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Detection of Neurodegenerative Disease in Ageing Adults: A Systematic Review

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Abstract:
Abstract—In the present day, neurodegenerative disorders play a mammoth role in the long-termdysfunction in aging adults. The percentage of aging adults is comparatively much higher in developing countries, therefore the increase in the percentage of patients suffering from neurodegenerative disease levies a huge burden economically on the governments. Moreover, neurodegenerative diseases are mostly progressive in nature and to date, no therapies or treatments have been found which can completely eradicate the disease from the body of a person. Therefore, the primary concern that needs to be addressed right at this point in time with regard to the neurodegenerative diseases is an effective diagnosis by avoiding the error in misdiagnosis rate and proper drug delivery to the patients to control the progression which can help them lead a better life. Now with the advent of computer-aided detection, the process of diagnosis has become seamless and also offers a multitude of assistance to the physicians and the doctors. Also, for the detection of the neurodegenerative disorder there is a number of parameters and modalities that need to attend by the doctors, therefore, leveraging computer-aided detection systems for the diagnosis might help the researchers and the doctors to explore multiple dimensions and fetch a unified and weighted response. In this paper, we have discussed multiple modalities with respect to the diagnosis of neurodegenerative disease and also its progression.

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I. INTRODUCTION

One of the primary concerns of the countries with a mammoth aging population is neurodegenerative diseases. Neurodegenerative diseases encircle a group of hereditary and occasional health conditions caused by the degeneration of the neural tissue. The most commonly observed degenerative diseases presently known are Alzheimer's disease and Parkinson's disease. The diseases are particularly much troublesome to the individuals as well as their families because such diseases are irremediable in nature and are also progressive of a kind. Neurodegenerative diseases have also invoked a huge burden worldwide as based on the World Alzheimer Report 2015, it was stated that around 46.8 million people across the globe are suffering from dementia and estimated that it could raise up to 74.7 million by 2030 [1]. Therefore, to tackle the progression of the neurodegenerative diseases at the early stages some great efforts have been made [2,3].

Alzheimer's Disease (AD) is primarily considered as the primarycauseof dementia. It has been observed that Alzheimer's Disease is progressive and irreversible which further leads to the decline in normal cognitive functioning of a person. The commonly observedsymptom of AD is the difficulty in remembering the latest events [4]. Moreover, as the progression occurs in a person, it can include symptoms like issues with the language, mood swings, and behavioral issues. As for the particular disease, no cure has been found out yet, to completely eradicate the disease from the body, therefore

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

detection in advance of the disease has proven to be effective in improving a person's life. Moreover, misdiagnosis of neurodegenerative disease may lead the physician in prescribing drugs which may turn the situation more hostile.

Parkinson's disease (PD) the second most commonly observed neurodegenerative disease in aging adults. PD usually affects the nerve cells which are responsible for producing dopamine, an organic chemical that acts as the neurotransmitter to send signals between multiple nerve cells. The deficiency of dopamine that is caused by Parkinson's disease incrementally worsens the motor capabilities of a person which further leads to muscle stiffness, tremors, and impairment of posture and balance. Similarly, like Alzheimer's disease, there is no cure available at present that completely eradicates the disease from a person's body. But advanced detection, of PD, can improve the life of a person suffering from it by providing proper medication to control the symptoms [5]. Moreover, the detection of PD can be achieved using gait analysis and neuroimaging techniques. Also, the detection of Parkinson's disease at the early stages is quite difficult and a lot of misdiagnoses happens which further leads to an increase in cost for the patients [6].

The flow of the study is as follows: In the second section, we have discussed the detection of AD using Wearable sensors and gait pattern analysis and the third section discussedthe detection of Alzheimer's disease using neuroimaging data. The fourth and the fifth section discusses in depth the work that has been performed for the detection of PD by leveraging wearable sensors and the neuroimaging data respectively and finally, the paper is concluded in the sixth section.

II. Detection of Early Stage Alzheimer Disease: Using Wearable Sensor Data

For the advanced detection of AD using wearable sensor data, multiple methods have been proposed which provided the community with some state-of-the-art methods. Varatharajan et al [7], emphasized on the early detection of Alzheimer's disease by monitoring the patterns of foot movement in patients. The work implemented a dynamic time warping algorithm for comparing the patterns in the foot movement of individuals suffering from AD and healthy people. Furthermore, comparative analysis in the gait pattern was performed between the individuals suffering from AD and the healthy people by leveraging a mid-cross-function. The cross levels for both the type of patients were further classified using classification algorithms such as K Nearest Neighbours (KNN) and Support Vector Machines(SVM) and it was found in the from the study that Dynamic Time Warping method proved to have high specificity and sensitivity while detecting Alzheimer's disease. Ardle et al. [8], also performed a gait pattern analysis for the detection of Alzheimer's disease using body-worn sensors. In this particular study, participants aged between 55 to 80 participated were, a lightweight triaxial accelerometer-based wearable was attached non-invasively to the fifth lumbar vertebra using double-sided tape. The complete experiment was performed for a duration of 7 days and was performed out in an independent free-living environment. The participants of the experiment underwent three gait assessments and also a neuropsychological assessment where the participants undertook the Mini-mental state exam. The results of the examination were discussed separately, where the CLOX and GDS scale were used for the neuropsychological assessment and regarding the gait assessment multiple gait parameters were obtained from the data and the relationship between the micro characteristics and cognition from the sensor data and neuropsychological data were examined.

Similarly, Hsu et al [9]. performed a balance and gait analysis for the detection of AD using a wearable device. In this study, 50 parents underwent a gait analysis by using two inertial sensors on the foot and balance analysis by using an inertial sensor that was placed on the back of the waist. Further, in the study, multiple algorithms were devised for gait parameter

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

analysis and gait cycle decomposition. Also, the study discussed the development of a balance analyzing algorithm for determining the path of the body's center of mass projection. The participants in the study undertook a dual-task walking test and a single-task walking test which was further analyzed by using the sensor data that was fetched during the test. Upon analysis, it was found that the participants suffering from AD showed a vast difference in gait parameters for the single-task walking tests and the double task walking test than the healthy participants. Kourtiset al. [10], on the other hand, discussed multiple digital biomarkers that can be derived from mobile and wearable devices. For the detection of AD, the author mentioned a few things which are as follows, gross motor function, where the gait pattern analysis can be performed using the IMU data, fine motor control, where using the sensor data from the mobile touch screen, keyboard and stylus, multiple artifacts can be observed. From the perspective of visual stimulus, the author suggested that the data from oculomotor can be used for understanding the visual preference, pupillary reflex, and eye movements during reading. Moreover, as we know [11], Alzheimer's disease causes the deterioration of the cholinergic system of the brain, therefore the author suggested the usage of PPG, ECG and ballistocardiography sensors for understanding the involuntary actions of the body, with the response to the disease stages.

III. DETECTION OF EARLY STAGE ALZHEIMER'S DISEASE: USING NEUROIMAGING DATA

The detection of AD using neuroimaging has provided with some great reliability, where previously for diagnostic purposes the neuroimaging was used for an exclusionary purpose but right at this time the neuroimaging has attained the central position [12]. The inclusion of neuroimaging methodologies for the detection of AD got much attention after it was found that the neuroimaging provides insights regarding the spatial and temporal evolution of AD progression. In a better sense, it can be duly observed that neuroimaging helps to depict the possible physical locations in the brain which have suffered effects from the enablement of AD. Also, with the topographical entropy of the brain, the reasoning of AD can now be easily quantified and can be related to each other effects [13]. Therefore, the prognosis in the neuroimaging for certain time intervals can now be easily correlated with the clinical biomarkers to simplify the biological cause of AD.

Kruthika et al [14], studied the multistage classification technique for the prediction of AD. In the performed study, the data was gathered from the Alzheimer's disease Neuroimaging Initiative (ADNI) database and the data of the subjects concluded as Alzheimer's disease, Mild Cognitive Impairment (MCI) and healthy control were chosen. The extraction of the features from the MRI images were extracted by leveraging Particle Swarm Optimization. For the classification of the features generated from the MRI Images, a Multistage classification routine was developed which used Gaussian Naïve Bayes in the first stage and SVM and KNN in the second stage respectively. The method of classifying was planned in such a way that at the first level, a Gaussian Naïve Bayes model was trained to predict whether the particular scan in AD or MCI or Control. Now if the first stage predicts the scan to be AD with high confidence then the particular scan is accepted and classified as AD. But if the scan is predicted as MCI or control with high probability, then the particular scan will be transferred to the second classifier which acts as the binary classifier for determining whether the image is MCI or control. The work pursued some astonishing results by leveraging the stage-based classifiers further the best model was evaluated with a precision of 96.05. Similarly, Moscoso et al. [15], studied to plot the implication of multiple classifiers or the design of classifiers on the detection of AD. For the study, authors leveraged data from ADNI but used only the data that was captured using the 3T scanners and also the data of only those patients were taken who were Normal control (NC), Late MCI and AD. In the

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

classification step, 4 different models were developed at the baseline where in the first model a logistic regression was fitted on normal control (NC) and AD patients. The other three models were computed using different outputs such as hippocampal volume, entorhinal cortex volume and both the volumes together respectively. Further, three different sets of analyses were performed by taking AUC, Specificity, and sensitivity as evaluation metrics. In the first sub-analysis, progressive MCI (pMCI) sensitivities were compared between the pMCI’s which converted in 2 years and 5 years respectively. The first sub-analysis primarily investigated the way the model performed with regard to the way how a control patient progressed in a period of 5 years. In the next sub-analysis, which was the sub-analysis part 2 the specificity of the model was checked with the data of stable MCI (sMCI) that converted in two years to the one which remained stable for 5 years. Further the 3rd sub-analysis, the MCI to AD converting patients were separated into two cohorts namely short-term convertors which converted in 2 years and the midterm convertors which converted in 5 years. This study finallyplotted that MCI patients remain stable for anamicable period of time and further progress to become an AD.

From the type of studies that were performed by the researchers, it was noted that the type of features that are being extracted from the MRI images also plays a ratheressential role in the prediction and progression of AD. So, the study of the different types of feature extraction methods plays a very essential role in classification purposes. Therefore, multiple works in the field of neuroimaging have been performed where different approaches based on the type of features have been proposed. Similarly, Luk et al [16] performed a study, where he extracted the features from the whole 3D brain MRI using texture analysis. The 3D voxel-based texture analysis [17] was performed by calculating a texture map for each voxel by taking the mean of the texture feature in all the three orthogonal plains namely, axial, coronal and sagittal. 8 different texture-based features were calculated for the study that has previously proved to be helpful to differentiate between dementia and non-dementia [17]. Following a comparative analysis was performed between the MCI Converters and Non-Convertors under an observation period of 3 years and a predictive model was designed to predict the conversion of the patients to AD from MCI. The predictive model at the end plotted an accuracy of 76.2% for the conversion of patients from MCI to AD. In another study, Beheshti et al. [18] discussed a feature ranking by leveraging the genetic algorithm approach regarding the classification of AD of its progression from MCI states. The authors in the work designed a computer-aided detection system where in the first stage a morphometry technique was devised based on the scan voxels to compare the grey matter atrophy in the scans of the patients suffering from AD and the normal patients. The second stage consisted of fetching volume of interests (VOI’s) which had a low level of Grey Matter volume. Further, the extracted voxel values from the VOI’s were induced to a feature vector that ranked the features based on t-test and genetic algorithm. At the penultimate, all the features were used to develop the classifier that leveraged support vector machine to classify the AD, control, sMCI, and pMCI patients. Another very effective approach was discussed by Long et al [19]The experimental where the primary proposition of the work suggested classifying a patient as AD based on the MRI deformation. The work demonstrated the method of analyzing regional morphological differences between the AD or MCI patients from the healthy controls and conversion to AD from MCI. The proposed method analyzed the deformation analogy by calculating the distance between the subject’s groups using asymmetric diffeomorphic registration and an embedding algorithm. Further, into the study, a classifier was leverage using a support vector machine algorithm which propelled an accuracy of 96.5% for segregating AD from healthy control adults, 91.74% for segregating progressive MRI from healthy

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

controls and lastly 88.99% in segregating progressive MCI from stable MCI.

However, a combination of biomarkers with neuroimaging has also shown many relevant effects when it comes to the predictive power of computer-aided detection systems. Therefore, multiple studies have been performed based on neuroimaging where particular biomarkers have also been included in the system. The study performed by Davatzikos et al. [20], leveraged cerebrospinal fluid (CSF) biomarkers together with MRI images for the prediction of MCI to AD conversion. For the analysis of short-term conversion from MCI to AD, the spatial pattern of aneurysms for the detection of early AD (SPARE-AD) score was utilized. It was derived that MCI subjectsthat converted to AD showeda positive baseline score and atrophy was observed in temporal grey and white lobe matter. Moreover, it was also found that MCI patients that converted to AD had CSF biomarkers similar to AD patients and MCI patients who did not convert to AD had a mixed baseline of CSF and SPARE-AD. In another study, Wang et al [21], trained the machine learning model on brain morphometry and white matter connectomes. The author leveraged a dataset of 422 patients which had a varied distribution of control, AD, MCI, and memory complaints respectively. For the classification purpose three most commonly used algorithms were used namely Random Forest, logistic regression and support vector machine with morphometric and connectome estimates as features. And it was found that the classification accuracy propelled to 97% for AD and controlled patients, 83% for MCI and SMC patients and 83% for AD and MCI patients respectively.

IV. Detection of Parkinson Disease: Using Wearable Sensor Data

PD which is considered as the second most commonly observed neurodegenerative disease and patients suffering from PD have always shown gait impairments which are also considered as one of the most important biomarkers. Therefore, wearable devices and biosensor data of PD patients have been widely utilized for gait pattern analysis by leveraging Spatio-temporal features and to analyze the PD progression. Aich et al. [22], performed quantitative and qualitative analyses on the gait patterns of PD patients and healthy patients to detect the freezing of gait (FoG). For the study accelerometer data were collected from 51 patients with 36 patients with FoG and 14 patients without FoG. The accelerometer data were collected by using two wearable accelerometers placed on both the knees. For the detection of FoG, 5 different parameters were extracted from the walking course data of the patients namely, stride velocity, stride length,step length, stride time and step time. The five features along with statistical features based on the accelerometer data were further used to develop an automated system using machine learning techniques which propelled an accuracy of 88% using SVM as the classifier. Bernard et al [23], performed a study for gait and balance analysis using wearable sensors placed on both ankles and on the lower back. The wearable sensors used in the study were packaged with accelerometer, gyroscope and magnetometer. The experimental process of the study assessed multiple tests such as a single-tasking test, dual tasking test, static balance test, Timed-Up-and-Go test (TUG), functional reach test. For the gait analysis, 3 different gait parameters were used namely, stride velocity, stride length and stride time.

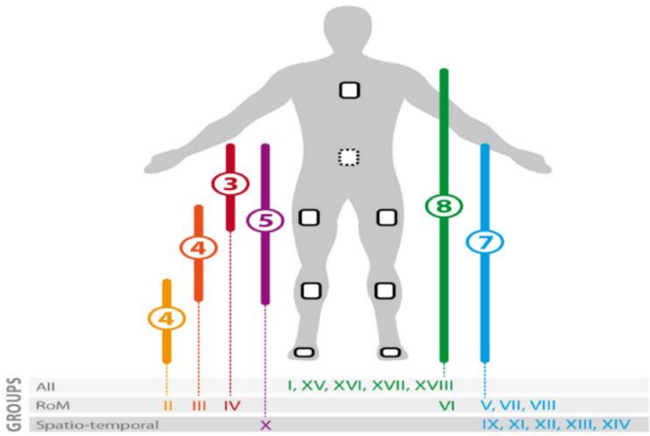

Figure 1: Sensor locations and the number of sensors.[24]

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

As the use of sensors for detecting gait patterns is important, perhaps the location where the sensor is placed on the body also holds importance. Therefore, Caramia et al [24] performed a study on gait patterns by positioning the sensors in different parts of the body. For the particular study, data from 27 patients suffering from idiopathic PD and 27 healthy controls were fetched. The features fetched from the sensors were particularly of two categories namely Spatio-temporal features and range of motions (ROM's) and the grouping of sensory locations was based as in figure 1. Further, into the study, multiple classification algorithms were used to check the prediction capability and classification of patients into Parkinson and healthy and it was found that when the sensors are placed as of "Group VI" maximum accuracy can be obtained. Similarly, Fortaleza et al [25], discussed the interference of dual-task on postural transitions, postural sway and gait patterns in PD patients. For the study, 56 patients have recruited in which 30 patients had FoG and 24 with no FoG. The sensors were placed on the feet, shanks, wrist and chest. It was observed that during walking, the patients with FoG exhibited difficulties in performing dual-task than the patients without FoG. And also, during standing patients with FoG plotted a larger postural sway compared to the patients who did not have FoG. Ireland et al [26], proposed the study of the classification of the movements in the people suffering from Parkinson's disease using wearables. The data was fetched from 14 patients who were suffering from PD and have been diagnosed with PD in the duration of the last 3.8 – 6.3 years respectively. The sensors were placed on both the legs, both the arms and on the back. The features were extracted from raw data of accelerometer and gyroscope using empirical mode decomposition. Further, into the study, an SVM classifier was used to classify the patients as Parkinson or healthy.

V. Detection of Parkinson Disease: Using Neuroimaging Data

The neurodegeneration in a prospective Parkinson's patient starts way before the onset of the motor systems that have been clinically identified for the detection of PD. The delay in the diagnosis often calls for the huge loss of brain cells. Also, the period between the inception of neurodegeneration and the development of motoric abnormalities is enough for the medical intervention to control the progression of PD. Therefore, multiple studies have been undertaken for the development of state-of-the-art techniques for the timely detection and diagnosis of PD. In the work devised by Xu et al [27] for the detection ofPD, leveraged multi-modality MR images. The images used in the study were considered from two modality cohorts namely, T1 and PET. The study leveraged the neuroimages from 49 Parkinson's subjects and 18 normal subjects. The 3D MRI images were segmented using pre-trained atlases to fetch the RoI's. After segmentation, all the anatomical MRI ROI was registered with PET images. Further from the PET images features were extracted and all the data was trained using an SVM classifier and the classifier showed perfect accuracy. Vlachostergiou et al [28] on the other hand performed multi-task learning for the prediction of PD. The study leveraged MRI Scans of the brain, scintigraphy images, epidemiological data, treatment data and clinical data of 55 patients altogether. The imagery data were trained using ResNet architecture and further clinical data were added to the system via auxiliary inputs. The complete deep neural network architecture propelled an accuracy of 0.91% with precision and sensitivity of 83% and 100% respectively. Moreover, in another study performed by Long et al [29], a classification technique using multi-modal MR imaging for the early detection of PD. For the study, the resting-state functional MRI (rsfMRI) and structural MRI were used from 19 patients suffering from PD and 27 healthy volunteers. The features extracted from the rsfMRI were the amplitude of low-frequency fluctuations,regional functional connectivity strength and regional

January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

homogeneity. And from the structural MRI images features based on the volume of grey matter, cerebrospinal fluid,the white matterwas used. Further, all the features were trained using an SVM classifier which plotted an accuracy, sensitivity and specificity of 89.96%, 78.95% and 92.59% respectively.

However, with the advent of deep learning and specifically convolutional neural networks (CNN), the analysis of image data has become much more accurate and definite [30], also the diagnosis and detection of early-stage Parkinson's disease have reached new heights. Moreover, having deep learning leveraged for the volumetric analysis of the neuroimaging data has also made the system more precise and accurate. Similarly, Sivaranjini et al [31], performed a study on the detection of PD using CNN. The work utilized the data from the public data PPMI and extracted the data of 182 patients where 82 were healthy patients and 100 were the patients suffering from PD. All the image data in the study were preprocessed by using a Gaussian filter. Post preprocessing all the data were trained using the well-known CNN architecture AlexNet. For the training purpose, transfer learning was performed where the pre-trained Alex Net weights were utilized to initialize the initial weights of the architecture and the last fully connected layer was used for the prediction purposes. The complete work demonstrated an accuracy of 88.9% and a sensitivity of 89.3%. With regard to the 3D volumetric analysis of the brain MR images, Esmaeilzadeh et al. [32], performed a study for the diagnosis of PD using a 3D-CNN network. The data for the study was extracted from the PPMI database, and it contained the data of 452 patients suffering from Parkinson's disease and 204 healthy adults. The MRI data were further subjected to pre-processing where skull stripping using the Brain Extraction Technique (BET) was performed. After the pre-processing, the feature data were trained using a 3D CNN architecture of 13 layers (including input and output). Moreover, the study also performed multiple experiments by changing the internal parameters of the architecture and also by changing the normalization criteria and regularization and at the end a comparative analysis was shown, where it was found that the architecture with Simplified Model, Age and Gender features, Group Normalization and Bias and Kernel regularization demonstrated a perfect validation accuracy. Also, Martinez-Murcia et al [33], developed a 3D CNN for the diagnosis of PD. The authors acquired Single Photon Emission Computed Tomography (SPECT) scans using the Ioflupane drug DaTSCAN which is one of the radiopharmaceutical drugs injected to the patients for performing a quantitative analysis of the spatial distribution of presynaptic dopamine transporters in the striatum [34]. The data for the study was extracted from the PPMI database and contained the data of 154 patients suffering from Parkinson’s disease, 32 patients without evidence for the dopaminergic deficit and 111 normal people. Further, the SPECT images were subjected to a 3D convolutional neural network with 7 layers combining the input and output layer. The 3D CNN architecture was later found to have propelled an accuracy of 95.5% accuracy and 96.2% sensitivity for the diagnosis of PD.

VI. Conclusion

The paper discussed a wide range of methods and studies that were performed over the last decade until now on the detection of neurodegenerative diseases such as Alzheimer’s and Parkinson's. To be more specific the study discussed the detection technique of both the diseases using wearable sensors (IMU) and neuroimaging. As the diseases are progressive in nature, therefore detection of these diseases at a very early stage is important so that the progression of the degeneration can be slowed down and the patient can live a better life. Now when wearable sensors are used they particularly allow us to detect neurodegenerative disease only at the onset of clinical symptoms but in reality, the neurodegeneration starts way before the arrival of clinical symptoms. Therefore, leveraging

TEST Engineering & Management
January - February 2020
ISSN: 0193 - 4120 Page No. 8982 - 8990

neuroimages data for the identification and detection of neurodegenerative diseases can be regarded as the best solution for the early detection part and followed by clinical analysis using the wearable devices.

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