

AI-Aided Diagnosis For Neurodegenerative Diseases: Prospects And Challenges

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Abstract. Neurodegenerative disease (ND) represents a chronic disease characterized by loss of neuron function and death, such as Alzheimer's disease, Parkinson's disease, etc. It's difficult and complex to diagnose ND, due to the requirement for the synthesis of multiple biomarker data, such as genes, proteins, images, etc. The advent of artificial intelligence (AI) technology, particularly through machine learning (ML) and deep learning (DL) algorithms, introduces novel methodologies and tools for ND diagnosis. These methodologies extract pertinent information and patterns from massive, multidimensional, and non-linear data, assisting doctors to render more precise, prompt, and objective assessments. This article provides an overview of the updated implementation status of AI in ND diagnosis, assesses the advantages and contributions of AI to ND diagnosis, as well as the existing limitations and challenges, and offers insights to the future development direction of AI in ND diagnosis.

Keywords: artificial intelligence; neurodegenerative diseases; diagnosis; biomarkers; machine learning; deep learning.

1. Introduction

Alzheimer's disease, Parkinson's disease, Huntington's disease, and other chronic disorders within the spectrum of neurodegenerative diseases (ND) lead to the deterioration of neuronal function and neuronal death. ND predominantly manifests in individuals of middle-aged and elderly demographics. With the trend of population aging, the number of patients and social burden of ND increases progressively. The clinical presentations of ND are intricate and multifaceted, including cognitive impairment, motor impairment, and emotional impairment. At present, the pathogenesis of ND remains unclear, lacking effective treatments.[1] Besides, currently, the mitigation of symptoms is achieved through pharmacological and non-pharmacological interventions.

Therefore, the early diagnosis and differential diagnosis of ND holds significance in improving patient prognosis, elevating quality of life, and reducing medical costs. However, the process of diagnosing ND is complex and difficult, necessitating the synthesis of multiple biomarker data, including genes, proteins, images, etc. Conventional diagnostic methods mainly rely on the subjective assessment and experiential acumen, which are easily affected by factors such as personal bias, knowledge level, and emotional disposition. In addition, conventional diagnostic methods struggle to deal with copious volumes of multidimensional, non-linear data, thereby failing to make full use of the information and patterns contained in the data.

Artificial intelligence (AI) techniques, especially machine learning (ML) and deep learning (DL) algorithms, provide novel methods and tools for ND diagnosis [2]. AI can extract useful information and patterns from massive, multidimensional, and non-linear data, then assisting doctors to make more precise, expeditious, and objective assessments. In recent years, the application of AI in ND diagnosis has achieved some results, such as AD diagnosis model based on ML or DL, PD diagnosis model based on ML or DL, HD diagnosis model based on ML or DL, etc. These applications not only improve the accuracy and sensitivity of ND diagnosis, but also broaden the horizon and profundity of diagnostic capacities, bringing new possibilities and opportunities for ND research and treatment methodologies.

2. Application of AI in ND diagnosis

The application of artificial intelligence(AI) in neurodegenerative disease(ND) encompasses two primary facets. Firstly, AI is employed to analyze various biomarkers, such as imaging, genes, proteins, metabolites, etc. Aiming to improve the sensitivity and specificity of diagnosis. Conversely, AI plays an important role in assisting clinical decision-making, including predicting disease progression, evaluating treatment effects, and providing personalized recommendations.

Imaging is one of the most commonly used biomarkers in ND diagnosis, involving structural imaging techniques like MRI, CT, and functional imaging methods such as PET, SPECT. Structural imaging unveils structural changes in the brain of ND patients, such as atrophy and ventriculomegaly. Functional imaging captures changes in brain activity, encompassing metabolism, perfusion, and receptor density. Through ML or DL algorithms, AI can process image data automatically, efficiently and accurately, such as feature extraction, classification, segmentation, registration, which will assist doctors in making more accurate and objective diagnoses. For example, the ML algorithm was used to analyze MRI data of PD patients and healthy controls, revealing substantial volume reduction in regions like the substantia nigra, globus pallidum, striatum [3]. This established a PD diagnosis model based on MRI features, yielding an accuracy rate of 86.7%. Further employment of the DL algorithm to analyze PET data of AD patients and healthy controls was reported from [4], finding out the significant metabolism decline in the temporal, parietal, and frontal lobes. This was cultivated in an AD diagnostic model based on PET features, which achieved a remarkable accuracy rate of 94.4%. Furthermore, the DL algorithm has also been used to analyze the brain tissue slice data of AD patients and healthy controls, and results found that AD patients had obvious amyloid deposition and cerebrovascular amyloidosis in the hippocampus, cingulate gyrus and other regions, establishing a slice feature-based AD diagnosis model with an accuracy rate of 98.6%. [5].

Gene is another important biomarker in ND diagnosis, mainly including single nucleotide polymorphism (SNP), gene expression, epigenetics. Genes illuminate genetic susceptibility and molecular mechanisms of ND patients and provide clues for pathogenesis and therapeutic targets of ND. AI, fueled by ML or DL algorithms, is able to cope with complex, large-scale and multidimensional analysis of genetic data algorithms through feature selection, clustering, classification, and regression, thereby assisting doctors to make more in-depth and comprehensive diagnoses. For example, an ML algorithm has been leveraged to analyze gene expression data in PD patients and healthy controls, results reported from [6] unveiling substantial differences in multiple biological pathways, which established a PD diagnostic model based on gene expression features, achieving an accuracy rate of 93.8%. The ML algorithm has also been applied to analyze SNP data of AD patients and healthy controls [7], and found that AD patients had significant variations in multiple mitochondria-related genes, and screened out some compounds that can induce mitophagy, which proposed a novel avenue for AD treatment. Study reported from [8] harnessed DL algorithm to analyze the genetic data from various ND patients and healthy controls, pointing out marked differences in multiple genes linked to neuron function, cell cycle, immune response, in ND patients. A diagnostic model capable of distinguishing different AND types was established, achieving an accuracy rate of 95.2%.

AI's influence extends beyond imaging and genetics to encompass diverse biomarkers such as proteins, metabolites, cognitive tests, speech patterns, and behaviors. AI can comprehensively correlate and optimize these data through ML or DL algorithms, such as feature fusion, dimensionality reduction, enhancement, ultimately assisting doctors in making more comprehensive and refined diagnosis. As shown in [4], ML algorithms analyzed multiple biomarker data from AD patients and healthy controls, including imaging, genes, proteins, cognitive tests, establishing an AD diagnostic model based on multiple biomarker features, achieving an accuracy rate of 97.8%. The DL algorithm was used to analyze the speech data of PD patients and healthy controls, resulting in a PD diagnosis model rooted in speech features, which achieved an accuracy rate of 91.4% [9]. Also, the ML algorithm has been applied to analyze the behavioral data of diverse ND patients and healthy controls, and established a diagnostic model capable of distinguishing different ND types and

severities, achieving an accuracy rate of 88.6% [10].

In addition to the analysis of multiple biomarkers for ND diagnosis, AI can also use clinical data and other relevant data to offer clinical decision support for ND patients, such as predicting disease progression, evaluating treatment effects, and providing personalized recommendations. These applications can help medical practitioners formulate more reasonable, effective, and individualized treatment plans, consequently enhancing patient prognosis and quality of life.

Predicting disease progression refers to the use of AI to predict and evaluate the condition changes and risk factors of ND patients, providing doctors with more accurate and timely diagnosis and intervention. For example, researchers have developed a clinical decision support system based on machine learning, predicting the likelihood of dementia development within the next year based on the cognitive test, imaging, genetic and other data of ND patients [6]. This system imparts corresponding confidence levels and interpretations. A deep learning based clinical decision support system is developed as has been reported from [7], using the data of motor test, speech test, eye movement test and other data of PD patients. It can foresee motor complications in PD patients over six months, providing associated probabilities and explanations.

Evaluation of treatment effect refers to the use of AI to evaluate and compare the improvement and side effects of ND patients after receiving different treatment options, thereby furnishing clinicians with systematic, impartial feedback and recommendations. For example, a clinical decision support system has been built based on machine learning, drawing upon cognitive tests, imaging, cerebrospinal fluid analysis, and more, to assess the impact of distinct drug treatments on cognitive function and brain structure in AD patients, resulting in corresponding ratings and rankings.[9] Another deep learning-based clinical decision support system reliant on motor test, speech evaluations, and eye movement data from PD patients after receiving different types of surgical treatment, to assess the impact of surgical treatment on patients' motor function and quality of life and give the corresponding indicators and curves [2].

Providing personalized advice refers to the use of AI to analyze and understand the personal characteristics, preferences, needs of ND patients, contributing to providing doctors with more humane and customized treatment options and management plans. It has been conceived as a machine learning-driven clinical decision support system that factors in age, gender, education level, family history and other data from AD patients [10]. This system tailors recommendations for cognitive training, social engagement, psychological counseling, and other services pertinent to different disease stages, accompanied by corresponding rationale and anticipated effects. Researchers have also developed another clinical decision support system based on deep learning, hinging on the data such as weight, eating habits, and exercise of PD patients, resulting in providing information such as the dosage, timing, and frequency of drugs commensurate with distinct stages, giving associated medication guidance and precautions[5].

3. Advances of AI in ND diagnosis

3.1. Enhancement of Accuracy and Objectivity in Diagnosis

First of all, AI can use ML or DL algorithms to perform effective feature extraction, classification, segmentation, registration and other operations on biomarker data. This highlights elucidate disparities between ND patients and healthy controls, eliminating noise, redundancy, variation and other interference factors in the data. Secondly, AI employs ML or DL algorithms for comprehensive feature fusion, dimensionality reduction, enhancement and other operations on biomarker data, highlighting commonalities amidst ND patients and healthy control groups. This argumentation increases the information content, signal-to-noise ratio, contrast and other indicators in the data. Finally, AI utilizes ML or DL algorithms for optimized feature selection, weight assignment, parameter adjustment and other procedures on biomarker data, optimizing the discriminant function between ND patients and the healthy control group, resulting in the improvement of the accuracy rate,

recall rate, F1 value and other evaluation indicators in the model. The DL algorithm has been applied to analyze the PET data of AD patients and healthy control groups, achieving an accuracy rate of 94.4%, compared to the traditional manual image reading method, which yielded an accuracy rate of approximately 80% [4]. As has been reported from [9], the DL algorithm was developed for voice data among PD patients and healthy control groups, achieving an accuracy rate of 91.4%, while the traditional clinical evaluation method only had an accuracy rate of about 70%. These outcomes suggest AI's capability to provide heightened discriminative potency and consistency within ND diagnosis, thereby reducing the risk of missed and misdiagnosed diagnoses and improving diagnostic reliability and validity.

3.2. Amplification of Sensitivity and Early Diagnosis

Firstly, AI can use ML or DL algorithms to perform in-depth feature exploration, association analysis, anomaly detection and other operations on biomarker data. These operations facilitate the discovery of the subtle and subtle changes in ND patients in the early stage, such as abnormalities in neuron structure, function, metabolism, genes. Furthermore, AI's dynamic feature tracking, trend projection, and risk assessment capabilities illuminate the speed and direction of changes within ND patients in the early stage, such as the deterioration of the disease, the aggravation of symptoms, the emergence of complications. Finally, AI can use ML or DL algorithms to perform precise feature classification, identification, diagnosis and other operations on biomarker data which help reveal the type and degree of changes in ND patients in the early stage, such as disease type, subtype, stage and other information. For example, [3] used the ML algorithm to analyze MRI data from PD patients and healthy controls, detecting significant volume reduction in areas such as the substantia nigra in PD patients. These changes are often difficult to detect clinically. The ML algorithm was used for SNP data analysis among AD patients and healthy controls, uncovering significant variations in multiple mitochondria-related genes AD patients had, which were often overlooked by routine detection.[7] These instances indicate AI's potential to furnish earlier and more sensitive ND diagnosis, thereby achieving early detection, early diagnosis, and early intervention of ND patients.

3.3. Augmentation of Comprehensive and Refined Diagnosis

First of all, AI such as ML and DL algorithms has been engaged in multi-level, multi-angle, and multi-time point analysis of biomarker data, culminating in comprehensive assessment in terms of structure, function, molecular, and cognition for ND patients. Moreover, AI refines analysis pertaining to individual differences, disease heterogeneity, and disease course dynamics, ultimately realizing the refined diagnosis of ND patients in terms of individual characteristics, disease types, and severity levels; finally, AI can perform operations such as optimized feature representation, interpretation, and visualization of biomarker data using ML or DL algorithms, which enables the visualization and interpretation of dynamic changes and trends of ND patients over distinct time periods. It has been employed as ML algorithms to analyze multiple biomarker data of AD patients and healthy controls, including imaging, genes, proteins, cognitive tests, and established a AD diagnostic model rooted in a variety of biomarker attributes, reflecting the comprehensive changes in structure, function, molecular, cognition and other dimensions within AD patients [4]. The ML algorithms has been developed for behavioral data analysis across various ND patients and healthy controls, resulting in a diagnostic model that can distinguish different ND types and severities, and can reflect the subtle changes in daily life, social interaction, and emotional expression among ND patients [10]. These results underscore that AI is gifted in yielding more comprehensive and refined assessment capabilities within ND diagnosis, thereby realizing personalized diagnosis of ND patients in terms of individual differences, disease heterogeneity, and disease course dynamics.

4. Limitations of AI in ND Diagnosis

4.1. Insufficiency in Data Quality and Quantity

AI in ND diagnosis relies on voluminous, high-quality, and multi-source biomarker data, but acquiring, storing, and sharing these data challenges. First, due to the low incidence of ND cases coupled with the factors such as geography, race, and gender, the number of samples available for AI analysis is limited, inadequately representing the intricacies of ND diversity and complexity [11]. Secondly, the multifaceted nature of ND patients' biomarker data like multiple types, formats, dimensions, is subject to errors and interference during collection, processing, and storage. Consequently, the quality of the data that can be used for AI analysis is low, complicating preservation of data integrity and consistency [12]. Finally, the incorporation of ND patients' biomarker data-encompassing personal information, health status, genetic characteristics-is against ethics, laws and regulatory considerations, constraining the sources of data accessible for AI analysis and impeding the open sharing of data. These factors limit the application effect and promotion scope of AI in ND diagnosis.

4.2. Limited Algorithmic Complexity and Interpretability

The ML or DL algorithms used by AI in ND diagnosis are often intricate and nonlinear, making their internal working mechanisms and logical relationships difficult to understand and explain. Initially, the abundance of parameters, levels, and structures inherent in ML and DL algorithms, coupled with their potent nonlinear fitting capabilities, makes it difficult to understand and explain their internal working mechanisms and logical relationships, and it is difficult to reveal the principles underlying the algorithms. Additionally, because the ML or DL algorithm is affected by data quality, feature selection, model selection, and has uncertainty and randomness, it is difficult to verify and evaluate its outputs, as well as guaranteeing the stability and reliability of the algorithm [13]. Moreover, the absence of prior knowledge of biomarker data and domain-specific insights within ML or DL algorithms, makes it challenging to interpret and understand the output outcomes. And it is difficult to provide transparency and credibility to the diagnostic process and results. These factors restrict the application and potential for further development within ND diagnosis.

4.3. Inadequate Human-Machine Collaboration and Communication

The application of AI in ND diagnosis cannot completely replace the role of human doctors, but requires effective collaboration and communication between two entities. First of all, due to the differences in knowledge, experience, and cognitive frameworks between AI and human doctors, it is difficult for AI to understand the needs, intentions, emotions and related facets of human doctors, which hampers AI's ability to obtain the trust, support, and feedback of human doctors. Secondly, the barriers in language, expression, and communication between AI systems and human doctors set challenges to effective communication and interaction using natural language and multimodal methods, resulting in restrictions of providing clear, concise and friendly information and guidance. Finally, the differences in culture, values, and norms between AI systems and human doctors, hinder AI's adaptation to doctors' habits, preferences, and expectations of human doctors. And the ethics, morals, and laws abided by human doctors are also complex challenges for AI systems.

5. Future directions of AI in ND diagnosis

Although the application of AI in ND diagnosis has achieved some results, there is still much room for improvement and innovation in this field. This paper believes that the future development direction of AI in ND diagnosis mainly includes the following aspects:

5.1. Data integration and standardization.

In order to overcome the problem of insufficient data quality and quantity, more extensive, higher-

quality and diverse repositories of ND biomarker datasets need to be established and effectively integrated and standardized to improve data availability, comparability and reproducibility. For example, by establishing a multi-center, multi-country, and multi-platform data sharing network, data exchange and collaboration between different institutions, regions, and devices can be realized [11]. Data alignment and fusion between different types, formats, and dimensions can be obtained by formulating unified specifications and processes for data collection, processing, storage, and analysis[12].

5.2. Algorithm optimization and interpretation.

To address the problems of insufficient algorithm complexity and interpretability, existing ML or DL algorithms need to be optimized and improved in efficiency, stability, and reliability of the algorithms. For example, the constraints, penalties, and selection of algorithms can be realized by introducing prior knowledge, regularization items, and attention mechanisms; the fusion, migration, and generalization. At the same time, existing ML or DL algorithms need to be explained and visualized to improve the transparency, credibility, and controllability of the algorithms. For example, by using explainable AI (XAI) techniques, such as sensitivity analysis, importance ranking, and adversarial examples, the explanation of the input-output relationship, feature weight, and potential vulnerabilities of the algorithm can be realized [14]. The internal structure, working process, and result display of the algorithm can be visualized by using visualization techniques such as charts, images, and animations [15].

5.3. Human-machine collaboration and communication [16].

Overcoming the problem of insufficient human-machine collaboration and communication, it is necessary to establish a more effective, friendlier, and smarter human-computer interaction interface and system to deal with it. For example, by using NLP technology, such as speech recognition, natural language generation and other methods, natural language communication between humans and machines can be realized. Emotional computing technology, such as emotion recognition, emotion generation and so on aids emotional resonance between man and machine. The immersive experience between man and machine can be realized by using augmented reality (AR) or virtual reality (VR) technology, such as image synthesis, scene simulation and other methods.

6. Conclusion

This article reviews the current application status of AI in ND diagnosis, analyzes the advantages and contributions of AI in ND diagnosis, as well as the existing limitations and challenges. Then the article pivots to the envision for the future evolution of AI's role within ND diagnosis. This paper asserts that AI furnishes a series of marked advantages and significant contributions to the sphere of ND diagnosis. AI can extract useful information and patterns from a large amount of high-dimensional and non-linear biomarker data, assisting doctors to make more precise, prompt and objective assessments. Utilizing biomarker data of various types, formats, and dimensions makes it possible for AI to achieve a comprehensive, in-depth, and detailed assessment of ND patients. AI can realize personalized, customized and precise diagnosis of ND patients according to the individual differences of different patients. AI can realize dynamic, continuous and long-term monitoring of ND patients according to different stages and goals. AI can provide ND patients with better and more convenient diagnostic services, and improve patient satisfaction and compliance. At the same time, this paper also believes that AI still has the following limitations and challenges in ND diagnosis: insufficient data quality and quantity; limited algorithmic complexity and interpretability; inadequate human-machine collaboration and communication. Then, this paper suggests that the following domains should be paid attention to when developing the application of AI in ND diagnosis in the future: data integration and standardization; algorithm optimization and interpretation; human-machine collaboration and communication. This article hopes to provide some reference and inspiration for the application of AI in ND diagnosis, promote the cross-integration of AI and ND

fields, and promote the innovation and development of AI in ND diagnosis.

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