

Artificial intelligence-powered analysis of medical images for early detection of neurodegenerative diseases

Samuel Fanijo ^{1,*}, Uyok Hanson ², Taiwo Akindahunsi ³, Idris Abijo ⁴ and Tinuade Bolutife Dawotola ⁵

¹ Department of Computer Science, Iowa State University, USA.

² Department of Educational Psychology, Texas A&M University, Texas, USA.

³ Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, Maryland, USA.

⁴ Department of Physics and Astronomy, University of Tennessee, Knoxville, USA.

⁵ Department of Mathematics and Philosophy, Western Illinois University, Illinois, USA.

World Journal of Advanced Research and Reviews, 2023, 19(02), 1578–1587

Publication history: Received on 07 June 2023; revised on 20 August 2023; accepted on 23 August 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.19.2.1432>

Abstract

Neurodegenerative diseases including Alzheimer's, Parkinson's, and Huntington's offer serious health issues to people all over the world, due to their progressive nature and lack of effective therapies. In order to improve patient outcomes and allow for prompt action to limit the progression of the disease, early identification is essential. With a focus on deep learning methods, this study investigates the use of AI-powered analysis of medical images for the early detection of neurodegenerative disorders. The use of several medical imaging modalities, such as PET, CT, and MRI, in identifying disease biomarkers at an early stage is investigated. The usefulness of deep learning techniques to automate feature extraction, categorize illness states, and track disease progression is highlighted. These techniques include convolutional neural networks [CNNs], recurrent neural networks [RNNs], and generative adversarial networks [GANs]. The study also discusses the difficulties in using AI implementation, including data quality, image variability, and the interpretability of AI models. Furthermore, the study explores possible regulatory and ethical considerations in clinical adoption. It also examines AI's growing role in clinical settings and its ability to work with personalized medicine which present promising opportunities for improving the diagnosis and management neurodegenerative disease. The final section of this paper outlines important future directions for increasing the use of AI in clinical care, including multi-modal fusion and transfer learning.

Keywords: Artificial Intelligence; Deep Learning; Neurodegenerative Diseases; Medical Imaging; Early Detection.

1. Introduction

Over time, neurodegenerative diseases are growing in importance as a public health issue [1]. They include a variety of progressive, long-term conditions marked by the slow deterioration of nerve cells, or neurons, resulting in problems with cognition, movement, and function [2]. The three most common of these diseases are Huntington's disease [HD], Parkinson's disease [PD], and Alzheimer's disease [AD], all of which have a significant effect on people, families, and healthcare systems around the world [3, 4]. Early discovery is essential for symptom management, slow progression of disease, and improved patient outcomes because of the incurable and irreversible nature of many diseases [4].

One cannot stress the value of early detection. Early-stage interventions for neurodegenerative disorders can improve quality of life, lessen the financial strain on healthcare systems, and delay the onset of severe symptoms [5]. Clinical evaluations, cognitive testing, and medical imaging are frequently used in the conventional diagnostic process for neurodegenerative diseases [6]. Subjectivity and the possibility of human error, however, can have limitations with

* Corresponding author: Samuel Fanijo

these approaches [7]. As a result, there is increasing interest in applying artificial intelligence [AI] to improve medical image analysis's precision and effectiveness [7].

Medical image analysis is one of the many domains that artificial intelligence, especially deep learning, has drastically altered [8,7]. Convolutional neural networks [CNNs], one type of deep learning technology, have proven to perform exceptionally well in tasks like image identification and classification, often outperforming classic machine learning techniques [8]. These methods can help with early and more precise diagnosis of neurodegenerative diseases by identifying patterns and features in medical images that could be invisible to the human eye [9,7].

This research paper explores the application of AI-powered analysis, specifically using deep learning techniques, to medical imaging for the early detection of neurodegenerative diseases. The objectives of this study are to evaluate the effectiveness of these techniques in accurately diagnosing neurodegenerative conditions at an early stage, compare different deep learning models and approaches, and assess the potential for integrating these technologies into clinical practice.

2. Overview of Neurodegenerative Diseases and Medical Imaging modalities.

Neurodegenerative diseases are conditions marked by a steady deterioration of the nervous system's structure and functionality [2,3]. Chronic and frequently incapacitating symptoms are the result of these disorders, which are usually related to aging and have no known solution. [4]. According to [3], Huntington's disease, Parkinson's disease, and Alzheimer's disease are some of the most prevalent and well researched neurodegenerative illnesses.

A neurological ailment that affects millions of individuals worldwide, Alzheimer's disease [AD] is the most frequent cause of dementia [1,3]. According to [10], its main symptoms include memory loss, cognitive deterioration, and behavioural abnormalities. Amyloid-beta plaques and tau tangles build up in the brain during the pathological stages of Alzheimer's disease, causing neuronal death and brain atrophy [11]. As AD progresses, mild cognitive impairment [MCI], which is one of the most common early symptoms, can turn into severe dementia [12].

[13] state that Parkinson's disease [PD], the second most common neurodegenerative disorder, mostly affects motor function and affects 2-3% of those 65 years of age or older. According to [14], it is typified by symptoms such as bradykinesia, stiffness, tremors, and postural instability. In the substantia nigra, a part of the brain essential for motor control, dopaminergic neurons are lost in Parkinson's disease [PD] patients [15]. According to [16], as the disease advances, non-motor symptoms such as mood problems and cognitive impairment are also frequently observed.

Huntington's disease [HD] is a genetic neurodegenerative disorder caused by a mutation in the huntingtin gene [17]. It is characterized by a combination of motor dysfunction, cognitive decline, and psychiatric symptoms [18]. HD typically presents in mid-adulthood and progresses over 10 to 20 years, eventually leading to severe disability and death [19]. The striatum, a brain region involved in motor control, is particularly affected in Huntington's disease, leading to the hallmark symptoms of chorea [involuntary, erratic movements] later progressive bradykinesia, incoordination and rigidity [motor impairment] [20].

Medical imaging plays a crucial role in the diagnosis and monitoring of neurodegenerative diseases [21]. Several imaging modalities are used to visualize brain structure and function, each offering unique advantages in assessing different aspects of neurodegeneration [22]. Magnetic Resonance Imaging [MRI] is a non-invasive imaging technique that provides high-resolution images of soft tissues, making it particularly useful for assessing brain anatomy [23]. MRI is widely used in the diagnosis of neurodegenerative diseases, as it can detect structural changes such as brain atrophy, white matter lesions, and hippocampal shrinkage, which are indicative of diseases like Alzheimer's [22].

Computed Tomography [CT] scans use X-rays to produce detailed images of the brain's structure [24]. Although less commonly used than MRI for neurodegenerative diseases, CT is valuable in detecting brain atrophy, especially in the later stages of diseases such as Alzheimer's [25]. It is also used to rule out other causes of cognitive decline, such as strokes or tumours [24].

Positron Emission Tomography [PET] imaging measures metabolic activity in the brain by detecting the distribution of a radioactive tracer [26]. PET is particularly useful in differentiating Parkinson's diseases from other movement disorders [27]. PET can also assess glucose metabolism in the brain, providing insights into functional changes associated with neurodegeneration [28].

Deep learning, a subset of AI, has shown tremendous potential in medical image analysis [8]. Unlike traditional machine learning methods that require manual feature extraction, deep learning models, particularly Convolutional Neural Networks, can automatically learn and extract relevant features from raw data [29]. This ability makes deep learning especially suitable for analysing complex medical images, where subtle patterns and abnormalities need to be detected [8].

Convolutional Neural Networks [CNNs] are a type of deep learning model that is particularly effective for image analysis tasks [29]. They consist of multiple layers of neurons, each of which detects different features in the input image, such as edges, textures, and shapes [30]. CNNs have been successfully applied to various medical imaging tasks, including disease diagnosis, segmentation, and classification [29]. In the context of neurodegenerative diseases, CNNs can be used to identify biomarkers such as brain atrophy or amyloid plaques from MRI and PET scans [31].

Recurrent Neural Networks [RNNs] are designed to process sequential data, making them useful for analysing time-series data in medical imaging [32]. For example, RNNs can be used to track changes in brain structure over time, helping to predict the progression of neurodegenerative diseases [8]. In this way, RNNs complement CNNs by adding the capability to model temporal dynamics in addition to spatial features [32].

Generative Adversarial Networks [GANs] are a class of deep learning models that consist of two neural networks—a generator and a discriminator—that work together to create realistic synthetic images [33]. GANs can be used in medical imaging to generate synthetic data for training purposes or to enhance the quality of medical images by reducing noise and artefacts [34]. In the context of neurodegenerative diseases, GANs could be used to simulate brain images at different stages of disease progression, providing valuable data for training diagnostic models [35].

2.1. AI-Powered Analysis of Medical Images

Medical images must undergo pre-processing to enhance their quality and remove any artefacts that could affect the results before any meaningful analysis can be conducted [36]. Pre-processing typically involves several steps, including noise reduction, contrast enhancement, and normalization [37]. These steps are crucial in ensuring that the images are of sufficient quality for accurate analysis. Noise reduction is crucial to ensure accurate analysis. Noise in medical images can arise from various sources, including the imaging equipment and the patient's movement during scanning [38]. Techniques such as Gaussian smoothing and median filtering are commonly used to reduce noise while preserving important features in the image [37]. Noise reduction is particularly important in MRI scans, where small anatomical features need to be clearly visible for accurate diagnosis [23]. Contrast enhancement improves the visibility of structures within an image by increasing the difference in intensity between adjacent regions. This is particularly useful in detecting abnormalities in brain scans, such as tumours or areas of atrophy [22]. Histogram equalization and adaptive contrast enhancement are commonly used techniques in medical imaging to enhance contrast [38]. Normalization is the process of adjusting the intensity values in an image so that they fall within a specific range. This step is important for ensuring consistency across different images, particularly when they are acquired from different patients or using different imaging equipment. Normalization allows for more accurate comparison and analysis of images [39]. Image segmentation is the process of dividing an image into meaningful regions, such as separating the brain from surrounding tissues in an MRI scan [40]. In the context of neurodegenerative diseases, segmentation is crucial for isolating regions of interest, such as the hippocampus in Alzheimer's disease, where early signs of atrophy may appear [22]. Deep learning techniques, particularly CNNs, have been widely used for image segmentation tasks due to their ability to automatically learn and identify relevant features [40]. For example, U-Net, a popular CNN architecture, has been used to segment brain MRI images with high accuracy [41].

Once the images have been pre-processed and segmented, the next step is feature extraction, where specific characteristics of the images are identified and quantified [42]. In the context of neurodegenerative diseases, features might include the volume of certain brain regions, the thickness of the cortex, or the intensity of PET signals [22]. Feature extraction involves identifying relevant patterns in the image that can be used to differentiate between healthy and diseased states [42]. In neurodegenerative diseases, this might include measuring the volume of the hippocampus in Alzheimer's disease or the intensity of dopaminergic pathways in Parkinson's disease [43]. Deep learning models, particularly CNNs, can automate this process by learning to identify the most relevant features for distinguishing between different disease states. For example, CNNs have been used to extract features related to brain atrophy in Alzheimer's patients, which can then be used for early diagnosis [42]. After feature extraction, the next step is to select the most informative features for analysis. Feature selection is important for reducing the complexity of the model and improving its performance [44]. In deep learning, feature selection can be achieved through techniques such as principal component analysis [PCA] or through the use of specific layers in the neural network that prioritize certain features

over others [44]. For example, in Alzheimer's disease, features related to hippocampal atrophy might be prioritized, while other less relevant features are discarded.

After feature selection, the next step is to classify the images or detect the presence of disease [43]. Deep learning models, particularly CNNs, are often used for this purpose due to their ability to learn complex patterns and relationships between features [42]. In the context of neurodegenerative diseases, classification algorithms are used to differentiate between healthy individuals and those with early signs of disease [45]. CNNs are particularly well-suited for this task, as they can learn to identify subtle patterns in the images that may not be discernible to the human eye [41]. For example, CNNs have been used to classify MRI images of the brain to differentiate between patients with Alzheimer's disease and healthy controls [45]. Detection algorithms are used to identify specific areas of interest within an image, such as regions of atrophy or amyloid plaques in the brain [43]. These algorithms can be trained to detect these features automatically, allowing for quicker and more accurate diagnosis. For example, CNNs have been used to detect amyloid plaques in PET scans of Alzheimer's patients, providing an objective measure of disease severity [43]. In addition to CNNs, Recurrent Neural Networks [RNNs] can be used for analysing sequential data, such as changes in brain structure over time [46]. RNNs are particularly useful for predicting the progression of neurodegenerative diseases, as they can model temporal dynamics in the data. For example, RNNs have been used to predict the progression of Parkinson's disease [46]. Generative adversarial networks [GANs] can be used to generate synthetic medical images for training deep learning models [35]. This is particularly useful in the context of neurodegenerative diseases, where acquiring large datasets can be challenging. By generating realistic synthetic images, GANs can augment the training data and improve the performance of the models [35].

To ensure the accuracy and reliability of the AI-powered analysis, performance evaluation metrics are used to assess the model's performance [47]. Common metrics include accuracy, sensitivity, specificity, and the area under the receiver operating characteristic [ROC] curve [48]. Accuracy measures the overall correctness of the model's predictions, defined as the proportion of true positive and true negative predictions out of the total number of cases. High accuracy is essential in medical diagnosis to ensure that the model reliably identifies patients with neurodegenerative diseases [48]. Sensitivity, also known as the true positive rate, measures the proportion of actual positive cases that are correctly identified by the model [47]. Specificity, or the true negative rate, measures the proportion of actual negative cases that are correctly identified [47]. Both metrics are crucial in evaluating the model's ability to correctly diagnose patients with and without the disease [47]. Receiver Operating Characteristics [ROC] curve is a graphical representation of the model's performance across different classification thresholds [49]. The area under the curve [AUC] is a single scalar value that summarizes the model's ability to distinguish between classes. A higher AUC indicates better performance, with a value of 1.0 representing perfect classification [49].

3. Applications in Neurodegenerative Diseases

Alzheimer's disease [AD] is a significant focus of AI-powered medical image analysis due to its prevalence and the importance of early detection. Deep learning models, particularly Convolutional Neural Networks, have been extensively applied to Magnetic Resonance Imaging and Positron Emission Tomography scans to identify early biomarkers of Alzheimer's, such as hippocampal atrophy and amyloid-beta accumulation [50]. The hippocampus is one of the first brain regions affected by Alzheimer's, making it a critical area of focus for early detection [50]. Convolutional Neural Networks trained on large datasets of Magnetic Resonance Imaging scans have been shown to detect hippocampal atrophy with high accuracy, even in the preclinical stages of Alzheimer's [50]. Early detection allows for the implementation of therapeutic interventions that can slow disease progression and improve quality of life. AI models can also assist in the differential diagnosis of Alzheimer's by distinguishing it from other forms of dementia [51]. For instance, Convolutional Neural Networks can be trained to classify Magnetic Resonance Imaging and Positron Emission Tomography scans as indicative of Alzheimer's, frontotemporal dementia, or healthy aging, providing a more accurate diagnosis than traditional methods [51]. This capability is particularly valuable in clinical settings, where early and accurate diagnosis is critical for effective treatment planning. Monitoring the progression of Alzheimer's disease is essential for evaluating the effectiveness of treatment and planning future care [42]. Artificial Intelligent models can analyse longitudinal Magnetic Resonance Imaging and Positron Emission Tomography data to track changes in brain structure and function over time [42]. For example, Recurrent Neural Networks have been used to predict the future trajectory of cognitive decline in Alzheimer's patients based on baseline imaging data, helping clinicians anticipate the patient's needs and adjust treatment accordingly [42].

Parkinson's disease [PD] presents unique challenges and opportunities for AI-powered medical image analysis, particularly in the assessment of motor symptoms and the tracking of disease progression. The motor symptoms of Parkinson's, such as tremors, rigidity, and bradykinesia, are primarily caused by the degeneration of dopaminergic neurons in the substantia nigra [52]. AI models can analyse Magnetic Resonance Imaging scans to detect structural

changes in this region, providing early indicators of Parkinson's disease [52]. In addition to structural imaging, AI can analyse functional MRI [fMRI] data to assess changes in brain activity associated with motor symptoms [53]. For example, AI models can identify abnormal patterns of connectivity in the basal ganglia and motor cortex, which are correlated with the severity of tremors and bradykinesia [53]. Tracking the progression of Parkinson's disease is critical for managing symptoms and evaluating the effectiveness of treatment [Chen *et al.*, 2017]. AI models can analyse longitudinal Magnetic Resonance Imaging and Diffusion Tensor Imaging data to monitor changes in brain structure and connectivity over time. For example, Convolutional Neural Networks have been used to track the degeneration of white matter tracts in Parkinson's patients, providing a quantitative measure of disease progression [54]. Additionally, AI models can be used to predict future changes in motor function based on baseline imaging data, allowing for more personalized treatment planning [54]. AI-powered analysis of medical images can be integrated with clinical assessments to provide a more comprehensive evaluation of Parkinson's disease. For instance, AI models can analyse video recordings of patients' movements to assess the severity of motor symptoms, such as tremors and bradykinesia, in a more objective and quantifiable manner than traditional clinical assessments [55]. This integration of imaging and clinical data can improve the accuracy of diagnosis and the precision of treatment.

Huntington's disease [HD] is a genetic disorder with well-defined biomarkers, making it a compelling case for the application of Artificial Intelligence in medical imaging [56]. AI models can help identify early imaging biomarkers and predict the onset and progression of the disease in individuals who carry the genetic mutation [56]. Magnetic Resonance Imaging is commonly used to assess brain atrophy in Huntington's patients, particularly in the striatum, a brain region that is severely affected by the disease. Deep learning models, such as CNNs, have been trained to detect early signs of striatal atrophy, even before clinical symptoms appear [56]. These models can also be used to quantify the extent of atrophy and track its progression over time, providing valuable insights into the disease's pathophysiology. Predicting the onset of Huntington's disease in individuals who carry the genetic mutation is a significant challenge. AI models can analyse longitudinal Magnetic Resonance Imaging data to identify patterns of brain atrophy that are associated with the onset of motor symptoms [57]. By combining imaging data with other biomarkers, such as genetic and clinical data, AI models can provide more accurate predictions of disease onset and progression [57]. This information is crucial for planning early interventions and improving patient outcomes. AI models can be used to analyse data from longitudinal studies of Huntington's patients, providing insights into the disease's progression and potential therapeutic targets. For example, Recurrent Neural Networks can be used to model the progression of motor symptoms over time, helping clinicians predict the future trajectory of the disease and adjust treatment plans accordingly [58]. Additionally, AI models can be used to identify subgroups of patients who are likely to respond to specific treatments, paving the way for personalized medicine in Huntington's disease [58].

4. Challenges and Limitations

One of the primary challenges in AI-powered analysis of medical images is the quality and availability of data [29]. High-quality, annotated datasets are essential for training effective deep learning models. However, acquiring such data is often difficult due to the rarity of certain neurodegenerative diseases, variability in imaging protocols across institutions, and privacy concerns [29]. Limited access to large, diverse datasets can lead to models that are biased or less generalizable, reducing their effectiveness in clinical settings.

Medical images often exhibit significant variability and heterogeneity due to differences in imaging modalities, equipment, and patient populations [59]. This variability can pose a challenge for AI models, which may struggle to generalize across different types of data. For instance, an AI model trained on Magnetic Resonance Imaging scans from one institution may not perform as well on scans from another institution with different imaging protocols [59]. Techniques such as data augmentation and domain adaptation are often employed to address these challenges, but they may not fully eliminate the impact of image variability on model performance.

Another major limitation of AI-powered medical image analysis is the interpretability and explainability of the models [60]. Deep learning models, particularly those with many layers and parameters, are often considered "black boxes" because their decision-making processes are not easily understood by humans. In the context of medical diagnosis, this lack of transparency can be problematic, as clinicians need to understand how and why a model arrived at a particular conclusion [60]. Efforts are being made to develop more interpretable models, such as those that provide visual explanations of their predictions, but this remains an ongoing challenge in the field.

The integration of Artificial Intelligence into clinical practice also raises important regulatory and ethical considerations [61]. Ensuring that Artificial Intelligence models are safe, effective, and unbiased is critical, particularly when they are used to make decisions about patient care. Regulatory agencies, such as the Food and Drug Administration, are beginning to establish guidelines for the approval and oversight of AI-based medical devices, but the field is still evolving

[61]. Additionally, ethical concerns related to data privacy, informed consent, and the potential for AI to exacerbate healthcare disparities must be carefully addressed as these technologies are implemented in clinical settings [62].

5. Future Directions

The field of AI-powered medical image analysis is rapidly evolving, with several emerging trends and techniques poised to further enhance the early detection of neurodegenerative diseases. Transfer learning, which involves using pre-trained models as a starting point for new tasks, is gaining popularity as it allows for the efficient development of models with limited data [63]. Additionally, multi-modal fusion, which combines data from multiple imaging modalities [e.g., Magnetic Resonance Imaging and Positron Emission Tomography], offers a more comprehensive view of the brain and has the potential to improve diagnostic accuracy [64]. Transfer learning can be particularly useful in the context of neurodegenerative diseases, where large datasets are often not available. By leveraging pre-trained models that have already learned to identify relevant features from similar tasks, researchers can reduce the amount of data and computational resources needed to train new models [65].

Multi-modal fusion involves combining data from multiple imaging modalities to provide a more comprehensive assessment of the brain. For example, integrating Magnetic Resonance Imaging and Positron Emission Tomography data can provide both structural and functional information, improving the accuracy of diagnosis and the ability to monitor disease progression [66]. Deep learning models that can effectively integrate multi-modal data are likely to play a key role in the future of neurodegenerative disease diagnosis. As AI models continue to improve, there is significant potential for their integration into clinical practice. AI-powered tools could assist clinicians in diagnosing neurodegenerative diseases more quickly and accurately, leading to earlier interventions and better patient outcomes. Furthermore, the ability of AI to analyse large datasets and identify patterns specific to individual patients opens the door to personalized medicine [7].

Artificial Intelligence integration into clinical practice, it must be user-friendly and seamlessly integrated into existing workflows. This includes developing AI tools that can provide clear, actionable insights to clinicians and integrating these tools with electronic health records [EHRs] to provide a comprehensive view of the patient's health [67]. Artificial Intelligence has the potential to revolutionize personalized medicine by providing more accurate diagnoses and predicting individual responses to treatment. By analysing large datasets of imaging and genetic data, AI can identify patterns and biomarkers that are specific to individual patients, allowing for more targeted and effective treatments [68].

Table 1 Abbreviations and their meanings

Abbreviations	Meaning
AI	Artificial Intelligence
AD	Alzheimer's Disease
PD	Parkinson's Disease
HD	Huntington's Disease
MRI	Magnetic Resonance Imaging
CT	Computed Tomography
PET	Positron Emission Tomography
CNN	Convolutional Neural Network
RNN	Recurrent Neural Network
GAN	Generative Adversarial Network
fMRI	Functional Magnetic Resonance Imaging
DTI	Diffusion Tensor Imaging
AUC	Area Under the Curve
ROC	Receiver Operating Characteristic
FDA	Food and Drug Administration

6. Conclusion and Recommendation

In summary, Artificial Intelligence-powered analysis of medical images using deep learning techniques offers a powerful tool for the early detection and monitoring of neurodegenerative diseases. Techniques such as Convolutional Neural Networks, Recurrent Neural Networks, and Generative Adversarial Networks have shown great promise in identifying early biomarkers of diseases like Alzheimer's, Parkinson's, and Huntington's, often before clinical symptoms appear. However, challenges related to data quality, model interpretability, and ethical considerations must be addressed to fully realize the potential of these technologies. As research in this field continues to advance, the integration of Artificial Intelligence into clinical practice could revolutionize the diagnosis and treatment of neurodegenerative diseases, leading to more personalized and effective care.

It is also recommended that efforts should focus on enhancing data quality and standardization to ensure consistent and high-quality datasets across institutions. Additionally, improving the interpretability of AI models is essential to build clinician trust, enabling better understanding and integration of AI tools in medical practice.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

References

- [1] Prince, M., Wimo, A., Guerchet, M., Ali, G.C., Wu, Y.T. and Prina, M., 2015. *World Alzheimer Report 2015. The Global Impact of Dementia: An analysis of prevalence, incidence, cost and trends* [Doctoral dissertation, Alzheimer's Disease International].
- [2] Piemonte, M.E.P., Kumar, K.R., McConvey, V., Zhang, B., Tan, E.K. and Savica, R., 2022. Age Cutoff for Early-Onset Parkinson's Disease: Recommendations from the International Parkinson and Movement Disorder Society Task Force on Early Onset Parkinson's Disease.
- [3] Feigin, V.L., Vos, T., Alahdab, F., Amit, A.M.L., Bärnighausen, T.W., Beghi, E., Beheshti, M., Chavan, P.P., Criqui, M.H., Desai, R. and Dharmaratne, S.D., 2021. Burden of neurological disorders across the US from 1990-2017: a global burden of disease study. *JAMA neurology*, 78(2), pp.165-176.
- [4] Cummings, J., Morstorf, T. and Lee, G., 2016. Alzheimer's drug-development pipeline: 2016. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, 2[4], pp.222-232.
- [5] Brookmeyer, R., Abdalla, N., Kawas, C.H. and Corrada, M.M., 2018. Forecasting the prevalence of preclinical and clinical Alzheimer's disease in the United States. *Alzheimer's & Dementia*, 14[2], pp.121-129.
- [6] Winblad, B., Amouyel, P., Andrieu, S., Ballard, C., Brayne, C., Brodaty, H., Cedazo-Minguez, A., Dubois, B., Edvardsson, D., Feldman, H. and Fratiglioni, L., 2016. Defeating Alzheimer's disease and other dementias: a priority for European science and society. *The Lancet Neurology*, 15[5], pp.455-532.
- [7] Esteva, A., Robicquet, A., Ramsundar, B., Kuleshov, V., DePristo, M., Chou, K., Cui, C., Corrado, G., Thrun, S. and Dean, J., 2019. A guide to deep learning in healthcare. *Nature medicine*, 25[1], pp.24-29.
- [8] LeCun, Y., Bengio, Y. and Hinton, G., 2015. Deep learning. *nature*, 521[7553], pp.436-444.
- [9] Liu, S., Liu, S., Cai, W., Pujol, S., Kikinis, R. and Feng, D., 2014, April. Early diagnosis of Alzheimer's disease with deep learning. In 2014 IEEE 11th international symposium on biomedical imaging [ISBI] [pp. 1015-1018]. IEEE.
- [10] Querfurth, H.W. and LaFerla, F.M., 2010. Mechanisms of disease. *N Engl J Med*, 362[4], pp.329-344.
- [11] Scheltens, P., Blennow, K., Breteler, M.M., De Strooper, B., Frisoni, G.B., Salloway, S. and Van der Flier, W.M., 2016. Alzheimer's disease. *The Lancet*, 388[10043], pp.505-517.
- [12] Petersen, R.C., Lopez, O., Armstrong, M.J., Getchius, T.S., Ganguli, M., Gloss, D., Gronseth, G.S., Marson, D., Pringsheim, T., Day, G.S. and Sager, M., 2018. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*, 90[3], p.126.

- [13] Tysnes, O.B. and Storstein, A., 2017. Epidemiology of Parkinson's disease. *Journal of neural transmission*, 124, pp.901-905.
- [14] Kalia, L.V. and Lang, A.E., 2015. Parkinson's disease. *The Lancet*, 386[9996], pp.896-912.
- [15] Poewe, W., Seppi, K., Tanner, C.M., Halliday, G.M., Brundin, P., Volkman, J., Schrag, A.E. and Lang, A.E., 2017. Parkinson disease. *Nature reviews Disease primers*, 3[1], pp.1-21.
- [16] Chaudhuri, K.R., Healy, D.G. and Schapira, A.H., 2006. Non-motor symptoms of Parkinson's disease: diagnosis and management. *The Lancet Neurology*, 5[3], pp.235-245.
- [17] Bates, G.P., Dorsey, R., Gusella, J.F., Hayden, M.R., Kay, C., Leavitt, B.R., Nance, M., Ross, C.A., Scahill, R.I., Wetzel, R. and Wild, E.J., 2015. Huntington disease. *Nature reviews Disease primers*, 1[1], pp.1-21.
- [18] Roos, R.A., 2010. Huntington's disease: a clinical review. *Orphanet Journal of rare diseases*, 5, pp.1-8.
- [19] Walker, F.O., 2007. Huntington's disease. *The Lancet*, 369[9557], pp.218-228.
- [20] Ross, C.A. and Tabrizi, S.J., 2011. Huntington's disease: from molecular pathogenesis to clinical treatment. *The Lancet Neurology*, 10[1], pp.83-98.
- [21] Weiner, M.W., Veitch, D.P., Aisen, P.S., Beckett, L.A., Cairns, N.J., Green, R.C., Harvey, D., Jack, C.R., Jagust, W., Liu, E. and Morris, J.C., 2013. The Alzheimer's Disease Neuroimaging Initiative: a review of papers published since its inception. *Alzheimer's & Dementia*, 9[5], pp.e111-e194.
- [22] Jack Jr, C.R., Bennett, D.A., Blennow, K., Carrillo, M.C., Dunn, B., Haeberlein, S.B., Holtzman, D.M., Jagust, W., Jessen, F., Karlawish, J. and Liu, E., 2018. NIA-AA research framework: toward a biological definition of Alzheimer's disease. *Alzheimer's & dementia*, 14[4], pp.535-562.
- [23] Oishi, K., Faria, A.V., Van Zijl, P.C. and Mori, S., 2010. *MRI atlas of human white matter*. Academic Press.
- [24] Papageorgiou, N., Briasoulis, A., Androulakis, E. and Tousoulis, D., 2017. Imaging subclinical atherosclerosis: where do we stand? *Current cardiology reviews*, 13[1], pp.47-55.
- [25] Frisoni, G.B., Fox, N.C., Jack Jr, C.R., Scheltens, P. and Thompson, P.M., 2010. The clinical use of structural MRI in Alzheimer disease. *Nature reviews neurology*, 6[2], pp.67-77.
- [26] Sarikaya, I., 2015. PET imaging in neurology: Alzheimer's and Parkinson's diseases. *Nuclear Medicine Communications*, 36[8], pp.775-781.
- [27] Politis, M., Wu, K., Loane, C., Kiferle, L., Molloy, S., Brooks, D.J. and Piccini, P., 2010. Staging of serotonergic dysfunction in Parkinson's disease: an in vivo 11C-DASB PET study. *Neurobiology of disease*, 40[1], pp.216-221.
- [28] Mosconi, L., 2005. Brain glucose metabolism in the early and specific diagnosis of Alzheimer's disease: FDG-PET studies in MCI and AD. *European Journal of nuclear medicine and molecular imaging*, 32, pp.486-510.
- [29] Litjens, G., Kooi, T., Bejnordi, B.E., Setio, A.A.A., Ciompi, F., Ghafoorian, M., Van Der Laak, J.A., Van Ginneken, B. and Sánchez, C.I., 2017. A survey on deep learning in medical image analysis. *Medical image analysis*, 42, pp.60-88.
- [30] Krizhevsky, A., Sutskever, I. and Hinton, G.E., 2012. Imagenet classification with deep convolutional neural networks. *Advances in neural information processing systems*, 25.
- [31] Zhao, Y., Guo, Q., Zhang, Y., Zheng, J., Yang, Y., Du, X., Feng, H. and Zhang, S., 2023. Application of deep learning for prediction of alzheimer's disease in PET/MR imaging. *Bioengineering*, 10[10], p.1120.
- [32] Lipton, Z.C., Berkowitz, J. and Elkan, C., 2015. A critical review of recurrent neural networks for sequence learning. *arXiv preprint arXiv:1506.00019*.
- [33] Goodfellow, I., Pouget-Abadie, J., Mirza, M., Xu, B., Warde-Farley, D., Ozair, S., Courville, A. and Bengio, Y., 2014. Generative adversarial nets. *Advances in neural information processing systems*, 27.
- [34] Frid-Adar, M., Diamant, I., Klang, E., Amitai, M., Goldberger, J. and Greenspan, H., 2018. GAN-based synthetic medical image augmentation for increased CNN performance in liver lesion classification. *Neurocomputing*, 321, pp.321-331.
- [35] Bowles, C., Chen, L., Guerrero, R., Bentley, P., Gunn, R., Hammers, A., Dickie, D.A., Hernández, M.V., Wardlaw, J. and Rueckert, D., 2018. Gan augmentation: Augmenting training data using generative adversarial networks. *arXiv preprint arXiv:1810.10863*.

- [36] Zhou, S.K., Greenspan, H., Davatzikos, C., Duncan, J.S., Van Ginneken, B., Madabhushi, A., Prince, J.L., Rueckert, D. and Summers, R.M., 2021. A review of deep learning in medical imaging: Imaging traits, technology trends, case studies with progress highlights, and future promises. *Proceedings of the IEEE*, 109[5], pp.820-838.
- [37] Pham, D.L., Xu, C. and Prince, J.L., 2000. Current methods in medical image segmentation. *Annual review of biomedical engineering*, 2[1], pp.315-337.
- [38] Gonzalez, R.C., 2009. *Digital image processing*. Pearson education India.
- [39] Nyúl, L.G., Udupa, J.K. and Zhang, X., 2000. New variants of a method of MRI scale standardization. *IEEE transactions on medical imaging*, 19[2], pp.143-150.
- [40] Ronneberger, O., Fischer, P. and Brox, T., 2015. U-net: Convolutional networks for biomedical image segmentation. In *Medical image computing and computer-assisted intervention–MICCAI 2015: 18th international conference, Munich, Germany, October 5-9, 2015, proceedings, part III 18* [pp. 234-241]. Springer International Publishing.
- [41] Çiçek, Ö., Abdulkadir, A., Lienkamp, S.S., Brox, T. and Ronneberger, O., 2016. 3D U-Net: learning dense volumetric segmentation from sparse annotation. In *Medical Image Computing and Computer-Assisted Intervention–MICCAI 2016: 19th International Conference, Athens, Greece, October 17-21, 2016, Proceedings, Part II 19* [pp. 424-432]. Springer International Publishing.
- [42] Liu, S., Liu, S., Cai, W., Che, H., Pujol, S., Kikinis, R., Feng, D. and Fulham, M.J., 2014. Multimodal neuroimaging feature learning for multiclass diagnosis of Alzheimer's disease. *IEEE transactions on biomedical engineering*, 62[4], pp.1132-1140.
- [43] Klöppel, S., Stonnington, C.M., Chu, C., Draganski, B., Scahill, R.I., Rohrer, J.D., Fox, N.C., Jack Jr, C.R., Ashburner, J. and Frackowiak, R.S., 2008. Automatic classification of MR scans in Alzheimer's disease. *Brain*, 131[3], pp.681-689.
- [44] Halgamuge, M.N., 2020. Supervised machine learning algorithms for bioelectromagnetics: Prediction models and feature selection techniques using data from weak radiofrequency radiation effect on human and animals cells. *International Journal of Environmental Research and Public Health*, 17[12], p.4595.
- [45] Farooq, A., Anwar, S., Awais, M. and Rehman, S., 2017, October. A deep CNN based multi-class classification of Alzheimer's disease using MRI. In *2017 IEEE International Conference on Imaging systems and techniques [IST]* [pp. 1-6]. IEEE.
- [46] Ahmed, S., 2020. Prediction of Rate of Disease Progression in Parkinson's Disease Patients based on RNA-Sequence using Deep Learning [Doctoral dissertation, Université d'Ottawa/University of Ottawa].
- [47] Powers, D.M., 2020. Evaluation: from precision, recall and F-measure to ROC, informedness, markedness and correlation. *arXiv preprint arXiv:2010.16061*.
- [48] Fawcett, T., 2006. An introduction to ROC analysis. *Pattern recognition letters*, 27[8], pp.861-874.
- [49] Hanley, J.A. and McNeil, B.J., 1982. The meaning and use of the area under a receiver operating characteristic [ROC] curve. *Radiology*, 143[1], pp.29-36.
- [50] Lin, W., Tong, T., Gao, Q., Guo, D., Du, X., Yang, Y., Guo, G., Xiao, M., Du, M., Qu, X. and Alzheimer's Disease Neuroimaging Initiative, 2018. Convolutional neural networks-based MRI image analysis for the Alzheimer's disease prediction from mild cognitive impairment. *Frontiers in neuroscience*, 12, p.777.
- [51] Bäckström, K., Nazari, M., Gu, I.Y.H. and Jakola, A.S., 2018, April. An efficient 3D deep convolutional network for Alzheimer's disease diagnosis using MR images. In *2018 IEEE 15th International Symposium on Biomedical Imaging [ISBI 2018]* [pp. 149-153]. IEEE.
- [52] Li, M., Liu, Y., Chen, H., Hu, G., Yu, S., Ruan, X., Luo, Z., Wei, X. and Xie, Y., 2019. Altered global synchronizations in patients with Parkinson's disease: a resting-state fMRI study. *Frontiers in Aging Neuroscience*, 11, p.139.
- [53] Helmich, R.C., 2018. The cerebral basis of Parkinsonian tremor: a network perspective. *Movement Disorders*, 33[2], pp.219-231.
- [54] Chen, X., Zhang, H., Zhang, L., Shen, C., Lee, S.W. and Shen, D., 2017. Extraction of dynamic functional connectivity from brain grey matter and white matter for MCI classification. *Human brain mapping*, 38[10], pp.5019-5034.

- [55] Drotár, P., Mekyska, J., Rektorová, I., Masarová, L., Smékal, Z. and Faundez-Zanuy, M., 2016. Evaluation of handwriting kinematics and pressure for differential diagnosis of Parkinson's disease. *Artificial intelligence in Medicine*, 67, pp.39-46.
- [56] Tabrizi, S.J., Leavitt, B.R., Landwehrmeyer, G.B., Wild, E.J., Saft, C., Barker, R.A., Blair, N.F., Craufurd, D., Priller, J., Rickards, H. and Rosser, A., 2019. Targeting huntingtin expression in patients with Huntington's disease. *New England Journal of Medicine*, 380[24], pp.2307-2316.
- [57] Kloeppel, S., Henley, S.M., Hobbs, N.Z., Wolf, R.C., Kassubek, J., Tabrizi, S.J. and Frackowiak, R.S.J., 2009. Magnetic resonance imaging of Huntington's disease: preparing for clinical trials. *Neuroscience*, 164[1], pp.205-219.
- [58] Aylward, E.H., Nopoulos, P.C., Ross, C.A., Langbehn, D.R., Pierson, R.K., Mills, J.A., Johnson, H.J., Magnotta, V.A., Juhl, A.R., Paulsen, J.S. and PREDICT-HD Investigators, 2011. Longitudinal change in regional brain volumes in prodromal Huntington disease. *Journal of Neurology, Neurosurgery & Psychiatry*, 82[4], pp.405-410.
- [59] Panayides, A.S., Amini, A., Filipovic, N.D., Sharma, A., Tsafaris, S.A., Young, A., Foran, D., Do, N., Golemati, S., Kurc, T. and Huang, K., 2020. AI in medical imaging informatics: current challenges and future directions. *IEEE journal of biomedical and health informatics*, 24[7], pp.1837-1857.
- [60] Doshi-Velez, F. and Kim, B., 2017. Towards a rigorous science of interpretable machine learning. *arXiv preprint arXiv:1702.08608*.
- [61] Topol, E.J., 2019. High-performance medicine: the convergence of human and artificial intelligence. *Nature medicine*, 25[1], pp.44-56.
- [62] Morley, J., Machado, C.C., Burr, C., Cowls, J., Joshi, I., Taddeo, M. and Floridi, L., 2020. The ethics of AI in health care: a mapping review. *Social Science & Medicine*, 260, p.113172.
- [63] Pan, S.J. and Yang, Q., 2009. A survey on transfer learning. *IEEE Transactions on knowledge and data engineering*, 22[10], pp.1345-1359.
- [64] Song, J., Zheng, J., Li, P., Lu, X., Zhu, G. and Shen, P., 2021. An effective multimodal image fusion method using MRI and PET for Alzheimer's disease diagnosis. *Frontiers in digital health*, 3, p.637386.
- [65] Shin, H.C., Roth, H.R., Gao, M., Lu, L., Xu, Z., Nogues, I., Yao, J., Mollura, D. and Summers, R.M., 2016. Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning. *IEEE transactions on medical imaging*, 35[5], pp.1285-1298.
- [66] Suk, H.I., Lee, S.W., Shen, D. and Alzheimer's Disease Neuroimaging Initiative, 2015. Latent feature representation with stacked auto-encoder for AD/MCI diagnosis. *Brain Structure and Function*, 220, pp.841-859.
- [67] Jha, S. and Topol, E.J., 2016. Adapting to artificial intelligence: radiologists and pathologists as information specialists. *Jama*, 316[22], pp.2353-2354.
- [68] Jain, K.K., 2015. *Textbook of personalized medicine*.