Gray and White matter changes of the Brain for Medical Diagnosis

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Abstract

To facilitate fast diagnosis and to get accurate result of complex diseases in the individual patients it is necessary to have some automatic classification of diseases. The main objective of this paper is to utilize AI for diagnosis. This paper proposes to take into account the changes in white matter and the gray matter of the brain and its association with global disease severity in patients. The volumes were processed to perform a voxel based analysis of gray matter and white matter volumes. The gray matter and white matter volumes and their correlation with cognitive functions was investigated using SVM classifier .The support vector machine is a increasingly popular tool for machine learning tasks such as classification. SVM, a powerful machine method has been developed from statistical learning and has significant achievement in some field. The foundations of SVM have been developed by Vapnik and are gaining popularity in field of machine learning due to many attractive features and promising empirical performance. Introduced in the early 90's, they led to an explosion of interest in machine learning. SVM method does not suffer the limitations of data dimensionality and limited samples [13]. The proposed method showed high accuracy and therefore may help in early diagnosis of diseases.

Keywords: Gray matter; white matter; SVM classifier; CT; MRI; neurodegenerative diseases.

I. INTRODUCTION

Early stage diagnosis followed by proper treatment may result in saving life of the patient. But accurate diagnosis is not easy. Due to this complexity there is a need for automation of the process of medical diagnosis that can help doctors in the diagnostic process. Therefore an efficient support system has to be developed to support diagnostic process to decrease time and improve accuracy. This paper looks into the diagnosis of neurodegenerative diseases. Neurodegeneration is the gradual deterioration in a person's cognitive abilities, such as memory. This loss may be due to either structural changes which prevents neurons (brain cells) from functioning normally, or lead to cell death. Neurodegeneration is a key feature of several diseases that are referred to as "neurodegenerative diseases". The most common among them are: Alzheimer's disease(AD), Parkinson's disease, Huntington's disease, Amyotropic Lateral Sclerosi(ALS), Frontotemporal Lobar Degeneration (FTLD).Out of these, the most common is the AD. AD is mostly age dependent. 5-10% individuals over the age of 65, and more than 30% over age of 85 are affected. The reason for this is amyloid plaques, which are dense deposits of protein, accumulates outside and around nerve cells and neurofibrillary tangles, which are twisted fibers that build up inside the nerve cell[1]. There are various computer-aided techniques proposed in the past and they include the study of texture changes in signal intensity [2], gray matter (GM) concentrations differences [3].

Estimates have shown that gray and white matter changes are with age. There are a number of modalities for identifying changes in gray and white matter and they have been found to be effective. They include structural MRI[4]–[6] functional imaging modalities like single-photon emission computed tomography (SPECT) [7] positron emission tomography (PET) [8], synchronous neural interactions obtained using magnetoencephalography [7]central spinal fluid (CSF) [3] and electroencephalographic (EEG) rhythms [9][10]. These modalities have been widely used to guide doctors for planning a course of action. Moreover, combinations of two or more modalities have also been done to improve the results of the diagnosis [4]–[6], [11]-[12]. For example, combination of MRI and CT will provide better accuracy than when using any one of the modalities alone [4]–[6]. In combination of two modalities, Fan et al. combined MRI and PET modalities [2]. Walhovd et al.

and Zhang et al. reported that combination of MRI,PET, and CSF modalities helps to get the most suitable and complementary indicators for the diagnosis of AD (or Mild Cognitive Impairment) [4], [11]-[12].

The cause or causes of Alzheimer's diseases are not yet known. However, most experts agree that the cause of Alzheimer's, like other common chronic diseases, develops as a result of multiple factors rather than a single cause. These factors may include a variety of brain changes that begin as many as 20 years before the symptoms start to appear. The "continuum" of Alzheimer's is the time between the initial changes of the brain of Alzheimer's and the symptoms of advanced Alzheimer's. At the initial stage of the continuum, the individual is able to function normally even though there are changes in the brain. Moving along the continuum, the brain can no longer compensate for the increased neuronal damage caused by brain changes, and the individual shows slight decline in cognitive function. In some cases, physicians identify this point in the continuum as MCI. Toward the end of the continuum, neuronal damage and death is so significant that the individual shows obvious cognitive decline, such as memory changes or confusion as to time or place. At life's other pole, the aging brain is characterized by a selective decrease of cerebral white matter. According to the 1984 criteria for Alzheimer's, physicians would diagnose the individual as having Alzheimer's disease only when reaching the last stage of continuum. But the new criteria will diagnose the full swing of continuum as the Alzheimer's. This is because of the Biomarkers used today for finding the changes that occur in the brain.

Researchers are on the lookout of why some individuals who have the brain changes associated with the earlier points of the continuum do not go on to develop the over symptoms of the later points of the continuum. The accumulation of the protein beta-amyloid outside neurons in the brain and the accumulation of the protein tau inside neurons are the main contributors in the development of the Alzheimer's disease. A healthy adult brain will contain 100 billion neurons, each with long, branching extensions. These extensions will help individual neurons to form specialized connections with other neurons. These specialized connections are called synapses, and information flows in tiny chemical pulses released by one neuron and detected by the receiving neuron at these synapses. The brain contains 100 trillion synapses. They allow signals to travel rapidly and constantly through the brain's circuits, creating the cellular basis of memories, thoughts, sensations, emotions, movements and skills. When a patient develops Alzheimer's disease, information transfer at synapses will begin to fail and the number of synapses decreases and neurons gradually die. The beta-amyloid accumulated outside the neurons will interfere with the neuron-to-neuron communication of synapses and this leads to cell death. Inside the neuron, tau form angles which are abnormally high and will block the transport of nutrients and other essential molecules throughout the cell. This process will result in cell death. The patients with advanced Alzheimer's show shrinkage from cell loss and widespread debris from dead and dying neurons.

One known cause of Alzheimer's is genetic mutation. These mutations involve the gene for the amyloid precursor protein and the genes for the presenilin1 and presenilin2 proteins. Inheriting any of these genetic mutations guarantees that an individual will develop Alzheimer's disease. In such individuals, the disease tends to develop before age 65, sometimes in individuals as young as age 30.Alzheimer's is also considered as a disease of gray matter. But there are suggestions that white matter abnormalities also constitute for Alzheimer's.

White matter is the tissue through which messages will pass between different areas of gray matter within the central nervous system. The white matter is white because of the fatty substance (myelin) that surrounds the nerve fibers (axons). This myelin is found in almost all long nerve fibers, and acts as an electrical insulation. This is important because it allows the messages to pass quickly from place to place. White matter abnormalities not only represent an early neuro pathologist event in AD but also plays important role in pathogenesis and diagnosis of AD. In an dissection study of normal brains from age 20 to 90, white matter loss, by volume, was 28 percent, but gray matter loss, was 12 percent, less than half of white matter loss. This greater loss of white matter, with its special role in connectivity and efficient brain communication, suggests a cause for slowed speed in information processing, diminished attentional capacity, and forgetfulness which represents some of the typical cognitive changes of aging. The figure 1(a) shows

deposition of beta-amyloid protein in the hippocampal volume of an Alzheimer's affected patient. The figure 1(b) shows hippocampal atrophy of an Alzheimer's affected patient in the coronal regions.

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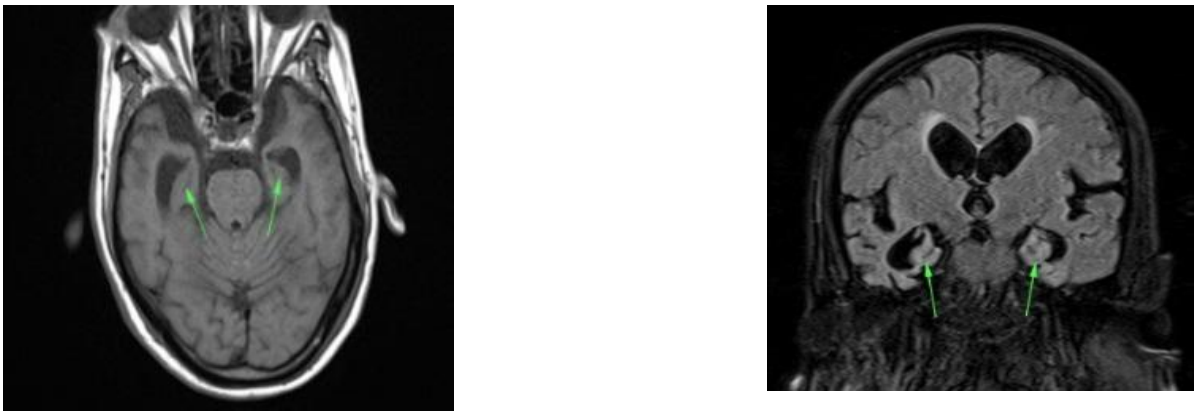
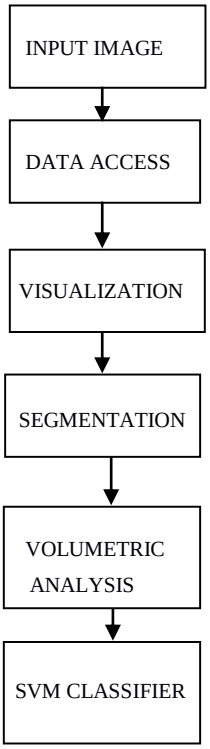


Fig. 1. (a) Beta amyloid protein in hippocampal volume; (b) Hippocampal Atrophy

I. METHODOLOGY

The Block diagram of the proposed work is as follows.



The general structure of the proposed approach is presented in Figure above showing the main steps of the whole process from acquisition process, through the sorting and selection of variables or features using the well-established SVM classifier. The proposed approach is also open to the use of other alternative classification algorithms such as artificial neural networks, optimal discriminant analysis, and so on. This study is opted for SVM only because of its implementation simplicity. Here MRI scans of dicom file type of Alzheimer's affected and not affected patients were collected. Dicom images are the images that contain slices of images. One dicom image may contain upto 60 slice images or more. From each slice of image, get the slice thickness and pixel spacing. Read each slices of images from the obtained scans to get the whole data of the Alzheimer's affected patients and those that are not affected.

A. Visualization

After data accessing, the next step is to visualize. In visualization, images are read from only 30 slices because images from this range, i.e 30 to 60 contains 99.5% of total image content and also has higher sensitivity and specificity, a criterion that is essential while passing to the SVM classifier. Then squeeze the image into one dimensional image. The maximum level is set to twice the maximum of dimension of the matrix. After setting the maximum level, permutation has to be done for rearranging in the order of rows, columns and slice numbers.

B. Segmentation

Segmentation is actually meant to filter the required portions of the image. For doing so, a threshold is set. The value that exceed threshold is considered as 1 and below as 0. Rotation has been done on the image by

using imrotate function of MATLAB to get a clear angle of the image. Original data is duplicated for later reference.

Apply the thresholding rule to ignore unnecessary portions. The thresholding values are set based on the intensity values shown in the input image. When the set threshold falls below or equal to 40, it allows the removal of lower levels that might include the cerebro-spinal fluid and the air. The threshold value that falls above or equal to 100 of the set threshold value ignores the higher levels that include the skull and other hard tissues. To erode away the thick layer or dissolving the thin surrounding tissues is done by padding ones to the rows and columns.

At this phase, the biggest area and its area content is considered to analyse the Alzheimer's affected regions. To grow back the original, the Matlab function imdilate is used. From the obtained brain image, gray matter and white matter are separated on the basis of setting a threshold value 67, which when exceeds this value is regarded as white matter and below are regarded as gray matter and that equals zero as head or skull portion.

C Volumetric Analysis

AD patients suffer from cerebral atrophy, which can be distinguished from normal aging, and specific regions are more atrophied along the progression of AD. The adjusted volumes and ICV of the volumetric variables are then combined to generate a variable vector discriminator for each subject. Test is carried to determine the significance of each variable in the classification outcome and are selected and ranked in the order of Alzheimer's affected and those not affected. The slice thickness and the pixel size multiplied by the area of the segmented portion gives the volume of Alzheimer's affected region. Also found the separate volumes of gray matter and white matter, and also their densities which is to be given as an input to the SVM classifier.

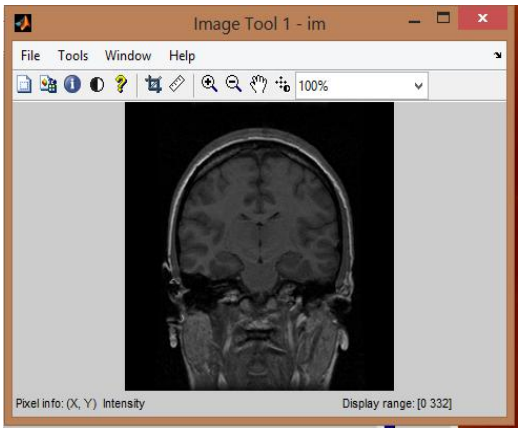
D SVM classifier

SVMs are set of related supervised learning methods used for classification and regression [13]. They belong to a family of generalized linear classification. SVM classifier shows good performance in classification of datas. The SVM implemented is a soft-margin SVM classifier. SVM maps the original features via a kernel function to construct a maximum margin classifier in a high-dimensional feature space. SVM map input vector to a higher dimensional space where a maximal separating hyperplane is constructed. Two parallel hyperplanes are constructed on each side of the hyperplane that separate the data. The separating hyperplane is the hyperplane that maximize the distance between the two parallel hyperplanes. An assumption is made that the larger the margin or distance between these parallel hyperplanes the better the generalization error of the classifier will be [13].

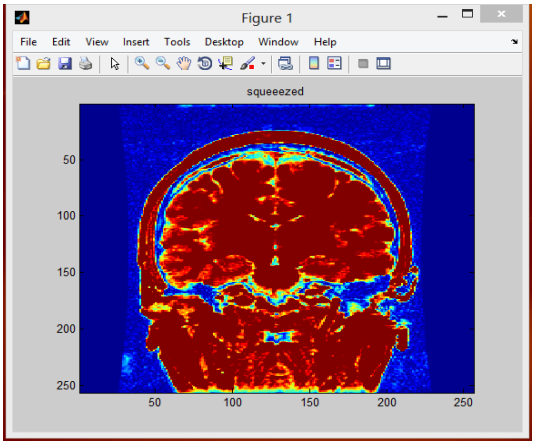
II. RESULTS AND DISCUSSIONS:

A. Visual Analysis:

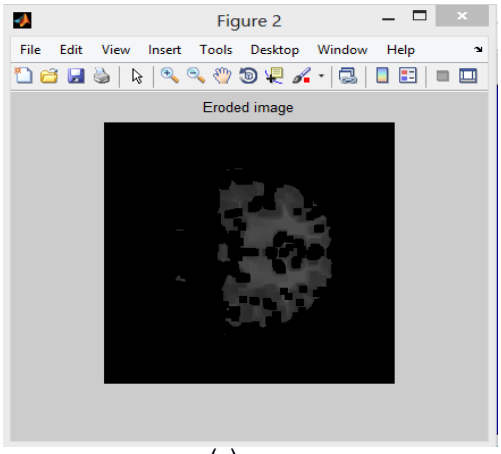
The figure below shows the various stages of the processing in identification of the neurodegerative disease.



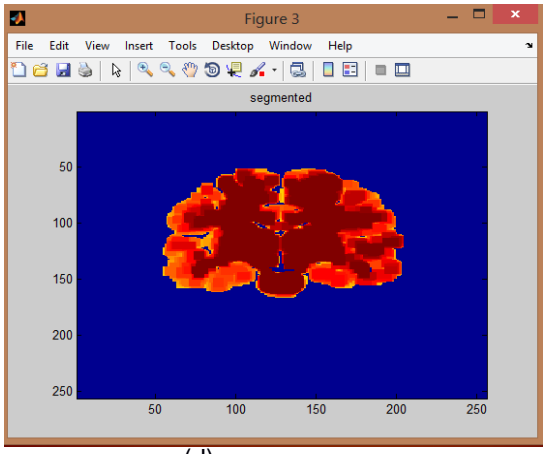
(a)



(b)



(c)



(d)

Fig. 2. (a) image showing pixel variations (b) squeezed image (c) eroded image (d) segmented image

B Quantitative Analysis

The quantitative analysis of the images were done by considering the voxel size, brain volume , gray volume, white volume and the fractions of gray and white matter. The output of the neurodegenerative affected image produced the following output.

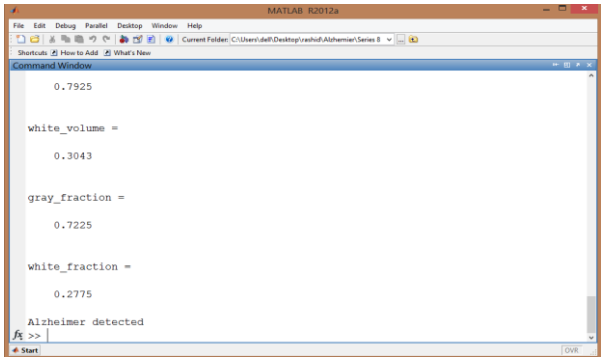


Fig.3 Output

voxel_size =0.8594 0.8594 3.0000

brain_volume= 1.0969

gray_volume = 0.7925

white_volume = 0.3043

gray_fraction = 0.7225

white_fraction = 0.2775

III. Conclusions

The main aim of using Image processing is to make the physician confident in their diagnosis by offering quantitative assessments of brain images, especially neurodegenerative disorders. We have presented a methodology for computer-aided diagnosis and demonstrated using real data. .It is found that SVM produced correct output while giving any of the untrained image included in our database as input whereas with KNN some did not work. SVM assumes there exist a hyper-plane seperating the data points , while kNN attempts to approximate the underlying distribution of the data in a non-parametric fashion Therefore it is found that SVM performed better with high accuracy when the data is preprocessed and given as input.

References

[1] S. H. Braak and E. Braak, “Evolution of the neuropathology of alzheimer’s disease,” Acta Neurol. Scand. Suppl., vol. 165, pp. 3–12, 1996

[2] Y. Fan, S. M. Resnick, X. Wu, and C. Davatzikos, “Structural and functional biomarkers of prodromal Alzheimer’s disease: A high-dimensional pattern classification study,” Neuroimage, vol. 41, no. 2, pp. 277–285, Jun. 2008

[3] G. B. Frisoni, C. Testa, A. Zorzan, F. Sabattoli, A. Beltramello, H. Soininen, and M. P. Laakso, “Detection of grey matter loss in mild alzheimer’s disease with voxel based morphometry,” J. Neurol. Neurosurg. Psychiatry, vol. 73, pp. 657–664, 2002.

[4] DN. C. Fox and J. M. Schott, “Imaging cerebral atrophy: Normal ageing toAlzheimer’s disease,” Lancet, vol. 363, no. 9406, pp. 392–394, Jan. 31,2004..

[5] K. B. Walhovd, A. M. Fjell, J. Brewer, L. K. McEvoy, C. Fennema-Notestine, D. J. Hagler Jr., R. G. Jennings, D. Karow, and A. M. Dale,"Combining MR imaging, positron-emission tomography, and CSFbiomarkers in the diagnosis and prognosis of Alzheimer disease," AJNRAmer. J. Neuroradiol., vol. 31, no. 2, pp. 347–354, Feb. 2010.

[6] E. Westman, J. Muehlboeck, and A. Simmons, "Combining MRI and CSFmeasures for classification of Alzheimer's disease and prediction of mildcognitive impairment conversion," Neuroimage, vol. 62, no. 1, pp. 229–238, 2012.

[7] P. Vemuri, H. J. Wiste, S. D. Weigand, L. M. Shaw, J. Q. Trojanowski, M. W. Weiner, D. S. Knopman, R. C. Petersen, and C. R. Jack Jr., "MRI and CSF biomarkers in normal, MCI, and AD subjects: Predicting future clinical change," Neurology, vol. 73, no. 4, pp. 294–301, Jul. 28, 2009.

[8] K. A. Johnson, K. Jones, B. L. Holman, J. A. Becker, P. A. Spiers,A. Satlin, and M. S. Albert, "Preclinical prediction of Alzheimer's dis-ease using SPECT," Neurology, vol. 50, no. 6, pp. 1563–1571, Jun. 1998.

[9] G. Henderson, E. Ifeachor, N. Hudson, C. Goh, N. Outram,S. Wimalaratna, C. Del Percio, and F. Vecchio, "Development and assessment of methods for detecting dementia using the human electroen-cephalogram," IEEE Trans. Biomed. Eng., vol. 53, no. 8, pp. 1557–1568,Aug. 2006.

[10] R. Hornero, J. Escudero, A. Fernandez, J. Poza, and C. Gomez, "Spec-tral and nonlinear analyses of MEG background activity in patients withAlzheimer's disease," IEEE Trans. Biomed. Eng., vol. 55, no. 6, pp. 1658–1665, Jun. 2008.,

[11] C. Huang, L. Wahlund, T. Dierks, P. Julin, B. Winblad, and V. Jelic,"Discrimination of Alzheimer's disease and mild cognitive impairment by equivalent EEG sources: A cross-sectional and longitudinal study,"Clin. Neurophysiol., vol. 111, no. 11, pp. 1961–1967, Nov. 2000.

[12] D. Q. Zhang, Y. P. Wang, L. P. Zhou, H. Yuan, D. G. Shen, andA. D. N. Initia, "Multimodal classification of Alzheimer's disease and mild cognitive impairment," Neuroimage, vol. 55, no. 3, pp. 856–867,Apr. 1, 2011.

[13] V. Vapnik. The Nature of Statistical Learning Theory. NY: Springer-Verlag. 1995Y. Fan, S. M. Resnick, X. Wu, and C. Davatzikos.,