Diagnosis of Alzheimer's disease using artificial intelligence

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Abstract

In this article, we explain the importance of early detection Alzheimer's disease and the reason why we should use AI for that. After that, we discuss a little about the past research in this area with machine learning. Moreover, we introduce Deep learning methods such as image processing and signal processing.

Keywords: CNN , EEG , MRI , Artificial Intelligence , Alzheimer's disease , Deep learning

Introduction

Alzheimer’s Disease (AD) is the most common type of dementia. Dementia refers to diseases that are characterized by a loss of memory or other cognitive impairments, and is caused by damage to nerve cells in the brain. In 2010, the number of people over 60 years of age living with dementia was estimated at 35.6 million worldwide. This number is expected to almost double every twenty years. In the United States, an estimated 5.2 million people of all ages have AD in 2014. The Alzheimer′s association claims that AD is the sixth leading cause of death in United States [2]. It is prominent in elderly people with age greater than 65 years but an early onset is also observed in some cases. Good care giving arrangements are thus needed for older people. According to Alzheimer′s association, in 2017, AD will cost about approximately 259 billion US dollars to the US nation. [1]

Alzheimer’s disease is a disease which becomes worse gradually as time passes. It is observed that Alzheimer’s disease embarks 20 years or more prior to beginning of symptoms, which are noticeable after many years of brain modifications. the persons start to get affected by loss of memory and language complications. As time passes, the symptoms increase, become more severe and hinder the capability of people to undertake everyday activities. At this instant, the person is observed to have dementia because of Alzheimer’s disease. [3]

The cerebral cortex of a brain gets severely damaged and shrinks greatly. Cerebral cortex lies in the cerebrum which is largest part of the brain and is associated with memory, logical and critical thinking, reading, spatial orientation, and other voluntary activities. Hippocampus, associated with short term memory and spatial direction, shrinks up and ventricles of brain become large. The damage of cortex is, thus, very destructive for a person′s normal life. It is progressive in nature and leads to ultimate death of brain tissues. The rate of progression of AD is different from person to person owing to different genetic and clinical history. Early and reliable diagnosis of AD is very crucial for providing better treatment and healthcare. [1]

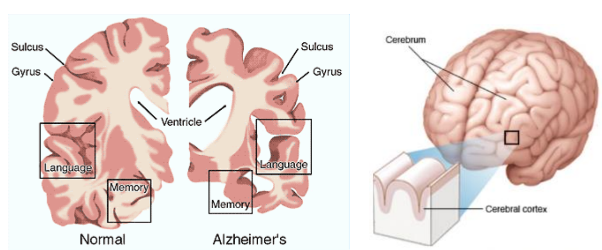

Fig1: Cerebrum, a normal brain and an Alzheimer brain

Artificial intelligence is one of the most trending fields in many expertise like automation, IOT, image processing, machine learning. Beyond general usages, there is a domain in which AI is flourishing path

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breaking innovations is medical science. The performance of a clinician is affected by a number of factors like fatigue, stress, distractions, and inherent cognitive bias towards a specific disease condition. When a radiologist views a medical report a magnetic resonance imaging (MRI) scan of a patient, a biased thinking for a disease would result in missing the chance of detecting other disease conditions. Thus, it leads to considering only a subset of causes and conditions. About 74% of diagnostic errors were attributed to cognitive and approximately 75% of all the medical errors occurred due to diagnostic errors by the radiologists. An increased workload, stress, fatigue, cognitive bias, and poor system are some of the factors behind it. In this situation, smart diagnostic systems provide a safe clinical support to the clinicians. These systems are made to learn and detect several diseased conditions simultaneously. However, these systems are still not able to replace the need of a human expert. These systems provide a supporting or complementary information for improved decisions. [1]

In this article first we examine some old research in this area and then explain some new methods in deep learning such as 2d and 3d convolutions and eeg.

Related works

Over the past few years, various of classification models have been tried for the discrimination of subjects using structural MRI and others modalities in Alzheimer disease. Among these approaches, traditional machine learning methods especially support vector machines (SVM) and its extended algorithms have been used widely in the area. Among these techniques, the best ones are mostly dependent on fusion of multiple biological features and multi-modal imaging data. Another research used a combined kernel technique to fuse structural magnetic resonance imaging MRI, positron emission tomography (PET), and cerebral spinal fluids (CSFs) features and applied a support vector machine (SVM) classifier to perform binary classification. Another research calculated cortical thickness measurements, volumetric measurements, hippocampal shape, and hippocampal texture from MRI scans and obtained results for multi-class classification. In a recent work, Another research used hybrid features, based on imaging and clinical data of patients, followed by SVM classification. [1]

However, with the continuous development of deep learning methods, which has left an impressive result in many big data application fields such as image recognition, text mining and natural language processing in recent years, more and more researchers have similarly explored it for medical images analysis.

Experimental data

The MRI data used in the preparation of this article were a subset obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The ADNI has been validating the use of biomarkers including blood tests, tests of cerebrospinal fluid, and MRI/PET imaging for AD clinical trials and diagnosis since 2004. ADNI is the result of many coinvestigators from a broad range of academic institutions and private corporations.

The raw MRI images from the ADNI database were provided for both three groups (AD, MCI, NC) with different resolution in both depth and dimension. First of all, MRI images all have been spatially normalized by SPM to guarantee that each image voxel corresponding to the same anatomical position. Next, all non-brain tissues, including skull and neck voxels, were remove from the images using CAT, an extension toolbox for SPM, by adopting a voxel-based morphometric (VBM) method. In this step, a study specific grey matter template was then created using the VBM library and relevant protocol. After that, all brain-extracted images were segmented to grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF). GM images were selected and registered to the GM ICBM-152 standard template using non-linear affine transformation.

In 2D form, all horizontal slices from preprocessed 3D GM are split apart as the training data.[2]

2D convolution

Convolutional neural networks (LeCun 1998), also known as CNNs, are a specialized kind of neural network for processing data hierarchically that were inspired by the human visual system. CNNs have been tremendously successful in practical applications such as handwritten digit recognition, image segmentation and object detection.

Equation below describes convolution operation in machine learning application. The input is usually a tensor of data and the kernel is usually a tensor of parameters that are adapted by the learning algorithm. Here we use a two-dimensional image I as our input, we probably also want to use a two-dimensional kernel.

$$S(i,j) = (I * K)(i,j) = \sum_m \sum_n I(i+m, j+n)K(m,n) \quad (1)$$

A hidden layer has several feature maps and all the hidden units within a feature map share the same parameters. The parameter sharing feature is useful because it further reduces the number of parameters, and because hidden units within a feature map extract the same features at every position in the input. At a convolution layer, the previous layer's feature maps are convolved with learnable kernels and put through the activation function to form the output feature map. Each output map may combine convolutions with multiple input maps. In general, we have that:

$$x_j^l = f\left(\sum\nolimits_{i\in M_j} x_i^{l-1} * k_{ij}^l + b_j^l\right) \tag{2}$$

Where Mj represents the input feature maps, f is the activation function, and * denotes the convolution operation. In the computation the scalar term b^l_j is added to every entry of the array $x^{l-1}{}_i * k^l{}_{ij}$. Convolutional layers are followed by pooling layers. [2]

Some work applies the famous GoogLeNet and ResNet model for the diagnosis of AD. GoogLeNet architecture has 22 layers and focuses on a careful increase of: modules in width and depth of the network. It is also known for its Inception module. Multiple filters in the module extract multi-scale information which is combined before passing to the next layer. The architecture keeps track of the computational budget by incorporating dimensionality reduction before each filter in the module. [1]

3D Convolution

Similar to 2D convolution, the 3D convolution is achieved by convolving a 3D kernel to the cube (block) formed by stacking multiple consecutive slices together. Moreover, we adopt ReLU activation function, Batch Normalization, Dropout and L2 regularization in order that accelerate the convergence of the model and prevent overfitting. The final outputs are then flattened and used as inputs for a 3-layer fully connected neural network (i.e. with two hidden layers and an output layer). We choose two hidden layers with ReLU activation function. And an output layer with 3 units with a softmax activation function for 3-way classification. The 3 units in the output layer represent the posterior probability that the input belongs to each of the classes (AD, MCI and NC).

The 3D-CNN is trained by backpropagation (BP) algorithm. [2]

Electroencephalogram

The brain's electrical fluctuations within the neurons create currents that emit through the scalp. As electrodes of electroencephalograph are adhered to the scalp; they detect particular interpretable electrical currents and convert them into corresponding electric waveforms widely acknowledged as in electroencephalogram which depicts induced seizures. Hence, an EEG showcases the succinct timeline of electrical activities happening in the cerebral cells. A set of EEGs could be utilized as a baseline differentiation to scrutinize cerebral function. Identification of various trait of EEG patterns is necessary for evaluation of sleep and its abnormalities. The phenomenon of EEG is showcased by frequency in cycles per second (hertz [Hz]), amplitude [microvolts (lv)] and shape [3].

Electrodes

The information regarding electric signals produced by brain from different scopes is extracted in an EEG record. These distinct scopes are called electrodes technically. The primary EEG electrodes are attached on different lobes of the brain—frontal, frontopolar, temporal, central, parietal, occipital, auricular. All these lobes are shown in Fig. 2. The effects of Alzheimer's majorly hinder the frontal lobe of the brain. The three leads that show major impact due to Alzheimer's are Cz, Fz and Pz [3]. Figure 1 depicts positioning of electrodes respective to brain.

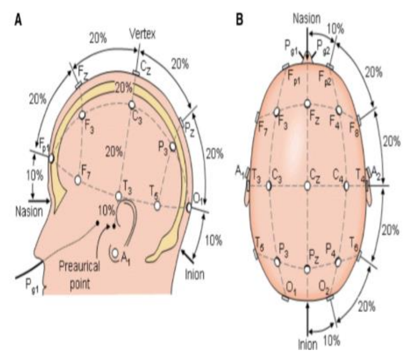

Fig 2

Cz Strip

The examination of EEG widely relies on examination of rhythm strip, which is produced by brain's electrical momentum during the observation period. Mainly for the analysis during the detection of Alzheimer's, the Cz lead is used. The interpretation of Cz is done from the data extracted from the EEG. The observation period of Cz strip [3].

Cz Complexes

The EEG complex depicts the electrical impulses occurring in the EEG periodic cycle. In stage 2 of NREM sleep, there are 2 complexes which mainly occur in the Cz lead. Those complexes are sleep spindle and K-complex [3].

K-Complex

Actually, K-complex is a type of waveform usually observed in EEG. This phenomenon is the authentication mark of stage 2 of NREM sleep [4fall]. It is the biggest and one of the most prominent events in EEG. K-complex has a couple of functions—first is the oppressing cortical aroused in reaction against stimuli that the sleeping brain assesses not to trigger danger. And second is aiding sleep relied memory consolidation. K-complex is interpreted as an acute negative waveform quickly accompanied by a positive waveform with the following traits: (1) at least 0.5 s period , (2) a minimal amplitude of 75 lV for negative waveform from the baseline of EEG [3].

Sleep Spindle

Sleep spindle are tears of neural oscillatory which are produced by the interaction of the thalamic reticular nucleus and other thalamic nuclei occurring in stage 2 NREM sleep having a frequency domain of approximately 11–16 Hz, having a period of 0.5 s or more. Figure 2 represents complexes of Cz lead with patterns of K-complex and sleep spindle in graphical form [3].

Pre-processing

Each EEG signal is normalized with Z-score normalization. The CNN architecture consists of three different types of layer: (1) convolutional layer, (2) pooling layer, and (3) a fully connected layer.

(1) Convolutional layer: It consists of filters (kernels) which slide across the EEG signal. A kernel is the matrix to be convolved with the input EEG signal and stride controls how much the filter convolves across the input signal. This layer performs the convolution on the input EEG signals with the kernel using equation (3). The output of the convolution is also known as the feature map. The convolution operation is as follows[4]:

$$y_k = \sum_{n=0}^{N-1} x_n h_{k-n} \qquad (3)$$

Where x is signal, h is filter, and N is the number of elements in x. The output vector is y. The subscripts denote the nth element of the vector.

(2) Pooling layer: This layer is also known as the down-sampling layer. The pooling operation reduces the dimension of output neurons from the convolutional layer to reduce the computational intensity and prevent the overfitting. The max-pooling operation is used in this work. Max-pooling operation selects only the maximum value in each feature map and consequently reducing the number of output neurons [4].

(3) Fully connected layer: This layer has full connection to all the activations in the previous layer.

Two types of activation functions are used in this work: (1) Rectified linear activation unit and (2) soft max.

(1) Rectified linear activation unit: After every convolutional layer, it is a common practice to employ an activation function. Activation function is an operation which maps an output to a set of inputs. They are used to impart non-linearity to the network structure. The rectifier linear unit is an established activation function for deep learning [4]. The leaky rectifier linear unit (relu) is used in this work as an activation function for the convolutional layers (1, 3, 5, 7, 9, 11, and 12). Relu has properties which adds nonlinearity and sparsity in the network structure. Therefore, providing robustness to small changes such as noise in the input. Equation (4) shows the relu function [4].

$$f(x) = \begin{cases} x & if\ x > 0 \\ 0.01x & otherwise \end{cases} \qquad (4)$$

(2) Soft max: This function computes the probability distribution of the output classes. Hence, Layer 13 uses soft max function to predict which class the input EEG signal (NC, MCI or Alzheimer's) belongs to [4].

$$p_j = \frac{e^{x_j}}{\sum_1^k e^{x_k}} \quad \text{for } j = 1, \ldots k \qquad (5)$$

Where x is the net input. Output values of p are between 0 and 1 and their sum equals to 1.

Training of CNN

A conventional backpropagation (BP) with a batch size of 3 is employed in this work to train CNN. BP is a method to calculate the gradient of the loss function with respect to the weights. BP passes error signals backwards through the network during training in order for the weights to get updated to the network. A batch size is the number of signals used for each training update [4].

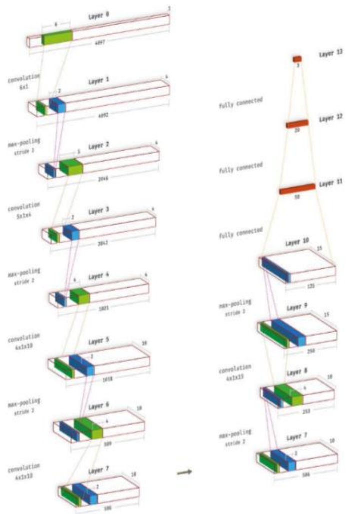

Fig.3

Identifying Alzheimer's

The CNN trained by the EEG signals of Alzheimer then it can diagnosis of the disease, when the input is new EEG signals.

Accurate diagnosis of Alzheimer's disease is made on the K-complex signal.

CONCLUSION

In this paper as mentioned, the Alzheimer's has high cost for goverments.so it is very important to detect Alzheimer's disease in preliminary steps.

In this century the progress of Deep learning especially in image processing and signal processing is helping clinicians to detect disease specially brain's.

We hope that we can prepare an AI system without errors to detect Alzheimer's so we can replace it with a human expert.

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