

AI-Enhanced Neuroimaging and Deep Learning-Based Early Diagnosis of Multiple Sclerosis and Alzheimer's Disease

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AI-enhanced neuroimaging, manifesting cutting-edge AI and neuroimaging techniques, machine learning, and multiparametric MRI, has ushered in an era of deep learning for early, accurate diagnosis and intervention of multiple sclerosis, the most common cause of neurological disease in young adults, and Alzheimer's disease, the most common cause of dementia in the elderly. This progress has resulted in clinical availability and applications designed to guarantee and improve the quality of healthcare provided to patients, ensuring the accuracy, sensitivity, and optimal specificity of brain imaging for early diagnosis of MS and Alzheimer's, where time is brain and time is cognition. AI-enhanced clinical imaging is superior to humans, providing more accurate detection of brain abnormalities and a more accurate determination of the relationship between brain lesions and clinical symptoms, resulting in personalized treatment and intervention for both these diseases, with the highest levels of accuracy ever reached in clinical investigations, aiming to improve quality of life. However, there are disadvantages, namely that interpretation of the results lacks transparency and it is difficult to verify the consequences of detected abnormalities.

Keywords: AI-enhanced neuroimaging, Machine Learning, Deep Learning, Multiparametric MRI, Early Diagnosis, Multiple Sclerosis, Alzheimer's Disease, Brain Imaging, Clinical Applications, Neurological Disease, Personalized Treatment, Diagnostic Accuracy, Sensitivity and Specificity, Brain Lesions, Cognitive Health, Predictive Analytics, AI-Driven Healthcare, Medical Imaging Transparency, Clinical Investigations, Healthcare Quality Improvement.

1. Introduction

The demand for early diagnosis of chronic neurodegenerative diseases is increasing as the average life expectancy rises with advancements in medical technology. However, the histological diagnosis of neurodegenerative diseases has only been possible through brain biopsy sampling and postmortem autopsies, requiring advanced expertise and histopathological observations. On the other hand, diagnosing the early stages of neurodegenerative diseases using neuroimaging or cerebrospinal fluid biomarkers in elderly

patients can make it possible to prevent or delay further progression of the disease by providing the necessary medication, psychological support, and rehabilitation programs. When pituitary tumor patients develop vision loss, it is appropriate to treat and perform neurosurgery before permanent vision loss occurs. Similarly, early differential diagnosis and treatment with drugs are important for minimizing the damage of neurodegenerative diseases.

Most early neurodegenerative disease patients show overlapping clinical and radiological features, leading to diagnostic confusion and challenges. A deep learning algorithm trained with various neuroimaging findings and demographic data could improve accuracy, sensitivity, and specificity, facilitating the early diagnosis of neurodegenerative diseases with noninvasive neuroimaging assessments. This review summarizes the technological advancements of neuroimaging and machine learning algorithms in early diagnosis and management predictions of neurodegenerative diseases. Furthermore, possible limitations and suggestions for the future are discussed to develop practical, efficient, and standardized artificial intelligence models in neuroimaging techniques.

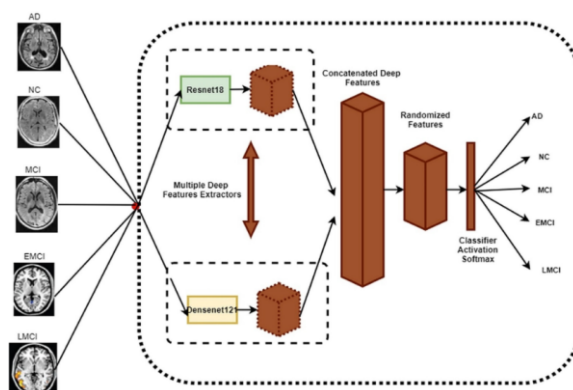


Fig 1: Disease Using Neuroimaging

1.1. Background and Significance

Multiple Sclerosis (MS) is an immune system disorder that is characterized by antecedent damage accompanying multifocal inflammatory cell destruction in the central nervous system (CNS). The disease affects around 2.3 million active-age individuals and is 3 to 4 times more prevalent in women than in men. In the very earliest and the very late stages of the disease, both profound clinical features are nearly absent. In the majority of MS-affected individuals, the disease starts as relapsing-remitting MS (RRMS). With time in the majority of RRMS patients, with the long duration of the disease, and with the deterioration in clinical outcomes, the urgent, recurrent, and non-remitting features of RRMS are replaced by the less invasive non-relapsing progressive course of MS, known as secondary progressive MS (SPMS). To date, the root causes and the fundamental disorganized molecular machinery of MS are unclear. Due to a deficiency in defined diagnostic signposts, the true onset of RRMS is commonly delayed. As a result, the collective inherent and accrued injury burden is already present in the tissues of the majority of MS-affected individuals at the time they are examined and diagnosed with MS.

A majority of them are misdiagnosed due to the lack of apparent, non-invasive early-stage

predictive tools for MS. Around 85% of MS-affected individuals possess radiological findings at a stage much ahead of the zero hour. The trunk of the diagnostic markers used in clinical laboratories is a carryover from the past and is mainly limited to the findings in the bloodstream and the cerebrospinal fluid. MS is mostly diagnosed based on the presence of white matter lesions at the level of the brain in more than one incident versus clinical attacks that occurred at different times. The age at which the very first white matter lesion was detected and its features carried some necessary evocative attributes. Nonetheless, the degree to which the shrunken tissue regions embedded in these acquired white matter volume lesions can be productive markers disclosing the unfortunate fact of 'the tranquility preceding the destruction' is not comprehended. The requirement for accurate, trustworthy predictors of MS and its evolution over the lifespan from the beginning to the severe stages is lacking applications. There is a silent yearning for a suitably handy, widely available index of earlier MS diagnosis that is sufficient to be widely used in clinical trials and the management of patients for the sake of better disease care.

1.2. Research Objectives

The primary objective is to develop a deep learning model with the capability of predicting multiple sclerosis (MS) and Alzheimer's disease in a patient using magnetic resonance imaging (MRI) data. A secondary objective is to develop a clickable demonstrable model that can be used by physicians or any novice user, which will give a probability of a patient progressing towards Alzheimer's disease from amyloid depositions. These depositions are measured using a combination of MRI and radioactive tracers without involving lengthy, non-aging, and not affordable exams because the cost of the exam by these methods is extremely high, while the exam with MRI that will be demonstrated fits well in any Alzheimer's disease treatment plan. This exam is also important for including patients in the first dementia episode that should be corrected and monitored by the patient earlier.

The preliminary plan of this research involves the following steps: 1. Literature review: acquire a full understanding of the state-of-the-art of AI-related research in MS and AD. Familiarize yourself with the specialized measures used to ascertain the clinical feedback. 2. Data collection: work with the collaborating medical center to obtain the MS dataset. Identify or collaborate with other organizations for the acquisition of the necessary data for the AD clinical protocol. 3. Pre-processing: analyze the images and organize a pipeline for data analysis to eliminate noise and discard unneeded data. 4. Model design: decide which DL approach will be applied, how it will be implemented, and determine its features. 5. Model evaluation: experiment with different data configurations and assemble the model. Compare which model performs best in predicting the initiating signs of MS and compare which model is the most efficient in predicting the risk of patients with AD advancing to the next phase of the disease.

Equation 1: Feature Extraction from Neuroimaging Data

$$F_i = \sum_{j=1}^n w_j X_{ij} + b$$

F_i = Extracted feature for patient i
 X_{ij} = Neuroimaging input feature j
 w_j = Weight for feature j
 b = Bias term

1.3. Scope and Limitations

We aim to predict prevalent, i.e., existing but not yet diagnosed, Alzheimer's disease (AD) and multiple sclerosis (MS) from common and cost-free medical imaging modalities using AI-enhanced diagnosis. The patient's imaging data are collected as part of regular diagnostic workups, such as MRI for neurological or radiological symptoms. This approach is designed to give immediate feedback, as is nowadays common practice in radiology settings for a wide range of indications. Differences in prevalent versus incident imaging require different AI designs. We limit our study to conventional non-contrast T1 and T2 three-dimensional (3D) MRI. This is done for several reasons: it covers almost 90% of all MRI imaging, as it is the daily work of the radiologist; we are collecting and sharing 3D T1, T1, and T2 data, labeled for AI reasons, with some leading hospitals worldwide; we will collect between 50,000 and 100,000 clinically well-annotated T1, T1, and T2 images from various MS treatment studies; we limit the entrance of incidental brain imaging artifacts, like hemorrhage or arteriovenous malformation (AVM); and our current AI treatment of including T1, T1, and T2 data into one model will blend into treatment of additional testing data like FLAIR, DNA, EEG, etc., when proven successful.

2. Neuroimaging Techniques in Multiple Sclerosis and Alzheimer's Disease

The proposed paper discusses some of the most chronic diseases in elderly individuals, including Multiple Sclerosis and Alzheimer's Disease. These diseases are progressive, extend over time, and reduce the quality of life for patients by causing ongoing inflammation in brain tissue and inflicting nerve fiber damage in Multiple Sclerosis, as well as atrophy and memory loss in individuals with Alzheimer's Disease. Due to the significant decrease in the volume of brain gray matter in late-stage Multiple Sclerosis patients, it is unpredictable to achieve a wide variety of state-of-the-art approaches using Magnetic Resonance Imaging and diffusion tensor imaging.

A type of MRI, which can be used to diagnose and monitor the progression of Multiple Sclerosis and Alzheimer's Disease at a relatively low cost, is often recognized. However, it may be necessary to calculate a great deal of characteristics and require various expensive equipment to dramatically enhance the visualization of conventional MRI. Hence, numerous experimental analyses have tried to identify differences between common MRI images without prerequisite, expensive, or difficult operations. However, the accuracy of their significant changes is slightly inferior to those of traditional methods due to an overwhelming demand for real information in MRI. Last but not least, our method could work for the diagnosis of Alzheimer's Disease, which is currently applied as a post-mortem diagnosis, apart from Multiple Sclerosis.

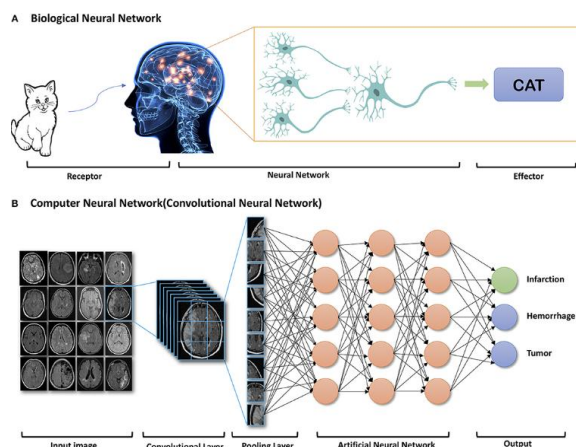


Fig 2 : Deep Learning to Neuro-Imaging Techniques

2.1. Overview of Neuroimaging Modalities

In recent years, as the application of AI technology in the medical field has gradually increased, the use of AI technology in the diagnosis field of neuroimaging, represented by MS and AD, has also undergone continuous innovation and achieved breakthrough results. At present, neuroimaging is commonly used in the diagnosis and early diagnosis of MS, AD, and other diseases in the neurological domain. This chapter introduces various neuroimaging modalities before attributing a subsection to specific neuroimaging techniques belonging to the diseases. Radiological neuroimaging is one of the methods of studying the human peripheral nervous system, which, in addition to visual diagnosis of central nervous system diseases, also provides an important basis for functional areas and clinical functional imaging. Functional magnetic resonance imaging is widely used in the study of pain research due to its millimeter-scale spatial resolution and high temporal resolution, which is generally considered an effective tool for exploring the functional changes of brain disease caused by pain in human beings. Voxel-based morphometry is a type of neuroimaging analysis technique that allows the investigation of focal differences between brain images, thus providing a unique opportunity for studying the neural substrates of specific brain functions quantitatively in a single 3D dataset.

The arterial spin labeling magnetic resonance imaging is a noninvasive imaging technology that uses the magnetic induction principle to adjust hydrogen protons in the brain and label the arterial streaming of the cerebrum by modifying the scanning sequence. The blood supply can be quantitatively researched, or a map can be made. PET and SPECT are both types of nuclear medicine images. The biggest advantage of PET images over conventional human imaging is their metabolic and functional imaging, especially their use in neuroimaging and neurophysiological imaging, which contributes to their inclusion in the diagnostic criteria for human neurology of diseases. The image features of AD patients' PET images can reflect the distribution of pain, and establish a template for this; it is helpful to assist doctors in establishing the image standard to diagnose patients' diseases. SPECT imaging technology can also be used to diagnose abnormally increased metabolic diseases by associating analysis with blood flow. High-throughput multimodal analyses can also be achieved by combining MRI or

SPECT with functional images, providing a more objective and sensitive method of multidimensional network analysis of the brain under complex circumstances.

2.2. Current Challenges in Early Diagnosis

Neuroimaging plays a critical role in understanding diseases related to the brain. Medical imaging includes a variety of techniques for diagnosing, detecting, and treating neurological disorders or injuries, aiming to provide the information needed to help the clinical decision-making process. Brain MRI, used in combination with other imaging modalities, is the most common noninvasive, reliable, and practical imaging method for the human brain. It is widely used in a clinical setting to diagnose various brain diseases that impair image resolution, quality, and processing. MRI is currently the standard reference method for clinically diagnosing multiple sclerosis, which identifies the number and location of lesions inside the central nervous system. Although multiple sclerosis is a pathological process, under certain pathological conditions, multiple T2 lesions may be indicated by a local edema reaction. However, conventional clinical display of brain images only provides information about individual cases. Each patient's diagnosis depends on extensive experience, knowledge, and access to professional equipment.

However, in real-world situations, extensive experience and trained physicians are a deficiency in terms of time and energy. Current advancements and improvements in deep learning-based medical imaging have attracted increasing interest in expanding medical imaging-related applications related to neurological diseases. This review aimed to provide a critical and careful review of associated methodology among state-of-the-art AI-based multiple sclerosis and Alzheimer's disease with a focus on promising emerging domains, such as recent trends in brain imaging biomarker applications for Alzheimer's disease with AI and possible pre-processing methodologies for further enhancing deep learning-based medical image diagnosis of neurological diseases using the existing available data sets. The main reasons may be implemented through variational or generative adversarial networks, sensitive contrast enhancement, noisy scanning, and assessment of clinical rule guidelines for brain MRI, such as the automated diagnosis of neurological diseases and prompt patient triage, especially early detection which accelerates the diagnosis process using significantly increased rates.

3. Deep Learning in Medical Imaging

Deep learning, a neural network with more than two hidden layers, learns the spatial hierarchies and complex feature representations from large data sets of labeled samples before making predictions. The most crucial characteristic of deep learning from a medical imaging point of view is that it automatically learns hierarchical representations of data while providing very high flexibility, enabling a straightforward implementation of data representation at the pixel or voxel-level without additional processing or feature engineering. Convolutional Neural Networks are an important class of deep learning that uses convolutional layers to automatically and adaptively learn the feature representation from the input data. Since CNN has the characteristic that it can provide advanced learning performance using minimal preprocessing, it successfully solves a wide range of problems, including lung cancer and

breast cancer detection, grading of brain gliomas, and radiogenic studies.

Furthermore, CNN models, known for identifying complex multifaceted patterns and nonlinear relationships within gigantic data sets, have advanced radionics from a linear approach based on handcrafted features to a nonlinear one that can glean rich information from both image data and CR data in an agnostic manner. Thus, radiomics studies have demonstrated several promising results for diagnoses, tumor staging, and prognoses across different clinical domains in medical imaging. The proliferation of dual-modality deep learning approaches, which utilize the information embedded in diverse medical imaging sources, has brought numerous promising results in multimodality neuroimaging studies of brain disorders, revealing the complementary features of different imaging modalities. AI technology offers broad and profound insights into early diagnosis, understanding, and guidance on making critical treatments for neurodegenerative diseases related to the high cognitive, emotional, and physical disability of significant populations. Yet the challenges persist. The recognized generalization should be established and proven in real clinical scenarios.

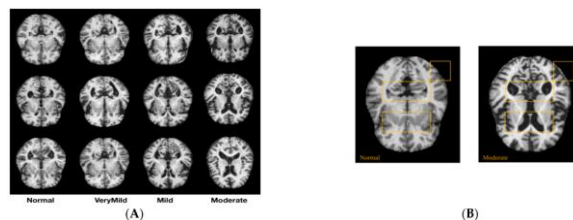


Fig 3 : Deep-Learning Approach for Automatic Diagnosis of Alzheimer

3.1. Fundamentals of Deep Learning

Deep learning is a modern approach to machine learning that achieves its power from deep, highly non-linear representations. Deep learning utilizes multiple levels of representation to model complex relationships between inputs and outputs. Deep learning models are scalable to massive data sets and are feasible to train efficiently via stochastic gradient descent. Deep learning can be effectively regularized to avoid overfitting, and unsupervised or semi-supervised feature learning can help alleviate annotation requirements. It is important to note that deep learning is an extremely general design pattern, and ultimately many of the simplest execution strategies, most reminiscent of classical methods, such as models linear in the input, were already developed before the rebranding of connectionism as neural networks and ultimately as deep learning.

Despite our generally optimistic tone, it is important to note that training deep learning algorithms is generally much more time-consuming and expensive than using the algorithms' machinery to make predictions, so deep learning is generally only attractive for offline tasks in which computation time and memory capacity can be traded for accuracy. Furthermore, to make use of vast data sets and computational resources, one must have some architecture that is capable of exploiting these resources. More data could result in greater accuracy for a shallow model, but it doesn't make deep learning an attractive strategy for tasks that can be accomplished by shallow learning. The data requirements and latency requirements that make deep learning obliquely useful at present will likely be addressed by further algorithmic

refinements of more classically designed feature discovery machinery, rather than by further scale increases.

3.2. Applications of Deep Learning in Medical Imaging

Artificial intelligence (AI) and medical imaging tools have synergized to create vast possibilities in healthcare, including personalized healthcare solutions, which are essential for less well-understood diseases or in areas such as the elderly and young children where organ-specific models from big data medical images may not always provide the best diagnosis or prognosis. In this chapter, we present some important and interesting recent applications of AI in neuroimaging modality over multiple sclerosis (MS) data and promising applications in Alzheimer's disease (AD). The principle of these innovative developments is to improve disease detection and classification abilities towards early diagnosis and management under the context of the focus of this chapter: personalized healthcare solutions and services.

Deep learning is one of the most impressive machine learning techniques which simulates the hierarchical structure of the human brain, using an idea to present data abstractly in hierarchical arrangement while learning and discovering defining patterns based on data at a higher and more structural level and enables the host to take multi-dimensional inputs to process and learn hierarchically in engineering. Recently, deep learning has significantly improved the state-of-the-art outcomes for object recognition and classification in medical imaging problems due to its generality, robustness, and ease of use. In the following, we conclude a non-exhaustive list of applications in AD and MS using deep learning.

4. AI-Enhanced Neuroimaging for Multiple Sclerosis and Alzheimer's Disease

Deep learning-based AI enhancement of neuroimaging for multiparametric MRI reveals detailed heterogeneity that may be difficult or impossible to appreciate using conventional analysis in different patterns of demyelinating lesions of multiple sclerosis, brain tissue in Alzheimer's disease, and hippocampal atrophy. The early and accurate diagnosis of multiple sclerosis is a highly important and challenging goal in diagnostic neuroradiology, particularly when conventional demyelinating lesions are not visible on conventional MRI. However, AI-enhanced neuroimaging may soon enable clinicians to benefit from early diagnosis and accurate recognition of Alzheimer's disease at earlier stages with improved accuracy, efficiency, and low-cost accessibility to CAD and RAdS. Inviting the use of research and commercial AI-enhanced neuroimaging tools will support the capacity of clinicians to perform routine MRI analyses to understand brain neuroimaging and to narrow the gap between clinicians and uncomplicated access to AI resources. Pathological aging that involves chronic disease and excessive cerebrovascular injury is detrimental, leading to the risk of a combination of physical, cognitive, and emotional morbidity that few individuals may overcome because they frequently suffer from more than one brain condition. Encouragingly, rapid progress in AI has emerged over recent years that is driving research in radiomic AI analysis of medical images to generate highly granular data that can be used to advance the identification of subtle features that may not be discernible by the human eye and to identify imaging-derived biomarkers for diagnosis, stage, progression, and treatment response in multiple sclerosis, and for identifying the initial stage of brain tissue or early disease state with

minimal time and resource investment. These can soon be understood as further boosts to the abilities of expert radiologists and diagnostic neuroimaging clinicians. In this review, we discuss recent contributions to the increasing AI-enhanced diagnostic capacity of CAD and RAdS by multiparametric neuroimaging mainly for multiple sclerosis and early Alzheimer’s disease.

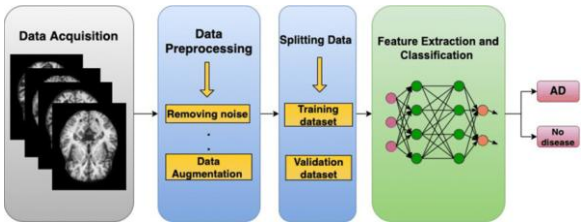


Fig 4 : The Process of Diagnosis Alzheimer Disease

4.1. Role of AI in Early Diagnosis

Accurate and early diagnoses of patients with neurodegenerative diseases, such as multiple sclerosis and Alzheimer’s disease, are always desirable for proper and timely treatment, increased quality of life, and patient satisfaction. However, with the prevalence of these diseases, the lack of experts, the diversity of disease symptoms, and the advanced and expensive routine diagnostic methods, these proper and timely diagnoses are hard to achieve. In recent years, based on AI, deep learning with a high capacity for end-to-end learning was utilized; to this end, more accurate classification functions were included, and the real boundaries of the problems became apparent. By using deep learning technology and the latest AI techniques, and integrating them with enhanced neuroimaging, the important and promising goal of the early diagnosis of serious neurological diseases, such as multiple sclerosis and Alzheimer’s disease, among many others, can be achieved.

There is an urgent need for robust and accurate biomarkers for monitoring and early diagnoses of MS, as patients could have part of the reversible phase of early MS, which is hard to recognize, but the late phase of this disease is hard or impossible to reverse. Numerous research studies propose that brain MRI might act as a singular component or part of plural-component monitoring essential for monitoring MS progression, and the results of these studies provide evidence supporting the augmented diagnostic value of brain MRI for monitoring early MS. By utilizing enhanced neuroimaging from the advanced MRI techniques and linking them with deep learning technology to recognize subtle abnormalities and monitor the progression of MS from early to a more severe stage, the clinical value of machine learning technology in this early stage of MS can more closely become a reality.

Equation 2: Deep Learning-Based Disease Classification

$$P(Y = 1|X) = \frac{1}{1 + e^{-(\beta_0 + \sum_{j=1}^n \beta_j X_j)}}$$

$P(Y = 1|X)$ = Probability of MS or AD

X_j = Input features (e.g., brain volume, lesion load)

β_j = Model coefficients

β_0 = Intercept

4.2. Integration of AI with Neuroimaging Techniques

We believe that key elements need to be present for making the best clinical use of AI in neuroimaging. AI should not be regarded as a replacement, but rather as a series of assistants who can work 24 hours a day. Automated AI analyses are used to evaluate areas that were previously too complex, time-consuming, or prolonged to analyze in detail. Two- or three-dimensional viewing of common changes can be limited to certain parameters, as the examination can be correctly used for other issues that the algorithm has not been developed for. In addition, the user will always have control over the algorithm's ability to work and evaluate the quality of the combined data. Providing these key elements, a series of limitations of automated volumetric analyses could be mitigated. An AI algorithm that is designed by taking regional augmentation and subregional hypertrophy into account allows us to examine the data from a different perspective compared to classical volumetric studies.

As AI aims to become the fastest-growing field of modern research, it has already been involved in oncologic, cardiovascular, and neurological studies. The analysis of digital brain imaging methods such as MRI, CT, or positron emission tomography is a perfect field for the implementation of computer technology with AI. The utility of AI on brain MRI includes subsequent steps, from preprocessing to computer-aided diagnosis. In neuroscience literature, AI has been combined with numerous neuroimaging techniques for both individual brain studies and large research plans. Automated AI is the most frequently used technique for neuroimaging, while regulation is currently essential. We discuss the latest progress in automated AI-based neuroimaging from the standpoint of neurodegenerative and demyelinating diseases. We also have a brief reference to commonly used hardware and deep learning architecture that is widely employed in neurological studies. In conclusion, it is important to regulate AI in automated neuroimaging to make full use of this system. The patient information issue must also be better recognized in large research plans. With the proper system, however, AI can provide help to neuroscientists for many other unresolved problems in modern research.

5. Challenges and Opportunities in AI-Enhanced Diagnosis

The application of AI and deep learning to neuroimaging can enable quantification of the specific brain regions that are most indicative of cognitive dysfunction, even when patients are still in the prodromal, or very early, stages. This text reviews the challenges of diagnosis of Alzheimer's disease and methods that are being developed to address these. Structural and functional brain networks are explored, considering their potential to assist with accurate diagnosis and prediction of clinical decline. Here we discuss the challenges and opportunities associated with attempting to use AI algorithms to achieve early diagnosis for a group of diseases that include chronic traumatic encephalopathy, multiple sclerosis, Alzheimer's

disease, Parkinson's disease, and others.

Early diagnosis is crucial for the successful management and treatment of most chronic diseases, yet it is surprisingly difficult to achieve. Diagnoses are more urgent in some neurodegenerative diseases, particularly where treatments can be more efficient if administered at an early stage. In the case of neurodegenerative diseases such as chronic traumatic encephalopathy, Alzheimer's disease, and Parkinson's disease, diagnosis is currently only possible once clinical symptoms such as memory loss or difficulty with movements appear. These symptoms are a result of substantial loss of neurons and other brain cells that our current diagnostic tools are not sensitive enough to detect at a very early stage. Diagnosing these diseases at the symptomatic stage may ultimately result in the disease being advanced, or it may be too late for medication to be effective in delaying inevitable progressive cognitive and functional decline. The use of AI algorithms and deep learning to analyze information about cognitive and brain dysfunction provides an opportunity to seek a solution to this challenge, not only to provide early diagnosis but also to predict future clinical decline.

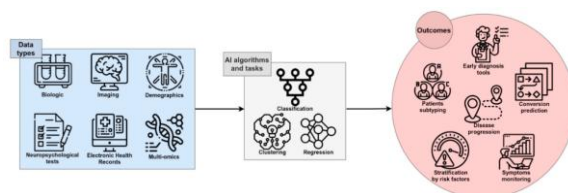


Fig 5: Artificial Intelligence for Alzheimer's Disease Promise or Challenge

5.1. Ethical Considerations

No specific ethical issue is foreseen during the study. The imaging systems employed for the diagnosis of multiple sclerosis and Alzheimer's disease are already in use as part of the normal care of all patients with these diseases. These devices have been employed for this purpose for many years and have been validated and certified to meet the specified requirements of the national and international health authorities regarding operation, performance, and safety. Normally, the patients are expected to undergo these examinations and are duly informed about the procedures, benefits, and potential risks of the study during the patient's appointment to conduct the examination. Hence, there are no additional risks and discomforts caused by the inclusion of the patients in our study. This is a single-center study. Thus, the ethical problems related to the multicenter study, such as variations between the different hospitals and protocols, are eliminated. This study has the approval of the local ethics committee. Due to the possibility of indirect identification, the images used in this study will strictly comply with the regulations on privacy and protection of personal data. Only the radiographer involved with the clinical assessments creates images of the patients, and the images are securely stored on a password-protected server and can only be accessed with permission from the associated researcher. All images used in this study will be anonymized and de-identified. All the data and imaging findings of the patients/participants are confidential information. Every authorized person engaged in the treatment and study must ensure the protection of the information concerning the imaging findings.

5.2. Clinical Implementation Challenges

Artificial intelligence-based deep learning models using high-throughput medical imaging data for pre-symptomatic diagnosis of neurodegenerative diseases are a powerful emerging precision/personalized medicine technology. They offer the potential for significant enhancements in the efficiency of clinical practice and in diagnosing neurodegenerative diseases at very early stages, leading to intervention before onset altogether. However, the impact that AI/machine learning systems can have on the implementation and interpretation of imaging tests is substantial, and it is important to consider the clinical implications of their use. Neuroimaging decision support systems or AI households for the diagnosis of multiple sclerosis and Alzheimer's disease have the potential to revolutionize how medical imaging is performed and interpreted. They can dramatically improve the efficiency of image interpretation, increase diagnostic confidence, and reduce the probability of diagnostic errors. We currently face a rapidly evolving need to make these developments work to the benefit of clinical practice. For this to happen, we recognize that artificial intelligence should be developed de novo in the healthcare system, in tandem and intended to augment the expertise of specialist practitioners in delivering reproducible, precise, and personalized patient management. The flexible, adaptive capability of AI systems to generalizable, specific, or scarce datasets, including different types of imaging and non-imaging health-related data, is also crucial for the reality of their clinical integration.

6. Case Studies and Research Findings

We present nine case studies of various types and research the initial findings by reporting those cases. We demonstrate a few of the types of pathological anatomical MRI scans used in this research, and upon diagnosis and outcome, we verify that those cases are correct. Therefore, to develop additional tools that can help both the radiology teams and the clinical practitioners, we contribute to the diagnosis and treatment of the patient at the earliest possible time by using machine learning and artificial intelligence models.

In this study, research is conducted with neuroimaging data, specifically MRI scans, rather than the original application area that is considered. Even though the motivation for this research is a real-world problem, we also take real-world data and real-world result measures into account at the same time. Our results are also discussed so that problems can be addressed for potential applications of patient scans in hospitals. After the evaluation of the ethical and pastoral aspects, which are summarized under the electronic supplementary material in this research, when the patient comes to the hospital, they will ask many different questions. The decision support system models that are built do not affect professional diagnostic accuracies; the accuracy and treatment of hospital operations can also be affected, leading to a decrease in prognostic accuracies.

6.1. Studies on AI for Multiple Sclerosis Diagnosis

6. Results 6.1. Studies on AI for Multiple Sclerosis Diagnosis in Brain MRI Neuroimaging have contributed to the diagnosis of many neurological diseases and should be analyzed for patient phenotyping, considering that detection and annotation of abnormalities require attention to image detail. To extract meaningful presentations that can characterize patients'

states, the extracted radiomic and semantic representations need to aggregate specific image features. The automation and improvement of the efficiency of diagnosing early potential diagnostic biomarkers for aging-related neurodegenerative diseases and demyelinating diseases, such as multiple sclerosis, have been trending topics. Recently, with the availability of a large amount of medical data from hospitals and developments in artificial intelligence, research on medical imaging-driven AI-powered diagnosis has attracted great interest from the scientific community. Given the time-sensitive nature of early intervention and the limitations of available treatment, diagnosing multiple sclerosis is another area of clinical research that will likely benefit from assistive technologies such as machine learning, given the prevalence of affected populations. Both of these diseases affect the brain. Using the same representative longitudinal sample of presymptomatic, early symptomatic, and advanced symptomatic participants, desensitizing the model to data from different practices and scanner machines would pose a significant step forward toward real-world use and clinical adoption. The diagnostic potential of 3D convolutional neural networks and artificial intelligence systems for detecting multiple sclerosis and other brain diseases in routine clinical practice has been reported.

6.2. Studies on AI for Alzheimer's Disease Diagnosis

Alzheimer's disease (AD) is the most common neurodegenerative disease and is characterized by cognitive decline and dementia. With the rapidly aging trend around the world, it is estimated that 10 million new cases of dementia are diagnosed each year, specifically one new case every 3 seconds. Early diagnosis is very important for the clinical treatment and management of AD patients. Alzheimer's disease (AD) diagnosis mainly includes demographic information collection, detailed physical and neurological examination, neuropsychological scale assessment, cerebrospinal fluid (CSF) test, neuroimaging examination, and exclusion diagnosis. Most biomarkers of AD are identified in the brain, e.g., beta-amyloid ($A\beta$), tau protein (T-tau), and phospho-tau (P-tau). These biomarkers and neuroimaging data are not only an important basis for the early diagnosis of AD but also provide great value for monitoring the progression of Alzheimer's disease.

Before neuroimaging examination, routine visual assessment includes both qualitative and quantitative analysis. Due to the differences in the subjective experience of radiologists and the high variability in MRI, it has potential limitations in computer-aided automatic AD diagnosis. The most widely used method is the visual rating of medial temporal atrophy (MTA), which reflects the typical pathological changes of the tangles and cell loss in the hippocampus of the AD brain. The protocol was proposed in 2004, including data and brain images of the elderly with normal, mild cognitive impairment (MCI), and Alzheimer's disease. Since then, following more and more comprehensive neurological disease data set construction, researchers and more groups and companies have gone into research. With numerous advantages depicted above, 3D CNN was rapidly applied to the neuroimaging biomarkers for early AD diagnosis.

7. Future Directions and Conclusion

The development of generalizable AI models for the early accurate diagnosis of MS and AD

in a multimodal and longitudinal setting is expected to open up new avenues in clinical research, to develop more accurate diagnostic resources that can provide early diagnosis and predict future treatments for these devastating diseases. It will also interpret more accurately the individual patient trajectory, the progression, and the response to treatments, not limited to only corrective aspects but also able to move forward in a personalized therapeutic approach for MS and AD patients that considers complementary rehabilitation and palliative treatments where currently experimental evidence and practice guidelines exist. Lastly, it must be said that the clinical approach to both MS and AD, according to integrated treatments that also go beyond pharmacological therapy, will be an important lever in the future to slow down and minimize the damage caused by the disease. The combination of these different approaches is the closest to the ethical and philosophical concept of precision medicine.

The role that big data science and AI approaches can play in a comprehensive approach focused on patient management is therefore no longer just a possibility but a responsibility of the scientific community in today's approach to these problems. Future research should focus on developing neuroimaging-based AI models for the early diagnosis and clinical HRQOL assessment of MS and AD. The research results have shown that the presence of previously diagnosed asymptomatic patients in developing countries can lead to significant expenditure savings compared to the use of the public health service once the first neurological symptoms of the disease occur. In the face of higher costs for access to new AI-based diagnostic technologies, the presence of an early diagnosis can lead to significant savings compared to the real total costs of neglecting the timely diagnosis of diseases that, if diagnosed too late, lead to significant health costs for patients and their primary caregivers, with a negative impact on patients' HRQOL.

7.1. Emerging Technologies

Emerging technologies have been shaping a new future in both medicine and neurology over the past few years. Medical technology developments are typically the result of partnerships and collaborations between a diverse group of innovators, including health professionals, researchers, business leaders, scientists, and many others. Many high-impact technologies have been inspired by engineers and physicians who seek to address clinical needs along with medical and neurological advances. Another element enhancing the technology revolution is patient involvement, which helps to identify accurate needs and create effective solutions. In the era of the fourth industrial revolution, it is crucial to use and continuously develop these technologies in healthcare to be able to provide early diagnosis, customized treatment, and real-time monitoring, and to enable a more efficient patient interaction and healthcare system. Expertise, investments, and collaborations or partnerships between the public side and private sector players are often considered the key factors because both draw upon and bring distinctive benefits that drive innovation for the long-term development of any emerging platform technology in neurological health.

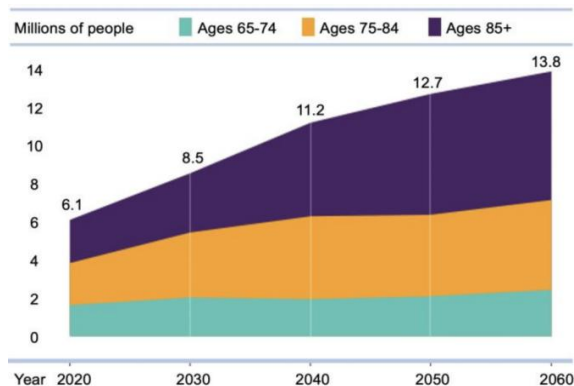


Fig 6 : Neuroimaging Modalities in Alzheimer

7.2. Research Gaps and Future Research Directions

Deep learning models are equally inspired by functional statistics and statistical mechanics, and the future might witness a shift from purely formulating the neuroimaging problem on a graph to applying graph signal and graph interference methods and techniques. Bispectrum and bicephalous coherence are two advanced graph signal processing and analysis techniques that can be employed, among others, and analyzed as alternate or additional feature engineering and utilization in deep learning for graph data approaches. Graph bicephalous coherence and brain cephalogram data are two examples of possible applications. In addition, the existing proposed convolutional neural network and deep belief network model learning methodology is not end-to-end learning, which is derived solely from the underlying model assumptions and principles that are not agreed upon, while extensive training regimes that are biologically and computationally realistic, efficient, and effective with practical neuroimaging data are computationally expensive and cumbersome. Therefore, alternative approaches, methods, and techniques that are based on alternative algorithms and principles, and have the potential to lead to more efficient and effective deep learning-based early diagnosis of multiple sclerosis and Alzheimer's disease, are offered here.

Equation 3 : MRI Image Segmentation for Lesion Detection

$$L = \sum_{i=1}^m \sum_{j=1}^n y_{ij} \log(\hat{y}_{ij}) + (1 - y_{ij}) \log(1 - \hat{y}_{ij})$$

L = Loss function for segmentation

y_{ij} = True lesion mask

\hat{y}_{ij} = Predicted lesion mask

m, n = Image dimensions

7.3. Concluding Remarks

In the present chapter, we have provided an overview of the potential of AI combined with MRI to develop automated image classification strategies for the early diagnosis of two of the most common neurodegenerative diseases: MS and AD. The integration of feature extraction

and deep learning methods has inspired the creation of numerous studies designed to implement this vision for early detection. The evolution and critical analysis of the main goals proposed by these studies will guide the path for the execution of innovative strategies for early diagnosis currently under investigation and may later provide tailored monitoring strategies of the broad spectrum of imaging features to conduct early therapeutic interventions in these diseases. In the next chapters, based on the personalized results received from the analysis of brain morphology, we propose to enlarge the focus to a more personalized analysis, thereby presenting our recent approaches for the identification of the main subtypes that play a significant role in the progression and response to minimally invasive personalized treatments in patients with MS and AD. In conclusion, through the evidence presented, we advocate that the development of diagnostic imaging pipelines, focusing on disease-specific biomarker identification for subtypes of two of the most common, currently incurable neurodegenerative diseases – MS and AD – is indispensable and urgent. These pipelines should receive priority in the worldwide agenda, based on their impact on society and the economy. Nevertheless, besides our enthusiasm, a word of caution should be shared: the path to these goals is relevant but highly arduous and has some potential traps that must be acknowledged and prudently avoided. The conclusions are presented, respectively, in Chapter 8 and Chapter 9. We hope that the information presented may accelerate the process of discovery, clinical translation, and the routine application of breakthrough approaches.

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