

# Towards Detecting Dementia via Deep Learning

Deepika Bansal, NorthCap University, India

\*Kavita Khanna, NorthCap University, India

Rita Chhikara, NorthCap University, India

Rakesh Kumar Dua, Fortis Hospital, India

Rajeev Malhotra, Max Hospital, India

## ABSTRACT

Dementia is a brain disorder that causes loss of memory leading to disruption in the normal course of life of an individual. It is emerging as a global health problem in adults with age 65 years or above. Early diagnosis of dementia has gone forth as a key research zone with the aim of early identification for hindering the advancement. Deep learning provides path-breaking applications in medical imaging. This study provides a detailed summary of different implementation approaches of deep learning for detecting the disease. Transfer learning for multi-class classification has also been explored for detecting dementia. The pre-trained convolutional network, AlexNet, is used with three optimizers, SGDM, ADAM, RMSProp. A dataset of 60 MRI images is taken from the OASIS dataset. Accuracy of the methods has been compared and the best parameters including classifier, learning rate, and a batch size of the model have been identified. SGDM classifier with a learning rate 10<sup>-4</sup> and a mini-batch size of 10 have shown the best performance in a reasonable time.

## KEYWORDS

Dementia, Machine Learning (ML), Deep Learning (DL), Magnetic Resonance Imaging (MRI), Convolutional Neural Networks (CNN), Alexnet

## 1. INTRODUCTION

Dementia is a neuropsychological disorder that causes loss of memory leading to disability and thus dependency on others for survival. Dementia is commonly found in adults above the age of 60 years. Alzheimer's disease (AD) is a type of dementia, being most prominent in almost 75% of the cases. Different sorts of dementia incorporate Frontotemporal Dementia, Vascular Dementia, Parkinson's disease, Dementia with Lewy Bodies, etc. As indicated by the World Health Organization (WHO), almost 50 million people are experiencing Dementia across the world and about 10 million new cases are expected to emerge every year (Dementia, 2020). The treatment of dementia at an early stage is very important for the social and economic impact of the disease.

Progression of dementia can be determined with a timely diagnosis and neuro-imaging analysis can be substantially helpful in its detection (Altaf et al., 2017). Various machine learning techniques implemented for the detection of the disease have been reviewed by various researchers (Bansal et al. 2018; Mirzaei et al., 2016; Ahmed et al., 2019). The multi-class classification of a subject into

DOI: 10.4018/IJHISI.20211001.0a31

\*Corresponding Author

This article published as an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and production in any medium, provided the author of the original work and original publication source are properly credited.

demented, very mild demented, and normal is the foremost for the diagnosis. But before classification, irrelevant and redundant features are removed through efficient feature selection techniques for achieving a better classification accuracy (Bansal et al., 2018; Bansal et al., 2019; Dallora et al., 2017).

The performance of machine learning approaches is relatively lower with a large amount of data. It can be a challenge for the diagnosis of brain disease. Deep learning approaches can overcome the pitfalls of machine learning approaches. It can also recognize the new features using self-learning of features for the quantitative analysis of MRI. Deep Learning has gained a lot of attention in various medical fields (lin et al., 2016), for example, histopathological disease (Litjens et al., 2016), pulmonary modules (Cheng et al., 2016), and breast lesions (Kooi et al., 2017).

This study would help the researchers to get answers to various research questions listed below pertaining to the implementation of Deep Learning for detecting dementia using MRI images.

RQ1: What are the available pre-trained architectures for Deep learning?

RQ2: What are the various software platforms which can be applied in this area?

RQ3: What kind of preprocessing techniques are necessary for MRI Images?

RQ4: What are the different types of deep learning models used for detecting Dementia?

A comparative analysis of different optimizers and hyperparameters is also presented in this study using transfer-learning. AlexNet architecture is used for tweaking the hyperparameters. Multiclass classification is performed for the detection of dementia using MRI images obtained from the OASIS dataset.

The remaining part of the paper is sorted out as follows: A comprehensive literature survey is given in Section 2. Section 3 outlines the experimental results and analysis, followed by a conclusion of the complete work.

## 2. LITERATURE SURVEY

Deep Learning is contributing a lot in the early detection and restriction of the progression of Dementia (LeCun et al., 2015). A great number of architectures (Ravi et al., 2017) stand out in vogue, among different methodological renditions of deep learning. The Convolutional Neural Network (CNN) (Lecun et al., 1998) is one of the most accepted algorithms utilized for deep learning in medical imaging. The idea of CNN roused from the neurobiological model of the visual cortex (Hubel and Wiesel, 1962). Other credible architectures for Deep Learning incorporate Deep Belief Networks (DBNs) (Hinton et al., 2006), Restricted Boltzmann Machines (RBMs) (Hinton and Sejnowski, 1986), Deep Boltzmann Machines (R. and Hinton, 2009), Deep Autoencoders (Hinton, 2006), and Recurrent Neural Networks (RNNs) (Williams and Zipser, 1989).

### 2.1 Pretrained Architectures

The ImageNet project runs a yearly programming challenge, as the ImageNet Large Scale Visual Recognition Challenge (ILSVRC), in which algorithms wrestle for effectively classifying and detecting objects. The available popular pre-trained CNN networks with their performance in ILSVRC are briefly explained below and summarized in Table 1 (CNN Architectures, 2020).

- LeNet5 is a simple CNN architecture proposed by Yann LeCun (LeCun et al., 1998) in 1998. The number 5 in LeNet5 represents the number of convolutional (2) and fully connected layers (3) used in the architecture. The convolutional layer has 3 parts: convolution, pooling, and non-linear activation functions. The convolution layer is used for extracting the spatial features from the images. A multi-layer perceptron is used in the last layer as a classifier. It has about 60,000

parameters and the activation function used is tanh. The recognition of simple digit images is the most popular application of LeNet.

- AlexNet designed by Alex Krizhensky won the ImageNet challenge in 2012 showing the reduction from 26% to 15.3% in the top-5 error rate (Krizhevsky et al., 2017). The architecture consists of 5 convolution layers and 3 fully connected layers. ReLU activation function was implemented in this architecture for the first time. A few more layers are stacked onto LeNet-5 for the origination of AlexNet. It considers 60 million parameters.
- ZFNet achieved a 14.8% top-5 error rate in the challenge in the year 2013 (Zeiler, & Fergus, 2014). It is similar to the architecture of AlexNet only tweaking the hyper-parameters. It used the small size filters of 7 x 7, to prevent the loss in pixel information. The number of filters keeps on increasing as the network goes deeper. The network is trained using batch stochastic gradient descent and ReLU activation function.
- In 2014, GoogleNet won the ImageNet challenge (Szegedy et al., 2015). A LeNet inspired CNN is used in GoogleNet and a new inception module is also implemented. It used an RMSprop optimizer. The total number of layers is 22. It eliminates all the fully connected layers using average pooling from 7 x 7 x 1024 to 1 x 1 x 1024. The number of parameters is 4 million with a top-5 error rate of 6.67%.
- VGG Net was developed by Simonyan and Zisserman (Simonyan & Zisserman, 2014). It won the ImageNet competition in 2014. The architecture consists of 16 convolutional layers. The filter size of 3 x 3 is used. As compared with AlexNet and ZFNet, VGGNet is also widely used. It consists of 138 million parameters.
- ResNet was developed by Kaimin, which reduced the top-5 error rate to 3.6%, in the year 2015. It consists of 152 layers. The complexity of this architecture is lower than VGGNet. ResNet has residual collections. It introduced “identity shortcut connection” which allows skipping one or more layers (He et al., 2016).

**Table 1. Various pre-trained CNN Architectures**

Year	CNN	No. of Layers	Developer	Place	Parameters	Top-5 error rate
1998	LeNet 5	7	Yann LeCun		60 thousand	-
2012	AlexNet	8	Krizhevsky	1 <sup>st</sup>	60 million	15.3%
2013	ZFNet	8	Matthew Zeiler and Rob Fergus	1 <sup>st</sup>	-	14.8%
2014	GoogleNet	22	Google	1 <sup>st</sup>	4 million	6.67%
2014	VGG Net	16	Simonyan, Zisserman	2 <sup>nd</sup>	138 million	7.3%
2015	Resnet	152	Kaiming He	1 <sup>st</sup>	-	3.6%

## 2.2 Popular Software Packages For Deep Learning Implementation

Deep Learning software packages provide the building blocks to design, train, and validate the deep networks (Comparison of deep-learning software, 2020). A high-level programming interface is used in the available software. A variety of packages depend on GPU-accelerated libraries such as CuDnn and TensorRT for attaining high performance. The details of diverse software packages of deep learning are given below and summarized in Table 2.

- Caffe was created by Yangqing Jia at UC Berkeley during his Ph.D. It is hosted at GitHub and written in C++, with an interface of Python. It provides support for CNN, RCNN, LSTM. Later, Facebook announced Caffe2, which includes RNN as a new feature (Caffe | Deep Learning Framework, 2020).
- The Microsoft Cognitive Toolkit (CNTK) is a toolkit for deep learning which considers networks as a series of computational steps through a directed graph. The users can simply combine DNN, CNN, and RNN using CNTK. It is open-source software (CNTK, 2016).
- Deeplearning4j is the only framework written in Java for Java Virtual Machine. It offers support for various deep learning algorithms such as RBM, DBN, Deep Autoencoder, stacked denoising autoencoder, etc.. Python API is served by Keras. The performance of Deeplearning4j is equal to Caffe on multi-GPUs (Deeplearning4j, 2020).
- Wolfram Mathematica is a computing system conceived by Stephen Wolfram. The language used is Wolfram. It is used in many technical, engineering, scientific, mathematical, and computing fields (Wolfram Mathematica: Modern Technical Computing, 2020).
- TensorFlow is an open-source software library originated by the Google Brain team. It allows users to train machine learning models very easily with high-level APIs (TensorFlow, 2020).
- Theano is a python library and open source project developed at Universite' de Montreal. It is written in Python and CUDA. The computations are expressed using Numpy Syntax. It can be efficiently run on either CPU or GPU architectures (Welcome — Theano 1.0.0 documentation, 2020).
- The Torch is an open-source and scientific computing framework. It is a scripting language based on Lua programming. It also offers various algorithms for deep learning (Torch, 2016).
- Keras is an open-source neural network library. It is written in Python by Francois Chollet. It is proficient in working on top of Theano, TensorFlow, CNTK, R, or PlaidML (Team, 2020).
- Neon is a deep learning framework developed by Nervana Systems of Intel. It supports RNN, GRU, LSTM, BatchNorm layers. It commits for the best performance on all hardware (NervanaSystems/neon, 2020).
- Dlib is open-source software released by Davis E. King. It is written in C++. It provides a variety of tools for dealing with networking, threads, machine learning, and image processing, etc. (King, 2009).
- Matlab is a multi-paradigm numerical computing environment created by Mathworks. It provides a Deep learning toolbox for designing and implementing deep neural networks. The training can be speeded up using GPU architectures (Deep Learning Toolbox, 2020).
- Chainer is a framework for deep learning written in Python. It follows the define-by-run approach (Chainer, 2020).
- Neural Designer is used for data analytics based on neural networks. The graphical user interface makes data entry and interpretation of results easy (Data science and machine learning platform | Neural Designer, 2020).
- OpenNN is written in the C++ language. It is used to implement the main area of deep learning, i.e. neural networks. It is developed by Artenics (OpenNN | Open Neural Networks Library, 2020).
- Apache SINGA is written in C++, Java, and Python. It is developed by Apache Software Foundation. It focusses on health-care applications (Apache SINGA · Distributed deep learning system, 2020).
- Apache MXNet is an open-source framework for deep learning. It is used for training and deploying deep neural networks. It is portable and can scale to multiple GPUs (Apache MXNet, 2020).
- PlaidML is a portable tensor compiler. It supports Keras, ONNX, and nGraph machine learning libraries. It achieves comparable performance without using CUDA or cuDNN (PlaidML - Intel AI, 2020).

- BigDL is created by Jason Dai at Intel. It is a distributed deep learning framework for Apache Spark. It is hosted at GitHub (BigDL, 2020).

### 2.3 MRI Image Preprocessing Software

Several publicly available datasets can be obtained from Open Access Series of Imaging Studies (OASIS) (OASIS Brains, 2007) and Alzheimer's Disease Neuroimaging Initiative (ADNI) (ADNI | About, 2004) which includes both longitudinal (Marcus et al., 2010) and cross-sectional studies (Marcus et al., 2007). ADNI established in 2004 provides us with various types of data being used for the treatment of dementia, for example, clinical data, genetic data, biospecimen data, and few neuroimaging data. The neuroimaging data includes magnetic resonance images (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT) which are being utilized for the detection of diseases (Jack et al., 2008).

MRI is used in the current study, as it distinguishes the healthy and diseased tissue. The complexity of MRI scans is very high since it comprises of a very large number of features. Therefore, MRI preprocessing plays a vital role in medical applications. A variety of software's available for visualization, preprocessing, and analysis of MRI images such as SPM, AFNI, FSL, FreeSurfer, MRICro, BrainVoyager, etc. are described below: (Behroozi & Daliri, 2012; Bernstein et al., 2018). The most commonly used functions for the preprocessing of MRI include Skull-stripping, Bias-correction, Coregistration, Segmentation, Normalization & Smoothing. Table 3 provides a detailed summary of the various software used for processing MRI.

- Statistical Parametric Mapping (SPM) applies brain imaging data sequences for analyzing brain images (SPM - Statistical Parametric Mapping, 2020). It can be used for fMRI, SPECT, PET, EEG, and MEG data. It is the freely available software that implements the theoretical concepts of SPM. The current version is SPM12 which performs temporal and spatial processing (Friston et al., 1994).
- Analysis of Functional Neuro Images (AFNI) was developed by Robert Cox (AFNI, 2020). AFNI is used to process and display the fMRI data. For processing, visualizing, and analyzing the three-dimensional human brain MRI, the software uses the C programs. It is freely available in both source code and binary executable files (Cox, 1996).
- FMRI Software Library (FSL) was written by the Analysis Group (FSL - FslWiki, 2020). It provides the GUI and CLP-based image analysis of fMRI, MRI, and DTI brain images. The installation process of AFNI is very easy. It is available for Windows, Linux, and Apple. The tools available can be executed from the command line and GUIs, both (Smith et al., 2004).
- Free Surfer is an analysis software for MRI and fMRI data (FreeSurfer, 2020). It is used in Linux, macOS, and Windows (via Virtual Box). It is available freely for analysis. It is developed by CorTechs and the Athinoula A. Martinos Center (Fischl et al. 2002). It provides various analysis tools: skull stripping, bias field correction, non-linear registration, measuring cortical thickness, etc.
- MRICro was proposed by Chris Rorden (MRICro, 2000). It is a standalone program for analyzing MRI, fMRI, and PET images. It can be used on Windows and Linux systems (Rorden and Brett, 2000). It provides the only visualization of the fMRI brain images. It can convert images to SPM friendly Analyze format.
- Brain Voyager is a software package for fMRI, EEG, and DTI data (Brain Innovation - Home, 2020). It was developed by Rainer Goebel. It works on Windows, Linux, and Mac OS. It is written in C++ and provides cross-platform usage (Goebel et al., 2006).
- BrainSuite is an open-source software tool for processing MRI (BrainSuite | magnetic resonance image analysis tools, 2020). It provides several tools for data visualization and interaction. The latest version is v.19a. It provides new automated skull-stripping parameter tuning. The source

**Table 2. Popular software packages used for providing the implementation of Deep Learning**

Name	Initial Release	Creator	License	Platform	Interface	Written In	Open Source
Caffe	2013	Berkeley Center	FreeBSD	Windows, Linux, Android, OSX	Python	C++	Yes
CNTK	2016	Microsoft	MIT	Linux, Windows	Command Line	C++	Yes
Deeplearning4j	2014	SkyMind	Apache ver. 2.0	Linux, OSX, Windows, Android	Clojure, Scala, Java	C++, java	Yes
Wolfram Math	1988	Wolfram Research	Proprietary	Linux, OSX, Cloud, Windows	C++, Java	C++, Wolfram Language, CUDA	No
TensorFlow	2015	Google	Apache ver. 2.0	Linux, OSX	Python	C++, Python, Cuda	Yes
Theano	2007	Universite de Montreal	BSD	Cross-platform	Python	Python	Yes
Torch	2002	Ronan Collobert et al.	BSD	Linux, Windows, OSX, Android, iOS	LuaJIT, C, Lua	C, Lua	Yes
Keras	2015	Francois Chollet	MIT License	Linux, Windows, OSX	Python	Python	Yes
Neon	-	Nervana Systems	Apache ver. 2.0	Linux, OSX	Python	Python	Yes
DLib	2002	Davis E. King	Boost	Cross-platform	C++	C++	Yes
Matlab	-	MathWorks	Proprietary	MacOs, Linux, Windows	Graphical User Interface	C++	Yes
Chainer	2015	Preferred Networks	BSD	Linux, MacOS	Python	Python	Yes
Neural Designer	-	Artemics	Proprietary	Linux, MacOS, Windows	Graphical User Interface	C++	No
OpenNN	2003	Artemics	GNU LGPL	Cross-platform	C++	C++	Yes
Apache SINGA	2015	Apache Incubator	Apache 2.0	Linux, macOS, Windows	C++, Java, Python	C++	Yes
Apache MXNet	2015	Apache Software Foundation	Apache 2.0	Linux, macOS, Windows, AWS, JavaScript, Android, iOS	C++, Julia, Python, Matlab, Perl, JavaScript, RScala	Small C++ core library	Yes
PlaidML	2017	Vertex.AI, Intel	AGPL	Linux, macOS, Windows	Python, C++	Python, C++, OpenCL	Yes
BigDL	2016	Jason Dai (Intel)	Apache 2.0	Apache Spark	Scala, Python	Scala	Yes

code is written in C++ and Matlab. The GUI is available for Windows, Linux, and macOS (Shattuck and Leahy, 2002).

- Nilearn is a python module for statistical learning on Neuroimaging data (Nilearn: Machine learning for NeuroImaging in Python — Machine learning for NeuroImaging, 2020). It performs multivariate statistics. It supports the general linear model (GLM) based analysis. It uses the scikit-learn Python toolbox (Abraham et al., 2014).
- Multi-Image Analysis GUI performs analysis and navigates through image volumes (Research Imaging Institute — Mango, 2020). It has three versions, different for each platform – Mango (Desktop), Papaya (Browser), and iMango (Mobile). It performs ROI editing, Surface Rendering, Image registration, Image Stacking, Analysis, and Processing of brain images (Kochunov et al., 2002).

**Table 3. Detailed summary of the most popular & conventional software**

Software	Year	Developed By	Citation (till 17 Jan 2020)	Operating System	Base language	G U I	Source Code Availability	Functionality
SPM	Late 1980s	Karl Friston	9738	Linux, Windows	Matlab	Yes	Yes	Visualization, Preprocessing Analysis
AFNI	Mid-1990s	Robert Cox	7842	Unix, Linux	C	Yes	Yes	Visualization, Preprocessing Analysis
FSL	2000	Analysis Group	9150	Linux, Windows	C++	Yes	Yes	Visualization, Preprocessing Analysis
FreeSurfer	-	Bruce Fischl	5420	Linux, Mac, Windows	Stand-alone	Yes	Yes	Visualization, Preprocessing Analysis
MRICro	2000	Chris Rorden	1979	Windows, Linux, Solaris	Stand-alone	Yes	Yes	Preprocessing Analysis
Brain Voyager	1996	Rainer Goebel	921	Windows, Linux, Ubuntu, Mac	C++	Yes	No	Visualization, Analysis
BrainSuite	2001	Shattuck Group & Leahy Group	695	Windows, Linux, Mac	C++, Matlab	Yes	Yes	Preprocessing Analysis, Visualization
Nilearn	2014	INRIA	368	Windows	Python	No	Yes	Preprocessing Analysis
Mango	2002	Jack L. Lancaster, and Michael J. Martinez	150	Linux, Mac OS, and Microsoft Windows	Java	Yes	Yes	Preprocessing Analysis, Visualization

## 2.4 Deep Learning Implementation for Detecting Dementia

A concise summary of varying deep learning approaches for the identification of dementia is presented and summarized in Table 4. Brosch et al. (2013) performed the learning of manifold for 300 MRI brain images taken from the ADNI dataset using deep belief networks. The skull-stripping, bias field correction, and registration of images were done and a high classification accuracy with a p-value of  $8.24 \times 10^{-9}$  was obtained. Suk et al. (2013) presented a multi-model data fusion deep learning feature representation using stacked auto-encoder with MRI, PET, and CSF image modalities. The three-way classification was performed using 202 subjects. The segmentation was performed to obtain gray matter, white matter, and CSF images. High classification accuracy of 95.8% (for AD), 85.0% (for MCI) and 75.8% (for MCI-converter) was obtained. Liu et al. (2014) presented an early diagnosis of AD using Deep Learning feature selection with Elastic Net. The architecture contains a stacked autoencoder and softmax output layer and the results are compared with single-kernel SVM and multi-kernel SVM. An accuracy of 87.76% was obtained using the proposed method for the classification of AD and normal.

Payan et al. (2015) predicted AD with CNN using auto-encoder where preprocessing of MR images is done using SPM. The ICBM template registration was performed and a sparse auto-encoder was used for both 2D and 3D images. It had been observed that the performance of the model was better with 3D images for all the experiments. The accuracy obtained was 89.47% for 3-way classification and 95.39% for 2-way classification of AD vs HC. Hosseini et al. (2016) successfully predicted AD by extracting brain features using a 3D auto-encoder. The preprocessing of the brain images was done using SPM. The ADNI dataset of 210 subjects was used, of which 30 images are considered for validation. The accuracy of 94.2% was obtained and compared with previous models. Sarraf et al. (2016) successfully classified fMRI data of AD from normal controls reaching an accuracy of 96.85%. The motion correction is performed for preprocessing using MCFLIRT. CNN and LeNet-5

are used with no. of epochs 30, batch size 64, learning rate 0.01 which drops initially after each 10th epoch. Ortiz et al. (2016) explored the deep learning-based classification method applicable for brain regions which are defined by Automated Anatomical Labelling (AAL) using Deep Belief Networks (DBN) as feature extractors obtaining the best classification outcomes. The spatial normalization of 275 brain MRIs obtained from ADNI was performed using PET and VBM-T1 templates. The accuracy of 90% is obtained using the hybrid model. In (Sarraf & Tofighi, 2016), the author extracted the shift and scale-invariant features using CNN from fMRI of 43 patients. The data were preprocessed using the FMRIB Software Library. The preprocessing steps were motion correction, skull stripping, and spatial smoothing. The LeNet-5 was trained for 126990 iterations, with 30 epochs, 64 batch size. The accuracy obtained was 96.85%.

Saman Saraf et al. (2016) considered MRI and fMRI images from the ADNI dataset for distinguishing the Alzheimer's brain and normal subjects using Deep CNN adopting LeNet and GoogleNet. The preprocessing of the datasets is done with the help of Brain Extraction Tool FSL-BET (Smith, 2002) and FSL-VBM (Douaud et al., 2007) library. Both the models are initialized with 30 epochs with Stochastic Gradient Descent base learning rate 0.01,  $\gamma = 0.1$ , momentum = 0.9, weight decay 0.0005. GoogleNet showed slightly better accuracies than LeNet, 99.9% for fMRI data, and 98.84% for MRI data. A 4-way classification using DCNN with 3 frameworks of CNN namely, GoogleNet, ResNet18, and Resnet 152, was proposed adopting 100 epochs Xavier initialization of weights (Farooq et al. 2017). The accuracies obtained with GoogleNet- 98.88%, ResNet18- 98.01% and ResNet152- 98.14%. The SPM-8 tool was used for preprocessing 149 subjects and the main steps are skull stripping, gray matter segmentation, bias correction, and modulation. The detection of dementia and the classification of MRI with deep neural networks and transfer learning was performed by the author (Bidani et al. 2019). The OASIS dataset of 416 subjects was used and the images were resized using interpolation. An accuracy greater than 80% was achieved. The 2D CNN with ResNet-18 was used for diagnosis and classification of different AD stages by Ramzan et al. (2020). The dataset of 138 fMRI subjects from ADNI was used. The brain extraction, motion correction, intensity normalization, image registration was used for preprocessing the images. An accuracy of 97.88% was acquired.

Maqsood et al. (2019) proposed a system using transfer learning. The fine-tuned AlexNet was used for the study. The images were obtained from the OASIS dataset and segmented into gray matter, white matter, and cerebrospinal fluid. The experiment was conducted using both segmented and non-segmented images. The results showed an overall accuracy of 92.85% for the classification of unsegmented images. Gorji et al. (2019) used the approach of deep learning for distinguishing between MCI and healthy subjects. A network with 3 convolutional layers and 1 fully connected layer was used. The dataset of 600 subjects was collected from ADNI in three categories normal, EMCI, and LMCI. The best accuracy of 94.54% was obtained for the classification of CN and LMCI. Jiang et al. (2020) classified the early MCI from normal subjects using the VGG-16 network for transfer learning, along with Lasso, for feature selection and SVM for classification. The ADNI dataset of 120 subjects was skull-stripped, normalized, and registered for processing. The 3D images were converted to 2D and only 32 slices are retained for the experiment. The ratio of 8:2 was used and an accuracy of 89.40% was obtained. The author used structured MRI images from OASIS and MIRIAD dataset for the diagnosis of AD (YİĞİT and IŞIK, 2020). The images were skull-stripped, augmented, resized and only 10 slices were retained for processing. The three models of CNN were observed by tweaking the number of layers. The best accuracy of 82% was observed with a 0.0002 learning rate. Castro et al. (2020) compared two datasets for the diagnosis of AD. The 1743 images from ADNI and 416 images from the OASIS dataset were considered. The data was augmented for processing. Resnet was used for extracting the features and SVM for classification of sagittal MRI. The age and sex of the patient were added after the 47<sup>th</sup> layer for further classification. The accuracy of 86.81% was achieved with the OASIS dataset and 76.84% from ADNI data.



### 3. EXPERIMENTAL RESULTS AND ANALYSIS

#### 3.1 Dataset

The publicly available OASIS dataset of magnetic resonance images is used in this work. It includes two types of data – cross-sectional and longitudinal. This study prefers the cross-sectional dataset as we do not require the dataset acquired over a long period for this study. The dataset of 60 subjects aged between 18 to 96 years is used, including (20 normal, 20 AD, and 20 MCI). A sample of demented, normal, and mild cognitive impaired MRI is shown in Fig. 1.

#### 3.2 Image Preprocessing

Preprocessing plays an important role in MRI images due to their high complexity. The dataset includes segmented images from which facial features are removed using the Brain Extraction Tool (fMRIDC, 2020). The MRICro software is used for converting 3D images into 2D images (MRICro | CRNL, 2020). The middle 50 slices out of 176 slices are extracted. The images are converted into RGB format and resized to 227 x 227. A total of 3000 images are used for implementation.

#### 3.3 Training Network and Fine-Tuning

AlexNet is used for transfer learning which is trained for 1000 classes on the ImageNet dataset. For training the pre-trained model, CNN layers are fine-tuned according to the dataset used. The high-level features of the network are changed by configuring the three fully connected layers available at the end of the network. The proposed method was trained using three optimizers, namely, stochastic gradient descent with momentum (SGDM), adaptive moment estimation (ADAM), and RMSprop (root mean square propagation). The loss function is minimized and bias and weight parameters are adjusted using the optimization algorithms. SGDM is SGD with momentum, incorporating the past gradients for each dimension (Qian, 1999) (Sutskever et al. 2013). It develops the high “velocity” having a consistent gradient. RMSprop uses a learning rate and the gradient is accumulated as an exponentially decaying average of squared gradients (Hinton et al. 2012). ADAM utilizes the first and second moments for computing the adaptive learning rates for each parameter (Kingma et al. 2014). The Mini Batch Size, Learning Rate, Verbose, Epochs, Validation Frequency are included in the options for training. The bias learn factor and weight learn factor is considered as 20 each. For training the network, a mini-batch size of 10 and a learning rate of  $10^{-4}$  is used. The maximum no. of iterations is 840, forming 210 iterations per epoch. The total no. of epochs used is 4.

#### 3.4 Classification Results

The network is trained for multi-class classification of Normal, Demented, and Mild cognitive impaired subjects. The training and validation ratio is 7:3. Classification accuracy and duration of the experiment is considered as the evaluation metrics. Alexnet is trained for three optimizers SGDM, ADAM, and RMSProp, using a learning rate of 0.0001 and a mini-batch size of 10. For validation, we tweaked the parameters, learning rate, and mini-batch size. The learning rates of 0.01, 0.001, 0.0001, and mini-batch sizes of 10, 20, 30 are considered. A learning rate of 0.0001 and a mini-batch size of 10 have been found as optimal for the trained network. The training and validation ratio is 7:3. The best classification accuracy of 81.89% is obtained using the SGDM classifier in 18 min 32 seconds. The accuracy obtained using ADAM is 78.11% in 20 min 18 seconds and 64.56% for RMSProp in 7 min 45 seconds.

**Table 4. Survey of Deep Learning Techniques used for the Detection of Dementia**

Ref.	Year	Image Modality	Dataset	No. of Subjects	Preprocessing	Technique	Accuracy
(Brosch et al. 2013)	2013	MRI	ADNI	300 subjects	Skull-stripped, Bias field corrected, registration	Deep belief networks or Conv RBMs	p-value = $8.24 \times 10^{-9}$
(Suk & Shen, 2013)	2013	MRI, PET, CSF	ADNI	51 AD, 99 MCI 52 healthy	AC-PC, skull-stripping, segmentation into GM, WM, and CSF	Stacked Auto encoder	95.9%, 85.0%, and 75.8% accuracy for AD, MCI, and MCI-converter.
(Liu et al. 2014)	2014	MRI	ADNI	311 subjects	Registration to ICBM_152 Grey matter extraction.	Deep learning using Elastic Net	83.75%
(Payan & Montana, 2015)	2015	MRI	ADNI	755 patients	Normalize to ICBM template.	CNN Auto Encoders	89.47%
(Hosseini et al. 2016)	2016	sMRI	ADNI	210 subjects	Extracted Brain features using conventional 3D autoencoder	Deep 3D-CNN	94.8%
(Sarraf & Tofighi, 2016)	2016	fMRI	ADNI	28 AD 15 NC	Motion correction (MCFLIRT),	CNN and LeNet-5	96.85%
(Ortiz et al., 2016)	2016	MRI	ADNI	68 NC, 111 MCI, 70 AD, and 26 Late MCI	Spatial normalization with PET and VBM-T1 templates.	Deep Belief Network as feature extractors	90%
(Sarraf & Tofighi, 2016)	2016	fMRI	ADNI	300 subjects	Motion correction, skull stripping, and spatial smoothing registered to the MNI152	CNN with LeNet	96.85%
(Sarraf & Tofighi, 2016)	2016	MRI, fMRI	ADNI	144 fMRI 302 MRI	ICBM 152 template registration	Adopted LeNet and GoogleNet	98.84%
(Farooq et al. 2017)	2017	MRI	ADNI	33 AD, 22 LMCI, 49 MCI, 45 healthy	Skull stripping, gray matter segmentation, bias correction, modulation using SPM - 8 tool.	4-way classification using DCNN with 3 frameworks	98.88% GoogleNet
(Bidani et al. 2019)	2019	MRI	OASIS	416 subjects	Resizing using Interpolation	DCNN and Transfer Learning	Accuracy >80%.
(Ramzan et al. 2020)	2019	fMRI	ADNI	138 subjects	Brain extraction, Motion Correction, Intensity Normalization, Image Registration	2D CNN, ResNet-18, Transfer Learning	97.88%
(Maqsood et al., 2019)	2019	MRI	OASIS	382 subjects	Segmentation	Transfer Learning	92.85%
(Gorji and Kaabouch, 2019)	2019	MRI	ADNI	200 Normal, 200 EMCI, 200 LMCI	Segmentation, Normalization, Smoothing	Variant of CNN	CN and LMCI - 94.54% 93.96% and 93.00% for EMCI/LMCI and CN/EMCI
(Jiang et al., 2020)	2020	MRI	ADNI	70 EMCI, 50 Normal	Skull-stripping, Normalization, Registration	Transfer Learning Using VGG-16	89.4%
(YİĞİT and İŞİK, 2020)	2020	MRI	OASIS + MIRIAD	416 OASIS, 69 MIRIAD	Skull-stripping, augmentation, contrast enhancement	Variants of CNN	82%
(Castro et al. 2020)	2020	MRI	OASIS, ADNI	1743 ADNI, 416 OASIS	Augmentation	ResNet + SVM	86.81% - Oasis 78.64% - ADNI

Figure 1. Sample MRI (a) Normal, (b) Demented and (c) Mild cognitive Impaired

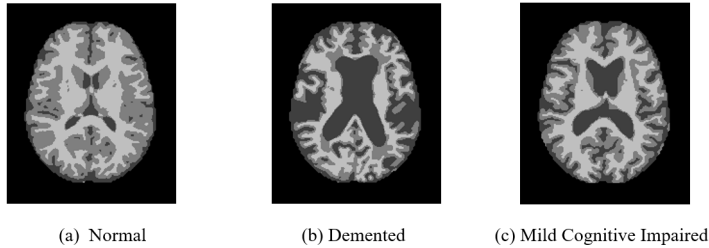


Table 5. Clinical brain MRI dataset

Image Class	# MRI slices
Normal	20 (subjects) x 50 slices = 1000 slices
Demented	20 (subjects) x 50 slices = 1000 slices
Mild Cognitive Impaired	20 (subjects) x 50 slices = 1000 slices
Total	3,000 slices

Table 6. Comparative Analysis of the Optimizers for Transfer Learning using AlexNet

Optimizer	Accuracy	Duration
SGDM	81.89%	18 min 32 sec
ADAM	78.11%	20 min 18 sec
RMSProp	64.56%	7 min 45 sec

## CONCLUSION

Dementia is a brain disorder, where the early detection of the disease is a challenging task. For the same purpose, deep learning has captivated a great consideration in recent years. This paper starts with the basic concepts including the definition of Dementia, its types, and prevalence, followed by the available datasets for the disease and related biomarkers, for example, MRI, fMRI, PET, etc. It is highly recommended that the combination of these neuroimaging modalities along with neuropsychological tests can help us to convey a more promising diagnosis. Considerably more research is required with the combination of modalities for finding the multi-modal biomarkers.

Further, an introduction of Deep Learning is discussed with various architectures, and listed research questions are addressed in various subsections. Various available architectures for deep learning and popular software packages for preprocessing and implementing deep learning are explored and it has been observed that SPM is the most widely used preprocessing software over the various studies. In terms of preprocessing, skull stripping, normalization, and image registration to a template are recommended. A detailed literature survey of various deep learning techniques used for the detection of dementia has been presented with a comparison of the existing techniques over various image modalities, data sets, and preprocessing techniques used. A comparative analysis using three optimizers, SGDM, ADAM, and RMSProp has been performed. The two hyperparameters,

learning rate and mini-batch size of AlexNet architecture are tweaked for validating the accuracy obtained with multiclass classification.

To conclude, this study provides a complete framework of the detection of dementia with varied aspects catering to its diagnosis and thus can form a base for the future researchers in the field.

## **ACKNOWLEDGMENT**

The research was funded by the Department of Science and Technology DST, New Delhi, Reference number DST/CSRI/2017/215 (G).

## REFERENCES

- Abraham, A., Pedregosa, F., Eickenberg, M., Gervais, P., Mueller, A., Kossaifi, J., Gramfort, A., Thirion, B., & Varoquaux, G. (2014). Machine learning for neuroimaging with scikit-learn. *Frontiers in Neuroinformatics*, 8. PMID:24600388
- ADNI | About. (2004). <http://adni.loni.usc.edu/about/>
- Afni. (2020). Available at: <https://afni.nimh.nih.gov/afni/>
- Ahmed, M. R., Zhang, Y., Feng, Z., Lo, B., Inan, O. T., & Liao, H. (2018). Neuroimaging and machine learning for dementia diagnosis: Recent advancements and future prospects. *IEEE Reviews in Biomedical Engineering*, 12, 19–33. doi:10.1109/RBME.2018.2886237 PMID:30561351
- Altaf, T., Anwar, S., Gul, N., Majeed, N., & Majid, M. (2017). Multi-class Alzheimer disease classification using hybrid features. *Proceedings of the Future Technologies Conference (FTC)*.
- Apache MXNet. (2020). Available at: <https://mxnet.incubator.apache.org/>
- Bansal, D., Chhikara, R., Khanna, K., & Gupta, P. (2018). Comparative analysis of various machine learning algorithms for detecting dementia. *Procedia Computer Science*, 132, 1497–1502. doi:10.1016/j.procs.2018.05.102
- Bansal, D., Khanna, K., Chhikara, R., Dua, R., & Malhotra, R. (2019). Analysis of Classification & Feature Selection Techniques for Detecting Dementia. *SSRN Electronic Journal*. 10.2139/ssrn.3356886
- Bansal, D., Khanna, K., Chhikara, R., Dua, R. K., & Malhotra, R. (2019, October). A study on dementia using machine learning techniques. In *Communication and Computing Systems: Proceedings of the 2nd International Conference on Communication and Computing Systems (ICCCS 2018), December 1-2, 2018, Gurgaon, India* (p. 414). CRC Press.
- Behroozi, M., & Daliri, M. R. (2012). Software tools for th analysis of functional magnetic resonance imaging. *Basic and Clinical Neuroscience*, 3(5), 71–83.
- Bernstein, A., Akzhigitov, R., Kondrateva, E., Sushchinskaya, S., Samotaeva, I., & Gaskin, V. (2018). MRI brain imagery processing software in data analysis. *Trans. Mass-Data Analysis of Images and Signals*, 9(1), 3–17.
- Bidani, A., Gouider, M. S., & Travieso-González, C. M. (2019, June). Dementia Detection and Classification from MRI Images Using Deep Neural Networks and Transfer Learning. In *International Work-Conference on Artificial Neural Networks* (pp. 925–933). Springer. doi:10.1007/978-3-030-20521-8\_75
- Bigdl. (2020). <https://software.intel.com/en-us/frameworks/bigdl>
- Brain Innovation. (2020). *Brain Innovation - Home*. Available at: <http://www.brainvoyager.com/>
- Brainsuite.org. (2020). *Brainsuite | Magnetic Resonance Image Analysis Tools*. Available at: <http://brainsuite.org/>
- Brosch, T., & Tam, R. Alzheimer's Disease Neuroimaging Initiative. (2013, September). Manifold learning of brain MRIs by deep learning. In *International Conference on Medical Image Computing and Computer-Assisted Intervention* (pp. 633–640). Springer. doi:10.1007/978-3-642-40763-5\_78
- Caffe. (2020). *Deep Learning Framework*. <http://caffe.berkeleyvision.org/>
- Castro, A. P., Fernandez-Blanco, E., Pazos, A., & Munteanu, C. R. (2020). Automatic assessment of Alzheimer's disease diagnosis based on deep learning techniques. *Computers in Biology and Medicine*, 120, 103764. doi:10.1016/j.compbiomed.2020.103764 PMID:32421658
- Chainer. (2020). <https://chainer.org/>
- Cheng, J., Ni, D., Chou, Y., Qin, J., Tiu, C., Chang, Y., Huang, C., Shen, D., & Chen, C. (2016). Computer-Aided Diagnosis with Deep Learning Architecture: Applications to Breast Lesions in US Images and Pulmonary Nodules in CT Scans. *Scientific Reports*, 6(1), 24454. doi:10.1038/srep24454 PMID:27079888
- CNTK. Build software better, together. (2016). *GitHub*. <https://github.com/Microsoft/CNTK>
- Comparison Of Deep-Learning Software. (2020). Available at: [https://en.wikipedia.org/wiki/Comparison\\_of\\_deep-learning\\_software](https://en.wikipedia.org/wiki/Comparison_of_deep-learning_software)

- Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, 29(3), 162–173. doi:10.1006/cbmr.1996.0014 PMID:8812068
- Dallora, A., Eivazzadeh, S., Mendes, E., Berglund, J., & Anderberg, P. (2017). Machine learning and microsimulation techniques on the prognosis of dementia: A systematic literature review. *PLoS One*, 12(6), e0179804. doi:10.1371/journal.pone.0179804 PMID:28662070
- Deep Learning Toolbox. (2020). <https://in.mathworks.com/products/deep-learning.html>
- Deeplearning4j.org. (2020). *Deeplearning4j*. Available at: <https://deeplearning4j.org/>
- Douaud, G., Smith, S., Jenkinson, M., Behrens, T., Johansen-Berg, H., Vickers, J., James, S., Voets, N., Watkins, K., Matthews, P. M., & James, A. (2007). Anatomically related grey and white matter abnormalities in adolescent-onset schizophrenia. *Brain*, 130(9), 2375–2386. doi:10.1093/brain/awm184 PMID:17698497
- Farooq, A., Anwar, S., Awais, M., & Rehman, S. (2017, October). A deep CNN based multi-class classification of Alzheimer's disease using MRI. In *2017 IEEE International Conference on Imaging systems and techniques (IST)* (pp. 1-6). IEEE. doi:10.1109/IST.2017.8261460
- Fischl, B., Salat, D. H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., & Montillo, A. et al. (2002). Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain. *Neuron*, 33(3), 341–355. doi:10.1016/S0896-6273(02)00569-X PMID:11832223
- fMRIDC.org. (2020). Available at: <http://www.fmridc.org>
- Freesurfer. (2020). <https://surfer.nmr.mgh.harvard.edu/>
- Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., & Frackowiak, R. S. (1994). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping*, 2(4), 189–210.
- Fsl. (2020). *FSL - Fslwiki*. <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>
- Goebel, R., Esposito, F., & Formisano, E. (2006). Analysis of functional image analysis contest (FIAC) data with brainvoyager QX: From single-subject to cortically aligned group general linear model analysis and self-organizing group independent component analysis. *Human Brain Mapping*, 27(5), 392–401.
- He, K., Zhang, X., Ren, S., & Sun, J. (2016). Deep residual learning for image recognition. In *Proceedings of the IEEE conference on computer vision and pattern recognition* (pp. 770-778). Academic Press.
- Hinton, G. (2006). Reducing the Dimensionality of Data with Neural Networks. *Science*, 313(5786), 504–507.
- Hinton, G., Osindero, S., & Teh, Y. (2006). A Fast Learning Algorithm for Deep Belief Nets. *Neural Computation*, 18(7), 1527–1554.
- Hinton, G., & Sejnowski, T. (1986). Learning and relearning in Boltzmann machines. *Parallel distributed processing: Explorations in the microstructure of cognition*, 1(2), 282-317.
- Hinton, G., Srivastava, N., & Swersky, K. (2012). Neural networks for machine learning. *Coursera, Video Lectures*, 264(1).
- Hosseini-Asl, E., Gimel'farb, G., & El-Baz, A. (2016). *Alzheimer's disease diagnostics by a deeply supervised adaptable 3D convolutional network*. arXiv preprint arXiv:1607.00556.
- Hubel, D., & Wiesel, T. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *The Journal of Physiology*, 160(1), 106–154.
- Jack, C. R. Jr, Bernstein, M. A., Fox, N. C., Thompson, P., Alexander, G., Harvey, D., & Dale, A. M. et al. (2008). The Alzheimer's disease neuroimaging initiative (ADNI): MRI methods. *Journal of Magnetic Resonance Imaging: An Official Journal of the International Society for Magnetic Resonance in Medicine*, 27(4), 685–691.
- Jiang, J., Kang, L., Huang, J., & Zhang, T. (2020). Deep Learning based Mild Cognitive Impairment Diagnosis Using Structure MR Images. *Neuroscience Letters*, 134971.
- King, D. E. (2009). Dlib-ml: A Machine Learning Toolkit. *J. Mach. Learn. Res.*, 10(Jul), 1755–1758.

- Kingma, D. P., & Ba, J. (2014). *Adam: A method for stochastic optimization*. arXiv preprint arXiv:1412.6980.
- Kochunov, P., Lancaster, J., Thompson, P., Toga, A., Brewer, P., Hardies, J., & Fox, P. (2002). An Optimized Individual Target Brain in the Talairach Coordinate System. *NeuroImage*, 17(2), 922–927.
- Kooi, T., Litjens, G., van Ginneken, B., Gubern-Mérida, A., Sánchez, C., Mann, R., den Heeten, A., & Karssemeijer, N. (2017). Large scale deep learning for computer aided detection of mammographic lesions. *Medical Image Analysis*, 35, 303–312.
- Krizhevsky, A., Sutskever, I., & Hinton, G. E. (2017). ImageNet classification with deep convolutional neural networks. *Communications of the ACM*, 60(6), 84–90.
- LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature*, 521(7553), 436–444.
- Lecun, Y., Bottou, L., Bengio, Y., & Haffner, P. (1998). Gradient-based learning applied to document recognition. *Proceedings of the IEEE*, 86(11), 2278–2324.
- Lin, D., Vasilakos, A., Tang, Y., & Yao, Y. (2016). Neural networks for computer-aided diagnosis in medicine: A review. *Neurocomputing*, 216, 700–708.
- Litjens, G., Sánchez, C., Timofeeva, N., Hermesen, M., Nagtegaal, I., & Kovacs, I. (2016). Deep learning as a tool for increased accuracy and efficiency of histopathological diagnosis. *Scientific Reports*, 6(1).
- Liu, S., Liu, S., Cai, W., Pujol, S., Kikinis, R., & Feng, D. (2014, April). Early diagnosis of Alzheimer's disease with deep learning. In *2014 IEEE 11th international symposium on biomedical imaging (ISBI)* (pp. 1015–1018). IEEE.
- Maqsood, M., Nazir, F., Khan, U., Aadil, F., Jamal, H., Mehmood, I., & Song, O. Y. (2019). Transfer learning assisted classification and detection of Alzheimer's disease stages using 3D MRI scans. *Sensors (Basel)*, 19(11), 2645.
- Marcus, D. S., Fotenos, A. F., Csernansky, J. G., Morris, J. C., & Buckner, R. L. (2010). Open access series of imaging studies: Longitudinal MRI data in nondemented and demented older adults. *Journal of Cognitive Neuroscience*, 22(12), 2677–2684.
- Marcus, D. S., Wang, T. H., Parker, J., Csernansky, J. G., Morris, J. C., & Buckner, R. L. (2007). Open Access Series of Imaging Studies (OASIS): Cross-sectional MRI data in young, middle aged, nondemented, and demented older adults. *Journal of Cognitive Neuroscience*, 19(9), 1498–1507.
- Medium. (2020). *CNN Architectures: Lenet, Alexnet, VGG, Googlenet, Resnet And More*. Available at: <https://medium.com/analytics-vidhya/cnns-architectures-lenet-alexnet-vgg-googlenet-resnet-and-more-666091488df5>
- Mirzaei, G., Adeli, A., & Adeli, H. (2016). Imaging and machine learning techniques for diagnosis of Alzheimer's disease. *Reviews in the Neurosciences*, 27(8), 857–870.
- MRicro. (2000). Available at: <http://www.cabiatl.com/mricro/mricro/mricro.html>
- Mricro | CRNL. (2020). <https://www.mccauslandcenter.sc.edu/crnl/mricro>
- Nervanasystems/Neon. Github. (2020). Available at: <https://github.com/NervanaSystems/neon>
- Neuraldesigner.com. (2020). *Data Science And Machine Learning Platform | Neural Designer*. Available at: <https://www.neuraldesigner.com/>
- Nilearn.github.io. (2020). *Nilearn: Machine Learning For Neuroimaging In Python — Machine Learning For Neuroimaging*. <http://nilearn.github.io/>
- OASIS Brains - Open Access Series of Imaging Studies. (2007). *Oasis-Brains*. <https://www.oasis-brains.org/>
- Opennn.net. (2020). *Opennn | Open Neural Networks Library*. <https://www.opennn.net/>
- Ortiz, A., Munilla, J., Gorriz, J. M., & Ramirez, J. (2016). Ensembles of deep learning architectures for the early diagnosis of the Alzheimer's disease. *International Journal of Neural Systems*, 26(07), 1650025.
- Payan, A., & Montana, G. (2015). *Predicting Alzheimer's disease: a neuroimaging study with 3D convolutional neural networks*. arXiv preprint arXiv:1502.02506.

- Plaidml - Intel AI. (2020) <https://www.intel.ai/plaidml/#gs.58mt3t>
- Qian, N. (1999). On the momentum term in gradient descent learning algorithms. *Neural Networks*, 12(1), 145–151.
- R., S., & Hinton, G. (2009). Deep boltzmann machines. *Proc. Int. Conf. Artif. Intell. Stat.*, 1(3).
- Ramzan, F., Khan, M. U. G., Rehmat, A., Iqbal, S., Saba, T., Rehman, A., & Mehmood, Z. (2020). A Deep Learning Approach for Automated Diagnosis and Multi-Class Classification of Alzheimer's Disease Stages Using Resting-State fMRI and Residual Neural Networks. *Journal of Medical Systems*, 44(2), 37.
- Ravi, D., Wong, C., Deligianni, F., Berthelot, M., Andreu-Perez, J., Lo, B., & Yang, G. (2017). Deep Learning for Health Informatics. *IEEE Journal of Biomedical and Health Informatics*, 21(1), 4–21.
- Research Imaging Institute — Mango. (2020). <http://ric.uthscsa.edu/mango/>
- Rorden, C., & Brett, M. (2000). Stereotaxic Display of Brain Lesions. *Behavioural Neurology*, 12(4), 191–200.
- Sarraf, S., & Tofighi, G. (2016). *Classification of alzheimer's disease using fmri data and deep learning convolutional neural networks*. arXiv preprint arXiv:1603.08631.
- Sarraf, S., & Tofighi, G. (2016). DeepAD: Alzheimer's disease classification via deep convolutional neural networks using MRI and fMRI. *bioRxiv*, 070441.
- Sarraf, S., & Tofighi, G. (2016, December). Deep learning-based pipeline to recognize Alzheimer's disease using fMRI data. In *2016 Future Technologies Conference (FTC)* (pp. 816-820). IEEE.
- Shattuck, D., & Leahy, R. (2002). BrainSuite: An automated cortical surface identification tool. *Medical Image Analysis*, 6(2), 129–142.
- Simonyan, K., & Zisserman, A. (2014). *Very deep convolutional networks for large-scale image recognition*. arXiv preprint arXiv:1409.1556.
- Singa. (2020). *Apache SINGA · Distributed Deep Learning System*. Available at: <https://singa.incubator.apache.org/>
- Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping*, 17(3), 143–155.
- Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E., Johansen-Berg, H., & Niazy, R. K. et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage*, 23, S208–S219.
- SPM - Statistical Parametric Mapping. (2020). Available at: <https://www.fil.ion.ucl.ac.uk/spm/>
- Suk, H. I., & Shen, D. (2013, September). Deep learning-based feature representation for AD/MCI classification. In *International Conference on Medical Image Computing and Computer-Assisted Intervention* (pp. 583-590). Springer.
- Sutskever, I., Martens, J., Dahl, G., & Hinton, G. (2013, February). On the importance of initialization and momentum in deep learning. In *International conference on machine learning* (pp. 1139-1147). Academic Press.
- Szegedy, C. (Ed.). (2015). *Going deeper with convolutions Proceedings of the IEEE conference on computer vision and pattern recognition*. IEEE.
- Taheri Gorji, H., & Kaabouch, N. (2019). A deep learning approach for diagnosis of mild cognitive impairment based on mri images. *Brain Sciences*, 9(9), 217.
- Team, K. (2020). *Keras: The Python Deep Learning API*. Available at: <https://keras.io/>
- TensorFlow. (2020). <https://www.tensorflow.org/>
- Torch. (2016). <http://torch.ch/>
- Welcome — Theano 1.0.0 Documentation. (2020). <http://deeplearning.net/software/theano/>
- Who.int. (2020). *Dementia*. <https://www.who.int/news-room/fact-sheets/detail/dementia>



Williams, R., & Zipser, D. (1989). A Learning Algorithm for Continually Running Fully Recurrent Neural Networks. *Neural Computation*, 1(2), 270–280.

Wolfram.com. (2020). *Wolfram Mathematica: Modern Technical Computing*. Available at: <https://www.wolfram.com/mathematica/>

Yiğit, A., & Işık, Z. (2020). Applying deep learning models to structural MRI for stage prediction of Alzheimer's disease. *Turkish Journal of Electrical Engineering and Computer Sciences*, 28(1), 196–210.

Zeiler, M. D., & Fergus, R. (Eds.). (2014). *Visualizing and understanding convolutional networks*. *European conference on computer vision*. Springer.