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Artificial Intelligence Techniques To Classify And Diagnose Alzheimer's Diseases

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Abstract: Alzheimer's disease (AD) is a neurological illness that worsens with time and mostly affects cognitive abilities. It causes memory loss, thinking problems, and ultimately the loss of independence. An accurate and timely diagnosis is essential for the disease's optimal treatment and intervention. The use of artificial intelligence (AI) methods to aid in the early diagnosis and categorization of Alzheimer's disease has gained popularity in recent years. An overview of the state of AI applications in AD diagnosis is given in this study, along with a discussion of the various methods, difficulties, and potential paths forward. According to the review, DL methods have demonstrated potential in the identification and treatment of AD. Natural language processing and picture categorization, in particular, have benefited greatly from the use of DL, which has advanced artificial intelligence. The work sheds important information on the wide range of this research and emphasises the potential of AI in AD genetic investigations.

Keyword: Alzheimer's disease, deep learning, early stage detection and diagnosis.

I.INTRODUCTION

A gradual and irreversible brain illness, Alzheimer's disease (AD) causes memory loss and cognitive impairment. It is a common kind of dementia that affects people 65 years of age and beyond. It is critical to diagnose AD accurately and promptly. Software technologies and diagnostic neuroimaging have become indispensable for diagnosing dementia in its early stages. This work aims to present an extensive overview of current studies that use deep learning (DL) methods for dementia evaluation, with a focus on AD in its early phases. Analysing the existing status of research and investigating potential future avenues for this topic are the goals. A comprehensive review of the literature on the use of DL approaches to the evaluation of dementia and the early detection of AD is part of this work. Examined are a number of datasets frequently used to predict AD. The paper includes a review of the many uses of modern AI algorithms for AD diagnosis, along with an analysis of their benefits, drawbacks, and effectiveness.

Alzheimer's disease (AD) is a neurological illness that is irreversible and gradually deteriorates cognitive abilities, eventually leading to dementia. Based on the existence of objective cognitive abnormalities (usually substantial memory problems), AD is clinically diagnosed. Atypical presentations of AD are possible in certain situations, characterised by deficits in non-amnesic domains such as language, attention, executive processes, and visuoconstructive practice [1]. To make an early and differential diagnosis, particularly in the early stages of the illness, is challenging since AD combines many clinical symptoms with other neurodegenerative diseases, such as Lewy body dementia [2], frontotemporal disorders [3], and vascular dementia [4,5]. Clinical signs of dysexecutive/behavioral changes, or fluent and non-fluent progressive aphasia, may overlap with frontotemporal dementia syndromes in atypical AD [6–7]. Similarly, posterior cortical atrophy (PCA) with underlying AD aetiology may overlap clinically with dementia with Lewy bodies or corticobasal syndrome. Lastly, a common characteristic of neurodegenerative diseases that have a common pathogenic mechanism—extracellular and/or intracellular insoluble fibril aggregates of abnormally misfolded proteins, such as the development of amyloid plaques, tau tangles, or α-synuclein inclusions—is the presence of co-existing pathologies. In this regard, the pathophysiological and molecular alterations typical of AD or other pathologies, as well as the corresponding clinical manifestations that occur, particularly in the pre-clinical stages, can be detected and recognised with the aid of the system biology approach, which strives to integrate clinical and multi-omics data [8].

The neuropathological features of the disease are amyloid plaques and neurofibrillary tangles [9]. These can be assessed in vivo by neuroimaging research and the evaluation of biomarkers in the cerebrospinal fluid (CSF); specifically, amyloidβ1-42 (Aβ42), its ratio with amyloid β1-40 (Aβ42/Aβ40), total tau protein (t-tau), and hyperphosphorylated tau (p-tau181).

Since AD is multifactorial, a wide range of disorders, including depression, hearing loss, traumatic brain injury, alcohol misuse, and metabolic impairments (diabetes mellitus, hypertension, obesity, and low HDL cholesterol), might affect an individual's risk and age of start [1]. Lifestyle variables that may be changed include smoking, inactivity, and social isolation. Some of these factors may also have reciprocal interactions and constitute early signs of dementia other than risk factors during the prodromal period [2]. All these clinical, biochemical, sociodemographic, and lifestyle variables help define the course of the illness and are therefore helpful in attempting to unravel the mystery surrounding AD's aetiology.

Many of the mechanisms in the development of the illness have been unveiled by decades of experimental and clinical study, including the β-amyloid hypothesis, but the mystery is still not fully solved. Big Data exploitation may be used to examine the theoretically infinite quantity of biological process information included in clinical and biological data from electronic health records and multi-omics sciences, including genomes, transcriptomes, and proteomes [8]. Tens of thousands of AD patients have had their data collected so quickly that it far outpaces human comprehension of the illness.

Although sophisticated AI-based models may successfully extract valuable information from Big Data, it is harder and harder to understand how they generate their output as they get more complicated. They have been dubbed "black-box models" as a result. In healthcare applications, where physicians and patients alike must trust research methodologies to make conclusions about people's health, making AI explainable is a major challenge of contemporary AI technology advancement [4].

II. LITERATURE SURVEY

In 2018, Liu *et al.* [7] suggested the use of cascaded CNNs because of their ability to progressively analyse different levels and characteristics of MRI and PET brain images. No expertise was required, as no image segmentation was involved in preprocessing the data. This feature generally serves as the advantage of this approach over the other methods. In the other methods, the features are retrieved and then fitted to the model. Their study involved 100NCcases, 93AD patients and 204 MCI patients based on the ADNI data A 93.26% efficiency was achieved.

Kruthika *et al.* [3] proposed a content-based image retrieval system that relied on 3D Capsules Network (CapsNets), i.e. a 3D CNN, and a pre-trained 3D auto-encoder technology to detect AD at its initial stages. They stated that 3D CapsNets are capable of performing rapid imaging. However, unlike the deep CNN, their method can only improve the detection. They achieved an accuracy of 98.42% in distinguishing AD.

Basaia *et al.* [4] examined subjects from an organisation in which 407 healthy controls and 418 AD, 280 progressive MCI and 533 stable MCI cases were involved. They used CNNs and practiced on the 3D T1-weighted images. Their dataset was ADNI. They investigated CNN activity to classify AD, progressive MCI and stable MCI. 75% accuracy was obtained when CNNs were used to segregate the progressive MCI patients from the stable MCI patients.

Payan and Montana [5] developed an algorithm that used MRI scans to evaluate the condition of a particular patient. They used a total of 2,265 cases, and they selected the ADNI dataset for their work.

Hosseini-Asl *et al.* [6] suggested the use of DSA-3D-CNN, which they found to be more precise than the other modern predictors in evaluating AD based on the MRI scans. By distinguishing the AD, MCI and NC cases, they showed that the retrieval of features can be enhanced in 3D-CNN. Seven metrics were utilised by the brain extraction tool for the analysis. They used the FMRIB software library. Apart from describing the process of using the data, this library contains tools to facilitate MRI, fMRI and DTI brain imaging data.

Overall, based on a high-level examination of the literature, we discovered that published articles in this field primarily address two areas of research: neuroimaging and biomarkers, with a growing amount of attention going towards image processing. Despite being viewed as comprehensive and carefully carried out, the work adds nothing to our understanding of AD early detection because most of the selected individuals have been diagnosed with the disease previously. This study examined a few of the significant relevant AD datasets, as well as diagnosis and detection methods. This strategy works well for preliminary neuroimaging studies.

III. ALZHIEMER'S DISEASE STORY

This section presents the history of AD as a compilation of results from Google Scholar searches for AD articles. Only articles published between 2008 and 2019 were chosen, and only the most recent publications were taken into consideration. Our study concentrated on datasets that were used to investigate AD and moderate cognitive impairment (MCI), which is the precursor to AD [8]. The methods and approaches employed by earlier researchers were examined.

Kraepelin discussed a unique group of cases in 1910's eighth edition of Clinical Psychiatry: A Text-book for Students and Physicians. These cases included excessive plaque formation, the death of approximately one-third of the cerebral cortex, and the replacement of those areas with particular bursts of coloured neurobrils. These cases also represented the most severe form of malnutrition. Kraepelin was the first to refer to the ailment as "Alzheimer's disease," having provided a description while the clinical diagnosis of the illness was not yet established.

The German doctor Alois Alzheimer initially described a case of Auguste Deter disease in 1906, but the diagnosis was not quite clear-cut. It took more than a century for reliable descriptions of the clinical criteria of AD to emerge. Neurobrillary portions and senile plaques were mentioned in the 1907 and 1909 descriptions of AD by Dr. Alois Alzheimerer and Proskin, respectively [10]. Nevertheless, no notable evidence of arteriosclerosis was discovered during a clinical examination of a patient's brain, despite the fact that this condition was thought to be included in the patient's diagnosis. Researchers from the Max Planck Institute of Neurobiology in Martinsried and the University of Munich, Germany, discovered in 1998 that amyloid plaques and neurobrillary cramping may have an impact on certain brain regions [1]. Since then, this research has been recognised as the first example of AD that has been documented; more significantly, the case satisfies the current definition of AD.

Dr. Gerber and his associates from the Max Planck Institute of Neurobiology's Psychiatric Department studied histological slices from F. Johan in 1997. Johan's brain tissues had been kept in good condition for more than 90 years. The study was considered the second example of AD to be published. After the wounds were examined, several amyloid plaques were found. According to the aforementioned research, it is feasible to do a mutational investigation on preserved brain tissue. Dr. Alzheimer's historic discovery was validated once more on the centenary of its discovery. A comparison of an AD-affected brain and a healthy brain is presented in Figure 1.

IV.RELATED WORK

A deep learning-based approach for evaluating structural MRI data is presented in this paper. Four kinds of patients are offered MRI scans: those with Alzheimer's disease (AD), mild cognitive impairment (MCI) in its early stages, moderate cognitive impairment (LMCI) in its later stages, and normal cognitive function (NC). Alzheimer's disease is classified as a neurological brain illness. It progresses gradually and eventually results in the destruction of brain tissue. A brain's cerebral cortex suffers significant damage and shrinks dramatically. The greatest portion of the brain, the cerebrum, contains the cerebral cortex, which is linked to voluntary movements like reading, remembering, logical and critical reasoning, and spatial orientation. The hippocampal region, which is linked to short-term memory and spatial orientation, decreases while the brain's ventricles enlarge. Thus, cortical injury is extremely detrimental to a person's ability to lead a regular life. According to the Alzheimer's Association, AD ranks as the sixth most common cause of mortality in the US [3]. Although an early beginning is occasionally seen, it is more common in older adults over the age of 65. For older individuals, appropriate care plans are therefore necessary. The Alzheimer's Association estimates that the US will have to pay around 259 billion dollars for AD in 2017 [3]. Each person's pace of AD development varies due to differences in their genetic makeup and clinical background. Getting an accurate and timely diagnosis of AD is essential to improving healthcare and treatment.

Zhang et al. [4] fused characteristics from cerebral spinal fluids (CSFs), positron emission tomography (PET), and structural magnetic resonance imaging (MRI) using a combined kernel approach. They then employed a support vector machine (SVM) classifier to carry out binary classification. Tong et al. [5] used the graph fusion approach to combine the best similarity vectors to create a single, unified graph for classification. For every modality, these vectors were produced by computing a pairwise similarity of characteristics. Using MRI images, Sorenson et al. [6] computed hippocampus texture, hippocampal shape, hippocampal thickness, and volumetric data to produce findings for multi-class categorization. In a recent study, Altaf et al. [7] employed hybrid features, which were based on patient clinical and imaging data, and then SVM classification.

But as deep learning becomes more and more popular, neuroscientists are also turning to artificial intelligence and pattern recognition to find answers to their difficulties [8]. A neural network called an autoencoder can extract meaningful features from input data, usually for feature learning and dimensionality reduction. It is mostly employed as a pre-training phase that is followed by a classifier phase. Lui et al. [9] developed a stacked autoencoder (SAE) network for classification utilising a zero-masking technique for combining data from MRI, PET, and CSF. In a separate study, Lui et al. [10] retrieved features at various stages, using multimodal imaging data as a high-level feature and clinical data as a low-level feature.

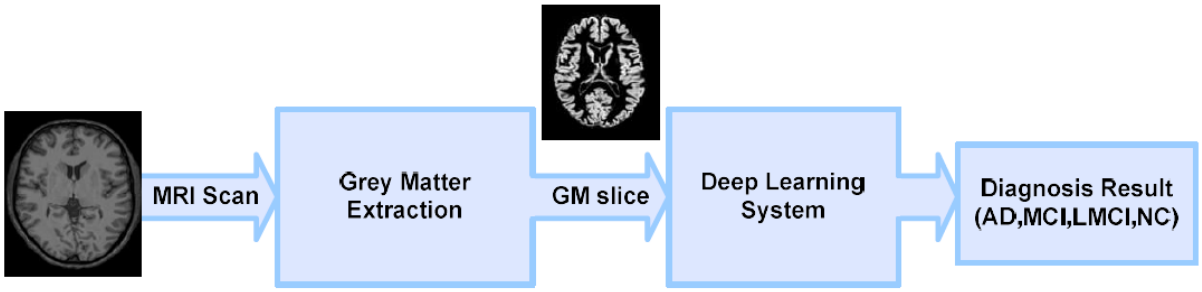

Figure 1. Diagnosis framework for Alzheimer's disease, early and late mild cognitive impairment and normal cognitive

On SAE, the feature learning was based. Multimodal stacked deep polynomial networks (SDPNs) were used for classification by Shi et al. [11]. From MRI and PET data, two different SDPNs extracted features; the outputs were then combined and sent to a final stage SDPN. Nonetheless, for binary or paired classification, the findings of these studies are good and similar; however, multiclass classification requires more work. A unique method of convolving test scans with pre-learnt feature bases was developed by Gupta et al. [12]. The SAE network was used to train the bases from independent sets of MRI and natural data. In their studies, they used both bases, and their 3-way classification accuracy was 85%. Using a similar technique, Payan et al. [13] classified AD, MCI, and normal with 89.5% accuracy in a single setup by performing 3D convolution of the pre-trained bases with MRI data and passing the feature maps to a fully connected network.

A 3D convolutional autoencoder (CAE) and convolutional neural network (CNN) based model was suggested by Hosseini et al. [14].

Three distinct scales' feature bases were extracted. These bases were then used in the CNN's convolutional layers as convolving filters. For class assessments, many fully connected layers were layered above convolutional layers. Good accuracy was attained by this strategy for both binary and multiclass diagnosis. But Sarraf et al. [5] were the first to use CNN architectures on unprocessed picture data directly. They used LeNet and GoogLeNet models to train their network independently for MRI and resting state functional MRI data. A CNN model using VGG architecture as inspiration was put into practice by Korolev et al. [16], who also produced results for the residual and sequential versions of the model for binary datasets. This work uses structural MRI scans to offer a 4-way convolutional neural network based diagnostic method for AD and MCI.

V.MODULES DATASETS TYPES FOR AD

This section explains the dataset modules and the types of AD. The widely utilised types of data are the neuroimaging _le formats. First, the AD dataset module loads the scans, then the image data from the Neuroimaging Informatics Technology Initiative (NIfTI) are utilised. NiBabel (one of the classic packages of Python) is configured by using pip. The NiBabel images are composed of the following.

Image data array: 3D or 4D array of image data.
An affine array: details about the image location.
Image metadata: describes the image.
Uniform dataset (UDS): The data in this dataset are gathered by evaluating the cases from the National Institute on Aging-Funded Alzheimer's Disease Centers. Evaluation is carried out annually. Each year, the cases undergo clinical examination to determine the neuropsychological
testing scores. Nearly 60% of all UDS cases have the apolipoprotein E genotype. The UDS can utilize structural MRI images and data for the cases, and it can subsequently implement enhancements by focusing on the latest factors emphasising frontotemporal lobar degeneration. More work is being conducted to enable researchers to obtain different types of images and biomarkers from biospecimens (i.e. CSF).

Neuropathology dataset: This dataset contains standardized neuropathology data from patients who died and whose bodies were autopsied.

Minimum dataset: Prior to the establishment of UDS in 2005, cross-sectional data on cases from the Alzheimer's Disease Center were gathered through previous research. Second, we need to determine the main types of AD, beginning with the datasets from the Alzheimer's Disease Neuroimaging Initiative, Harvard Medical School and Max Planck Institute Leipzig (Mind_Brain_Body Dataset-LEMON).

VI.METHODOLOGY

Figure 1 displays the suggested framework's block diagram. Using the SPM 8 tool, the first step processes the 3D input volumes and extracts grey matter (GM) for each volume. Neurons' cell bodies are composed of grey matter.

The conversion of each volume yields around 166 2D slices.

Only axial scans are acquired using the slices. These slices are then forwarded to the deep learning-based network, which is the following step.

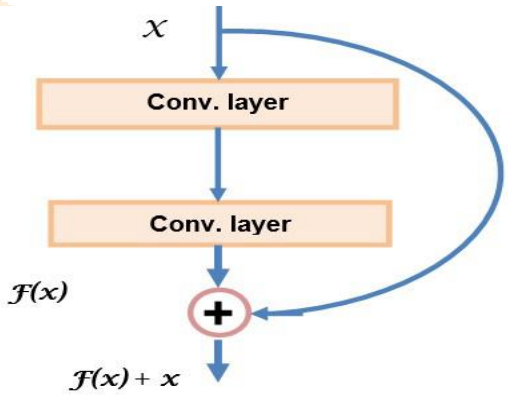

Figure 2. Residual Learning block for ResNets

Machine learning, a representational learning approach, has recently evolved into deep learning, which extracts unique characteristics straight from the raw input pictures. The foundation of deep learning systems is made up of intricate hierarchical neural networks. CNNs are feed-forward, deep networks consisting of many convolutional layers, as well as activation and pooling layers. By performing operations on its input receptive field, each convolution integrates local connections and spatial placement invariance to build feature maps. The annual ImageNet large scale visual recognition competition (ILSVRC) introduces a number of CNN-based models that are subsequently employed for tumour segmentation and medical picture retrieval. The well-known GoogleNet and ResNet models are used in this study to diagnose AD.

The 22-layer GoogLeNet design is centred on a methodical expansion of modules in both the network's breadth and depth.

Its Inception module has also gained notoriety. The module has many filters that extract multi-scale data, which is merged before moving on to the following layer. The design uses dimensionality reduction prior to each filter in the module to monitor the computational budget.

The architecture of the residual neural network (ResNet) is predicated on the residual learning principle. This approach offers reduced computing complexity, faster convergence, and a large increase in depth. As seen in Figure 2, it is made feasible by inserting identical connections between various convolutional layers, which carry the input and its converted or residual information F(x) straight to the layer's output. Hence, it facilitates learning and transfers the most information possible across layers. Eight times deeper than a VGG network, a ResNet with 152 layers has less parameters overall.

VII.RESULTS AND DISCUSSIONS

The Alzheimer's Disease Neuroimaging Initiative (ADNI) provided the MRI data utilised in this study [5]. Binary, unbalanced multiclass, and balanced multiclass data subsets are the three types of data employed. Data for 33 AD, 22 LMCI, 49 MCI, and 45 normal individuals are included. These individuals were scanned at various times, yielding a total of 355 MRI volumes. Binary data, which has 26784 slices, united all cases of AD, MCI, and LMCI into a single sick class. A total of 24668 photos with 4753 AD, 5823 LMCI, 6574 MCI, and 7518 normal class (NC) make up the unbalanced multiclass data. Data augmentation is used to prepare the balanced multiclass data for the class with fewer photos. All it takes to amplify a picture is to flip it along its horizontal axis. There are 9506 photos in each class, for a total of 38024 photographs in the balanced set.

Three stages of the experiment are: training on binary datasets, training on unbalanced and balanced multiclass data from scratch, and fine-tuning pretrained models for multiclass classification. 25% of the data are used for tests, while the remaining 75% are used for training in all studies.

The Torch7 framework is used for implementation. Nvidia GeForce Titan X graphics processing unit (GPU) devices are used for network training.

In the first step, binary classification is done, and Figure 3 displays the findings. The best accuracy results were achieved by ResNet-18 and GoogLeNet, with scores of 99.18% and 99.08%, respectively. The performance of all the models is on par with other cutting-edge methods that have been documented in the literature. The suggested approach is practical since it only needs one modality and little preprocessing, whereas the majority of approaches incorporate characteristics from several modalities.

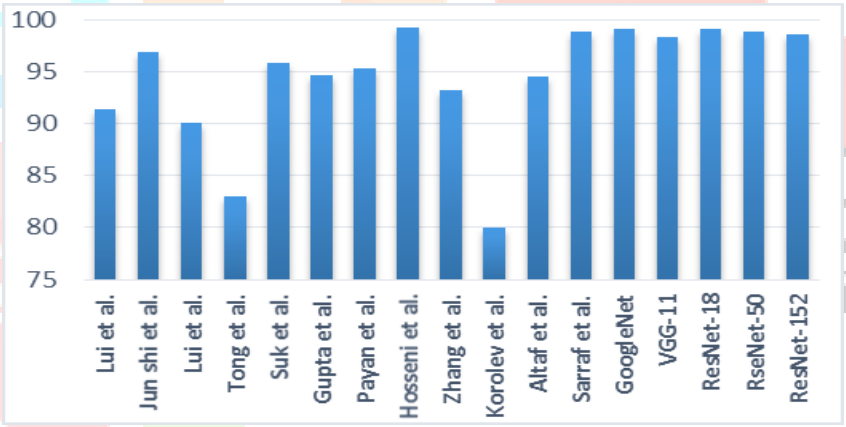

Figure 3. Accuracy performance and comparison for Binary Classification with other techniques.

Multiclass classification, which identifies all four classes in a single run, is carried out in the second phase. Findings for both balanced and unbalanced datasets indicate that the accuracy varies slightly depending on the data distribution.

The best scratch training accuracy results are 98.14% and 98.88%. The suggested strategy goes from 94% to 99.9% for all models and is successful in terms of both specificity and sensitivity. When the suggested approach for multi-class classification is compared to other cutting-edge techniques found in the literature, Figure 4 demonstrates a notable improvement.

The model is trained using a transfer learning strategy in the third experiment phase. With this method, weights may be learned on one set of data and then adjusted for the target dataset. When the dataset size is tiny, this is helpful. ResNet-152 performed poorly in the earlier tests when compared to other models. Because this model is deeper than others, it needs a substantial quantity of training data. 99.7% accuracy is attained when models trained on binary datasets are adjusted for multi-class data using the ResNet-152 model.

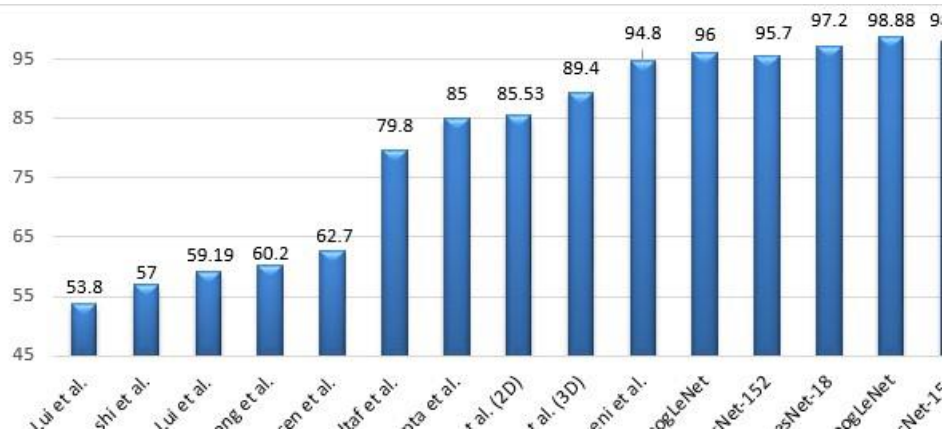

Figure 4. Accuracy performance comparison for Multiclass Classification with other state-of-the-art techniques

VIII.CONCLUSION

This study offered a quick and accurate artificial intelligence-based method for MRI image-based brain pattern diagnosis. In particular, it identified Alzheimer's and likely its early stages. Three phases of the tests were conducted using regular ADNI data. Results from the binary classification phase were on par with those obtained using existing methods. For both balanced and unbalanced data, multi-class classification yields performance accuracy that is noticeably greater than other methods. With training from scratch, the framework predicted the diagnostic groups with 98.88% accuracy; using a transfer learning technique from binary to multi-class, it obtained 99.7% accuracy. The suggested framework is trustworthy and competent to provide consistent outcomes. Since it can identify every group in a single setting, it shows how deep models may be used to diagnose medical conditions. These models' predictions are free from stress, tiredness, and cognitive biases. It proposes training our model on integrated MRI data for numerous diseases in order to create a generic model that can intelligently predict about multiple brain ailments in one setting. The whole model will pick up on every structural biomarker associated with a certain illness. In order to obtain the most intelligent and optimised model for brain illnesses, it may also integrate clinical data. Future research could use multi-modal data training. As a result, the suggested approach raises questions about the potential high-level uses of deep learning and pattern recognition in the creation of intelligent and portable healthcare apps.

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