Computer-Aided Classification of Multi-Types of Dementia via Convolutional Neural Networks

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Abstract— **With millions of people suffering from dementia worldwide, the global prevalence of dementia has a significant impact on the patients' lives, their caregivers' physical and emotional states, and the global economy. Early diagnosis of dementia helps in finding suitable therapies that reduce or even prevent further deterioration of patients' cognitive abilities. In recent years, state-of-the-art literature has proposed various computer-aided diagnosis systems based on 3-dimensional brain imagery analysis to identify early symptoms of dementia. These systems aim to assist radiologists in increasing the accuracy of diagnoses and reducing false positives. However, the early diagnosis of dementia is a challenging task due to the image quality, noise, and human brain irregularities. The state-of-the-art has focused on differentiating multi-stages of Alzheimer's disease, however, the diagnosis of various types of dementia is still a gap. This paper proposes a deep learning- based computer-aided diagnosis approach for the early detection of multi-type of dementia. To show the performance of the proposed CAD algorithm, three conventional CAD methods are implemented for comparison. The proposed algorithm yields a 74.93% accuracy in early diagnosis of multi-type of dementia and outperforms the state of the art CAD methods.**

Keywords—Alzheimer's disease; Brain imaging; Computer-Aided Diagnosis; Convolutional Neural Networks; Dementia; Early diagnosis; Magnetic Resonance Imaging;

I. INTRODUCTION

Dementia is a brain disorder that is characterized by a chronic decline in mental ability due to loss of, or damage to, neurons in the brain. Dementia can develop as a result of a number of risk factors; some of these factors are advanced age [2], genetic disorder [25], traumatic brain injuries, and environmental factors [21]. The term dementia is a widespread term for brain disorders that result in a set of symptoms that disturb normal brain functions, such as thinking, intellectual abilities, memory recollection, problem-solving, and use of language, serious enough to affect the patients' daily activities [19]. In recent years, the growing number of patients who have Alzheimer's disease (AD) and other dementias indicates the prevalence of such cognitive impairment. Accordingly, numerous researchers have been working towards the development of new or improved technologies to accurately detect dementia. The most prominent diagnostic technique that can capture early symptoms of dementia is through revealing the internal structure and the function of the brain. Through a quick overview of the state-of-the-art studies for diagnosing dementia, it has been noticed almost all of them suggested CAD systems in order to differentiate various stages of severity of Alzheimer's disease. However, this paper offers a novel computer aided diagnosis (CAD) system for early detection of multi-types of dementia.

The thematic development of the paper is as follows. Section II provides a general overview of dementia by presenting statistics of its prevalence, reviewing the risk factors that increase the chances of developing dementia, and discussing the most prevalent types of dementia, including AD, in greater Section III provides a comprehensive review of the CAD methodologies that have been implemented for early detection of dementia. Section IV presents the proposed approach for early detection of dementia. Then, the experimental setup is summarized and the experimental results are discussed in Section V. Finally, Section VI concludes this work.

II. OVERVIEW OF DEMENTIA

In recent years, the prevalence of dementia has risen incredibly throughout the world. In England alone, more than 500,000 people were diagnosed with dementia in 2011 [19]. This number has significantly increased. In 2015, it was reported that 46.8 million people worldwide were living with dementia. The projections indicate a significant increase which is estimated to be about 75.6 million by 2030, which will almost triple by 2050 to 135.5 million [6,4]. Total health-care costs for people with dementia amounted to more than 1 per cent of the global gross domestic product (GDP), or US$604 billion, in 2010. Generally, the number of cases with different types of dementia increases due to the exposure to various environmental and genetic factors that are discussed in the next section.

Dementia disorders have many forms whose signs are sometimes similar; nevertheless, some types of dementia are more popular than others. Alzheimer's disease (AD) is the most prevalent type of dementia, as can be noted from Fig. 1. AD accounts for nearly 63% of all diagnosed cases of dementia and it has been estimated that almost five million people from various age groups in the United States of America were diagnosed with AD in 2015 [3]. AD was discovered by Dr. Alois Alzheimer in 1906. It is defined as a neurological disorder caused by loss of brain cells that results in memory degeneration and cognitive impairment [32].

As illustrated in Fig. 1, the second most common type of dementia is called vascular dementia (VaD). Recently, the percentage of patients with vascular dementia has risen gradually and 10% of all patients diagnosed with dementia have been clinically diagnosed as having VaD [4]. Additionally, having abnormal characteristics from more than one type of dementia concurrently represents mixed dementia; which is the third prevalent type of dementia. Overall, many other forms of dementia have been clinically diagnosed, including Lewy Body dementia, Front temporal dementia,

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young onset dementia, mild cognitive impairment, and some other rare forms [8].

Some symptoms of dementia like memory loss, personality change, disorientation, mood swings, and bad concentration are shared among its various forms while some others are clearly distinct to some types [5]. The diagram shown in Fig. 2 clarifies the process that the human brain goes through as it develops dementia. When studying and investigating scans of normal brains and demented ones, many differential characteristics can be observed among them in terms of the cerebral cortex, hippocampus, and ventricles. First, as shown in Fig. 3(B) and Fig. 3(D), the cerebral cortex, the outer layer of the brain that is referred to by arrow 1, looks smaller in a brain with dementia compared to in a healthy brain. In terms of the hippocampus's size, referred to by arrow 2 in Fig. 3(B) and also Fig. 3(D), it can been seen that the hippocampus is shrivelling up in a demented brain while it looks bigger in a normal brain. The ventricle region, referred to by arrow 3 in Fig. 3(B), looks enlarged in a brain diagnosed with dementia compared to that in a healthy brain.

III. RELATED WORKS

Significant effort has been made to develop an effective approach to aid in the identification of early cases of dementia. Numerous work efforts have used Voxel-based morphometry (VBM) that computes the grey matter densities from medical images to classify the different stages of AD [1, 23, 34].

The second approach is based on the analysis of some features of regions of interest (ROIs) from medical brain images including volume and cortical thickness [32, 35, 13]. In 2014, some researchers attempted to improve the accuracy of multinomial classification [39] that is provided by the combination of three binary classification models; NC vs. AD, NC vs. MCI, and AD vs. MCI [20]. Other studies proposed algorithms that evaluate the changes of brain volume, measure the thickness of the cerebral cortex in the brain, and compute the hippocampal shape score, and the hippocampal texture score from MRI brain images [36, 10].

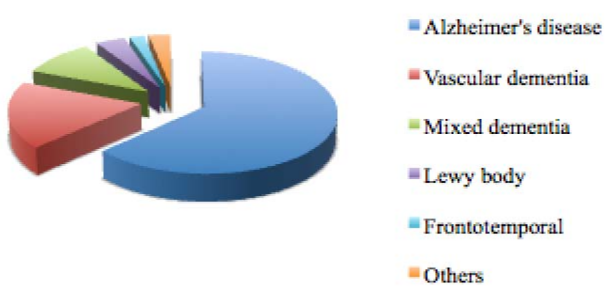

Fig. 1. The prevalence of common types of dementia in the US [14].

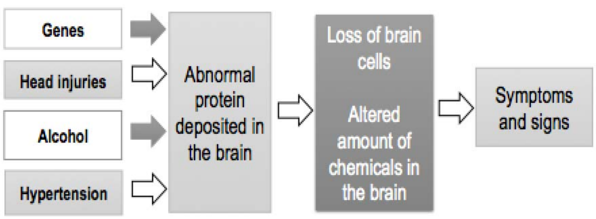

Fig. 2. What happens in Dementia?

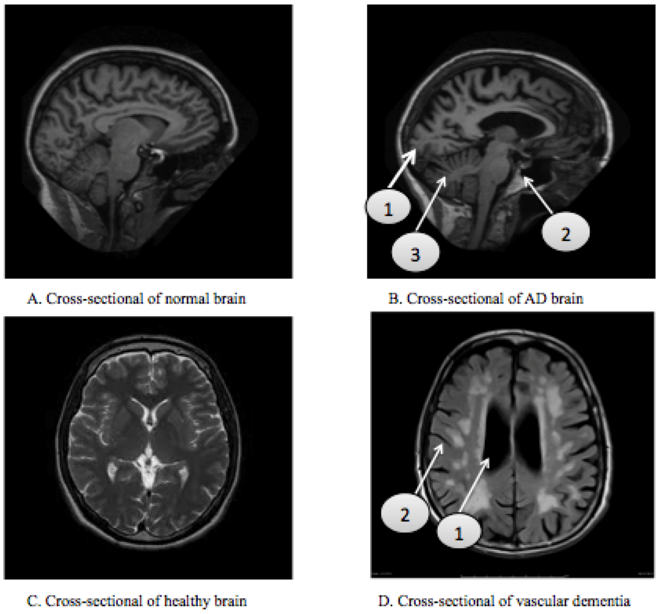

Fig. 3. The difference between normal brain vs. vascular demented brain and brain with AD [42,29].

A regularized linear discriminant analysis classifier is used to classify between healthy and demented brains based upon the aforementioned features. In [28], researchers proposed a CAD for dementia methodology that distinguishes patients with Parkinson's disease from NC by evaluating given samples using a calculation of sensitivity, MMSE, and specificity scores.

Several recent advances in research to obtain the accurate early diagnosis of dementia during its progress have been made by the use of any of the deep learning approaches. In 2015, some researchers sought to differentiate between patients with AD and healthy people using a new approach that combined a sparse auto-encoder [43] in order to learn features extracted from MRI images and learn filters of a convolutional layer under sparsity constraints as well as convolutional neural networks that are built to solve problems of image classification [12, 44]. As well, a new contribution has been introduced in [31] to improve accuracies of three suggested classifications: AD vs. NC, AD vs. MCI, and MCI vs. NC based on using a deep learning-based feature representation that has been developed with stacked auto-encoder (SAE) [20]. SAE has been used to explore a latent representation of input by extracting features like volume of grey matter tissue and intensity from MRI and PET, respectively.

Many Artificial Neural Network (ANN)-based diagnosis approaches have been applied in the literature to diagnosis dementia. In 2016, Sarraf and Tofighi developed in [46] a CAD method that classifies patients with AD and normal controls by classifying features extracted from converted MRI images using the LeNet architecture proposed in [47]. De Figueiredo et al. developed a new learning algorithm in order to differentiate between patients diagnosed with AD, patients diagnosed with VD and healthy controls. They initially extracted relevant features and removed redundant ones from Single-photon emission computed tomography (SPECT) images. Feature extraction has been applied by measuring of average of intensity. Then, an optimal interpolative neural network (OINN) was used to analyze these features, and then predict a diagnostic output accuracy of dementia based on using k-means clustering algorithm [45]. The work in [7] proposed an algorithm for pretraining ANN in order to enhance differentiating among various stages of AD. First, the authors employed FreeSurfer software for analyzing MRI images and producing feature vectors. Then, the projection matrix is produced for feature vectors by implementing and maximizing the centered kernel alignment (CKA) for enhancing classification task.

In this paper, a novel deep neural network-based CAD method has been proposed to aid in analyzing MRI neuroimages and then diagnosing dementia in its early stages. Unlike [46], CNN-based technique has been developed in this paper for purpose of differentiating among various types of dementia instead of focusing on differentiating of multi-stages of AD. Compared to previous work discussed in [46], our proposed approach addresses multi-class classification problem rather than addressing binary classification problems as in [46]. Also, proposed CNN based architecture consists of six convolutional layers and three fully connected layers while architecture of CNN in [46] consists of only two convolutional layers.

IV. PROPOSED METHOD

In this section, a new two- stage convolutional computer- aided approach illustrated in Fig. 4 has been proposed in order to detect and track the progression of dementia. This architecture initially builds CNN whose first layer takes the preprocessed images as inputs, and then builds logistic regression model to classify all examples of dataset into one of different classes of dementia. In section *A*, image preprocessing techniques that were used to improve the quality of gray scale images are presented, and in Section *B* the architecture of the CNN is detailed. The use of logistic regression is described in Section *C*.

A. Preprocessing images and extracting features

This section discusses several image preprocessing techniques that are proposed to enhance MRI scans before building a convolutional neural networks. Given the raw images as input: Initially, all MR images are resized into 176×208 for the preprocessing step. Then, they are preprocessed by image preprocessing techniques, including digital spatial filtering techniques [38] and image-adjustment techniques [43] because images acquired by neuroimaging techniques usually have a noise. Overall, the preprocessing step plays a significant role in increasing the reliability of the visual appearance of images and optimizing the images' quality.

In particular, normalization, Gaussian filter [52], and histogram equalization are some methods in image preprocessing that have been applied on the original MRI images for preparing them of CAD system. Gaussian filter has been developed to remove the noise from image signals. In addition, histogram equalization has been applied to improve low contrast of gray scale images by adjusting images' intensities [18].

Segmentation also has an important role in analyzing medical images of the brain and allowing interpretation for the better diagnosis of dementia. Image segmentation is the process of dividing the image [33] in order to differentiate various regions dissimilar characteristics in medical images. In this research, two different segmentation approaches are applied on MRI images of the brain to visualize anatomical structures of the brain, and then analyze changes of that brain:

a) Edge-based segmentation: Detection of a wide range of edges in an image is one of the important steps to retrieve the desired information from given images. Edges are lines identified on the basis of predicting the changes in some various properties of the image like brightness by using any of edge detectors [24]. In this paper, the Canny edge detection is performed to identify edges that represent one of significant features for analyzing brain images and prevent unconnected edges from continuing [38].

b) Region-based segmentation: An image could be also segmented into regions. Each connected region is comprised of a set of adjacent pixels with shared characteristics and the same grayscale values. For applying this kind of segmentation in this research, the watershed transform algorithm is used to produce better segmentation results [37].

B. Convolutional Neural Network (CNN)

Deep learning has been applied with success for a variety of computer vision tasks in recent years. It is shown as a new tool of machine learning that is relying on learning a hierarchy of representation like multiple levels of features. However, CNN is one of the most frequently used deep learning architectures, utilized in order to obtain an excellent performance in many computer vision applications. The typical CNNs are made of the input layer, set of conventional, local response normalization, and subsampling layers, and the output (fully connected) layer. Each of these layers takes a multi-dimensional array of numbers as input and produces an output that is another multi-dimensional array of numbers [22].

Input: a 176×208 pixel preprocessed image is rescaled in range 62×44×8 and then, reshaped to a 4D tensor.

Output: Given the whole preprocessed image as input, high level features are extracted and shaped in 4D tensor.

Architecture: The architecture of the CNN included in the proposed approach is comprised of six convolutional layers, six max-pooling layers, six local normalization layers, three fully connection layers, and two dropout layers. To simplify the description, the convolutional layer is denoted as $C\ (k, s)$, which indicates there are k kernels; each having the size of s x s and local response normalization is denoted as LRN. During each convolutional layer, the stride is set to 1. Convolution is applied to the output image after reshaping it to 4D tensor, and then, max pooling denoted as MP is applied to the output of the convolution to make the representation smaller and more manageable without loss of much information. The stride for pooling is 2. Then, the network architecture for the convolutional layers can be described as: *C* (16, 8) — MP— LRN— *C* (32,4) — MP— LRN— *C* (64,2)— MP — LRN — *C* (128,1)—MP— LRN— *C* (256,1) — MP—LRN— *C* (1024,1) — MP —LRN. For predicting accuracy of the diagnosis of dementia, the output of neurons in sixth convolutional layers is then fully connected to regression in order to analyze data and classify it into one of different categories of dementia. This convolutional neural network was built with Tensorflow. The architecture of the CNN is shown in Fig. 6.

C. Logistic regression as classifier:

The task of predicting the accuracy of CAD of dementia is treated as a classification problem. The output for this method is labels of types of dementia, including normal controls, uncertain dementia, incipient dementia PTP, and Dementia of Alzheimer's type (DAT)) are discrete output space and can be formulated as a classification problem. However, accuracy of correct prediction of dementia is continuous output space and thus need to be formulated as regression problem. In this paper, logistic regression is applied for classification of four aforementioned types of dementia from features extracted by CNN. Once regression model is built, the accuracy of correct diagnosis of dementia is predicted.

V. EXPERIMENTAL RESULTS

Dataset: A classification of dementia was tested on MR images collected from 74 different subjects. These images have been stored in the dataset that has been chosen among many datasets available on the Open Access Series of Imaging Studies (OASIS) for conducting our experiment. OASIS is a multicenter project that consists of many brains' MRI datasets, which are collected from various centers, including Washington University Alzheimer's Disease Research Centre, Howard Hughes Medical Institute, the Neuroinformatics Research Group, and the Biomedical Informatics Research Network. Overall, each patient record consists of at least three cross-sectional brain scans [42]. All healthy control subjects had a clinical dementia rating (CDR) of 0. On the other hand, subjects diagnosed with dementia had a CDR of at least 0.5. Fig. 5 shows an example of three slices of MRI brain images for each subject.

To evaluate the performance of the proposed model when deployed to make prediction on a new unseen data, 7- fold cross validation is performed on 734 MRI images. Cross validation assist in increasing the proposed system robustness against overfitting and enhance the estimation accuracy of proposed CAD method in predicting multi-type of dementia. After getting preprocessed dataset, seven random datasets are produced to repeat training and testing of model in which 60% of MRI images are assigned to the training set while 40% of images are used for testing the algorithm. The comparison among the proposed method and some state-of-the-art models, including Support Vector machine (SVM), logistic regression as well as LeNet-5 in [46] is made after training and testing them on the same MRI dataset in terms of following evaluation measures.

Evaluation measures: The performance of proposed algorithm is quantified through the calculation of various measures, which were implemented in Python Scripting Language (version 2.7.11) using Scikit-learn, pandas, and some other python packages.

A. Validity

The validity of the available set of screening tools in identifying early dementia is measured by investigating the ability of these tools to differentiate between healthy people and patients with dementia as well as investigating the ability to differentiate between subgroups of patients based on type of dementia [15]. This validation is evaluated by computing sensitivity, specificity, and predictive values of diagnosing dementia.

- **Sensitivity**: The probability of diagnostic tests to identify the subjects who have dementia [9]. The CAD sensitivity can be calculated by

$$Sensitivity = \frac{a}{a+c} \quad , \tag{1}$$

in which the value of a refers to the total number of patients having dementia as a positive result of the test while the value of c indicates the total number of people with dementia who tested negative. Thus, $a + c$ refers to the total number of subjects with dementia.

- **Specificity:** The probability of negative tests identifying subjects without dementia [9]. Specificity measures the total number of patients the system classifies as not having dementia, referred to by *d,* compared to the total number of subjects without dementia, refers to by $d + b$ in which b indicates the people without dementia who tested negative. The CAD specificity is given by

$$Specificity = \frac{d}{d+b} \tag{2}$$

- **Predictive values:** Predictive values (PV) are the sum of rates of people who are correctly identified as having dementia, *i.e.,* true positives (TrP), and rates of people who are correctly identified as not having dementia, *i.e.,* true negatives (TrN) [17]. PV is given by

$$PV = TrP + TrN \tag{3}$$

B. Accuracy for classification

The key performance measure for CAD is the accuracy of the image interpretation in differentiating normal controls from patients with cognitive impairment. The accuracy can be evaluated by a number of measures, some of them discussed below:

- **Classification Accuracy:** It is the percentage of correct predictions in identifying patients with early stages of dementia to the total number of examples of the dataset as given by Equation (4), in which the value of a + b + c +d refers to the total number of subjects.

$$acc = TrP + TrN/(a + b + c + d) \tag{4}$$

- **Confusion matrix:** It is a two dimensional matrix where each row of the matrix represents an actual class while each column represents a predicted class. By evaluating the performance of a CAD algorithm against a test dataset with known ground truth diagnosis, each matrix cell refers to the number of subjects of the predicted class with respect to their actual class.
- **Precision:** It refers to a proportion of correct predicted subjects to the total number of actual subjects. In order to get the high precision of dementia diagnostics, CAD systems provide consistent interpretations of medical images.

C. Missing values' amputation

The presence of missing values in the training data often affects the performance of the model and, worse, it may lead to wrong and imprecise predictions. To avoid the performance issues and improve the classification accuracy, various imputation methods have been suggested in [11] in order to treat these missing values.

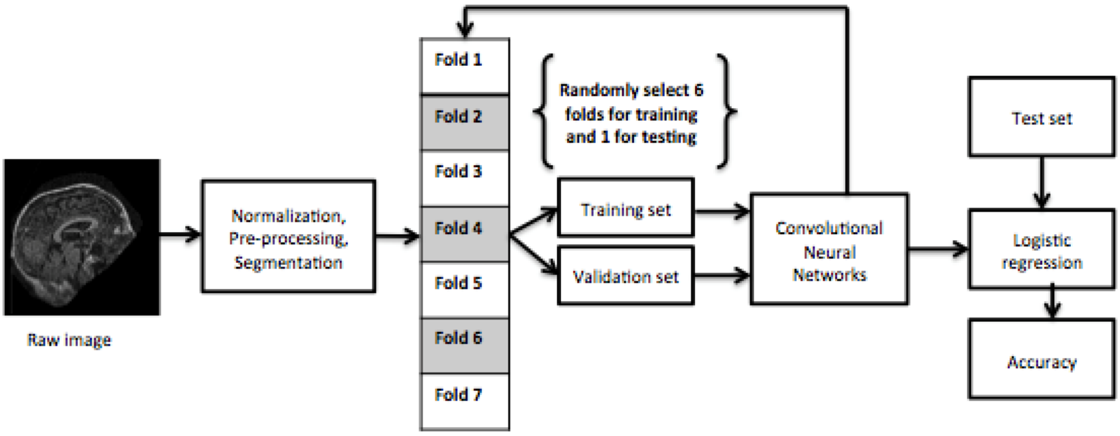

Fig. 4. Architecture of the proposed method for detecting dementia and predicting its accuracy.

However, calculation of the average of existing values for any of numeric variables and the most frequent value for categorical variables in a dataset is a chosen approach to fill missing values with estimated ones. For enhancing the accuracy of the classification of dementia in this study, means of CDR, estimated total interactional volume (eTIV), and normal whole brain volume (nWBV) calculated to fill missing values of CDR, eTIV, and nWBV are given by

$$mean = \left(\frac{Total\ of\ unmissing\ values}{total\ number\ of\ subjects\ with\ unmissing\ values}\right) \quad (5)$$

Various methods for multi-class classification have been built and evaluated based on using the same dataset. In case of multi class classification of dementia, the accuracy is assessed by summing of per class accuracies for all four classes divided by total number of classes denoted as C.

$$Total\ accuracy = \frac{1}{C}\sum\frac{TrP_i+TrN_i}{n} \quad (6)$$

Besides the measurement of accuracy, the sensitivity and specificity for multi-class classification were measured by making confusion matrix and then calculating true positive, true negative, false positive, and false negative rates.

Table 1 compares among the metrics' values obtained by applying our proposed algorithm and those obtained by applying SVM, logistic regression, and LeNet-5 in [46]. It shows for each network, maximum training accuracy reached by network, sensitivity, and specificity. However, the clinical diagnosis was used as the target during training and testing procedures. It is a categorical scale quantifying various types of dementia. As a result, Table 1 indicates that total accuracy of our proposed approach in classifying of five dementia types outperforms the accuracies of other compared models.

VI. CONCLUSION

In this paper, a new computer aided classification system for deffrintiating the different types of dementia in its early stages has been built and tested. This CAD method combines convolutional neural networks and logistic regression. Also, a comparison among the performance of the proposed model and three different models was conducted.The experiments indicate that our proposed model, merging the CNN with regression, achieves better accuracy than linear support vector machine, logistic regression, and CNN with softmax layer by training them on images.These investigations about the performance of our model could be improved in the future studies. For example, the first convolutional layer could be pre-trained with autoencoder. In addition, 3D convolutions could be used instead of 2D convolutions to boost the performance of the model and enhance its prediction.

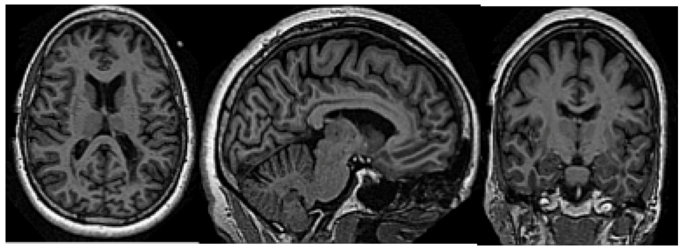

Fig. 5. Three slices of patient's brain with dementia [42].

Table 1: COMPARTIVE ANALYSIS. THE DATASET USED FOR TESTING ALGORITHMS IS FOUND IN SECTIN V. ACC=TRAINING ACCURACY AND AUC=TESTING ACCURACY

Model	ACC	AUC	Sensitivity	Specificity
SVM [32]	67.01%	70.09%	33.33%	77.2 %
Logistic regression	67.04%	68.36%	13.56%	85.53%
LeNet-5 [46]	61%	70.04%	31%	74%
Our model	70.97%	74.93%	46%	53%

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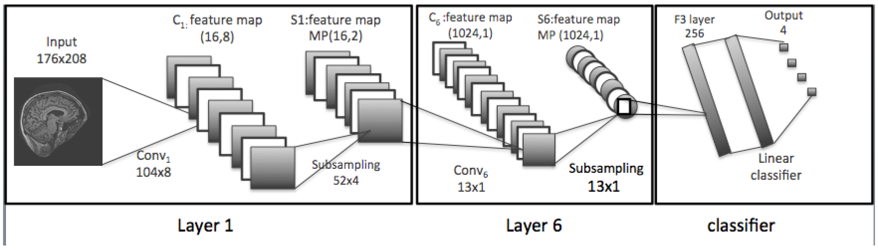

Fig.6. Architecture of Convolutional neural network.

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