Mini-Review

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Artificial intelligence technology in Alzheimer's disease research

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SUMMARY Alzheimer's disease is a neurocognitive disorder and one of the contributing factors to dementia. According to the World Health Organization, this disease has a sig-nificant impact on the global population's health, with the number of affected individuals steadily increasing each year. Amidst rapid technological development, the use of artificial intelligence has significantly expanded into the field of medical diagnostics, encompassing areas such as the analysis of medical images, drug development, design of personalized treatment plans, and disease prediction and treatment. Deep learning, which is an important branch in the field of artificial intelligence, is playing a key role in solving several medical challenges by providing important technical support for the early detection, diagnosis, and treatment of Alzheimer's disease. Given this context, this review aims to explore the differences between conventional methods and artificial intelligence techniques in Alzheimer's disease research. Additionally, it aims to summarize current non-invasive and portable techniques for detection of Alzheimer's disease, offering support and guidance for the future prediction and management of the disease.

Keywords Alzheimer's disease, mild cognitive impairment, artificial intelligence, machine learning, deep learning

1. Introduction

Alzheimer's disease (AD) is a progressive neurological disorder, with the highest in-cidence among individuals ages 65 and older. Current evidence suggests that the age range of the disease is gradually expanding, with middle-aged AD patients under the age of 65 years constituting the younger population affected by AD (*1*). Providing insight into the core mechanisms of AD, Jack *et al*. (*2*) found that the core pathological features of AD are amyloid pathology, tau protein pathology, and neurodegeneration. These three key pathological features are also key to predicting, diagnosing, and treating AD. Before the widespread adoption of artificial intelligence (AI) in healthcare, conventional testing for AD consisted of several approaches. Initially, physicians would rely on their professional expertise to evaluate whether a patient exhibited symptoms of the disease and assess its severity through in-person consultations and inquiries into the patient's medical history. Subsequently, cognitive assessment tools such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MOCA) were used to score the patient's cognitive abilities and determine their cognitive levels (*3*). Now that technology has advanced, magnetic resonance imaging (MRI), positron emission tomography (PET), diffusion tensor imaging (DTI), biomarkers, and cerebrospinal fluid (CSF) (*4*) are gradually being used to detect AD because they do not involve subjective intervening factors. MRI technology uses a strong magnetic field and harmless radio waves to generate high-resolution brain images, aiding physicians in observing the brain structure and detecting potential abnormalities. Biomarkers as described in (*2*) are used to detect AD by labeling specific markers such as amyloid and tau proteins and by ascertaining their presence and the degree of their accumulation. CSF involves the extraction of CSF samples from subjects' spinal region, which are then tested and analyzed to diagnose AD.

However, the aforementioned conventional methods for detection of AD have certain limitations. First, clinical assessment and cognitive testing methods rely to some extent on the subjective judgment of physicians. Second, due to the less distinct pathological features of AD in its early stages, brain imaging techniques such as MRI may lack the sensitivity required to predict this condition (*5*).

2. An overview of AI and its applications

2.1. An overview of AI

AI is a field focused on enabling computer systems to possess cognitive capabilities akin to human thinking. Its objective is to impart machines with the capacity to perceive their surroundings, comprehend natural language, acquire knowledge, engage in logical reasoning, problem-solving, and demonstrate adaptability to varying tasks (*6*). The study of AI extends across diverse domains, predominantly encompassing machine learning (ML) and deep learning (DL).

ML is an important branch in the field of AI that uses algorithms and statistical models to learn from large amounts of data to solve specific tasks (*7*). The core of ML is to perform tasks such as decision-making, classification, and prediction by analyzing and learning the features of data. Common ML models include decision trees (*8*), random decision forests (RFs) (*9*), logistic regression (*10*), support vector machines (SVM) (11), and Bayesian classifiers (*12*).

DL is a subfield of ML. Driven by the proliferation of data and enhanced compu-tational capabilities, ML has evolved into DL (*13*). DL emulates the functioning of neuronal networks in the human brain, acquiring an understanding of data relation-ships through multi-layered neural networks and autonomously extracting data fea-tures. The core of DL is deep neural networks such as the Convolutional Neural Net-work (CNN) (*14*), Long Short-Term Memory Network (LSTM) (*15*), and Transformer (*16*).

2.2. Widespread use of AI in medicine

The applications of AI in medicine are divided into two main categories, physical applications and virtual applications (*17*). Physical applications refer to the use of AI technology to invent and create medical robots and other medical devices in order to assist in medical research and clinical practice. Virtual applications are based on ML and DL and involve algorithmic and software analysis to assist medical research. The scope of virtual applications in healthcare is extensive, including medical testing and treatment, case analysis, and analysis of the progression of chronic diseases. Addi-tionally, the use of virtual applications in the field of AD has garnered significant attention.

The subsequent discussion will focus on the use of AI in the realm of virtual medicine. Its specific applications and potential value in AD detection, diagnosis, and case analysis will be delved into.

3. ML in AD

ML has been used in the field of medical imaging for several decades, with its appli-cations found in computer-aided diagnosis and functional brain imaging (*18*). In the early days, the main task of ML was to assist physicians in identifying and localizing obvious signs of disease. As ML techniques developed and matured, they were gradu-ally used to handle more complex medical detection tasks. By acquiring 18-month longitudinal trajectories of 1,909 patients with mild cognitive impairment (MCI) or AD, an unsupervised ML model, the Conditional Restricted Boltzmann Machine (CRBM), was utilized to simulate the disease trajectories of patients, ultimately doing so in a way that could accurately model the progression of AD (*19*). A study (*20*) summarized multiple brain regions that are closely associated with the pathological mechanisms of AD, including the hippocampus, the internal olfactory cortex, the basal ganglia, the rectus gyrus, the precuneus, and the cerebellum, and it used ML techniques to extract these multivariate biomarkers from structural MRI brain images in order to detect AD early. Studies such as the ones mentioned that utilized ML techniques to detect latent disease markers have made some progress (*20,21,22*). However, ML often requires manual extraction of features, which adds to the difficulty of analyzing large amounts of data.

4. DL in AD

DL performs better and has higher accuracy when dealing with complex data com-pared to conventional ML methods. In addition, DL models are more flexible in of-fering different architectures to adapt to different data characteristics, which is particularly important in AD research.

4.1. Early prediction of AD

The focus of research on early AD is mainly on MCI, because MCI is the transition state between normal aging and AD, and therefore accurate prediction of MCI is im-portant for early prediction of AD (*23,24*). In DL, LSTM performs well in processing time-related data and can be used in prediction problem. Patients' clinical or behav-ioral data usually contain extensive time-series information, and LSTM can capture the features in these time-series and they can be used to predict the changes in pa-tients' cognitive function and disease progression over future time intervals, rather than just a simple categorization of the current patient's disease status (*25,26*). More-over, Hong *et al*. (*25*) focused on predicting AD using five quantitative biomarkers, i.e., the cortical thickness standard deviation (TS), cortical thickness average (TA), WM parcellation volume (SV), surface area (SA), and cortical parcellation volume (CV), and the results of that study showed that all five biomarkers displayed excellent ability to predict AD. TA yielded the best results in prediction. In addition, some studies have explored AD prediction using only retinal pictures, and they have achieved a fairly high accuracy (*27*).

4.2. Diagnosis of AD

DL can be used to build models of disease progression. Unlike early prediction of AD, detection of AD focuses more on patients who already been diagnosed, utilizing DL techniques to assess the extent of cognitive impairment. Nowadays, the diagnosis of AD mostly utilizes MRI images. In the field of processing image data, the CNN ex-cels in processing neuroimaging data, and it can mine important pathologic features from these images to help doctors detect the progression of the patient's disease (*28,29,30*). Other studies have used eye-tracking data to diagnose AD. They track the eye movements and visual focus of test subjects to gather cognitive information (*31*). The studies (*25,26,32*) have integrated early prediction and diagnosis of AD, forming a comprehensive process or framework for predicting AD throughout its course. Medical imaging data are used in pre-trained DL architectures to accurately identify the stage of AD and to help physicians and researchers understand the progression of the condition. In addition, Ho *et al*. (*33*) attempted to use non-invasive near-infrared spectroscopy to diagnose AD, and the highest accuracy (90.91%) was achieved using a CNN-LSTM DL model. These methods enable effective diagnosis of AD in a non-invasive manner and portable format, helping to develop personalized treatment plans and monitor disease progression.

4.3. Treatment of AD

DL plays an important role in the treatment of AD. Transformer is a DL model that can flexibly process different types and lengths of sequence data. In addition, it can capture more detailed feature information. For example, a study used graph neural networks (*34*) to learn and capture structural features of drug molecules, with AD-related ApoE as a target, to search for corresponding acting drugs in the Kyoto Encyclopedia of Genes and Genomes (KEGG) database and PubChem database, to create drug–target interaction (DTI) data, to extract molecular structure information from the DTI data, and to utilize the Transformer network to fuse the features of dif-ferent layers in a graph convolutional neural network to predict potential therapeutics for AD. Amyloid-beta 42 (Aβ-42) is a high-risk factor for triggering AD. In order to predict the efficacy of drugs on AD, Kaushik *et al*. (*35*) used deep neural network technology to screen the PubChem compound library, and they discovered possible Aβ-42 inhibitors and assessed the effects of drugs on AD by observing the effects of inhibitors on Aβ-42.

5. Conclusion

This paper provides an overview of the role of existing AI methods in AD research (Table 1), with a focus

Table 1. Artificial intelligence-based studies related to Alzheimer's disease

Artificial intelligence approach	Main model	Primary data type	Task	*Ref.*
Machine learning	SVM	Magnetic resonance images of brain structures	Diagnosis of AD	*5,18,20*
	Boltzmann machine	Scales, tests, background and other clinical data	Prediction of the whole course of AD	*19*
	SVM, Logistic regression, Decision tree	Longitudinal MRI image	AD prognosis	*21*
	SVM, ANN	CSF data	Diagnosis of AD	*22*
Deep Learning	CNN, LSTM	Multimodal medical imaging, clinical data	AD diagnosis	*4,26*
	VGG-TSwinformer, CNN, LSTM	Magnetic resonance images of brain structures	Detection of early AD	*23,25,28,29,30,32*
	EfficientNet-b2	Retinal image	Detection of AD	*27*
	VGG, ResNet	Eye tracking data	Evaluation of the efficacy of drug therapy in AD	*31*
	CNN-LSTM	Functional near-infrared spectral data	Prediction of AD inhibitors	*33*
	Graph neural networks	Drug and target data	Detection of AD	*34*

on prediction, detection, and treatment. Historically, AD research and diagnosis usually relied on highly specialized techniques and equipment, including CSF, biomarkers, MRI, PET, and DTI. However, the rapid advancement of DL has opened new avenues. Presently, AD can be predicted using eye-tracking data, retinal images, and non-invasive near-infrared technology, offering a more accessible path to early intervention. In addition, DL technology can be used to determine drug efficacy by observing drug-inhibitor interactions, providing a convenient way to personalize treatment. The future will presumably offer more portable and advanced approaches for the prediction, detection, and treatment of AD. DL models are sure to continue playing a pivotal role in this endeavor.

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