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Survey Based Study: Classification of Patients with Alzheimer's Disease

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Abstract

Neuroimaging is a description, whether in two-dimensions (2D) or three-dimensions (3D), of the structure and functions of the brain. Neuroimaging provides a valuable diagnostic tool, in which a limited approach is used to create images of the focal sensory system by medicine professionals. For the clinical diagnosis of patients with Alzheimer's Disease (AD) or Mild Cognitive Impairs (MCI), the accurate identification of patients from normal control persons (NCs) is critical. Recently, numerous researches have been undertaken on the identification of AD based on neuroimaging data, including images with radiographs and algorithms for master learning. In the previous decade, these techniques were also used slowly to differentiate AD and MCI symptoms from structure classification methods. This review focuses on neuroimaging studies conducted to detect and classify AD, through a survey based on Google Scholar content. We explore the challenges of this field and evaluate the performance of these studies along with their negative aspects.

Keywords: Alzheimer's Disease, Neuroimaging, Magnetic Resonance Images, ADNI, OASIS.

دراسة بحثية: تصنيف المرضى الذين يعانون من مرض الزهايمر

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الخلاصة:

عادة ما يكون التصوير العصبي إما ثنائي أو ثلاثي الأبعاد وذلك للنظام الحسي عند الإنسان والتي تشمل بنية الدماغ ووظائفه التي سيتم فحصها. إن التصوير العصبي هو أداة واعدة لتشخيص الأمراض بشكل عام ، وهناك بعض الطرق التي يمكن للخبراء الطبيين استخدامها لالتقاط صور للنظام الحسي البؤري. يعد التصنيف الدقيق للمرضى الذين يعانون من مرض الزهايمر أو المرضى الذين يعانون من ضعف الادراك الخفيف ، وهي التي تعتبر المرحلة الاولى لمرضى الزهايمر ، أمر بالغ الأهمية للتشخيص السريري. لقد كان الاعتراف بمرض الزهايمر من معلومات التصوير العصبي ، على سبيل المثال ، الأشعة السينية بالاعتماد على التعلم الآلي موضوع بحث جدي في الآونة الأخيرة. علاوة على ذلك ، تم استخدام هذه الإجراءات على مدار العقد الماضي بشكل تدريجي لتمييز علامات الزهايمر بطرق هياكل التصنيف. استعرضنا تطبيق دراسات التصوير العصبي في مجال اكتشاف وتصنيف مرض الزهايمر. كماعملنا على استكشاف الصعوبات في هذا المجال وتحديد صفات هذا المرض والجوانب السلبية التي يجب تسويتها.

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1. Introduction

Alzheimer's disease is named after Alois Alzheimer; the specialist who originally described's the disease as a physical illness influencing the brain. AD is the leading cause of dementia and defined as an accumulation of side effects that can influence the loss of memory and the thought capacity of the brain when the disease is damaging [1]. In the United States, AD is the sixth leading cause of death in the general population and the fifth among Americans age around 65 years. Deaths from stroke, heart disease and prostate cancer decreased between 2000 and 2017, while AD deaths increased by 145% [2].

2. Brain Scanning Techniques

Cerebral changes caused by AD even precede the appearance of the amnestic side effects and they progress in a pattern that typically involves the temporal lobe and the hippocampus, as can be demonstrated by structural MRI imagery. An MRI scanner uses a powerful radio waves and magnetic field to produce digital images of tissues and structures in the brain that can detect abnormalities or tumors [3]. The performance of the nuclear resonance signals recuperated from various areas of the brain will improve the images. The relaxation times, i.e. T1 and T2, in addition to PD (proton density) are signal weighting parameters that are calculated after the pulse sequence of the scanner and are used to examine certain tissues in the brain (Figure-1) [4].

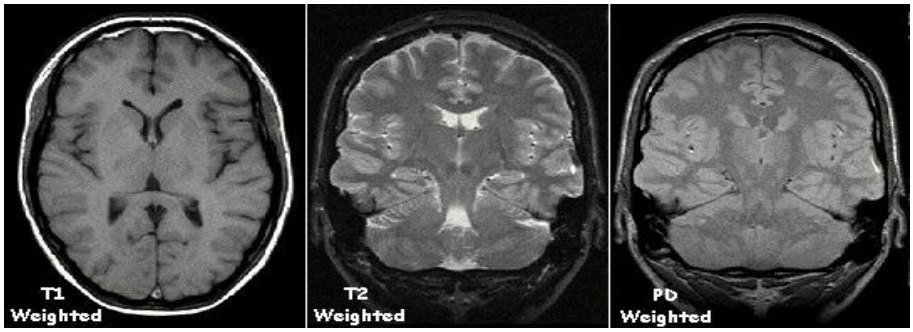

Figure 1-Examples of T1 weighted, T2 weighted and PD weighted MRI images [5].

Functional changes, connectivity, and metabolism may be detected with functional MRI (fMRI) by defining cerebral regions reacting to the patient into blood flow recordings. An fMRI scan is effortless and secure and can be performed routinely to monitor a patient's progress during treatment. Hemoglobin brings oxygen through the brain as oxyhemoglobin which is converted into deoxyhemoglobin once used. Where oxygen is "spent" close to an active location in the brain [6]. The image is then formed by looking at the proportion of small wave frequencies between these two states, while the patient is going to be treated, for example, by tapping the finger which is corresponding to the brain region in action, as shown in Figure-2.

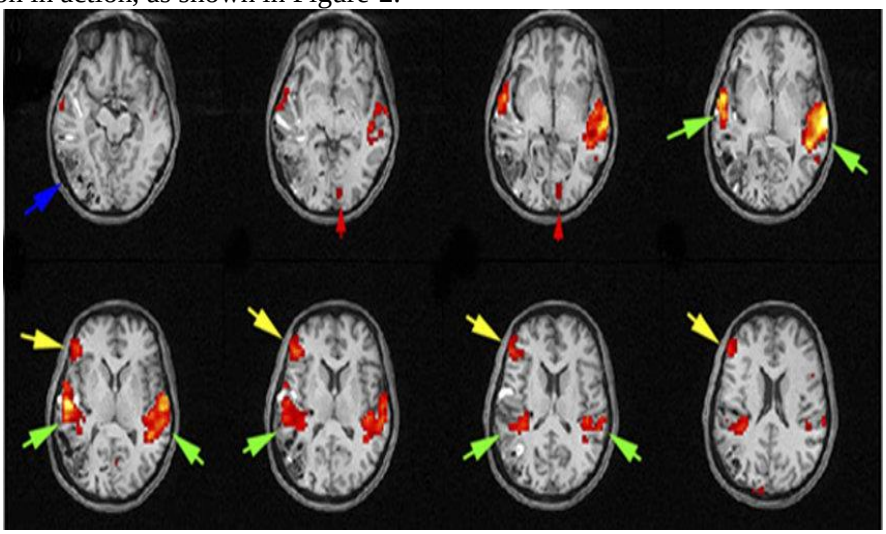

Figure 2- Axial TIWI in neurologic format with overlaid functional activation data demonstrate strong left dominance in the expressive speech area (yellow arrows) [7].

However, Figure-3 shows improvements in Fluoro-Deoxy-Glucose - Positron Emission Tomography (FDG-PET).

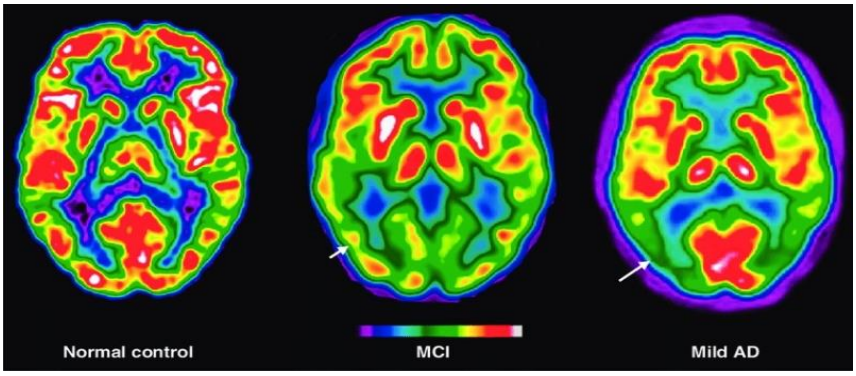

Figure 3-FDG-PET of control, MCI, and mild AD individuals. FDG-PET shows reduced uptake of regional CMRgl in the temporal-parietal cortex (shown as arrows) in MCI and AD patients [8].

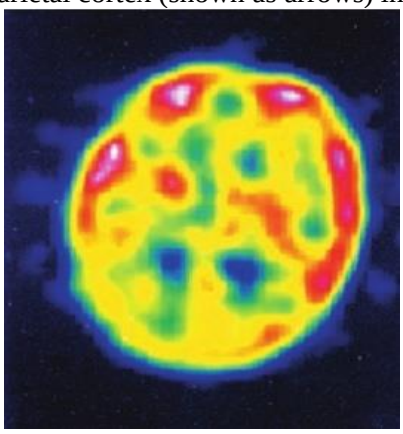

Figure 4-Single SPECT scan of a patient showing right temporoparietal hypoperfusion [9].

Single Photon Emission Computer Tomography (SPECT is a type of nuclear imaging that demonstrates how blood flows through tissues and organs, as shown in Figure 4. Experiments have shown that this can be more susceptible to brain damage than MRI scans, as it can recognize lower blood flow to damaged areas. This method is also useful in the diagnosis of spondylolysis and blood deprivation of the ischemic brain after stroke and tumors [10].

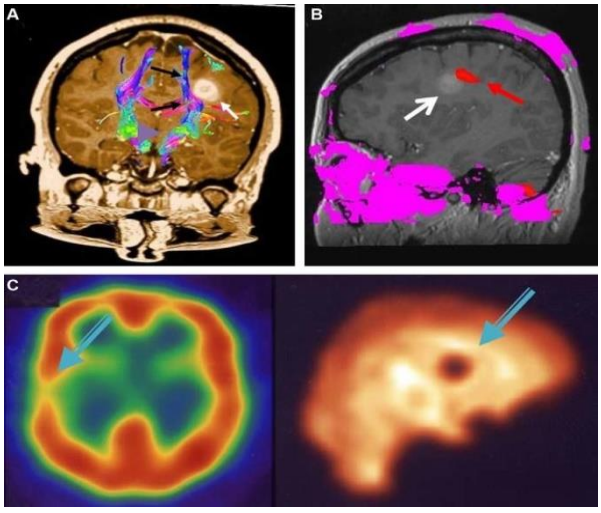

Figure 5-A DTI-derived tractography (1.5-T MRI scanner; diffusion gradients in 30 non-colinear directions [11].

3. Datasets

The image database is a crucial component for any recognition system because it contains photographs gathered from different sources or downloaded directly from multiple individuals using suitable tools.

3.1 Alzheimer's Disease Neuroimaging Initiative (ADNI) Dataset

ADNI has been developed as a prospective multicenter to identify biomarkers for early physiologic, genetic, and biochemical detection. ADNI was founded by Dr. Michael W. Weiner in 2003 as an independent private organization designed to determine the aggregation of serial MRIs and PETs, along with other natural markers and medical and neuropsychological assessments, to detect the development of MCI and early AD. ADNI includes different types of information, including medical, biological, rheumatoid, PET and biodiversity images (http://adni.loni.usc.edu/about/).

3.2 Open Access Series of Imaging Studies (OASIS) Dataset

The OASIS dataset was developed by Dr. Randy Buckner, from Howard Hughes Medical Institute (HHMI) at Harvard University, and it is a project to free the scientists ' communities from neuroimaging the brain data [12].

4. Literature Survey

AD diagnosis requires several measures that begin with pre-treatment and a complete evaluation to identify neurodegenerative patients.

4.1 Concatenation Features

Dukart *et al.* [13] reported 28 AD patients (Male / Female =19/9), 28 healthy controls (Male/Female = 20/8), and 56 individuals from the ADNI database. Knowledge research was carried out with their Leipzig cohort of 21 AD patients (Male / Female = 9/12) and 13 control subjects (Male/Female = 7/6). The FDG-PET and MRI pre-processing protocol included bias correction in the MRI results on inhomogeneous objects, partial volume-effect correction, masking in the FDG-PET data for non-gray material voxels, and the spatial normalization approach DARTEL to an average size model produced in all subjects. By drawing a circle of 5 mm diameter around the reporting co-ordinates, six VOIs are derived from each modality and limited to non-zero intensities in the sphere. Then, the average voxel for a Support Vector Machine (SVM)-based AD category from a picked Region of Interest (ROI) was taken. For the ADNI data collection, an accuracy rate of almost 88 % was achieved, while that for the Leipzig cohort was up to 100 %. The Leipzig cohort was discriminated against by a classification trained on ADNI data with an accuracy of 91%. Moradi *et al.*[14] selected subjects from the ADNI database, classified as (i) 200 NC (Male/Female = 103/97), (ii) 231 NC (Male/Female = 119/112), (iii) 164 stable (Male/Female = 97/67) (iv) 100 progressive (PMCI) (Male/Female = 66/34). The SPM8 package and VBM8 toolbox were used for preprocessing. Biologically precise, standardized, and segmented magnetic pictures of the gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) have been revised. Besides, 29852 GM density values have been extracted from the GM chart for each subject and used as MRI features. There were two stages in the identification process. The first stage was the role selection to choose a subset of the MRI voxel in the Regularized Logistic Regression (RLR). Secondly, an LDS semi-monitored system based on the transductive SVM classification was used for categorization. Also, an MRI biomarker was extracted from the LDS classification, together with age and cognitive evaluation, as input data for a Random Forest (RF) analysis. The classification included an RF classification. The RF reliability was tested with 10 times cross-validation, showing an accuracy of almost 82 % of the MCI-to-AD conversion. Combining the MRI data with the findings of the mental assessments resulted in an increase of the MCI-to-AD precision. While this concatenation of knowledge is simple and desirable, the method has the advantage of treating all characteristics as equivalent, since the characteristics obtained from different modalities can not be distinguished. Another study [15] argued that the complementary knowledge provided by these methods could also be ignored.

Liu *et al.* [15] also collected information from the ADNI dataset, which was composed of 202 people including 51 AD patients, 99 MCI patients (43 of which had been AD converters in one and a half year, whereas 56 were non-converters), and 52 NC patients. However, the use of integrated multi-modal information could greatly enhance AD work in the previous studies reported by Dukart *et al.* [13] and Moradi *et al.* [14]. Liu *et al.* [15] proposed a novel multi-task selection method to maintain additional intermodal information by controlling each modality by restriction. After the selection of the function, a multi-kernel SVM was used to incorporate each classification modality. This technique

resulted in 94.37% accuracy for the region under the REC or AUC curve of 0.9724 AD, 78.80% accuracy for the AUC of 0.8284 MCI classification, and 67.83% accuracy with AUC of 0.6957 for the isols of the RCI converters to AD and nonconverters. This shows the superiority of this technology over the other state-of-the-art classification strategies.

Hojjati *et al*. [16] used 34 patients with AD (average age 72.5 years, 18 female), 25 patients with MCI-C (average age 73 years, 11 female), 69 patients with MCI-NC (average age 72.9 years, 37 female), and 49 HC (average age 74.4 years, 28 female) from ADNI database. The methodology includes the use of the graph theory to characterize different aspects of the rs-fMRI brain network by calculating measures of integration and segregation. The cortical and subcortical measurements, e.g. cortical thickness, were extracted from sMRI data. The rs-fMRI graph measures were combined with the sMRI measures to construct input features of a support vector machine (SVM) for classification. Two feature selection algorithms were used for feature reduction and selecting a subset of optimal features, namely the the discriminant correlation analysis (DCA) and sequential feature collection (SFC). The resulting accuracy values were 67 and 56% for three-group (AD, MCI-C, and MCI-NC or MCI-C, MCI-NC, and HC) and four-group (AD, MCI-C, MCI-NC, and HC) classification, respectively, which were obtained with the SFC feature selection algorithm.

4.2 Papers Utilized Different Classifiers with High Efficiency in Separating AD From MCI

The data from 345 AddNeuroMed cohort participants, comprising 116 AD patients, 119 MCI patients and 110 Cognitively Normal (CTL) individuals, were reviewed by Aguilar *et al*. [17] in 2013. The purposes of this research were: first, to compare linear and nonlinear multivariate AD vs CTL techniques; second, to check subsequent CA transformation anticipating MCI, the prodromal phase of the disease; third, to evaluate the effects of age, education and the genotype of apolipoprotein E (APOE), in predicting AD against CTL; finally, to differentiate between the genetic effects in ageing, education, and APOE. Four supervised learning methods were used for characterizing AD patients and controls, as well as foreshadowing the transition from MCI to AD based on MRI tests. The MRI data was made available for FreeSurfer, which included Orthogonal Latent Structures Projects (OPLS), Decision Trees, Artificial Neural Network (ANN) and SVM, to analyze the classification performance. The classification assessments resulted in an effect of 83 % and a precision of 87 % for the best methods. They obtained an accuracy of almost 86% to predict the development of MCI patients into AD for a one-year follow-up. In the identification of MCI converters, the estimation of multivariate models derived from the AD-CTL classification also seemed robust and efficient.

4.3 Deformation-Based Morphometry (DBM)-Based Studies

E. MRI and 18FDG-PET data were collected from 93 AD subjects, 204 MCI subjects including 76 MCI-C convertors and 128 MCI non-converters (MCI-NC), and 101 NC subjects were used from ADNI dataset. The dataset was taken into consideration by March 18, 2007. Suk *et al*. [18] were the first who studied the usage of DBM to describe a sleeping trait from a volumetric patch and subsequently developed a strategy for defining a joint feature representation from the multi-modality. The proposed method resulted in 95.35% AD versus NC, 85.67% MCI versus NC, and 75.92% MCI-C versus MCI-NC classification accuracies. The approach requires a significant number of generalization training samples, which are not feasible, especially as neuroimaging studies take time with many parameters associated with DBM. The resulting representations of the features are hard to understand with only few data samples. Thus, DBM could not claim to provide useful clinical data.

4.4 Multi-Atlas Based Morphometry

In order to suggest a multi Atlas-based morphometry technique that calculates the morphometric representations of the same picture in different spaces of multiple atlases, Min *et al.* [19] tested a sample of 459 subjects consisting of 97 AD, 117 progressive MCI (p-MCI), 117 stable MCI (s-MCI), and 128 NC patients from ADNI databases. Their data are recorded in several atlases, in which adaptive regional characteristics are extracted. The relationships and the critical scheme follow a final identification with the SVM are all elements from different atlases. The results showed rating reliability values of 91.64% for AD / NC and 72.41% for p-MCI/s-MCI, which exceeded the values from previous methods based on the single atlas. The derived characteristics of each atlas were combined to fully represent the brain of the subject. The features created from the different atlases, which could include redundant information from similar atlases and contribute to high-dimensional representations, were however considered for the AD classification. Liu *et al.* [20] clarified that a

subject could be seen from the front and side pictures via multiview face recognition. Since the images contain distinctive information about the same person, the use of different sets of features from more than one perspective can maximize the individual's representation, which is a preferred way of learning in comparison to strategies with single views. Likewise, multiple atlases can be viewed in brain morphometry as various perspectives of the same brain. Hence, an image created from a specific atlas can be seen as a brain profile and used to collect valuable data from other atlases with different representations (i.e. views). The authors argued that the features isolated from K adaptive ROI sets are representations of the same subject separately, so they should not be related, as previously stated in Min *et al.* [19]. They reported the subjects to various selected atlases as a solution.

4.5 DTI Based Studies

Dyrba *et al.* [21] used European DTI Dementia Contemplates (EDSD) specimens, including 137 clinically probable AD (MMSE 20.6±5.3 of Minimal State Examination patients and 143 healthy elderly controls). In order to achieve the criterion for choice of discriminatory voxels and use the diffusion ratios of fractional anisotropy (FA), maximum density (MD), and the anisotropy mode of the chosen voxels as features for SVM-based AD distinction and the Naïve Bayes (NB) classification, the primordial components of the analysis (PCA) and entropy-based results were used. Proportions of 80% for FA and 83% for MD were reached by SVM. The SVM-NB accuracies were lower by 68 % and 75 %. This type of research supports the idea that machine learning algorithms allow for robust identification of information collections available from various scanners, regardless of whether another information collection from the scanner was not in the workout sample. Nir *et al.* [22] conducted a medical visualization study on 200-piece samples comprising 50 CTLs, 113 mild-cognitive impaired subjects, and 37 AD-patients. To evaluate the value of the white matter, a modern fiber-tract display technique was used. Tractography was used to locate fibers and then classify them into 18 fiber classes based on the 18 areas detected in the probabilistic WM tract atlas of the Johns Hopkins University. It used the shortest path map to reduce the fiber pack to a small, low dimension image based on the Maximum-Density Path (MDP) approach to determine the number of fibers passing through each voxel. The thickness map was measured. All MDPs were reported in various areas and FA and MD diffusiveness metrics measured in all MDPs were used for the classification of SVM-based AD and MCI. Overall, the MD features were higher than those of the FA and the precision was improved by increasing the dimension of selecting the average MDP points passing the FIS. Dyrba *et al.* [23] analyzed EDSD data, a model studies 13,17,32–34 that involved eleven European Centers with 35 negative MCI (Aβ42–MCI), 35 positive MCIs (Aβ42+ MCI-Aβ), as well as 25 Healthy Controls (HC). The subsequent information included the Early shifts in their particular WM white tissue which were identified iin the AD patients. In the predementia step of the MCI, they tested WM modifications with DTI. The DTI, the volumetric magnetic resonance imaging data, and the fractional anisotropy, which is consisted of an MD and anisotropy mode maps derived from DI, were linked to an SVM cluster. The classification was taken into account by a comparison based on the volumes of GM and WM dark tissue produced by their positive or negative amyloid weight. The results revealed a precision for MO of up to 68 % and for MCI-Aβ42 − and MCI-Aβ42 + of up to 63 %. The classifier was up to 77% accurate to MD, with an impressive 68% lower value for the GM volume, for the isolation of MCI-Aß42+ from HC. The reliability of the multimodal classification was not higher than the precision of the current methodology.

M. DTI scans of 150 subjects in the ADNI database were examined by La Rocca *et al.* [24] to compare the nested and unnestled features in the same dataset. The first work was to measure the distinctively unknown characteristic distribution and to extract from each subject the main white matter fiber tracts with the FA and MD values of every voxel in the skeleton. Approximately 120,000 voxels were required for each subject guide. The Relief algorithm was then applied according to the principle of evaluating the characteristics following the discrepancy between their values in the neighboring data instances within an unregulated and nestled process. After that, the characteristics were identified and sorted in order to decrease. Fifteen reduced datasets were created for each classification task by selecting an increasing numbers of voxels, which are most selective based on the performance of the feature selection presently. The study and classification cycle were completed with random forest algorithms. The findings showed that the voxel-based approach did not improve the grading process achieved with other methodological methods other than what the AUC did with HC

and AD segregation using FA. These findings suggest that DTI data offer better accuracy in predementia DA for predicting GM scale.

4.6 ROI Type Study

Patients from ADNI were identified by Eskildsen *et al*. [25] along with 226 age-matched CN patients. The pMCI subjects were defined by time periods which included 6, 12, 24, or 36 months, and each class was classified by sMCI subjects. The pMCI subjects had their ratings. Preprocessing opertations eliminated noise from the images with the determination of the approximate standard noise variance, bias field rectification, registration at the Montreal Imaging Industry (MNI) standard storage, skull removal, and Face Accurate Cortex Extraction (FACE) cortical thicknesses. Cortical divisions were manually checked by a specialist for errors; if errors were found in any picture at preprocessing, subjects were omitted from the dataset. The validation technique of Leave One Out (LOO) was used to create a classification model in which one subject is evaluated. In total, 876 MCI step categorized feature sets were identified, 388 pMCI–sMCI features were identified, and maximum relevance minimal-redundancy reduction (MRMR) was introduced. For the classification, Linear Discriminant Analysis (LDA) resulted in prediction accuracies which were artificially inflated between 73% and 81%. This study showed that the reliability of the transition from MCI to AD can be enhanced by studying the atrophy patterns of the different disease stages.

Xu *et al*. [26] used ADNI information, which included 113 AD patients, 110 MCI and 117 NC subjects and focused on extending the algorithm of multi-methodology by separating AD / MCI with a strategy assessment. Their approach suggested using the characteristics of GM size, regional average FDG-PET rate, and flowerbetapir images. Alternatively, they proposed employing a Sparse Representation-Based Classification (SRC) technique to a get-together of different weights to the different methods of classification of AD versus MCI and pMCI versus sMCI subjects. The accuracy of classification using Weighted Multi-Modality SRC (wmSRC) was 74.5% for AD versus NC and for MCI versus NC, whereas it was 94.8% for MCI versus NC and for pMCI versus sMCI . Zu *et al*. [27] used ADNI regular MRI and FDG-PET imaged data, which included 51 ADs, 99 MCIs and 52 NCs in 202 baselines MRI and FDG-PET registers. This work introduced a new model to learn how to define AD versus MCI multimodally by exploring the relationship between modalities and topics. The strategy involved the selection and multimodalizing of etiquette multi-tasks, where the selection of features is based on a range of modalities, and a group-sparse regularizer is needed to jointly select a subset of features. Next, an SVM multi-kernel combines the features selected for final classification from the multi-modality findings. The proposed strategy obtained 95.95, 80.26 and 69.78 % accuracies with respect to AD vs. NC, MCI vs. NC and MCI-C vs. MCI-NC, respectively. Jie *et al*. [28] utilized data from 51 AD, 99 MCI (43 MCI converters and 56 MCI non-converters), and 52 NC patientsfrom the ADNI database. Consequently, a multifunctional, regularized multi-tasking method of training was proposed, in order to both safeguard the characteristic relation of the different data modalities and to overcome the drawbacks of current multimodality techniques, ignoring the information distribution in every methodology that is necessary for. They were able to extract global topology and local connectivity features from the graph, while a multi-kernel SVM for the MCI class was used for the least absolute shrinkage and selection operator. The results showed that the technique could improve recognition and help to find the brain sites required for the diagnosis of disease.

Liu *et al*. [20] employed datga from 459 subjects from ADNI (97 AD, 117 progressive MCI, 117 s-MCI, and 128 NC). They suggested a new, vision-centralized, multitasking technique of employing useful evidence from multiple atlases in different representations. The brain pictures were captured separately in multiple atlases to obtain representations of features in each atlas region. With additional guidelines from various atlases, the proposed multi-atlas list method focuses upon the most restrictive features for each atlas. The SVM classifier then used the function chosen in every space of the atlas. Finally, the results from the SVM classifiers were taken together to make the final selection. This process achieved reliability of 92.51% with AD compared to NC and 78.88% with pMCI versus sMCI. Ota *et al*. [29] studied 80 individuals who underwent the systemic RIM, and 18 FDG-PET baseline scans with the amnesty RIM (40 of whom developed DI within three years) of an enhanced image-oriented prediction of transition from mild cognitive disability to DA. The selection of biomarkers for early detection of AD was important in that

approach. The functions were derived from the baseline data MRI and FDG PET using the Automatic Anatomical Labeling (AALs) and the LONI Probabilistic Brain Atlas (LPBA40) for each area of concern, which reflect gray density and relative brain metabolic levels for glucose. The identification output was evaluated by a linear SVM ensemble with bagging and a determined region under the ROC curve. The feature score was calculated using multiple SVM recurred role deletion (SVM-RFE). The resullts showed that the multimodal inclusion offers a clear improvement and that FDG-PET performed better than MRI in AD prediction, based upon the variance analysis of the average AUCs for eight sets of features. Evidence from the three ADNI cohorts and from the Australian Biomarkers Imaging and Lifestyle (AIBL) study were used in a paper by Sørensen *et al*. [30]. They tested the hypothesis of early cognitive impairment beyond those associated with volumetric changes as the hippocampal texture. The double-sided hippos are classified by using a delicate SVM edge with a radial Gaussian kernel based on their texture. The real-life decision-making feature for SVM was described as a single texture. The sign indicates whether the SVM classifies the patient as a commitment (+) or a command (-), and the sum is equal to the distance between the two classes and the selection limit. This research proposed and tested the hippocampal framework as a potential AD biomarker for early structural MRI detection. The data from the ADNI datasets were used by Lama *et al.* [31] with 214 sub-themes, including 70 NCs, 74 MCIs not modified in the AD, and 70 ADs. They used SVM and Import Vector Machine (IVM) along with Extremely Regularized Research Machine (RELM) with structural magnetic resonance imaging to discriminate against AD, MCI and HC subjects. The greedy feature selection strategy based on score chose main feature vectors and complex data distributions were performed by kernel-based discriminative methodologies. Studies of ADNI datasets showed that RELM substantially improves the accuracy of AD classification from MCI and HC subjects with the feature-selection methodology. In evaluating their strategy on 807 subjects, including 186 AD, 395 MCI, and 226 NC, Cheng *et al.* [32] used ADNI database. They conducted a collaborative research in multi-ailway environments and objective areas with a technique incorporating a new structure for early diagnosis of Multi-Domain Transfer Learning (MDTL). There were two sections in this method; First, an MDTFS model that selects the most useful subset of features from MDTF data. Second, MDTC model to classify early AD disease conditions in MDTC (Multidomain Transfer Classification). The results showed that multi-auxiliary domain information could be used in the MDTL technique to promote learning in the objective domain.

The ADNI and AIBL visualization systems, as well as software aided diagnosis of dementia (caddentia), were used by Sørensen *et al*. [33] for both freely accessible ADNI datasets. With several combined individual MRI biomarkers, including measurements of cortical thickness, volumetric measurements, the form of the hippocampus and hippocampus texture, their approaches included a biomarker that uses more information than a single biomarker method in the structural MRIs. By incorporating all biomarkers into the LDA classifier as a feature, they combined calculation of various MRI biomarkers which provided a Multi-CA value of 62,7 % on the datasets. In the CADDementia challenge, which was held in the event, a comparable CA of 63.0% was achieved. Rathore *et al*. [34] however noted that ROI forms of AD-related research rely only on early learning in order to control the selection of ROIs and features. This may lead to a propensity to see new information without taking into consideration changes in the brain outside the regions studied. With locally linear embedding (LLE) studies which unattend MRI features and can detect changes in the brain without direct feedback on the way the disease spread, Liu *et al.* [35] argued that LLE) has a benefit over various ROI approaches. Such inquiries included subjects chosen from the ADNI list, including 413 topics from 137 CN, 93 S-MCI, 97 c-MCI and 86 AD, collected between 2005 and 2008. LLE transformed the volume and cortical thickness information of local cerebrums into a locally linear space requiring less measurement, as well as the global nonlinear data structure. Embedded brain features were then used in the preparation of the classification calibrations, such as the RLR, SVM, and LDA. The findings were 68 % right, 80 % sensitive and 56 % special.

Liu *et al.* 2013 [35] argued that classifications that use embedded MRI features usually outweigh original classifications. In the three types of linear classification widely used for SVMs and LDA, changes in the classifications with LLE performed equally well. This finding showed that the benefit of LLE was important and not limited to a certain class of classifiers. Moreover,

and clinically important, LLE considerably increased the separation between the MCI subjects who changed into AD within three years of the MRI base and those persons who remained stable. Contrary to conventional dimensional reduction methodologies such as global linearity of PCAs or unique kernel shapes in supervised learning calculations such as LLE, a separation performed in the absence of LLE generated results worse than those from traditional models for supervised learning calculations.

4.7 Parameter Tuning

An ADNI database of 185 AD and 225 HC, which were arbitrarily assigned to training and testing datasets, was used by Lebedev *et al*. [36]. By monthly convert to dementia (based on four years of follow-up), 165 individuals with MCI were also reported. This study examined the efficiency of forest randegroups, trained with and without neuroanatomic detection limitations using different structural MRI measures, and the precision and intercohort robustness of AD prediction. The 1.5-T MRI structural scans using freesurfer segmentation and cortical reconstruction were processed. AD versus HC classifiers, including template tuning, were trained from the performance and evaluated using an off-bag estimate. The classifiers were therefore validated with the AD vs HC test set to foresee the transformation of MCI to AD. The ADNI dataset combined cortical thickness with volume measurement to ensure the best AD vs HC sensitivity and specificity, which had values of 88.6 % and 92.0 %, respectively, for test set. In comparison to the reference classifier Linear Support Vector Machine (L-SVM), this random forest model produced significantly more accuracy. The detection sensitivity of the transformation MCI-to-AD (but not the performance of the AD-to-HC classification) was also increased by a combination of morphometric measurements with a genotype and demographics (e.g., age, sex, and education) from 79.5% and 75%, respectively, to 83.3% and 81.3%. The typical subset in the ADNI data base was used with 170 subjects incorporating 54 AD patients, 58 MCI and 58 NC, by Beheshti *et al*. [37]. They proposed a combination of Voxel-based morphometry (VBM) and texture analysis to separate the more discriminatory characteristics to adapt the SVM-RFE with a covariation technique to choose a powerful sub-set of characteristics to overfit the combination of features. For AD and NC classification, the technique achieved a rating precision of 92.86% for MCI and NC, a rating accuracy of 97.22%, an accuracy of 91.18% for AD from the MCI, and a range accuracy of 85.59% for three-way classification. No optimal technique was identified for relegating the SVM1 parameter to the number of features which should have been selected in the SFS procedure.

Li *et al*. [38] included ADNI database from 113 AD patients, 111 MCI patients, and 117 CU subjects for the classification of AD versus Cognitively Unimpaired (CU), MCI versus CU, and AD versus MCI. The emphasis was on recognizing AD or MCI from the CUs topics based on a new technique called Dictionary Learning (DL). In addition to an active implementations in past acceptance, it was based on a Multi-Feature Kernel Supervised Within Class-Similar Discriminative Dictionary Learning (MKSCDDL), SMRI, FDG-PET, and florbetapir-PET. This merged approach was adopted in order to differentiate AD, MCI, and CU. The results from MKSCDDL were promising for the classification and determination of neuroimaging data diseases, which gave ratings accuracy of up to 98.18% of AD versus CU, 78.50% of MCI versus CU, and 74.47% of AD versus MCI. These results were better than those achieved from other state-of-the-art approaches, such as Multiple Kernel Learning (MKL) and Joint Regression. However, the drawback of these studies is that parameter tuning is important.

4.8 Radial Basis Function (RBF) Kernel

In order to introduce a new approach to statistic function reduction and selections in high dimensional MRI data based on the Probability Distribution Function (PDF), Beheshti *et al*. [39] used 3T MRI images obtained from the ADNI database. They selected the optimum number of bins in the intensity distribution between AD-and CN subjects used by the Fisher maximization criterion, which were then used to classify ADs for an SVM (i.e. SVM with a linear and RBF kernels). The results showed that the PDF-based selection methodology is a sound strategy that is highly competitive in the classification of DC from high-dimensional sMRI tests with other state-of-the-art technologies. Because vector machines support and various models that use the kernel method are not well suited to numerous training tests or features at the input space, there have been some approximations to the RBF kernel.

4.9 DMAF-Based Strategies

Möller *et al*. [40] had a dataset with 89 patients who visited the Alzheimer Centre, Vrije Universiteit of Amsterdam (VU) Medical Center or Erasmus Medical Center in Rotterdam, from September 2009 to October 2011, in addition to 53 patients with a behavioral variant Frontotemporal Dementia (bvFTD) and 53 patients with a Subjective Cognostic Deficits (SCDs). The findings of the machine-learning classification of AD versus bvFTD revealed a GM density map value for the SVM AD group, which is 88 % higher for patients who receive AD versus control subjects, 85 % higher for patients with bvFTD versus control items, and 82 % higher for patients with AD versus patients with AD. Nonetheless, Rathore *et al*. [33] reported that the number of features is generally larger than, or equal to, the number of subjects available, as features or DMAF-based strategies suffer as a consequence of dimensionality disadvantage. Overspent and unattended methods to minimize complexity have not been tested.

4.10 Neural Systems

In 2013, Mamood and Ghimire investigated the reliability of the system's diagnosis by 230 analyzed RMIs collected by means of the OASIS MRI database and tested by the professional neural systems on all 457 MRIs [41]. Current AD diagnosis strategies rely on a mental disability examination, which is not effective until the patient has progressed to a moderate AD. The approach, which relies on scientific and image management strategies, was devised to better classify AD using the PCA's research system computerized category model to increase the dimensionality of MRI images. A multi-organized, mixed class feed-forward neural network was then equipped with reduced dimensional information to accept the AD aspect in the MRI. Comprehensive OASIS MRI data collection experiments were correctly separated by an 89.22 % classification, since the system uses a neural network. Ram [42] used longitudinal MRI images from 138 subjects, including 68 patients with CN, and the ADNI database for 70 AD patients. Instead of looking for stable patterns in CN subjects or AD patients, the goal was to demonstrate the degeneration process in various areas of the brain from individual MRI images. The Apps relied on brain volumes at the Automatic Anatomic Labeling (AAL) atlas at such locations. To each subject with a smaller longitudinal model, the covariance values processed by SICE has to be determined using these qualities to prepare the deep neural structure. The findings showed the strategy's effectiveness, with 94% accuracy, to identify certain patterns for grouping CN and AD subjects, which exceeded the performance of previous strategies. Prásad *et al*. [43] examined 200 subjects in an ADNI-2 component, following up the ADNI database project where the MRI standard protocol was applied to diffusion imaging (amongst other outputs). The dataset included MRI disseminations from 50 NC monitors, 74 Early MCI subjects and 38 Late MCI subjects, as well as 38 AD subjects. Their method produced two communication networks that rely on the regional characteristics of the number and fiber flow. The SVM-based classification of the early and late-MCI subjects was used to include raw connectivity matrices and other network measures, such as global efficiency, transitivity, trajectory length, modularity, radius, and diameter. The results showed that, for the FI(N)¨and FL(N) controllers, the highest accuracy set was detected at 78.2 %, while the instance t-tests were used ($p > 0.05$). For the controls versus eMCI classifier, FI(N +M) had the highest accuracy of 59.2 %, but this was not the case for FI(N +Š)¨ FL(Ň+M). For the controls vs. LMCI, FL(N) was 62.8 % more accurate and much more desirable than any other function set. The best performance for EMCI versus LMCI was 63.4%, with FI(N) and FL(N), and it was significantly different from all other feature sets. Neural systems, however, have the drawback of the parameter tuning requirement. The machine learning techniques used by most of the present works relied on one classifier, with the most common classifier being the SVM, a binary classifier that is suitable for high-dimensional applications with few examples. Additionally, groups that combine the outputs of several classifiers to test the optimal combination of apps or models, otherwise randomly selected, are an alternative to a single classifier. After that method, Cabral *et al*. [44] used the ADNI database in several classifiers including subjects chosen from a class-adjusted subset of 177 volumes of the FDG-PET. They suggested an alternative approach in the organization of AD, MCI and CN cases in PET brain images to address the three-class problem. The study aimed to recognize FDG-PET brain images of CN, MCI, and AD through a ternary classification problem for the best group of RF and SVM classifiers. Their combination effectively overrated the corresponding SVM group’s single classifier, with the best result being 66.78%.

4.11 PET Scanners

Two databases including fMRI and SPECT brain images, as well as PET brain metaphors, were tested by Dinesh *et al*. [45]. In order to implement a computer-aided diagnostic (CADx) tool, the collection of PET data was collected from the ADNI. Only Normal (NOR) and AD groups of l05 subjects were given in the SPECT database. Their approach suggested a nonnegative matrix factorization (NMF) combination to be used for the production of assisted AD analyzes, as well as the reduction and the SVM classification. The results of the validation of that strategy showed high sensitivity and specificity more than 85 %, up to 91 % classification accuracy, respectively. Li *et al*. [46] applied their proposed deep learning model consisting of 51 AD patients, 99 MCI patients, and 52 normal controls to an overall society of ADNI data. They identified a comprehensive learning system for different stages of AD patients, which were pre-processed for the extract of characteristics, based on MRI and PET scans. The next move was to use PCA to acquire the PC in new features and to choose the most efficient features using stabilization selection techniques together with Lasso, the least absolute shrinkage and selection operator. The deep learning architecture subsequently treated these features. Unattended learning and finely tuned AD patient tags initialized template weights into the deep structure. The decomposition enhanced the generalization ability of the template during the fine-tuning process. Finally, an AD versus MCI classification by an SVM was applied to the learned functionality representation. The results showed that the classification accuracy was improved by 5.9% on average as compared with traditional deep learning methods, with 91.4% for AD versus the HC, 77.4% for the MCI versus the HC, 70.1% for AD versus the MCI, and 57.4% for the MCI versus the MCI.NC. Nonetheless, for clinical applications, PET scanners are more costly and a scanner for generating SPECT images is more reliable than a PET scanner.

4.12 Whole-Brain Analysis

A research of 202 MRI and structural MRI results from 16 sites between the United States and Canada was conducted by Zhan *et al.*[47], based on information collected from ADNI2. The brain networks were measured use 9 methods based on entire-brain tractography including the Functional Correlation Tensor (FCT) method, the Runge-Kutta second-order (RK2), SL and the Tensorline (TL), two FAD-focused deterministic orientation (FACT and RK2), and two ODF-based probabilistic approaches (Hough and PICo) within the main implementation for the four tensor-based deterministic Fiber assignment (FACT). The approach adopted five methods of selection of nine brain-wide tractography from brain networks for 3 classification tasks. Three possible factors might affect the accuracy of the classification, including the diagnostic complexity, the feature extraction method and the algorithm for tractography. The findings of the classification accuracy shown by the work team were closely associated using the diagnostic problem. Liu *et al*. [48] published a study of MRI images of 710 subjects from the ADNI list (200 AD, 120 MCIc, 160 MCInc, and 230 HC). Due to the noise and limited sample size of the available RIM images, they employed a wholly-brained hierarchic network (WBHN), as depictions of a single or multiple ROI may not be sufficient to reveal the anatomic distinctions underlying the groups of disease sufferers and the HC structures. Using a technique involving dividing each subject's entire brain into regions using the AAL atlas, the connectivity between each pair of regions was developed and calculated using Pearson's correlation coefficient. Instead They selected those with higher F-notes to reduce the dimensionality of the features. While, the classification process was based on a Multiple Kernel Boosting (MKBoost). The results showed an accuracy of 94.65% and an AUC-ROC of 0.954% for the AD vs. HC, an accuracy of 89.63% and an AUC of 0.907% for the AD vs. MCI, an accuracy of 85.79% and an AUC of 0.826% for the AUC vs. HC, and of 72.08% and a AUC of the MCIc vs. MCInc of the CVs. Using ADNI server information with a set of 427 topics, Long *et al*. [49] indicated an automated learning system to distinguish AD or MCI patients from stable elderly patients by recording and analyzing regional morphological differences of the brain across various classes for the expectation of AD transfer in MCI patients. After the separation of each combination of subjects was determined, a range matrix was constructed to integrate the idea of transforming the distance matrix into a cross-product matrix, where a Multi-Dimensional Scaling (MDS) algorithm was used. Thus, they were able to find their decomposition to obtain a PCA. The MATLAB ' libsvm' toolbox was used to implement an SVM with a linear kernel. separation accuracy values of 96.5% for AD versus healthy elderly, 91.74% for progressive MCI versus strong older, and 88.99% for progressive MCI versus healthy MCI, were demonstrated by the proposed algorithm. Wang *et al*. [50] noted that full-brain research relies heavily

on mathematical honesty and can not be carried out only by computer scientists after the facts are labeled as AD or safe by physicians. The study downloaded an open-access database of 126 examples (28 DBs and 98 HCs) including a variety of imaging studies. They tried to develop a new AD brain detection technique based on a method based on the 3D (DF) estimate between participants in the stable elderly control and AD classes. Three AD-related characteristics which are the distance of Bhattacharyya, the student's T-test, and Welch t-test (WTT) were identified for this 3D-DF. For classification, two non-Parallel SVMs, a generalized proximal SVM of its value, and a Twin SVM (TSVM) were then applied. The results showed that the "3D-DF+WTT+TSVM" combined value was best achieved with 93.05±2.18% accuracy, 93.57±3.80% sensitivity, 93.18±3.35 specificity, and 79.51±2.86 precision.

5. Validation Techniques

In order to test the proposed technique of a random forest classifier, Selvathi and Emala [51] used 416 subjects (healthy and pathological) from Open Access Series of Imaging Studies (OASIS) database to differentiate brain MRI-influenced patients from AD subjects. The unsubsampled contourlet transforms the input picture into several subgroups and distinguishes features from both input pictures and transformed images. The characteristics were given to compare the execution of algorithms to the random forest grade and the SVM. The results revealed that both the random forest classifiers are superior to the SVM classifier and other previous works in terms of accuracy, sensitivity and specificity. The identification precision values of the OASIS-G1, OASIS-G2, OASIS-G3, and OASIS-G4 datasets were 81.58%, 86%, 73% and 85%, respectively. While, the accuracy vallues of the random forest classification were 84.21%, 89%, 83% and 87% for OASIS-G1, OASIS-G2, OASIS-G2, and OASIS-G4 data, respectively. Lebedeva *et al*. [52] used two cohorts, the first was from the Prognosis of depression in the elderly (PRODE) that included 169 ADNI patients and 185 HC, whereas the second included ADNI patients (n=225). Their project aimed to test whether MCI or dementia could be predicted one year before diagnosis in structural brain MRIs in Late-Life Depression (LLD). Structural brain measurements were collected from T1-weighted brain MRI pictures using Freesurfer Technology (v.5.1). Random forest classification was based on MRI discriminated against patients with MCI and dementia who improved after a one-year follow-up and those with LLD who remained cognitively intact. In the LLD dataset, 185 patients with cognitively stable AD vs 22.5 elderly people from ADNI were also tested on a previously established random forest model. The study found that LLD patients with MCI or dementia who were diagnosed one year ago were classified with 76 % accuracy from those cognitively healthy LLD patients, using structural brain measurements. The best model calculated the MCI status alone with SVM and MMSE values, which were 89%, 85%, and 90%, respectively.

Ardekani *et al*. [53] used information from the ADNI database to assess 164 subjects with a progressive (n=86) and stable (n=78) diagnosis in two groups based on their possible transition into probable AD. The random forest category algorithm was used to determine the usefulness of Hippocampal Volumetrial Integrity (HVI) in the detection of healthy and dysfunctional MCI patients. The resulting identification accuracy was measured at 82.3% at a tolerance of 86.0%, 78.2% with considerably higher accuracy 89.1% than that for men 78.9% for women. This increased precision for women is the most commonly reported result of thhe use of AD machines in MCI. Nonetheless, they are not yet strong enough for routine clinical work, even with these enhanced studies. In order to understand the characteristics which are present in the iris, Hernández *et al*. [54] obtained real data from the foundation in Quito, which collaborated with coworkers to collect samples. The technique used a MATLAB- developed mathematical model to identify iris characteristics by specifying AD parameters or patterns. The first image was standardized by a Fourier transform, and then transformed to find circles. Specific training methods were used, including ZeroR, Naïve Bayes and Multi-layer Perceptron, using three multi-layer classifiers. Their analysis found that the best-results classification tool was Naïve Bayes with 61.96% accuracy, 74% probability that a sick patient will receive a positive diagnosis, and a 47.62% accuracy that the healthy person is considered not to be in a medical state. The data obtained by the Naïve Bayes prediction classifier required feedback on the method of generating the modeled function. Nevertheless, a technique of validation, such as that of 10-fold validation, was not included.

6. Multi-Kernel Learning

Data collected from the ADNI databases, including N-MCI (n= 120) and P-MCI (n= 139), were also used by Korolev*et al.* [55]. In this analysis, the multivariate prediction approach MCI-to-dementia was applied using a technique based on cortical and subcortical quantities, cortical thickness and surface area, as well as the structural MRI curvature, medical measurements and plasma measures, to resolve the perceptions of improvement in AD. The criterion for shared knowledge (MI) was used for the selection of functions and the classification of probabilistic multi-kernel learning (pMKL). The best model was to combine mental and functional markers with morphometric MRI measurements that projected development with a precision of 80% (83%, 76%, and AUC = 0.87). In this experiment, MKL had little impact on model execution, because it did not improve classification accuracy, but rather the multi-source display calibration, when using five kernels in Gaussian. The limited number of kernels (3-5), as in other recent studies, could explain the limited benefit observed, while further improvement in the predictive performance can be achieved with a larger number of kernels.

7. Heterogeneity

Varol *et al*. [56] used an ADNI dataset made up of 123 AD patients and 177 T1-weighted magnetic resonance volumetric frames. The genetic information set comprised 103 AD patients and 139 controls with a single nucleotide polymorphism information. The presentation of a new non-linear algorithm for simultaneous binary classification and subtype identification, Heterogeneity Through Discriminative Analytics (HYDRA). By defining the non-linear limits of classification developed by using various linear hyperplanes, HYDRA isolates two classes. The polytope calls the revealing diversity by assignment to various hyperplanes of subgroups of patients. HYDRA can be general in dealing with imaging and non-imaging data and can find applications beyond the clustering of brain images in exploratory investigations. Their results showed the ability of neuroimaging and genetic research to approach map disease heterogeneity. Heterogeneity in future research lines is important with this enticing promise.

8. Landmark-Based Feature Extraction Method

Zhang *et al*. [57] used ADNI server subjects consisting of all ADNI-1 MR images, including 199 AD and 229 matched-age HC images. The two sets were divided randomly; the D1 (100 AD and 115 HC) and the D2 (99 AD and 114 HC). Then, they proposed a pioneering approach of extraction to overcome the non-linear registration and tissue segmentation constraint. A pre-trained model for detecting landmarks in each test image was used for detecting AD landmarks. The linear SVM classifier then classifies a sample picture as HC or AD with characteristic morphological features from the training frames. The findings showed that the method had a grade accuracy of 83.1%. This approach, therefore, depends on the size of training datasets, so that the lower number of subjects adversely affects the reliability of recognizing landmarks and hence the learned seminal might not be sufficiently relevant for a new subject. ADNI1 information packages comprising a total of 207 HCs, 154 AD, and 346 MCI subjects were employed by Zhang *et al*. [58]. In this research, a novel extractor method for AD diagnosis was implemented using longitudinal, simple MR images. These observed landmarks removed peculiar spatial features and associated statistical properties. In particular, a word packing method removes abnormal state spatial features so that large spatial variations are obtained from all scanning times and are therefore invariant with the number of longitudinal scans as well. Finally, AD and MCI classification with these spatial and longitudinal characteristics is achieved by the linear SVM classification. Experimental results showed 88.30 % accuracy for AD versus HC and 79.02 % accuracy for MCI versus HC classifications. Zhang *et al*.[57] focused on offering a significant twofold approach to the discovery of anatomical landmarks. The proposed approach, as a result of its landmark conclusion design, is neither expected for non-linear imaging nor for brain tissue divisions. Also, they used a two-layer forest regression model that provides an efficient and reliable way to handle AD characteristics. While they often suggested a different technique to extract features based on the anatomy of space and longitudinal features, the main characteristics of this work are the adoption of a Bag of Word system to create high-level space characteristics for MR boards, where the normalized longitudinal deformations are used for supporting the MR images.

9. Kernel Weights Choice

Tong *et al*. [59] used ADNI database which included 37 AD patients, 75 MCI patients, and 35 NC patients. They introduced a multi-methodology classification system for the effective use of the multi-modal information complementarity. For each method, the similarity of regional MRI volumes, voxel-based FDG-PET signal intensities, CSF-biomarker measures, and categorical genetics information is calculated separately for each methodology. Different similarities of modalities can then be combined to generate a single graph for final classification in a non-linear graph fusion process. The accuracy of the API classification was 98.1% between AD subjects and NC, 82.4% between MCI subjects and NC, and 77.9% in three-way classification. This methodology is based on an AUC classification. Nevertheless, it is very time-consuming to pick the optimal kernel weights.

10. Classifying Using CDR Scale

Sivapriya *et al*. [60] acquired ADNI data that includeed neuropsychologic information, combined baseline, and composite data. In conjunction with the Merit Merge (CPEMM) process, the features selected for the proposed ensemble classifier C4.5 were better than those of SVM, NB, and random forest classifiers. The suggested collection from the CPEMM function showed the best subset of characteristics that distinguish normal people from patients with mild cognitive impairments and 98.7 % with Alzheimer's disease. Hon and Khan [61] tested the problem of reliance on a variety of training images using OASIS MRI datasets. They pursued the need to carefully refine the design of deep networks with transfer learning, state-of-the-art architectures such as the Visual Geometry Gruppe (VGG), and the release of pre-trained weights from large benchmark object datasets. The fully connected layer will then be re-trained with just a few MRI images with almost ten times less than state-of-the-art training. In assessing 150 members, including 75 NC and 75 early-stage AD patients, Cai *et al*. [62] used the OASIS database. They examined the sulcal width and three more important morphological measures of neuroimaging in order to differentiate early-stage AD. The IG technique selects a subset of features for a large data set for the separation of individuals from the NC and early-stage AD. In order to compare the classifications performance, three types of classifiers, Naïve Bayes, Logtical Regression and SVM were applied to each of the four modals, including sulcal measurement, cortical thickness, cortical volume, and subcortical volume, along with the combination of the various measures. Their results indicated that sulcal tests are higher than or similar to the other classification measures. The global Sulcal Index (g-SI) and Sylvian fissure width were two of the most important sulcal measurements which served as beneficial neuro anatomic markers for the identification of early-stage AD. When using similar neuroanatomic functions, there was no significant difference between the three groups. One drawback of this study is the identification of people with a Clinical Dementia Rating (CDR).

11. Voxel-Wise Studies

Gray *et al*. [63] selected a dataset of 147 ADNI subjects from 37 AD (14 women), 75 MCI patients from 34 sMCI (12 women), 41 advanced to AD (12 women), and 35 HC (12 women). All participants had 1.5 T MRI, fdg-PET and CSF analyzes in the baselineand movement-corrected by the structural MRI and FDG-PET objects. The MRI collected 83 field volumetric features and obtained 239,304 FDG-PET voxels. CSF-derived Aβ, tau, and ptau measurements were included in the biological features. Furthermore, a genetic variant of the ApoE genotype was used. In classification purposes (AD vs HC, MCI vs HC and sMCI vs pMCI), the random forest was developed with regional GM volumetric controls, CSF biomarkers, FDG-PET-intensities which are dependent on voxels, and APOE-genotype, for the identification of AD and MCI. The researchers measured similarities among pairs of RF classification examples and applied a multi-modality approach to data learning. Accuracy, tolerance, and particularity were tested with 100 tests, splitting the dataset into randomly selected training sets (75%) and test sets (25%). In the AD vs HC with data from FDG-PET, the single-mode score results were 86.4%, in addition to MCI vs Hc with data from genes and the sMCI vs pMCI, 73.8% with data from MRI, in the AD vs HC multimodality rating, 89% and in MCI vs HC, 75%. Those results are similar to those presented in other recent multi-kernel learning studies. Ségovia *et al*. [64] analyzed ninety seven SPECT images taken in a recent study containing AD1 possible AD, AD2 possible AD, and AD3 being definite AD, from Virgen de las Nieves hospital in Granada (Spain). There were 41 NORs (male / female,

46–85 years old), 30 AD1s (male / female, 23–81 years old), 22 AD2s (male / female, 46–86 years old) and 4 A D3s (male / female, 69–83 years old). Then the SPECT images were normalized by a general affinity with the SPM code and further standardized with respect to the maximum intensity by intensity. The partial least square algorithm (PLS) and the bag-out error were employed in order to select scores to identify characteristics for rating vector extraction. The class of the images was determined by an SVM-based classifier. This technique yielded precision values of 91.6%, sensitivity of 92.7% and accuracy of 91.1%. Nonetheless, the researchers used a small sample size, so that the input data for the majority of cases were transformed into small vectors in order to reduce the problem of small sample size.

Salvatore *et al*. [65] used 162 cognitually healthy elderly monitors in the ADNI database, 137 patients diagnosed as AD, 76 patients diagnosed as MCI converters with MCI in a year and a half, and 134 diagnosed MCI converters (MCIcs) in a year and a half as MCI non-converters. AD was not improved in 134 patients using a diagnosis of MCI over a year and a half. In addition, 509 individuals were considered from 41 radiological groups. The methodology involved extracting features and selecting them from the MR images, then selecting the most unequal features by using a PCA in accordance with the FDR criterion. A single topic classification was then carried out with an SVM-based machine learning method. Classification algorithm output was assessed with the nested 20-fold CV, with 0.76 for AD versus CN, 0.72 for MCIc versus CN, and 0.66 for MCIc versus MCInc. The results were superior to those of the 27 of the 28 algorithm configurations of the 3 classifications, as the 27 algorithms had an accuracy of 0.66 for the contrast between the MCIc and the MCInc. Khedher *et al*. [66] used 188 AD, 401 MCI, and 229 ADNI database command subjects. Their methodology implemented an early AD diagnosis CAD system using tissue-segmented brain images. The approach is based on multiple multivariate methodologies, such as PLS and PCA, between AD, MCI, and elderly NC subjects. The CAD frame demonstrated 85.11% sensitivity, 91.27% specificity, and 88.49% precision. In order to introduce a structured CAD template based on function ratings for the detection of AD using sMRI data, Beheshti *et al*. [67] used ADNI database, including 130 AD subjects and 130 HC subjects. Four phases were included in the approach. First, a voxel-based morphometrical technology analyzed the GM variations of AD patients compared to HC GMs, where the GM volume is known as a VOI. Second, the VOIs were extracted as raw characteristics by voxel intensity. The raw features from which higher scores were derived were the more discriminatory features, rated by 7 rankings, namely Statistical Dependency (SD), MI, IG, Pearson's Correlation Coefficient (PCC), Test Score (TS), Fisher's Criterion (FC) and Gini Index (GI). Third, the estimated classification error on the basis of the training set of the AD and HC classes was calculated with the vector size to determine the number of tops features the minimizes which error has been selected as the top discrimination function. Fourth, the evaluation was carried out by an SVM. A data fusion approach was also introduced to improve classification performance in the feature ranking methods. The score accuracy of the proposed automated AD diagnostic system was 92.48% with the sMRI results. Schouten et al. [68] had a group of participants containing only subjects screened at the University of Medicine in Graz. They used the voxel tensor measurements, which were skeletonized using spatial calculation on the tract. After that, by means of an Independent Component Analysis (ICA), they clustered vox-based diffusion interventions and separated the weights. Finally, they agreed on the structural availability of probabilistic tractography between Harvard Oxford Atlas regions and on the graphical measures that rely on those basic network charts. Vocal performance scores were obtained between 0.888 and 0.902 for the AUC rating of the measurements. The measures clustered by the ICA ranged 0.893 - 0.920 AUC. For the structural connectivity diagram, AUC was 0.900, while the graph measurements accordingly ranged 0.531 - 0.840 AUC. An AUC of 0.896 resulted in both measures along with insufficient lasso groups. The first group comprised 68 AD patients and 68 HCs and the second group comprised 92 AD, 94 HC, 65 sMCI and 71 pMCI subjects. Beheshti *et al*. [69] tested two groups. ADRNI was created as a new system to predict the transition of MCI into AD, one to three years before the clinical diagnosis, to assess the quality of their proposed CAD model for 458 subjects. The technique used the Fisher criterion to test the functional sub-sets, chosen from the best discrimination, which decreases the dimensionality of the vectors. Finally, an SVM with reliable results of 93.01% for AD vs. HC, relative to other recent classification studies to differentiate these two groups based on MRI data, was performed.

In the early stages of methodology development, Çevik *et al*. [70] analyzed data collected from the ADNI database of 508 subjects to establish a fully computerized voxel-based technique known as the Voxel-MARS for an order to identify AD and MCI. By means of a new three-step extraction process, the data were changed into a high-dimension space. The Multivariate Adaptive Regression Splines (MARS) technique was used for the first time to classify CN subjects from those diagnosed with AD and MCI in the area of brain RI. The results were comparable to those of the previously presented 28-voxel strategy studies. The technique was more sensitive than most other techniques, with 83.58% for AD vs CN and 78.38% for MCI vs CN. Lee, *et al.* used a voxel approach [71] focused on major structural adjustments that would subsequently have substantial limitations, for example, difficulties in representing the scanning's local data. In their study, 45 patients from ADNIas well as 52 NC and 58 MCI subjects were tested with a subset of ADNI. The approach included the extraction from DTI and sMRI of local image-based biomarkers to create multimodal AD signatures and the incorporation of complementary information using an AD recognition MKL model. The results showed that the accuracy of the classification for AD vs NC was 90.2%, MCI vs NC was 79.42, AD was 76.63% and MCI differential classification problems was 76.63%.

12. Small Samples Size

Eighty-four Diffusion Tensor Imaging (DTI) records from LONI photo collections were aggregated by Lee *et al.* [72]. Forty of these records were used for cross-validation and the creation of a prediction model, with 20 MCI and 20 NC. Early detection of AD is important because the use of drugs towards the start of the disease is more effective. The MCI is an intermediate disorder between usual olding and AD, so the early diagnosis of MCI is important. Their methodology developed an MCI and normal control subject classification model using probabilistic and TBSS analysis of the DTI data, which was randomly chosen from a fixed number of voxels. The SVM model used the FA of the voxels selected, the mean FA value, and the fiber path volume, to predict MCI. The results showed a 100 % reliability and precision and 10-fold cross-validation of 100 % sensitivity for an independent data set of 38 subjects, excluding the 40 subjects used to train the prediction models. In order to present a new ADNI diagnostic tool for AD by using MRIs, Ortiz *et al*. [73] used images collected from an ADNI containing 50 T1 weighted MR images, 25 of whom were normal and 25 AD. Their technique used data obtained through a non-supervised segmentation approach based on the distribution of GM and WM in the brain. The tissue distribution of the control (normal) and the AD pictures to generate a setup of representative models for each class were displayed using the Learning Vector Quantization (LVQ). The proposed technique included new images in the space for additional classification using SVM on the model vectors. The approach resulted in an accuracy of over 90% and a sensitivity of up to 95% for the tests of the normal subjects and AD patients.

Li *et al*. [74] used, together with 15 healthier people with no history of neurological or mental problems enrolled in Tongji clinic, 21 patients diagnosed with AD under Alzheimer's guidelines from the National Institute for Neurological and Communicative Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA). DTI's and T1 images from 36 subjects were examined based on four forms of AD characteristics, including WM atlas, tract-based FA, voxel-based FA, and GM volume. LOO technique was utilized to analyze and compared the characteristics of different markers with each other. The combined characteristics resulted in classification results with a precision of 94.3 %, sensitivity of 95.0%, specialty of 93.3 %, and a ROC area of 0.96. In the OASIS list of Chyzhyk *et al.* [75], there are 49 subjects diagnosed with moderate to medium DA and 49 unconscious to be selected. They proposed an evolutionary wrapper selection using Extreme Learning Machines (ELM) to explore the space of feature combinations in their basic classifier training algorithm, which consisted of a Genetic Algorithm (GA). The results of an AD database on the construction and location of CAD systems in the classification accuracy, sensitivity, and specificity of the features selected, were shown to be strong. By utilizing a dataset based on OASIS MRI scans Farhan *et al.* [76] used 37 AD and 48 NCs, with chosen distance, WM, CSF and hippocampus size features. The identification of the patients and controls was conducted using three different classification models, namely SVM, MLP, and J48. In addition, to resolve the error of an independent base classifier, an ensemble of classifiers based on majority voting was been included. The data showed 93.75% accuracy, 100% specificity and 87.5% sensitivity of the ensemble of classifiers.

Challis *et al*. [77] tested 77 subjects, 27 with potential AD and 50 with MCI, along with 39 control samples. All subjects were checked by 3T to obtain a resting-state scan of seven minutes and 20 seconds. Their study investigated the efficacy of the Gaussian System Logistic Regression (GP-LR) template of a particular multi-variate statistical machine learning software to stratify patients with functional communication patterns in the rest of the brains. They used covariance for the Gaussian period and the AD/MCI-based category of logistic regression as a correlation measure. The results showed that the connectivity strength between average structures and the best classified temporal and subcortical MCI regions as well as the connectivity strength between the frontal and other brain areas, is the best-classified AD. The results also backed the idea that GP-LR prototypes can communicate with patients. The model accurately measured 75 % ofthose with a mild amnesia cognitive impairment and 97 % of those with Alzheimer's disease, which were tested by screening, to disembark on a mild amnesic cognitive impairment. The ADNI dataset of 20 stable control with 20 AD-associated subjects was used by Khazaee *et al*. [78]. Their approach combines advanced machine learning methods to explore changes in functional brain networks in patients with ED, using graph computational methodologies. The capacity of the graph measures for the study of AD was investigated with an SVM model by using the fisher score for feature choice and the SV M in the AD classification. The combined mixture and isolation steps were analyzed. The system reached 100 % reliability.

MRI scans of 25 volunteers referred to the Radiology Department, through the Psychiatry, Neurology and Geriatrics Departments, Kasturba Medical College, Mangalore, were used by Fernandes *et al*. [79]. Their methods included the use of various techniques for image processing, such as K-means clustering, wavelet transforming, watershed algorithm, and a customized case-specific algorithm. These were introduced on Open CV with Qt open-source platforms which promote the production and use of the product without the need for proprietary software. The results can be used in detecting AD and linking clinical outcomes to assist clinicians in the early detection of AD. Zhang *et al*. [80] found 90 T2 images from the MRIs that belong to a server downloaded from Harvard University Medical School. Their technique was first used to eliminate the spectrum from each magnetic resonance image by using the weighted-type fractional Fourier Transform (WFRFT). Second, PCA was used to reduce the spectrum characteristics to only 26. Thirdly, these characteristics were combined and fed into two SVN variants with generalized own meaning proximal SVM and twin SVM. The 5x5-times cross-validation tests demonstrated sensitivity of 99.53%, precision of 99.53%, and reliability of 99.11%. is the results were comparable to the WFRFT-1PCA1-twin SVM. whereas they were superior to the proposed WFRFT1-PCA1-SVM. Their results showed the general self-value generalized proximal SVM of WFRFT1-PCA1. In order to study 75 subjects, of which 50 are normal, 17 are MCI, and eight have AD, an OASIS database was used by Ben Rabeh *et al*. [81]. The CAD model was proposed in their methodology for the early detection of AD, using three frontal sections to remove the Hippocampus (H), the sagittal analysis of the Corpus Callosum (CC), and the axial approach to function with a variety of Cortex features. This identification strategy relied on the SVM with the proposed structure, and resulted in an early AD diagnosis with accuracy of 90.66%.

Rabeh *et al*. [82] again used the database of the OASIS, which included 100 training subjects (50 normal, 25 MCI and 25 AD) and 75 test subjects (25 normal, 25 MCI, and 25 AD). Their work introduced another classification method to classify AD using a supervised classification system. Their approach took into account the four training samples of parts similar to the current passage X, as shown by the four divides between Euclidean, Manhattan, Hausdorff, and AMED, in which 92 % of AD detection was shown to be correct. The main disadvantage in their work was the use of small datasets.

13. Early and Late Fusion Methods

MNRIs were used by Ben *et al*. [83] for 218 subjects tested in a 3T-weighted contrast database called "Bordeaux Dataset". Their main contribution is the consideration of the visual features of the AD hippocampal area and the use of late fusion for enhanced precision results. In a sub-sample of a large French Epidemiological Study called "Bordeaux Dataset", the visual signatures based on CHF were first classified among two-by-two categories using the cutting-edge SVM approach and the Radial Basic (RBF) kernel. The results showed that the classification accuracies of ADNI subsets and the Bordeaux dataset reached 87% and 85% precision in classifying patients with AD

versus NC subjects. While, accuracies for MCI versus NC and MCI versus AD on reached 78.22% and 72.23%, respectively. Ben *et al*. [84] re-chosen ADNI sample subjects from data that included 137 patients with AD, 162 subjects with NCs, and 210 subjects with MCI. Their approach utilized the structural RIM information-dependent visual indexing framework and pattern identification to separate the three classes of NC, MCI, and AD subjects. This technique was used to derive local traits from the hippocampus and post-cingulate cortex (PCC) by circular harmonic functions (CHFs) [85]. The PCA method was also used to minimize dimensionality and then to classify the classes using SVM classifiers. Their findings demonstrated values of 83.77 and 78 % for the AD vs NC group, 88.2 and 80.4 % for organisms and 79.09 and 74.7 % for sensitivities. Their system also achieved 69.45% accuracy for NC versus MCI classification, a species of 74.8% and a sensitivity of 62.52%. The accuracy of AD versus MCI was 62.07%, the precision was 75.15%, and the sensitivity was 49.02% [86].

Dimitriadis *et al*. [87] selected ADNI MRIs that included an overall dataset of 400 subjects, divided into a 240-subject training dataset (60 of each of the four groups) and 160 testing subjects (40 of each of the four groups). This technique was based on a random forest algorithm of subsets of a complete set of characteristics (i.e., the whole set or the left/right hemispheric), as well as a random forest classification with an approach of fusion and a majority vote assembly. The results of these surveys were positive in the 61,9% four-class category by combining the MRI-based features with the random ensemble strategy for forests. The most detailed classification of all research groups participating in a neuroimaging competition was also achieved. However, features that have a low contribution and problems with dimensionality may affect early fusion efficiency. The correlations between the different modalities can not be used with late fusion methods because each modality is handled independently [88].

14. Conclusions

The literature progressively focused, over the previous decade, on the neuroimaging-based diagnosis of AD as a way to identify common biomarkers for these conditions. The ultimate aim of the AD group is to produce an individual diagnosed with a single MRI by using previously trained classification system models on a large pool of ill and healthy people. Many types of neuroimaging, including structural and MRI, were explored in this analysis and revealed typical changes in the brains of AD patients. No single modality of neuroimaging is adequate, because each of these has additional benefits and limitations. All works have seen improved classification performance for AD detection by incorporating information from various methods. However, the combination of neuroimaging features with population data, cognitive test results, CSF biomarkers, and genetic data was successful in obtaining correct classifications. Nevertheless, validation in a clinical environment and in databases that consist of extremely pre-selected subjects is important, that differ significantly from those seen in the clinical environment. Researchers in the field of AD classification face growing challenges, which make it difficult draw precision in classification, including the high dimensions of raw neuro-imaging data, the reduction of sample sizes, generalizability, and heterogeneity in AD. Neuroimaging remains, however, very promising for AD diagnosis as many of these problems can be solved.

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