Research Article

Classification of Brain MRI for Detection of Alzheimer's Disease

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Abstract

In this study, we propose a method for the classification of T1-weighted Magnetic Resonance Images (MRI) of the Brain in case of Alzheimer's disease based on extraction of different features. The dataset used comprises of right handed females of age group 18-96 years and is helpful to determine the onset and early detection of the disease. The processed MR images are used to obtain different features for training of classifiers. The whole Grey matter is considered as the Region of Interest (ROI) because it contains the Amygdala and Hippocampus, the regions most affected due to Alzheimer's. The features used for this study are some of the crucial second order features derived from Grey Level Co-occurrence Matrix (GLCM) such as Entropy, Energy, Homogeneity and Correlation and also the ratio of the Grey Matter Volume and the White Matter Volume to the Volume of the Cerebrospinal Fluid. An accuracy of 84% has been achieved with a sensitivity of 100%. This proves to be a better method than Voxel Based Morphometry extraction method which is cumbersome but has been proved to be more accurate but not as sensitive.

Keywords:

1. Introduction

A different neural network, consisting of multiple nerves and blood vessels forming the human brain, is the central nervous system. It weighs roughly 1 kilo and comprises of billions of synaptic structures comprising the Central Nervous System that governs all body movements (Mai et al. 2016). Neurons function as a contact pipeline for separate body parts. The effective handling of the brain depends on its neural connection efficiency. The brain accomplishes various activities, from thinking to walking and often helps to maintain hormonal equilibrium to help body movement (Durston et al. 2001).

The four lobes which make up the cortex are the frontal, occipital, parietal and temporal lobs. The front lobe regulates the decision-making and problem solving capability of an individual. The motor cortex of the frontal lobe uses the reaction to control data from various lobes Biological variations in the frontal lobe may often induce shifts in emotion and actions (Hall 2015; Bostan et al. 2013).

The temporal lobe at the base of the brain is responsible for the cognitive and retrieval skills of a person. Audience and sensory responses are tracked throughout the tempo lobe systems. Damage to the lobe creates complications with vision, hearing and voice (Jeneson & Squire 2012). The hippocampus, amygdala, entorhinal cortex and parahippocampal cortex are all on the inner side of the temporal lobe, responsible for the thinking, memory and emotional ability of the person. The centre for vision perception is the occipital lobe located at the rear of the brain. Occipital cortex biological disruptions lead to vision deficiencies (Raz & Levin 2015). The lobe is close to the centre of the brain. It makes communication with the brain and other parts of the body

smoother. It also helps to understand the spatial-visual relationship. The deficiency of this lobe affects changes in eye control and vocal power (Cappelletti et al. 2013).

The cerebellum under the occipital lobe tends to sustain the body's location by coordinating and controlling the activity of limbs. The brain stem links the brain and spinal cord and serves as a brain and body relay station. The brain has a defensive cloth consisting of bones such as the skull and a colourless substance called the cerebral fluid to cover the subanatomic components (CSF). Includes coating, mechanical protection and brain buoyancy. This safety case (Damasio 1995; Ungerleider & Haxby 1994).

1.1 Neurodegenerative Diseases

Irrespective of the defensive insulation, brain regions are susceptible to damage that can lead to many diseases similar to dementia (Bigler 2001). Diseases, including infection, pathology and brain lesions related to strokes and blood clots, can be caused by many factors. The regeneration ability of neurons is very little and they are more susceptible to damage. The origin of damage to neurons is neuronal loss and tissue deterioration. NEIMANN-PICK DISORSIONS, ADD, Fronto-temporal Dementia, Parkinson's disease, Amyotrophic lateral sclerosis and other diseases, such as Huntington's disease, tend to degenerate brain tissues (Parikshak et al. 2015).

Behavioral changes, cognitive loss and gait disorders are all manifestations of neurological illnesses, which are lethal if not early detected, assessed and treated (Mattson et al. 2001). Alzheimer's disease is one of the most prominent types of dementia and it progresses steadily and gradually. It induces multiple levels of cognitive impairment in a person (Prince et al. 2015; Ferreira et al. 2014).

The accumulation of tau-beta and amyloid-beta in the brain triggers the condition of Alzheimer. Plaques of amyloid develop in the MTL and cortex regions due to the excessive presence of amyloid-beta proteins, which cause neuronal problems and inhibit interaction between the brain regions (Brunnstrom & Englund 2010). Neurofibrillary tangles (NFTs), which cause neuronal breakdown and neuronal mortality of brain tissues, are produced in irregular deposition of tau proteins. Neuronal cells death induces morphological modifications in brain regions, which ultimately helps to shrink the brain.

The three stages of the disease pathway include preclinic Alzheimer's (preclinical AD), Mild Cognitive Impairment (MCI), and Alzheimer's (AD). There are multiple signs at each point that decide the magnitude of this illness (Amieva et al. 2008). The participants had longer periods of pre-existing Alzheimer's disorder before clinical symptoms are present. No noticeable memory failure or behavioural changes are present at this point (Petersen et al. 2001; Reisberg and Franssen 1999). Over this time the participants exhibit no symptoms of dementia, but the progressive deposition of abnormal proteins is causing neuropathological improvements in some subsound anatomical areas of the brain (Dubois et al. 2010). The two conditions consistent with this stage are aphasia and cortical atrophy. These persons are at substantial risk of psychological problems, which include preventive care (Dubois et al. 2010).

The second stage of Alzheimer's disease is miniature brain impairment in which the usual habits and processing capability of patients are not impaired. It is triggered by the transition from age to Alzheimer's disease (Ewers et al. 2012). Since Alzheimer's disease currently has little effective therapies, it is vital to recognise this disease at an early stage (da Silva Lopes et al. 2010; Dubois & Albert 2004). The participants have a variety of cognitive abilities and difficulties coping through language use efficiently (Nestor et al. 2004). Services suggest the early detection and action of cognitive and neuropsychiatric shifts at this period.

Alzheimer's participants have a brain dysfunction that impacts their daily lives (Dubois et al. 2010). Patients currently experience significant difficulties with carrying out personal activities such as feeding, listening and walking. The episodic deterioration of memory in typical Alzheimer cases, which increases as the disease progresses (Jellinger 2014). In both the neocortex and other regions of the brain, NFTs is discovered. Functions related to cognitive capacities for the performance of daily activities are of considerable difficulty for fully-developed AD sufferers. When Alzheimer's disorder advances, their reflexes get worse (Merriam et al. 1988).

1.2 Disease Diagnosis

A brain autopsy is the only traditional gold protocol to establish the origin of Alzheimer's disease. A rapid loss of the recollection is the strongest indication of Alzheimer's disorder (Petersen et al. 2014; Ewers et al. 2012). Among the measures that were used for diagnosis of Alzheimer's disorder are mini-mental status (Folstein et al. 1975), Clinical Dementia Rating (CDR) (Hughes et al. 1982), Montreal cognitive analysis (Nasreddina etal. 2005), geriatric distress scale(Yesavage et al. 1983). (Lawton & Brody 1970). During these tests, short-term memory, problem solving skills, alerting and language capacity are normally tested. The MMSE scale is between 27 and 30 and the average is taken into account. On average, the MMSE values are

reduced by 2 to 4 points a year (Kukull et al. 1994). The overvalued average of the total CDR score is 0 for healthy people, 0,5 for preclinical dementia, 1, 2 for scientifically verified dementia, and 3 for clinically established dementia.

In diagnosing Alzheimer's disorder, the cognitive test itself was found to be ineffective. For effective diagnosis of Alzheimer's disease it is important to identify biomarkers susceptible to brain changes linked with disease progression. Irregular protein accumulation causes chemical difference in the brain's CSF. CSF is therefore considered a possible biomarker for neurological disorders diagnosis (Susanto et al. 2015). The heterogeneity analysis of the CSF involves a lumbar puncture, on the other side. It has been found that the subject has several side effects following the operation. As a result, progress in the development of noninvasive testing approaches for Alzheimer's disease (Welge et al. 2009; Delano-Wood et al. 2008).

Neuroimaging is a successful instrument for early detection of Alzheimer's disease. Neuronal loss is observed through imaging methods in multiple systemic brain areas (Norfray & Provenzale 2004). Imaging techniques such as positron emission tomography, MRI, and computerised tomography can diagnose and quantify certain changes arising from multiple neurodegenerative diseases (Mueller et al. 2005; Soucy et al. 2012). Neuroimaging-based biomarkers may detect dementia well before clinical symptoms arise. It helps to improve strategies of prevention to reduce Alzheimer's symptoms.

Structural resonance imaging (SMRI), which allows non-invasive analysis of brain structures, is recognised for the higher tissue contrast and resolution (Bozzao et al. 2001; Vemuri & Jack 2010; Johnson et al. 2012). Structural MRI identifies the brain areas affected by Alzheimer's disease, and follow their progress in neuropathology (McEvoy & Brewer 2010; Chou et al. 2010). Data concerning anatomical brain deformation was obtained (Du et al. 2001). Appropriated comparison to brain anatomy view is given by T1 weighted MRI (Harper et al. 2013). Lesions are identified through axial perception, while a coronal view is used to analyse the internal structure of subcortical tissues (Konrad et al. 2009; Frisoni et al. 2010).

Since atrophy is reflected in MR images in sub-anatomic areas, measures taken from MR images are used in the evaluation of AD-binding neurosurgery (Holland et al. 2009; Lillemark et al. 2014). This regional neurodegeneration takes place during the early stages of Alzheimer's disease and helps with MCI diagnosis (Vos et al. 2012). GM atrophy is microscopically in line with MCI (Chou et al. 2010) and supports treatments that slow the rate of development of a disease a little (Zhang et al. 2011).

The hippocampus and entorinal cortex are the first brain regions in which Alzheimer's disorder is atrophied. There are differences of GM tissue in the temporal lobe, ganglia and thalamus. In addition to the temporal lobe, the frontal and parietal lobes display volumetric deformation to differentiate MCI and AD patients (Duara et al. 2008; Duara et al. 2013). Study into the regions of subcortical grey matter is therefore anticipated (Ryan et al. 2013).

Studies show a substantial increase in ventricular volumes in the case of Alzheimer's disease. Consequently, shifts in the ventricle influence the surrounding structures of white and grey matter according to AD (Carmichal et al. 2007). The Callosum corpus is part of the Callosum corpus

The (CC), adjacent to and above the brain ventricles, changes due to the ventricular dilation which signify the overall atrophic process of the brain (Ardekani et al. 2014). Aggregating AD condition, like cortical NFT, amyloid plaques and cognitive dysfunction, contributes to gradual dilution of the ventricular system (Chou et al. 2009; Chou et al. 2010).

Regional tests derived from ventricle enlargement and callosal atrophy characterise the essential morphometric measurements in neuropathological changes caused by AD and MCI (Pennanen et al. 2004; Ferrarini et al. 2008; Cho et al. 2014). Ventricular volume measurements are very sensitive to the prevalence of illness. Since the boundaries of cortical structures are freely defined, it is more accurate than measuring cortical structure to measure ventricular variations.

1.3 Brainstem Deformation

Alteration of the prefrontal system during development of the condition is consistent with cognitive impairment. In the fourth stages of seven-stage AD progression model, the incide of cognitive impairment is shown (Brodaty et al. 2003). However, like neurodegenerative illnesses, AD has an extended preclinical prodromal period marked by non-cognitive traits such as diminished physical capacities and behavioural difficulties.

Neuropsiatric symptoms (NSP) such as depression, apathy, turmoil, illusions and cognitive symptoms are present in the demented subjects (Ismail et al. 2016). Similar to the occurrence of AD, there is a very sparse perception that NPS incidence is involved with physiological causes. In neuropsychiatry, the emphasis is also on

the prefrontal areas that encourage a person's comportemental and cognitive ability. (APA 1994; Jayakar & Huang 2010; Morris 1993; Slats et al. 2013). More detail from APA 1994. Neuropathological findings have associated brainstrokes with different cognitive and behavioural disorders (Simic et al. 2009).

The brainstem consists of long axons and dispersed nuclei which bind several cortical structures and rule various cognitive functions and is an extremely complex neuronal structure. The brain stem consists of nerves that regulate many autonomous functions such as muscle control, pain modulation, autonomous reflection, excitement and awareness. The brainstem midbrain is susceptible to injuries of people that are malnourished. Atrophy of the brainstem, owing to its neuropatological modifications, is known to be a major pathological centre in the growth of AD.

For the performance of the executive tasks are accountable the prefrontal and anterior corticulate linked to the brainstem. Disorder in the frontal subcortical system influences the individual's concentration and management process. Differences in the dorsal raphe nucleus synthesis of serotonin and acetylcholine are responsible for disturbing mood and sleep throughout the existence and development of AD. The brainstem also remains a thoroughly researched organ, despite its considerable effect on neurodegenerative processes, since it has trouble overcoming the brainstem's design (Grinberg et al. 2011; Lee et al. 2015). In order to delineate the brainstem it is essential to accurately segment an algorithm to acquire the moral variance during development of disease.

1.4 Need for Shape Analysis

Shape measurements are gaining interest in neuroimaging analysis due to its ability in extracting the intrinsic morphometric changes of brain structures due to the incidence and progression of AD (Styner *et al.* 2006; Racine *et al.* 2014). Regionwise structural variations are not sufficiently depicted in the volume measurement as there exists a large overlap between normal and abnormal values. The accurate delineation of brainstem is essential to analyze its morphometric changes (Ng *et al.* 2014). Characterization of shape variation in brainstem region is possible by using shape measures (Wachinger *et al.* 2015). The identification of the local shape variations provides new insights about the underlying biological processes related to neurological disorders, and leads to accurate treatment and also help for developing better treatment strategies (Ng *et al.* 2014; Styner *et al.* 2003). Hence, this kind of analyses could further be involved for automatic diagnosis of diseases

2. Literature Review

Research has been carried out for detection of Alzheimer's disease from structural as well as functional MRI. In case of structural MRIs there has been a prime focus on the extraction of structures where maximum atrophy is seen in case of AD. These atrophies can be compared with perfectly normal brain structures and the disease can be detected.

A lot of work has been carried out by Voxel Based Morphometry (VBM) using Brain MRI. VBM preprocesses the images by standardizing images to same stereotactic space using linear affine transformation and further warps, smoothens and performs a statistical analyses. This has been carried out using different software on different kind of MR images of different age groups and interesting results have come up. The optimized VBM (SPM2) on cross sectional data (Good CD et al.)[7] showed a reduction in parietal and medial temporal gray matter structures as well as in white matter volume. The SPM99 on longitudinal (Resnick UM et al) and cross sectional (Matsuda H et al) proved a reduction in gray matter but in different regions. Savio et al. [8] obtained SPM using VBM extraction of two kinds of features: Mean and Standard Deviation of voxel values of Gray Matter (GM) and a high dimensional vector for GM segmentation values for different voxel locations.

Research not involving VBM has not been that popular but the few existing works have given concrete results. Saima et al proposed extraction by defining a rectangular ROI mask derived from manual segmentation of the hippocampal region on one half of the images which served as a training set for hippocampus area calculation. [9] These left as well as right hippocampal regions along with the GM, WM and CSF areas were fed as features to different classifiers and their performance was compared. SVM and J48 showed best results with an ensemble of features.

Another fascinating approach to the problem is by using second order features of Gray Level Co-occurrence Matrix. Daniela et al [10] calculated features like Entropy, Energy, Homogeneity and Correlation from the Hippocampus as an ROI to use as a basis for classification.

3. Methodology

In this approach, we simplify things and reduce computational time and instead of the cumbersome VBM approach, we try to improve the results by feeding a promising ensemble of features to the classifier – a

combination of textures extracted using GLCM, the ratio of the Gray Matter volume and the White Matter Volume to the Cerebrospinal Fluid Volume. Literature says atrophies are also seen in the CSF and other areas of GM apart from the Hippocampus. [4] Since concentrating just on the hippocampal region for volume calculation is narrow in approach and tedious because it cuts down the chances of other atrophies and also involves accurate extraction and subsequent calculation and cannot be done without help from a Neuro-radiologist, we can make use of the a ratio with the gray matter and the CSF and a similar ratio of the white matter and CSF and hence assure a more intensive learning, therefore, better results due to a reduced dataset.

3.1 Preprocessing

The dataset was processed so that it could properly cater to the method requirements. Each dataset consists of 3D MR images from the sagittal, coronal and transversal views. After acquisition, the images were first defaced and then ATLAS registered gain field corrected and motion corrected. Because brain scans may differ in size and shape for individual subjects, wrapping these to same template will help in identification of the anatomical structures. In our approach we used most widely used brain template, that is, Talairach and Tournoux coordinate system.[11]

The brain image primarily consists of the White Matter (WM), the Grey Matter (GM) and the Cerebrospinal Fluid (CSF). These important tissue intensities may overlap with the other regions of the head after thresholding like the bone and skin. Therefore, there is a strong chance that the presence of these non-brain pixels in MR image may reduce the reliability of identifying interested brain regions. For this purpose we require that non-brain pixels be trimmed off the MR image. Brain surface extraction [13] is a preprocessing step in which non-brain tissue is removed from the MRI. The extraction parameter is set to 0.5 for optimal results.

A subsequent step included increasing the contrast in the images such that there is a clear distinction between the WM, GM and CSF. The Finite Fixture Method has simple mathematics but is ineffective with high noise. Thus the Hidden Markov Random Field

Model and Expectation Maximization (HMRF-EM) [21] algorithm after Otsu's Thresholding [22] was used.

- The maximum interclass variance is the desired threshold. This gives us initial parameter set $\Theta(0)$ and initial labels x(0).

- In an HMRF-EM segmentation implementation, if

y=[y1, y2,….yn] represents an image where yi is the intensity of pixels,

x=[x1, x2,….xn] are all possible labels for classes

With the EM algorithm using Θ, a parameter set is obtained iteratively till $Q(\Theta|\Theta(t))$ maximizes.

For each parameter set, label sets are obtained. This repeats till total posterior energy is

minimized i.e $x^* = \arg\min x\in\chi \{U(y|x, \Theta) + U(x)\}$ (Hammersley–Clifford theorem).

The three intensities were labelled 1, 2 and 3 for White Matter, Gray Matter and CSF respectively.

4. Results

4.1 Case 1:

The MRI images are of 176 X 208 X 176 pixels. In the first case, we take 11 slices of the MR images, i.e. every 16 pixels, we take one slice and extract GLCM features. Then we average the features over all 11 slices. The Grey Matter and White Matter volume ratios are taken over the entire MR of the brain.

A 2-fold, 5-fold and 10 –fold cross validation process is carried out. The samples are divided into 5 (or 2 or 10) subsamples. One of the subsamples is retained as the testing data and the remaining 4 (or 1 or 9) subsamples are used as the training data. This is repeated for 5 (or 2 or 10) iterations, using one of the subsamples as testing data each time.

Average accuracy calculated was recorded as follows:

Folds	Accuracy
2	82%
5	73%
10	76%

4.2 Case 2:

In the second case, we only take the slices of the MR Images that contribute to the hippocampal and amygdala regions. The GLCM from these slices are averaged and fed to the classifier along with the Grey and White Matter volume ratios.

2-fold, 5-fold and 10-fold cross validations are carried out again and average accuracy was recorded as follows:

Folds	Accuracy
2	83%
5	73.3%
10	75%

4.3 Case 3:

In the third case, we only take 1 slice of the MR image, i.e. the centre slice. The hippocampal and amygdala regions are clearly visible in this slice. GLCM was calculated and fed to the classifier along with Grey and White Matter volume ratios.

2-fold, 5-fold and 10-fold cross validations are carried out again and average accuracy was recorded as follows:

Folds	Accuracy
2	84%
5	73.3%
10	78%

5. Conclusion

The results had a perfect sensitivity of 100% in each case. The accuracy is the highest in the 2-fold cross validation for Case 3 where only one slice of the MR image was considered. The high sensitivity shows that even though all cases were detected with dementia during the first MRI session, some were declared as non-cognitive after the subsequent session. The method proved to be 100% effective for diagnosing the patients based on their MR. The method has a higher efficiency as compared to the VBM method which has shown a sensitivity of 85% [16], although VBM helps show the comparison of MRI of patients with early and late onset of AD. The method although performs worse than methods which have used features localized to the Hippocampal area also, which have shown an accuracy of 87.5% with SVM. They have shown an accuracy of 93.75% when they have used an ensemble of classifiers like SVM, MLP and J48. [4]The same experiment was carried out with a limited dataset of female right handed patients between the ages 18-30 years. It showed an accuracy of 86.36% when 90% of the data was used for training and 10% for testing. The brain size and dementia levels do get affected with age. This shows that accuracy of classification increases when dataset within similar age group in taken. The limitations were in getting only the regions from the MR images that were atrophied in case of Alzheimer's. This is only possible if we have annotations by doctors. The closest we could get in this study was only considering the slice with the maximum hippocampal and amygdala regions (case 3) and it does show a higher accuracy in that case.

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