracting low-level to high-level features. We propose automated method for diagnosis Alzheimer's disease using Alex Net architecture and a convolutional neural network (CNN). This research aims to develop a helpful framework for the early identification of Alzheimer's disease using Magnetic Resonance Angiography (MRA) neuroimages.

Keywords: Alzheimer's disease, neuroimaging, Deep Learning, Convolutional Neural Network (CNN),Alex net.

I. Introduction

Alzheimer's disease is a brain ailment that steadily impairs memory and cognitive abilities and, ultimately, the ability to carry out the simplest activities. Alzheimer's is a kind of dementia. The two pathologies that define Alzheimer's disease are the growth of the protein beta-amyloid (plaques), which are found outside of neurons, and the tangles of the protein tau, which are found inside of neurons. These changes are followed by the death of neurons and brain tissue damage. Alzheimer's is a steadily worsening brain condition that develops years before symptoms appear.

Recent extensive post-mortem studies suggest that more than 50 % of patients with Alzheimer's dementia have Alzheimer's disease brain abnormalities (pathology) as well as brain alterations of one or more additional causes of dementia, such as cerebrovascular illness or Lewy body disease. If this is termed the mixed disease and, if identified throughout life, is called mixed dementia.

One of the most powerful areas of neuroscience is called "neuroimaging," which describes a collection of imaging methods used to look at the nervous system. The rapid advancement of these methods has led to the creation of new images that make it possible to extract meaningful information about the anatomy and function of the brain.

Researchers now utilize neuroimaging modalities, including MRI, CT, and PET, to develop novel methods for analyzing neuroimages. Extracting hidden features based on picture pixels is a crucial function of neuroimage processing in diagnostic classification. By recognizing the unique features of the picture, the precise processing results help distinguish between healthy and unhealthy situations.

Convolutional neural network (CNN), in particular, has demonstrated excellent performance in various computer vision applications, including object recognition, segmentation, and classification. Since it can be used for both feature extraction and classification, CNN's methods are distinguished by their high level of image processing performance. The process of extracting features from an image involves applying a transform filter to create a feature map, which is combined with a pooling layer to help reduce the size of the map. AlexNET is a convolutional neural network that is eight layers deep. The first five were convolutional layers, three max-pooling layers, and the last three were fully connected layers (the final layer is the softmax layer). AlexNET has got multiple convolutional layers and it might look similar to LeNET but it is much deeper. LeNET also had multiple convolutional layers but here number was really large. The goal of this research is to build a useful model based on magnetic resonance angiogram (MRA) neuroimages for the early diagnosis of Alzheimer's disease.

II. Literature survey

Deep learning algorithms have shown impressive performance in recent years. Due to deep learning's success in identifying 2D natural pictures, several research has tried to apply it to medical imaging [4, 5]. Strong deep learning models, in particular CNN, can decipher latent or hidden representations in neuroimaging data and efficiently identify pathologies associated with illness [1]. Additionally, CNN's may develop general cognition by connecting various elements of a picture. The complexity of medical imagery connected to Alzheimer's disease, however, means that there is still a long way to go before deep-learning algorithms can be used to identify the illness..

Medical imaging investigations using structural MRI, functional MRI (fMRI), PET, and diffusion tensor imaging (DTI) have all benefited from the use of deep learning models [6]. According to our literature evaluation, MRI is the most often used diagnostic tool for diagnosing AD. Hence, for this study's sake, we have concentrated on MRI scans. Deep models are typically ineffective because convergence takes too long and a huge dataset is needed, even though deep neural networks have been used to train from scratch in many studies [7]. Neuroimaging databases sometimes only include a few hundred photos, which leads to over fitting issues, even though image classification datasets for item classification typically comprise millions of images. In practice, it's common to use pre-trained CNNs for one domain-specific task as the initialization step, then retrain them for additional charges by fine- tuning their final layers [8, 9].

This is due to the more universal qualities present in CNNs' bottom layers, which are helpful for a wide range of tasks and may be transferred from one application domain to another. Transfer learning, a method for training large networks without over fitting, is compelling. It has been shown that transfer learning, particularly for cross-domain tasks, is quicker and yields better outcomes than initial training [10, 11].

To establish the first transfer learning method for AD diagnosis using deep learning, Gupta et al.
[1] first found a 2D CNN with one convolutional layer and a max-pooling layer, then used a neural network that included a single hidden layer for classification after feature extraction using a sparse auto-encoder. They demonstrated that training the auto encoder using real-world images enhances classification performance in higher layers.

Three 2D CNNs with two convolutional layers were trained using three slices in the core of the hippocampal region of specific MRI images. This transfer learning approach was created by Aderghal et al. [13]. Instead of beginning from scratch with a small dataset of DTI images, they utilized transfer learning to apply models trained on MRI images. They finally combined all the networks and used a majority voting method to arrive at a decision.

In recent years, deep learning systems have performed in a ground-breaking way. A rising numberof studies have attempted to use deep learning in medical imaging as a result of its effectiveness in classifying 2D natural images [4, 5]. Deep learning models, especially CNNs, may effectively detect disease-related pathologies and reveal latent or hidden representations in neuroimaging data by creating connections between distinct image areas. But before deep learning algorithms can be used to recognize the condition, researchers still have a long way to go, given the complexity of medical images associated with AD.

Recent technology advancements have paved the way for the introduction of beneficial new tools for healthcare professionals, such as advancements in the field of neuroimaging that have made it easier for researchers and medical personnel to acquire a vast array of various neuroimaging data sets.

Classical Machine Learning-Based Methods

Classical Machine Learning-Based Me Machine learning algorithms have also been included as part of the innovations, dramatically accelerating diagnosing and treating Alzheimer's disease. Researchers have employed well-known pattern analysis techniques, such as linear discrimination analysis (LDA), logistic regression (LR), and support vector machine (SVM), to create prediction models for the early identification of Alzheimer's disease [14]. The most significant obstacle to adopting these old categorization techniques is the time needed to accomplish these steps since their usage requires skill and numerous stages of development [15].

Research to create a diagnostic model for Alzheimer's disease was carried out by Lebedev et al. [16].185 Alzheimer's patients and 225 healthy participants' structural MRI scans from the ADNI database were utilized. The average morphometric characteristics, which include sulcal depth, Jacobian maps, and cortical thickness, were extracted using the Free-Surfer image analysis program, which contains the surface-based registration technique. When tuning and evaluating the model performance throughout the training process, they employed out-of-bag estimates, and RF achieved the best results with 88.6% and 92.0% of sensitivity and specificity, respectively.

The displacement field was provided as the features after being reduced using the principal component analysis approach for dimensionality reduction in Zhang and Wang's [17] 3D-MRI images of 28 patients with Alzheimer's disease and 98 healthy people from the OASIS database. According to the findings, the Twin-SVM classifier performed best, achieving accuracy, sensitivity, and specificity of 92.75%, 90.56%, and 79.61%, respectively.

Additionally, Beheshti et al. [18] employed structural MRI scans for 130 Alzheimer's patients and 130 healthy individuals from the ADNI database. Each participant had undergone neuropsychological testing, from which they had derived clinical markers such as the results of the clinical dementia ratio and the mini-mental state assessment. They also employed the voxel-based feature extraction approach to extract features from structural MRI images, as well as feature ranking that was determined by reducing the classification error. Their suggested model performed well based on the findings, achieving an accuracy rate of 92.48%.

In a different research, Zhang et al. [19] used the longitudinal structural MRI scans from the ADNI database for 207 healthy people and 154 Alzheimer's patients. After that, they used a data-driven method for landmark discovery to find landmarks and suggested a landmark-based feature extraction framework that employs a bag-of-words technique to extract statistical high-level spatial and contextuallongitudinal information. Based on their findings, the SVM classifier performed well, with an accuracy rate of 88.30%.

In their study, Zeng et al. [20] utilised MRI scans from the ADNI database for 82 patients with NC and 92 Alzheimer's patients. Then, they extracted voxel characteristics using the automated anatomical labelling template. They suggested a hybrid model that uses the switching delayed particle swarm optimization technique and principal component analysis to improve the kernel parameter and penalty factor of the SVM classifier. The suggested classifier has done better than existing machine learning classifiers with a level of accuracy of 71.23%, according to the results.

In a different investigation, Zhang et al. [21] examined the longitudinal structural MRI scans from the ADNI database for 207 healthy people and 154 Alzheimer's patients. After that, they used a data-driven method for landmark discovery to find landmarks and suggested a landmark-based feature extraction framework that employs a bag-of-words technique to extract statistical high-level spatial and longitudinal contextual information. Based on their findings, the SVM classifier performed well, with an accuracy rate of 88.30%.

In their study, Zeng et al. [22] utilized MRI scans from the ADNI database for 82 patients with NC and 92 Alzheimer's patients. Then, they extracted voxel characteristics using the automated anatomical labeling template. They suggested a hybrid model that uses the switching delayed particle swarm optimization technique and principal component analysis to improve the kernel parameter and penalty factor of the SVM classifier. The suggested classifier has done better than existing machine learning classifiers, with a level of accuracy of 71.23%, according to the results.

Recently, Koh et al. [23] employed MRI brain images from the Harvard Brain Atlas and the University of Malaya Medical Centre databases for 55 Alzheimer's patients and 110 healthy people. Then, they extracted features using the bidirectional empirical mode decomposition approach. According to the findings, RF classifiers and SVM with a polynomial kernel of one degree had the best performance,with an accuracy rate of 93.9%.

As a result, the main hurdle to using standard machine learning is the obligatory step of extracting features from various neuroimaging images and feeding them to classification algorithms.

Deep Learning-Based Methods

Researchers' challenges utilizing conventional machine learning methods to cope with pictures may be solved by deep learning. In the area of image processing, particularly in medicine, it sparked a lot of attention [24]. Deep learning algorithms are emphasized as the best approaches for working with picture datasets since their findings clearly outperformed those of classic machine learning techniques [25].

Research by Liu et al. [26] used FDG-PET neuroimaging to construct a model for diagnosing Alzheimer's disease using deep learning techniques. They divided the 3D-FDG-PET images into 2D slices and utilized them to compare 100 healthy participants and 93 patients with Alzheimer's disease from the ADNI database. Following that, slices were organized into nine-slice groups depending on how similar their structural characteristics were. In order to extract features, deep learning techniques were used. A 2D-CNN model was trained to extract intra-slice features, and a 2-stacked bidirectional-gated recurrent unit cascaded to extract inter-slice features. Based on feeding the created features into two fully linked layers and a softmax layer, the final classification output is produced. Based on the findings, the suggested model performs well, with an accuracy level of 91.2%.

Ge et al. [27] utilized 3D MRI images from the ADNI database of 139 healthy people and 198 Alzheimer's patients. Cerebrospinal fluid, white matter, and grey matter were the three sections of the tissue image that underwent concurrent 3D multiscale-CNN processing in order to extract the multiresolution features. Additionally, two distinct layers of fusion layer were carried out on various sizes of a tissue area as well as other tissue regions. After that, in addition to the classification job, dimensionality reduction of the obtained features was performed using XGBoost [28]. The suggested model has a degree of accuracy of 89.51% on datasets divided by topic, according to the findings.

In addition to 418 Alzheimer's patients and 407 healthy participants from the ADNI database, Basara et al. [29].'s MRI scans included 50 normal subjects and 124 Alzheimer's patients from the Milan database. The proposed model consists of a fully connected layer, an output layer for linear regression, and 12 convolutional layers of repeated blocks with the ReLU activation function. According to the findings, the suggested model performed well on both data sets, achieving an accuracy level of 98%.

Additionally, Pan et al. [30] employed three-axis slices from MRI scans of 162 healthy people and 137 patients with Alzheimer's disease from the ADNI database. The suggested model extracted features from a collection of coronal, sagittal, and transverse MRI slices using a variety of 2D-CNN models. After that, 2D-CNN models are combined to create a special ensemble model that produces theclassification result. The suggested model has achieved great performance with an accuracy level of 84% and 5% based on the results of using 10-fold cross-validation on the data set.

Additionally, Feng et al. [31] employed 3D MRI images from the ADNI database for 159 healthy people and 153 patients with Alzheimer's disease. The three models they presented are 2D-CNN, 3D-CNN, and 3D-CNN-SVM, where 3D-CNN extracts features from scans, and SVM is used to perform classification tasks using the retrieved features. Based on their experimental findings, the 3D-CNN-SVM model performed the best, with rates of accuracy, specificity, and sensitivity of 99.10%, 99.40%, and 98.80%, respectively.

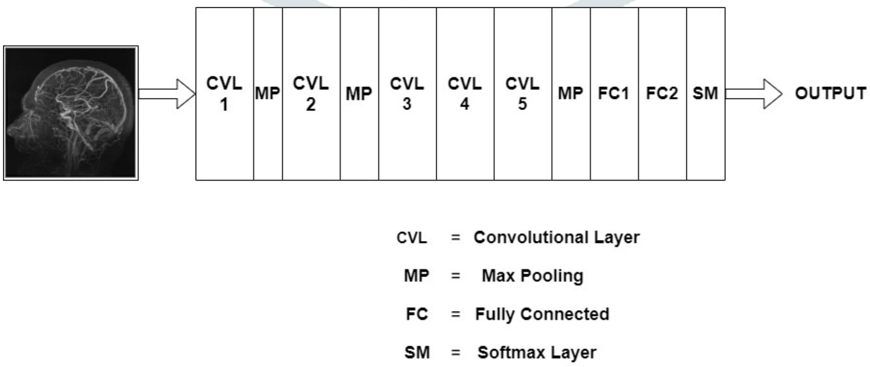
In a different research, Li et al. [32] employed 4D MRI images from the ADNI database for 174 healthy people and 116 patients with Alzheimer's disease. The suggested model was built utilizing two methods: 3D-CNN and Long-Short Term Memory (LSTM). Using 3D convolutional kernels, 3D-CNN was used to extract features from scans, and LSTM was used for the classification job based on the derived features. While 3D CNN could collect spatial information and LSTM could capture time-varying features, the suggested C3d-LSTM model has trained on 4D functional MRI scans without the requirement to slice it into 3D and 2D images. Based on their studies, the model has a high degree of performance with an accuracy of 97.37% and 0.56%.

Recently, Liu et al. [33] utilized MRI scans from the OASIS database for 30 patients with Alzheimer's disease and 332 healthy people. After using resampling methods on the data set, the final version of the data set had scans for 450 Alzheimer's patients and 532 healthy subjects. They also testedtheir model using a number of MRI images from the ADNI database. The suggested model can be separated based on depth. By dividing the convolutional layer into filtering and feature extraction layers, CNN varies from the basic CNN. Along with GoogLeNet and AlexNet [34,35], they also used the fundamental CNN paradigm via transfer learning. According to their tests, transfer learning produced the best results, with GoogleNet achieving an accuracy level of 93.02%.

The findings of earlier research have shown that using deep learning methodologies, which do not need a feature extraction step, is more accurate and efficient than using typical machine learning techniques. Additionally, findings are reliable and efficient because of the large number of images employed in Alzheimer's neuroimaging kinds. However, there is still room for improvement in deep learning methods for managing neuroimaging data, particularly datasets that include numerous frames for each patient, each of which has a unique collection of characteristics that are ultimately related to each other and signify crucial changes.

Additionally, it seems that no study has focused on the use of MRA scans or the cerebral bloodflow biomarker for the categorization of Alzheimer's disease in prior studies. This study is regarded as the first to focus on cerebral blood flow, a new biomarker investigated using MRA scans. Additionally, we develop a novel diagnostic strategy in which the outcomes are confirmed in collaboration with specialists in the field of interventional radiology. This is done by testing the accuracy of the results as necessary to maintain a competitive edge and by drawing conclusions about impaired blood flow and its impact on Alzheimer's patients.

Proposed Alexnet architecture



Alexnet Architecture

One thing to note here, since Alexnet is a deep architecture, the authors introduced padding to prevent the size of the feature maps from reducing drastically. The input to this model is the images of size 227X227X3.

Convolution and Maxpooling Layers

Then we apply the first convolution layer with 96 filters of size 11X11 with stride 4. Theactivation function used in this layer is relu. The output feature map is 55X55X96.

In case, you are unaware of how to calculate the output size of a convolution layerOutput= ((Input-filter size)/ stride) +1

Also, the number of filters becomes the channel in the output feature map.

Next, we have the first Maxpooling layer, of size 3X3 and stride 2. Then we get the resulting feature map with the size 27X27X96.

After this, we apply the second convolution operation. This time the filter size is reduced to 5X5 and we have 256 such filters. The stride is 1 and padding 2. The activation function used is again relu. Now the output size we get is 27X27X256.

Again we applied a max-pooling layer of size 3X3 with stride 2. The resulting feature map is ofshape 13X13X256.

Now we apply the third convolution operation with 384 filters of size 3X3 stride 1 and also padding 1. Again the activation function used is relu. The output feature map is of shape 13X13X384.

Then we have the fourth convolution operation with 384 filters of size 3X3. The stride along with the padding is 1. On top of that activation function used is relu. Now the output size remains unchanged i.e 13X13X384.

After this, we have the final convolution layer of size 3X3 with 256 such filters. The stride and padding are set to one also the activation function is relu. The resulting feature map is of shape 13X13X256.

So if you look at the architecture till now, the number of filters is increasing as we are going deeper. Hence it is extracting more features as we move deeper into the architecture. Also, the filter size is reducing, which means the initial filter was larger and as we go ahead the filter size is decreasing, resulting in a decrease in the feature map shape.

Next, we apply the third max-pooling layer of size 3X3 and stride 2. Resulting in the feature map of the shape 6X6X256.

Fully Connected and Dropout Layers

After this, we have our first dropout layer. The drop-out rate is set to be 0.5.

Then we have the first fully connected layer with a relu activation function. The size of theoutput is 4096. Next comes another dropout layer with the dropout rate fixed at 0.5.

This followed by a second fully connected layer with 4096 neurons and relu activation.

Finally, we have the last fully connected layer or output layer with 1000 neurons as we have 10000 classes in the data set. The activation function used at this layer is Softmax.

This is the architecture of the Alexnet model. It has a total of 62.3 million learnable parameters. AlexNet was the first convolutional network which used GPU to boost performance.

1. AlexNet architecture consists of 5 convolutional layers, 3 max-pooling layers, 2normalization layers, 2 fully connected layers, and 1 softmax layer.
2. Each convolutional layer consists of convolutional filters and a nonlinear activation functionReLU.
3. The pooling layers are used to perform max pooling.
4. Input size is fixed due to the presence of fully connected layers.
5. The input size is mentioned at most of the places as 224x224x3 but due to some padding which happens it works out to be 227x227x3
6. AlexNet overall has 60 million parameters.

Conclusion

Alzheimer's disease is incurable and has a long-term negative impact on the sufferer. It has recently been discovered that the number of Alzheimer's patients is rising. Alzheimer's disease must be identified early to prevent the patient's condition from worsening.This research presented a unique strategy based on a MRA scan.In future work, we want to gather additional data to create a new CNN architecture that produces more accurate findings in addition to doing segmentation studies to support radiologists' treatment plans.

References

1. Salehi, Ahmad Waleed, PreetyBaglat, and Gaurav Gupta. "Alzheimer’s disease diagnosis using deep learning techniques." *Int. J. Eng. Adv. Technol* 9.3 (2020): 874-880.

2. Khojaste-Sarakhsi, M., SeyedhamidrezaShahabiHaghighi, SMT FatemiGhomi, and Elena Marchiori. "Deep learning for Alzheimer's disease diagnosis: A survey." *Artificial Intelligence inMedicine* (2022): 102332.

3. Lin, Eugene, Chieh-Hsin Lin, and Hsien-Yuan Lane. "Deep learning with neuroimaging and genomics in Alzheimer’s disease." *International journal of molecular sciences* 22, no. 15 (2021):7911.

4. Litjens, Geert, ThijsKooi, BabakEhteshamiBejnordi, Arnaud ArindraAdiyosoSetio, Francesco Ciompi, Mohsen Ghafoorian, JeroenAwm Van Der Laak, Bram Van Ginneken, and Clara I. Sánchez. "A survey on deep learning in medical image analysis." *Medical image analysis* 42 (2017): 60-88.

5. Akhtar, Zahid, Gautam Kumar, SambitBakshi, and Hugo Proenca. "Experiments with ocular biometric datasets: a practitioner’s guideline." *IT Professional* 20, no. 3 (2018): 50-63.

6. Ker, Justin, Lipo Wang, Jai Rao, and Tchoyoson Lim. "Deep learning applications in medical image analysis." *Ieee Access* 6 (2017): 9375-9389.

7. Shen, Dinggang, Guorong Wu, and Heung-Il Suk. "Deep learning in medical image analysis." *Annual review of biomedical engineering* 19 (2017): 221-248.

8. Kumar, Gautam, Debbrota Paul Chowdhury, SambitBakshi, and Pankaj Kumar Sa. "Person Authentication Based on Biometric Traits Using Machine Learning Techniques." In *IoT SecurityParadigms and Applications*, pp. 165192. CRC Press, 2020

9. Gao, Linlin, Haiwei Pan, Fujun Liu, XiaoqinXie, Zhiqiang Zhang, Jinming Han, and Alzheimer's Disease Neuroimaging Initiative. "Brain disease diagnosis using deep learning features from longitudinal MR images." In *Asia-Pacific Web (APWeb) and Web-Age Information Management(WAIM) Joint International Conference on Web and Big Data*, pp. 327-339. Springer, Cham, 2018.

10. Garcia-Garcia, Alberto, Sergio Orts-Escolano, SergiuOprea, Victor Villena-Martinez, and Jose Garcia-Rodriguez. "A review on deep learning techniques applied to semantic segmentation." *arXiv preprint arXiv:1704.06857* (2017).

11. Su, Dong, Huan Zhang, Hongge Chen, Jinfeng Yi, Pin-Yu Chen, and YupengGao. "Is Robustness the Cost of Accuracy?--A Comprehensive Study on the Robustness of 18 Deep Image Classification Models." In *Proceedings of the European Conference on Computer Vision (ECCV)*, pp. 631-648. 2018.

12. Hon, Marcia, and NaimulMefraz Khan. "Towards Alzheimer's disease classification through transfer learning." In *2017 IEEE Information Technology (ICRTIT)*, pp. 1-5.

13. Gupta, Ashish, Murat Ayhan, and Anthony Maida. "Natural image bases to represent neuroimaging data." In *International conference on machine learning*, pp. 987-994. PMLR, 2013.

14. Aderghal, Karim, Alexander Khvostikov, Andrei Krylov, Jenny Benois-Pineau, KarimAfdel, and GwenaelleCatheline. "Classificatio of Alzheimer disease on imaging modalities with deep CNNs using cross-modal transfer learning." In *2018 IEEE 31st international symposium on computerbased medical systems (CBMS)*, pp. 345-350. IEEE, 2018.

15. Rathore, S.; Habes, M.; Iftikhar, M.A.; Shacklett, A.; Davatzikos, C. A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease andits prodromal stages. NeuroImage**2017**, 155, 530–548.

16. Samper-González, J.; Burgos, N.; Bottani, S.; Fontanella, S.; Lu, P.; Marcoux, A.; Routier, A.; Guillon, J.; Bacci, M.;Wen, J.; et al. Reproducible evaluation of classification methods in Alzheimer's disease: Framework and application to MRI and PET data. NeuroImage**2018**, 183, 504–521.

17. Lebedev, A.V.;Westman, E.; VanWesten, G.J.P.; Kramberger, M.G.; Lundervold, A.; Aarsland, D.; Soininen, H.; Kłoszewska, I.; Mecocci, P.; Tsolaki, M.; et al. Random Forest ensembles for detection and prediction of Alzheimer's disease with a good between-cohort robustness. NeuroImageClin. **2014**, 6, 115–125.

18. Zhang, Y.; Wang, S. Detection of Alzheimer's disease by displacement field and machine learning. PeerJ**2015**, 3, e1251.

19. Beheshti, I.; Demirel, H.; Farokhian, F.; Yang, C.; Matsuda, H.; Alzheimer's Disease Neuroimaging Initiative. Structural MRI-based detection of Alzheimer's disease using feature ranking and classification error. Comput. Methods Programs Biomed. **2016**, 137, 177–193.

20. Zhang, J.; Liu, M.; An, L.; Gao, Y.; Shen, D. Alzheimer's disease diagnosis using landmark-based features from longitudinal structural MR images. IEEE J. Biomed. Health Inform. **2017**, 21, 1607–1616.

21. Zeng, N.; Qiu, H.; Wang, Z.; Liu, W.; Zhang, H.; Li, Y. A new switching-delayed-PSO-based optimized SVM algorithm for diagnosis of Alzheimer's disease. Neurocomputing**2018**, 320, 195–202.

22. Koh, J.E.W.; Jahmunah, V.; Pham, T.H.; Oh, S.L.; Ciaccio, E.J.; Acharya, U.R.; Yeong, C.H.; Fabell, M.K.M.; Rahmat, K.; Vijayananthan, A.; et al. Automated detection of Alzheimer's disease using bi-directional empirical model decomposition. Pattern Recognit. Lett. **2020**, 135, 106–113.

23. Plis, S.M.; Hjelm, D.R.; Salakhutdinov, R.; Allen, E.A.; Bockholt, H.J.; Long, J.D.; Johnson, H.J.; Paulsen, J.S.; Turner, J.A.; Calhoun, V.D. Deep learning for neuroimaging: A validation study. Front. Neurosci. **2014**, 8, 229.

24. LeCun, Y.; Bengio, Y.; Hinton, G. Deep learning. Nature **2015**, 521, 436–444.

25. Liu, M.; Cheng, D.; Yan, W.; Alzheimer's Disease Neuroimaging Initiative. Classification of Alzheimer's Disease by Combination of Convolutional and Recurrent Neural Networks Using FDG-PET Images. Front. Aging Neurosci. **2018**, 12, 35.

26. Ge, C.; Qu, Q.; Gu, I.Y.-H.; Jakola, A. Multi-stream multi-scale deep convolutional networks for Alzheimer's disease detection using MR images. Neurocomputing**2019**, 350, 60–69.

27. Bonaccorso, G. Machine Learning Algorithms; Packt Publishing Ltd.: Birmingham, UK, 2017.

28. Basaia, S.; Agosta, F.; Wagner, L.; Canu, E.; Magnani, G.; Santangelo, R.; Filippi, M.; Alzheimer's Disease Neuroimaging

Initiative. Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks. NeuroImage: Clin.**2019**, 21, 101645.

29. 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.

30. Feng, W.; Van Halm-Lutterodt, N.; Tang, H.; Mecum, A.; Mesregah, M.; Ma, Y.; Li, H.; Zhang, F.; Wu, Z.; Yao, E.; et al. Automated MRI-Based Deep Learning Model for Detection of Alzheimer's Disease Process. Int. J. Neural Syst. **2020**, 30, 2050032.

31. Li, W.; Lin, X.; Chen, X. Detecting Alzheimer's disease Based on 4D fMRI: An exploration under deep learning framework. Neurocomputing**2020**, 388, 280–287.

32. Liu, J.; Li, M.; Luo, Y.; Yang, S.; Li, W.; Bi, Y. Alzheimer's disease detection using depthwise separable convolutional neural networks. Comput. Methods Programs Biomed. **2021**, 203, 106032.

33. Chollet, F. Xception: Deep learning with depthwise separable convolutions. In Proceedings of theIEEE Conference on Computer Vision and Pattern Recognition, Honolulu, HI, USA, 21–26 July 2017; pp. 1251–1258.

34. Train Your Own Image Classifier with Inception in TensorFlow, Google AI Blog, 09-Mar-2016. Available online: https://ai. googleblog.com/2016/03/train-your-ownimage-classifier-with.html. (accessed on 25 July 2021).