Brain Age Classification from Brain MRI using ConvCaps Framework

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Brain Age Classification from Brain MRI using ConvCaps Framework

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Abstract

Predicting brain age from brain Magnetic Resonance Imaging (MRI) can play a vital role in identifying various neurological disorders at an early stage. Change in brain contour is a great biomarker for onset of brain related problems. Artificial Intelligence has proven its applicability for image classification. However, higher complexity of the architecture and computational overhead are some of the reasons holding its application in actual medical scenarios. Use of conventional CNN has several pitfalls like positional invariance among the features and over-fitting with deeper network architectures. This study encompasses the application of novel Convolutional Capsule network, to inspect relevancy of spatial features and positional invariance while classifying brain age from brain MRI. Transfer learning based models like InceptionV3 and DenseNet were also considered for comparison an analysis. Models are trained on the OASIS (Open Access Series of Imaging Studies) dataset having 436 different brain MRI images and evaluated using model accuracy. In addition, benchmarks like Precision, Recall and F1-Scores were also applied. ConvCaps architecture reached an accuracy of 81% whereas InceptionV3 was slightly better with 85% accuracy. Both models have shown promising results for brain age classification and can be tuned for wider application.

1 Introduction

Brain is the most complex part of the human body and identification of neurological disorder has always been a tedious task. As per World Health Organization (WHO)[1] there is a population of around 50 million people who are suffering from neurological disorder and the number getting increased by 10 million every year with no effective treatment. It is expected that by 2050, 1 in 85 persons will be affected by Alzheimer Disease (AD) across the globe (Gaser et al.; 2013). Neurological disorders like AD make a person incapable to recognize even their family members are not able to manage their daily chores (Jiang et al.; 2019). The structure of the brain changes with age, which helps in deducing the physiological or biological age of a person (Huang et al.; 2017; Sturmfels et al.; 2018). An early detection of brain condition can supply more time to doctors for treating and managing the disease. Age estimation can be performed based on either cortical anatomy (Richard et al.; 2020) or the matters like Grey matter (GM), White matter (WM) and Cerebrospinal Fluid (CSF) present inside the brain (Franke et al.; 2010) as shown in Figure 1.

[1]https://www.who.int/news-room/fact-sheets/detail/dementia

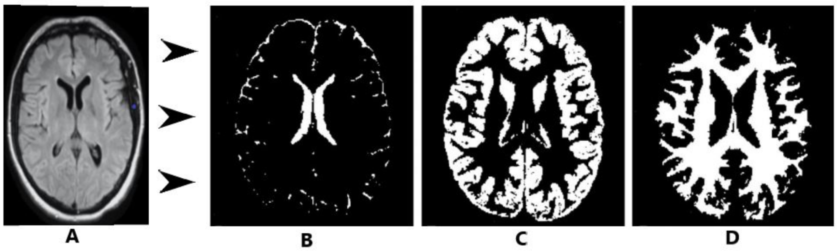

Figure 1: Brain MRI segmentation - A. T1-weighted brain MRI, B. Cerebrospinal Fluid C. Grey matter D. White Matter

Artificial Intelligence has changed the way of analyzing medical data in the last couple of years, especially image data like brain MRI. Deep learning algorithms like CNN have been used in various state-of-the-art for brain age classification (Basheera and Ram; 2020). However, it proved to be time-consuming and overhead computing (Pardakhti and Sajedi; 2019). Also, existing works lack region specific summary which can be paramount for predicting brain age and brain health (Richard et al.; 2020). A brain MRI image has large feature space which requires a special framework for extraction and processing of features. A novel approach of Convolutional Capsule Network has been proposed which consist of convolutional layer as first layer to tackle mentioned issue.

1.1 Research Question

The aim of this research is to examine the role of spatial feature while performing brain age classification from brain MRI using Convolutional Capsule Network architecture.

1.2 Research Objectives

The following sets of research objectives were derived to answer the above research question.

Table 1: Research Objectives of Brain Age estimation

Objective	Description	Metrics
1	Critical review of related work on Brain Age prediction using CNN techniques and highlight important elements	NA
2	Exploratory Data Analysis to identify features and perform data processing and transformation accordingly	NA
3	Implement and critically assess state-of-the-art experiment.	Accuracy, Recall, Precision, F1-score
4	Implement Convolutional Capsule Network architecture. Evaluate and discuss its results.	Accuracy, Recall, Precision, F1-score
5	Implement InceptionV3 transfer learning architecture. Evaluate and discuss its results.	Accuracy, Recall, Precision, F1-score
6	Implement DenseNet transfer learning architecture. Evaluate and discuss its results.	Accuracy, Recall, Precision, F1-score
7	Comparison of implemented models	NA

The main contribution of this research is the application of novel Convolutional Capsule Network on a highly varied OASIS dataset, whose age ranges from 18 years to 96 years. The model performance was given by testing accuracy and evaluated using benchmark metrics like Precision, Recall and F1 Score (Tharwat; 2020). Altogether, the new approach is the successor of the Capsule Network architecture with a more focused feature extraction algorithm.

The rest of the paper discusses related work in Section 2 categorized on the basis of various techniques applied for medical image classification. 1. Conventional machine learning techniques 2. Convolution neural network 3. CNN based transfer learning and 4. Capsule network. Followed by Section 3 and Section 4, with proposed methodology and design specifications, respectively. Section 5 analyses the model implementation; Section 6 evaluates and compares the implemented techniques. Later, Section 7 concludes the work under Conclusion and discusses the limitations and future scope

2 Related Work

This section discusses various approaches taken while analysing brain MRI images for diseases detection and classification. The techniques comprise various machine learning and deep learning methodologies ranging from conventional RVR and SVM to deep neural network architectures like CNN and transfer learning models. The literature review is divided into four subsections to discuss model architectures based on machine learning, basic CNN, transfer learning and capsule network algorithms, respectively

2.1 Application of conventional machine learning techniques

Before the rise of Neural Networks, analysis of the brain was mostly dependent on regression-based algorithms. Methods like Relevance Vector Regression (RVR) and Support Vector Machines (SVM) algorithm based on Bayesian formula were used to classify sample data.

Franke et al. (2013); Gaser et al. (2013) used same methodology of RVR which is the enhance version of SVM to detect Alzheimer Disease (AD) and brain age using brain MRI. The RVR has a self-learning mechanism to decide the parameters for best model fit unlike to the SVM (Gaser et al.; 2013). The results are calculated using Brain Age Gap Estimation (BAGE) metric which is the difference between actual and predicted age. It also explains the time of conversion to AD in years. The limitation with the former study was overlooking of white matter lesion in the study which is a biomarker for brain age prediction. Also, the latter research used BAGE to signifies the effect of diabetes mellitus on brain age. In study (Besteher et al.; 2019), another parameter of depression was included to analyse change in brain age. The result explained no major deviation in brain age due to depression disorder. Nakano et al. (2015) proposed an advanced machine learning approach to differentiate between normal and abnormal development in a newborn baby. The model consists of two architecture PCAR and ML-PCAR where latter one was used to derive growth index to feed in regression model. Result showed that ML-PCAR was more accurate than PCAR. The initial researches have at par accuracy in comparison to state-of-the-art in this field. However, these studies are the foundation of brain age analysis using Artificial intelligence.

2.2 Application of Convolutional Neural Network

With advancement in Artificial Intelligence, image detection and classification models get equipped with enhanced dimensionality reduction and feature extraction algorithms. The better input features fed into the model, the more efficient the model will perform.

The experiments for brain age detection has been re-performed with neural networks on both 2D and 3D brain images with CNN based architectures as shown in below researches. Huang et al. (2017) proposed a CNN architecture based on the VGG Net model with a stacked small kernel of size 3X3 and several max pooling layers. The idea behind the model is to provide good accuracy with limited samples and lesser time. With input brain MRI image segmented in GM, WM and CSF, the model gives MAE of 4 years on IXI dataset which is comparable to state-of-the-art as stated. However, the model is limited only to healthy brain prediction only. Qi et al. (2018) has enhanced the 3D CNN framework with an extra dense block to minimize gradient vanishing problem and to increase fitting ability of the model. The model is trained on the same IXI dataset and obtained a MAE of 4.28 across both healthy and unhealthy cohorts. With further enhancement in 3D CNN architecture, Ueda et al. (2019) introduced a model with 8, 16, 32, 64 feature channels in each block. The improved accuracy on 1000 Aoba centre collected dataset comes out as 3.67 MAE. With 3D CNN architecture a high dimensionality feature gets extracted from images. Due to which it can accommodate even smaller dataset with greater accuracy. However, the computational time and costing get affected due to complex architecture.

Bermudez et al. (2019) designed a combined architecture with amalgamation of conventional CNN architecture with volumetric feature processor to predict brain age. The architecture was applied on T1 weighted healthy brain MRI and computed tomography images. The model attained an accuracy of 4.08 MAE with OASIS and IXI based dataset. In another attempt to enhance 3D Rossi et al. (2019) introduced a novel technique to reduce computational time. The stated approach was to process different orthogonal planes that are axial, sagittal and coronal of an MRI image through different CNN blocks. The model is faster than other similar CNN based approaches, but at the cost of higher MAE scores of 5.94 than other studies. Wang et al. (2019) presented this study to investigate gray matter in brain atrophy as an established biomarker for dementia prediction. With CNN architecture the model provided a MAE of 4.45 +- 3.59 years but inefficient for healthy subjects (Wang et al.; 2019). In line with further enhancement in the CNN model, Qu et al. (2020) proposed a brain age estimation network called BAENET. To enhance the robustness of the model, outlier constraint loss and 3D skipping are integrated. The model attained an accuracy of 1.11 and 1.16 on ABIDE2 and ADHD200 datasets, respectively.

Shabanian et al. (2019) proposed a study to classify brain age of infants aged from 3 weeks to 3 years. Infant brain MRI shows changes in brain morphology since birth (Shabanian et al.; 2019) based on which a 3D CNN architecture is proposed in this study. The 3D CNN model is used to include maximum feature space and provides a sensitivity and specificity of 99% and 98% respectively. In further advancement of the 3D CNN network, He et al. (2020) introduced multiple 2D sequenced MRI image processing through 2D-Resnet18+LSTM model. A 3D MRI was split into multiple 2D sequences and processed through CNN based Resent18 with Long Short-term Memory (LSTM) as estimator at last. The study had an average accuracy of 0.78 MAE focusing only on age group between 0-6 years.

Siar and Teshnehlab (2019) proposed a novel technique for brain age classification using Alexnet based CNN architecture. The age categories were divided into 5 bins ranging from 10 years to 70 years. The model was executed with three different classification layers (SVM, Decision Tree, SoftMax) with SoftMax giving the highest accuracy of 79% on self-collected 1290 images. The accuracy with unequal age categories bins could be improved using spatial features of the image which is aim of the current study.

CNN based models are proved to be very efficient on large dataset using complex architecture like Resent and Alexnet as feature extractor. Such complex architecture takes time to process and increase computational overhead. Transfer Learning (TL) methodologies comes into picture to mitigate this issue.

2.3 Application of CNN based Transfer Learning techniques

With wide application of complex deep learning architecture instigated the need for more labelled data. The quench was solved by ImageNet which facilitates a wide range of labelled images, used for training a model by transferring the trained weights (Shao et al.; 2014). It has opened the doors for various CNN based complex architectures to be trained and tested to different datasets.

Transfer Learning (TL) technique was fully utilized in (Ren et al.; 2019) by training models on large dataset of UK Biobank and applying the weights on smaller dataset like NKI to get the result. The accuracy for brain age prediction is 4.20 MAE which is in line with other literature. (Jiang et al.; 2019) introduced TL methodology to pre-train only a limited number of layers while keeping others frozen. The prospect of the research is to predict brain age, as well as to identify the highest contributing factor for Alzheimer Disease (AD) detection. The results were slightly better than other similar work using DenseNet architecture. It also helped in determining that the frontal lobe has the highest involvement in AD detection (Jiang et al.; 2019).

TL mechanism has been implemented in several other brain analysis researches like brain tumor detection (Chelghoum et al.; 2020). The research compared 9 different TL models for predicting 3 classes of tumor (Glioma, Meningioma, Pituitary). As a result, models with fewer layers proved to be more efficient than the deeper layers. Ding et al. (2019) proposed a model to predict the diagnosis of AD in early stages using InceptionV3 TL architecture. The model accuracy predicted through the area under the ROC curve with 98% result at 95% confidence interval. The model on an average predicts 76 months before actual diagnosis of AD on ADNI dataset. TL models require a large dataset for initial training to assign weights. With smaller data, there is always a chance of an under fit model and lower accuracy.

2.4 Application of other frameworks

Other methods like (Al Zoubi et al.; 2018; Afshar and Sajedi; 2019) were also considered while deciding the architecture and process to be used in this literature.

Al Zoubi et al. (2018) used EEG signal to predict brain age on an OASIS dataset. The signals were amplified, processed and passed through Nested Cross Validation (NCV) architecture to achieve an accuracy of 6.87 MAE. Afshar and Sajedi (2019) study was focused on utilizing brain MRI images for brain age prediction to keep a check on computational complexity and time. An Extreme Learning Machine which is a combination of input neurons, hidden layers and sigmoid function mechanism is integrated for regression output. The model achieved an accuracy of 11.32 RSME but was inconsistent with train set error.

2.5 Application of Capsule Network

CNN is known for its enhanced feature extraction mechanism to differentiate complex features from the sample. However, a major limitation is the amount of labelled data requirement for such models which is extremely sparse in the medical domain (Jiménez-Sánchez et al.; 2018). Capsule network is introduced as an alternative for CNN architecture which keeps the spatial relationship and hierarchy intact while extracting features Hinton et al. (2011).

Adu et al. (2019); Afshar et al. (2019) explained the advantages of CapsNet over CNN for brain tumor detection. CapsNet architecture is more robust to affine transformation and rotation which is very common in medical images (Afshar et al.; 2019). The former proposed model attained 30% better accuracy than the traditional CNN model on brain tumor detection. The latter study incorporated a more enhanced feature extraction with segmented tumor images as input. The CapsNet had a minimal feature space to predict the output. The model attained an accuracy of 95.48 in classifying multi-class tumor. Pham et al. (2019) proposed a novel methodology using convolutional layers and capsule network known as ConvCaps. The model was able to classify tumors with 93.8% accuracy. Dynamic routing can be an expensive way of image processing depending on the problem type.

2.6 Literature Summary

From the above literature review we came to know about various techniques used for brain analysis. CNN and transfer learning proved to be the efficient way of brain classification and detection. However, the newly introduced Capsule Network has also shown promising results on various datasets. Use of convolutional layers on top of CapsNet can be a great addition. CNN models are quite focused on the required feature which causes the model to overlook its spatial relationship with the entire feature space. CapsNet models efficiently tackle this issue yet lack its efficiency with larger datasets (Pham et al.; 2019). This is where ConvCaps architecture originated to tackle both the problems effectively. There could be a possibility of vanishing gradient problem when various convolutional layers are used with max-pooling layers on top of CapsNet. However, in a controlled environment ConvCaps can be a game changer for computer vision in medical imaging. Current research is inspired to used ConvCaps architecture on Brain Age classification problem discussed in (Siar and Teshnehlab; 2019).

3 Methodology

Data mining research implementation and development requires a well-organized framework from the initial stage of data collection to the final results. This section discusses the step-by-step process followed while implementing this research. The project involves both image data and textual data to process, which requires individual processing architecture Figure 2.

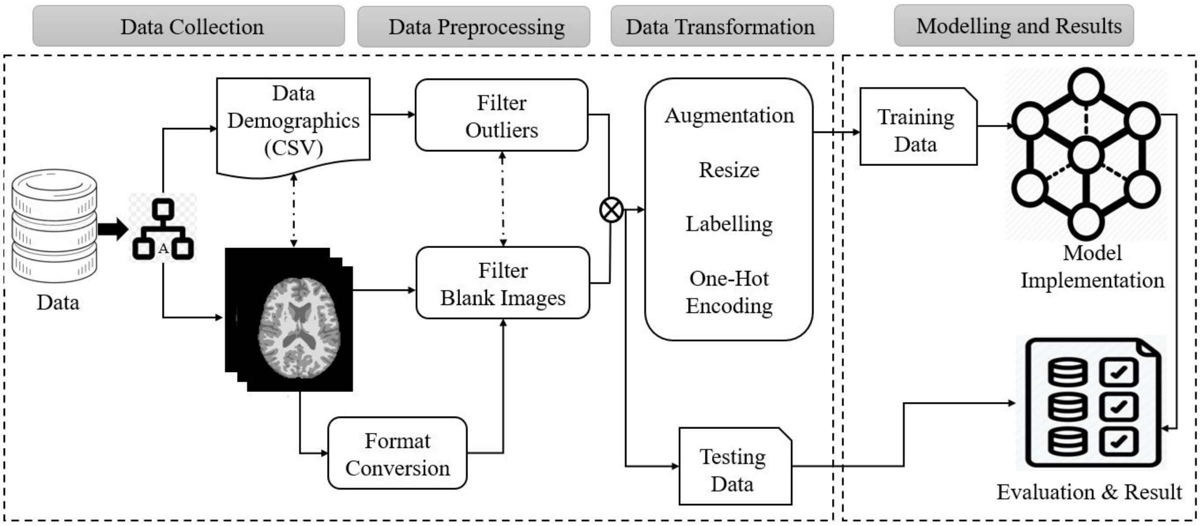

Figure 2: Process flow diagram

3.1 Process Design Flow

The collected and pre-processed data were present in the form of image and text containing labels. Images and labels were categorized (A) into 6 different age group bins as shown in table 2. Data were further classified into training and test sets before data augmentation. The testing set was taken as 20% of the dataset. The training set is augmented, resized and labelled as per the model requirement. Categorized test, train and validation data are fed into the model for feature extraction. The study encompasses the application of ConvCaps, Google InceptionV3 and DenseNet169 architectures. ConvCaps model is supplied with tokenized labels through one-hot encoding. Model weights and information per epoch is stored for further evaluation and analysis. Model Evaluation was performed using three classification metrics - Precision, Recall and F1-Score.

3.2 Data Selection

As noted from literature review, IXI (Information eXtraction from Image) and OASIS (Open Access Series of Imaging Studies) [2] are the most preferred dataset available publicly for research purposes. The OASIS dataset is used for this study, published by Marcus et al. (2010) and freely available to use by registering on the website. Data collection is available in three sequence T1 Weighted, T2-weighted and FLAIR data. Cross-sectional T1-weighted data having a shape of 208 X 176 pixels and 3 channels is used for this study. The data consist of a mean age of 51.35 with age ranging from 18 years to 96 years. The change in brain orientation is shown below in Figure 3.

[2]OASIS: Cross-Sectional: https://doi.org/10.1162/jocn.2007.19.9.1498

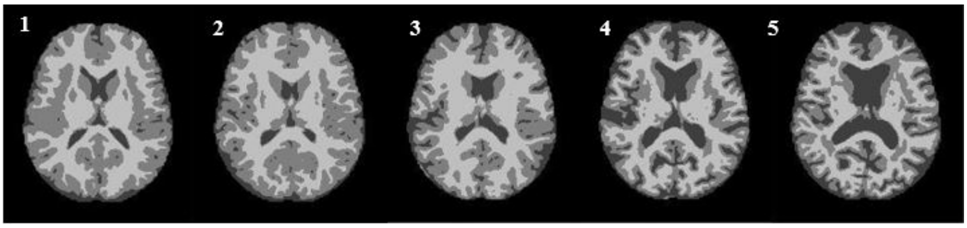

Figure 3: Change in brain orientation with ageing - 1) 20yr 2) 40yr 3) 60yr 4) 80yr 5) 96yr

3.3 Data Preparation

OASIS neuro-imaging dataset data consists of 436 cohort brain MRI scans in various masking forms. Initially, data are checked for missing labels in the demographic table and blank images in the dataset which acts as outliers. The data were present in GIPHY format, which is a short moving image, due to which it consumes large space. Each MRI was present in an individual folder with different sequences. The images were first extracted from FSL_SEG and PROCESSED folders and then converted into PNG (Portable Graphic Format) constituting a total image size of 872 (raw and masked). PNG is a lossless compression format which reduces the size of a GIPHY image by up to one-fourth. The pre-processed MRI images are resized into 175X175 and 3 channels using OpenCV2 library and saved with their unique ids in demographic CSV. The image size was decided after several iterations of the model run on various sizes. A dataset of 822 brain MRI images (outliers removed) and respective labels were divided into age group bins as shown in table 2.

Table 2: Class distribution according to age

Age Groups	**10-20**	**21-30**	**41-60**	**61-70**	**71-80**	**81-90**	**Total**
Bins	1	2	3	4	5	6	
Data	51	110	64	45	90	55	415

The saved images were augmented with 12 different filters as shown in Figure 4 (Mikołajczyk and Grochowski; 2018). For transfer learning based CNN models (InceptionV3 and DenseNet), MRI images are further passed through real-time augmentation using Image generator function.

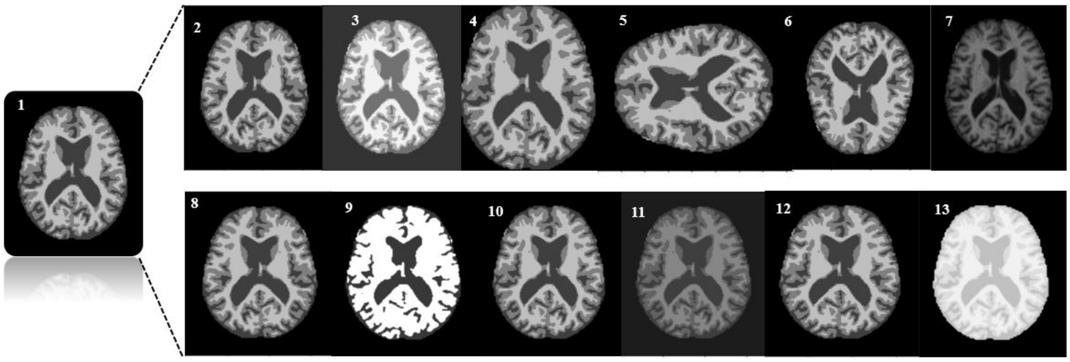

Figure 4: Data Augmentation - 1) Original Data 2) Left-Right Flip 3) Brightness(0.2) 4) Center Cropping (0.8) 5) Rotation 90 6) Upside Down 7) Random Contrast 8) Saturation (10) 9) Adjust Contrast (8), 10) Random Hue 11) Segmented 12) Random Gamma 13) Random Saturation

4 Design Specification

4.1 Convolutional Capsule Network (ConvCaps)

The proposed methodology was inspired by reviewed literature (Pham et al.; 2019). Implemented model was compared with baseline experiment (Siar and Teshnehlab; 2019) for further analysis. Capsule Network is an encoder-decoder framework. After combining with convolutional layers, it forms a novel architecture known as ConvCaps where conv layers present at the forefront followed by Primary Caps. The Input brain MRI image is first passed through a convolutional layer coupled with max pooling to maximize feature absorption and scale sample space. Features are then fed into a primary capsule layer for feature vectorization. Each vector now has a certain set of attributes which are further regulated through routing agreement. The top capsule layer of Digit caps sends capsule length having probability between 0 and 1 to decide the output. Decoder with 3 fully connected layers and sigmoid function helps in reconstructing input images (Sabour et al.; 2017).

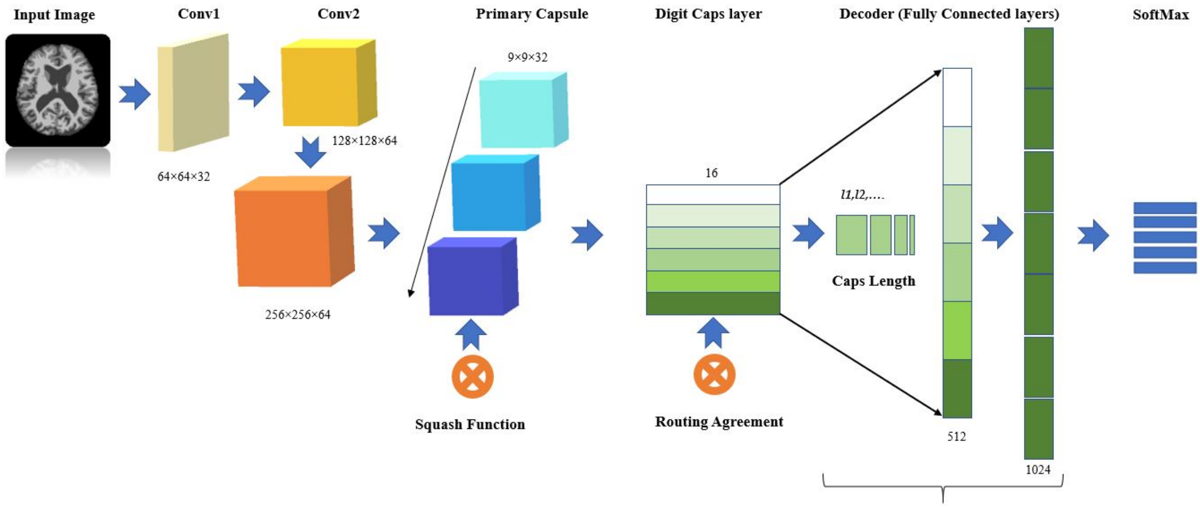

Figure 5: Convolution CapsNet design architecture (Pham et al.; 2019)

Detailed description of different modules of ConvCaps architecture discussed below (Sabour et al.; 2017; Afshar et al.; 2019):

1. **Convolutional layer** helps in extracting feature space from image by sampling through max pooling layer. Brain MRI images of size 175X175 were supplied to the convolutional layer.

2. Feature maps are vectorized By **Primary Caps** layer. Let say, 27 feature maps can be divided into three vectors of nine dimensions.

3. Vectors are assigned with probability value using **Squash function** which preserves the vector orientation while keeping the value between zero and one.

4. **Routing Agreement** decides confirmed position of an image using dot product of its own activation function (Ui) and transformation matrix (Wij) (U = Wij.Ui)

5. Only agreed positions are passed further to agreed class capsules for noise reduction.

6. **Decoder** is a collection of fully connected layers with sigmoid function as output layer.

7. Input images reconstruct by minimizing the squared difference between input and reconstructed images.

8. Image classification is based on **marginal loss** which should be minimum for better classification

9. **Loss Function** is defined as the sum of the length of rightly predicted vector and length of wrongly predicted vector.

4.2 Transfer Learning Technique

CNN architecture proved to be a great deep learning technique for computer vision. However, the amount of feature space it uses was never considered (Shao et al.; 2014). Getting a pre-labelled medical data is an expensive and cumbersome task. The Transfer Learning concept came into existence to mitigate this issue. The base concept of TL is to allow models to be trained on similar large dataset and the weights to be transferred on smaller dataset. The ImageNet challenge provided millions of labelled data for different models to compete. In this research TL based approaches like Google InceptionV3 (Ding et al.; 2019) and DenseNet 169 (Huang et al.; 2017) were also considered for the purpose of analysis and comparison.

5 Implementation

A brief overview of the implementation steps followed while executing Convolutional Capsule network, Alexnet-CNN, and pre-trained Inception and DenseNet architecture are discussed in this section. Deep learning implementation greatly depends on system specifications. Model training and execution was supported by Google Colab IDE which is a cloud based freely available platform with dedicated GPU access. Dataset was stored in google drive and accessed through local runtime environment. Deep learning models were implemented in Python language using Keras neural network library, integrated on top of TensorFlow framework. Data was further split into tests and training using the Sklearn library. A 20% testing ratio was taken as the overall dataset was smaller in size. The training data (658) was further augmented using 12 different filters as shown in figure 4 making a total of 7896 training data for model training. Model execution data like accuracy, validation and losses were stored in CSV file using csv logger and improved weights were stored in google drive for future reference. An early stopping mechanism was also integrated for efficient model run by checking overrun possibility. A generalized step per epoch and validation per epoch was assigned having value equals to the training or validation count upon batch size. Specific model implementations are discussed in next sections.

5.1 Alexnet based CNN Architecture

In an attempt to replicate state-of-the-art discussions by (Siar and Teshnehlab; 2019). An Alexnet based CNN architecture was implemented. The concerned architecture consists of 5 conv layer and 3 sub-sampling layers as discussed in the study. Model was supplied with an image size of 227 X 227 with 3 channels. Images were divided into respective class folders which acted as labels for the model. A SoftMax classifier was used as the final classification layer of the model.

5.2 Convolutional Capsule Network Architecture

ConvCaps Network has two different processes. Two convolutional blocks (Conv1, Conv2) coupled with max pooling and Relu activation function, sub-sample images at the beginning of the architecture. ConvCaps models require tokenized labels and the label needs to be preserved corresponding to their images. Same has been achieved using One-Hot Encoding mechanism on text class labels. Train dataset is further split into training and validation (20% of training data). Images of size 175X175 are fed with corresponding labels to the Conv1 having 64 kernels and size of (3,3) with max pooling of stride (2). Extracted feature spaces are then passed through Conv2 with 128 kernels and finally fed to the primary caps layer of 9X9X256 filters of stride 2. Each primary cap's location contains 32 capsules of 8 sizes. And each capsule stores different features of the images based on its orientation, shape, color and texture. The best position of the image is decided using a routing algorithm (num_routing = 3) and transferred into digit capsules. An elongated vector is then forwarded to decoder for image reconstruction and also to the SoftMax layers for image classification. Model with assigned weights was further used for testing and evaluation. Hyper-parameters considered for this study were - routing count of 3, learning rate as 0.001 and a batch size of 32 based on several model run.

5.3 Transfer Learning based InceptionV3 and DenseNet

There are two pretrained models (Google InceptionV3 and DenseNet) used for this research based on related work review (Huang et al.; 2017; Ding et al.; 2019). Inception nets are usually lighter and known for its parallel processing mechanism; however, DenseNet used to be quite complex due to its concatenated network architecture. Pretrained models like DenseNet and Inception have a definite set of layers with varied fully connected layers as per requirement. The dataset was first divided into folders of specific classes [1,2,3,4,5,6] which acted as a label for image data. Train and validation dataset were then passed through an image generator which automatically fetched labels and performed real-time augmentation. Corresponding pre-trained models were imported with trained weights from ImageNet. Hyperparameter tuning comprised a learning rate of 0.0001, batch size of 32, Adam optimizer and loss function as categorical cross-entropy based on dataset specifications.

Evaluation and Results are discussed in corresponding sections.

6 Evaluation and Results

Model implementation was followed by evaluation and results to analyze model performance, discussed in this section. Model performance is based on various metrics, out of which Accuracy, Precision, Recall, and F1 Scores (Tharwat; 2020) were considered. Accuracy is a great performance indicator; however, precision and recall represent the class-wise performance of a model which is paramount for unequally distributed class dataset. Model training time was considered for comparison which may vary depending on system configuration. The number of epochs (100) and image size 175X175 were decided based on several iteration of the model and were kept constant throughout the experiments for better comparison.

6.1 Baseline Experiment: Alexnet based Convolutional Neural Network

Mentioned experiment is the replication of state-of-the-art (Siar and Teshnehlab; 2019) which acted as the foundation of current research. The implemented model achieved an accuracy of 49% which was 37% less than the actual result (Siar and Teshnehlab; 2019). A major difference in both the implementation was of data pre-processing. Original work chose for brain masking and stripping technique using MATLAB, which is not in the scope of python language used in current research. Presented model has served its purpose of analysis, even though the experiment was not the mirror of actual work. The same procedure of classifying brain age was applied with newly proposed ConvCaps methodology as our next experiment.

6.2 Newly Proposed Experiment : Convolutional Capsule Network (ConvCaps)

Current research introduced a novel approach of ConvCaps architecture in order to assess the involvement of spatial features in brain age classification. The ConvCaps methodology achieved a training accuracy of 93.73 and a validation accuracy of 84.94. The model attained a testing accuracy of 81% which is comparable to the validation accuracy. Also, training loss and validation loss kept decreasing till 75th epoch as shown in figure 6, and are in line with model training, overrules any chances of model over-fitting. The result are encouraging and strengthen our initial prospect. It can be inferred that the spatial related features are having a strong correlation with brain age classification. Next experiment was performed to compare the proposed model with other state-of-the-art approaches like TL based InceptionV3 and DenseNet methodologies.

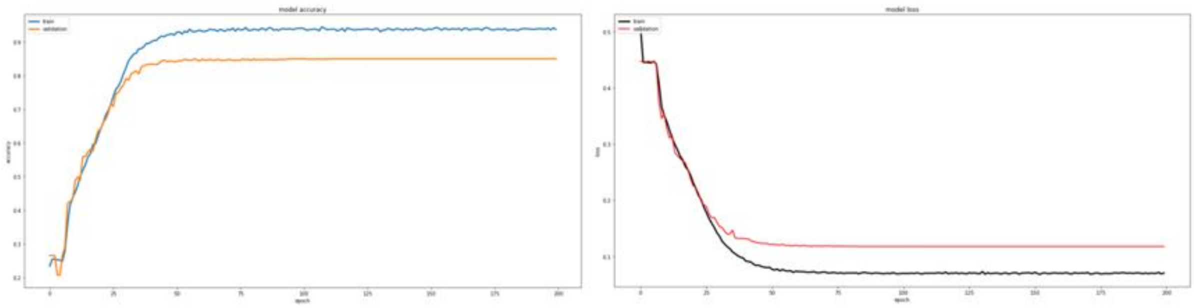

Figure 6: ConvCaps accuracy and loss curve

6.3 Supporting Experiments: Transfer Learning based InceptionV3 and DenseNet

TL based InceptionV3 and DenseNet architectures were applied for model comparison. The InceptionV3 model had a better accuracy (85%) than ConvCaps (81%) with slightly higher precision. DenseNet on the other hand, had least of all with only 60% accuracy and extremely low recall. Below graphs in figure 8 and 9 depict consistency of Inception over the entire range with constant increase in training and validation accuracy. Comparing ConvCaps with InceptionV3 framework makes it evident that ConvCaps has an encouraging result with medical images and can be applied to wider medical related problems.

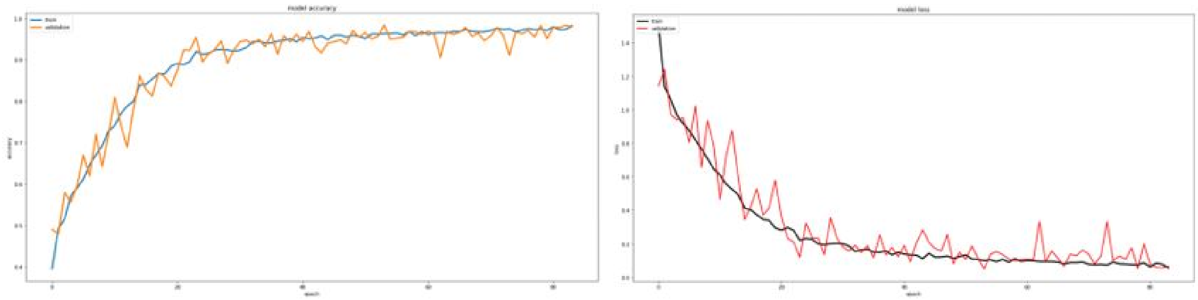

Figure 7: InceptionV3 accuracy and loss curve

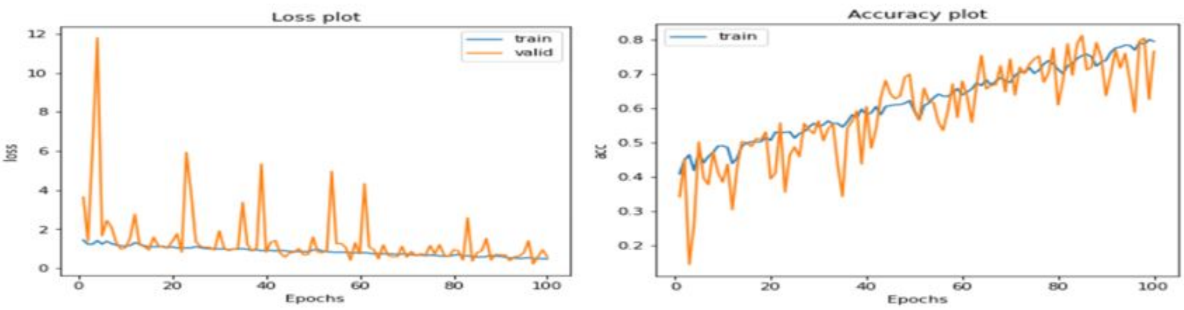

Figure 8: DenseNet accuracy and loss curve

6.4 Model Comparison, Discussion and Results

In this research, a novel approach of Convolutional Capsule Network was proposed to inspect the relevance of spatial features while classifying brain age from brain MRI. The model is inspired from (Pham et al.; 2019) research work on brain tumor. Pre-trained models like InceptionV3 and DenseNet were also considered as baseline comparison. Model execution was based on 436 different brain MRI images divided into six classes (10-20, 20-30, 40-60, 60-70, 70-80, 80-90) and collected from the OASIS database.

Model implementation was initiated with state-of-the-art architecture analysis. The Alexnet based CNN architecture was replicated on the OASIS dataset with a similar count of images (1310). The model accuracy was 37% lesser than the result suggested in the state-of-the-art. The cause of deviation found out to be the difference in data preparation techniques. Yet, the baseline experiment has provided a great aid to the current experiment. Transfer learning has given various state-of-the-art performance with small labeled dataset. Implementation of InceptionV3 and DenseNet was an attempt to utilize the same architecture on the brain age classification model. InceptionV3 has performed better than other two models. DenseNet validation curves has several spikes (as shown in figure 8) which explains the misinterpretation of validation set by the model and lower model accuracy.

The brain MRI images have large feature space unlike other similar problems like brain tumor. This increases the complexity for the model to detect and agree upon a particular orientation of the image. Furthermore, brain MRI image has a black background which again confuses the predicting model with other features. Initially, a simple Capsule

Network model had provided an accuracy of 35% due to aforementioned reasons. A novel approach of Convolutional Capsule Network was implemented to remediate these issues with advanced feature extraction framework. The enhanced ConvCaps architecture performed slightly better than the state-of-the-art (as shown in Table 3) with just 436 different cohort's data, augmented to 7,897 images dataset.

Table 3: Model comparison

Method	**Testing Accuracy**	**Precision**	**Recall**	**F1-Scores**
CNN (State-of-the-art)	79%	89%	50%	64%
ConvCaps	81%	83%	80%	80%
InceptionV3	85%	86%	85%	84%
DenseNet	60%	18%	17%	17%

The major implications of ConvCaps model is its limitation towards size of the image. The model requires smaller input size, however down sampling with traditional capsule algorithm drops several features from an image (Pham et al.; 2019). With complex images, the condition is even severe and prone to feature drop. The model requires a proper set sub sampling layers which can reduce the image size as well as keep the feature intact for complex data processing. To conclude, ConvCaps network architecture has shown promising results with small labelled brain MRI dataset. Yet are certain pitfall which needed to be enhance while using with complex feature dataset.

7 Conclusion and Future Work

The main aim of this research is to examine a novel Convolutional Capsule Network on the OASIS dataset. The purpose is to investigate the involvement of spatial relationship in brain age classification. The experiment has been performed in three stages - firstly, state-of-the-art work was replicated and studied, followed by the implementation of the proposed novel ConvCaps architecture and lastly, the implementation of TL based InceptionV3 and DenseNet for further comparison and analysis. The collected dataset consists of 436 brain MRI images of different cohorts which were further augmented, resized and filtered to get 7,897 brain MRI images. The pre-processed images were divided into six age groups (10-20, 20-30, 40-60, 60-70, 70-80, 80-90) used for modelling. The novel ConvCaps architecture is a combination of convolutional block at start and capsule network. A brain MRI with black background consists of large feature space, obstructing the capsule network to understand image orientation. Convolutional block was used to sub-sample the features and pass on to CapsNet block for further processing. TL based InceptionV3 and DenseNet models were used to explore the results. The ConvCaps model attained an accuracy of 81% complemented by pre-trained InceptionV3 architecture with 85%. Both InceptionV3 and DenseNet models were implemented with a transfer learning algorithm using "ImageNet" weights. Model performance was analyzed using benchmark metrics like Precision, Recall and F1-Score. The proposed ConvCaps gave encouraging results and can be adopted for wider application in brain related problems. The results also proved the viability of ConvCaps architecture on Brain MRI images for brain age classification.

7.1 Limitation and Future Work

This section discussed some limitation of ConvCaps model and future extension of this research. The model is prone to larger count of sub-sampling layer in ConvCaps architecture which can lead to drop of information while feature vectorization in the primary caps layer. Use of highly complex images in smaller dimensions can confuse the routing agreement while deciding best orientation for the capsule.

Convolutional Capsule Network has great potential for object detection by preserving spatial orientation. Thus, the next step could be to extend its application to more complex data and to test its applicability and accuracy on other medical problems.

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