Research Hotspots and Frontier Trends of Artificial Intelligence in Clinical Diagnosis and Treatment of Alzheimer's Disease: A Bibliometric Analysis of the Past 20 Years (Postprint)

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Abstract

Background Currently, the number of research papers applying artificial intelligence to Alzheimer's disease (AD) has increased significantly, and it is of great importance to identify the latest research hotspots and future development trends in this field. Objective To summarize relevant research on the application of artificial intelligence to AD and elucidate research hotspots and future research trends from 2004 to 2023 through bibliometric analysis. Methods Literature on the application of artificial intelligence to AD was retrieved from the Web of Science Core Collection database from January 2004 to June 2023. Microsoft Office Excel, CiteSpace, and VOSviewer software were employed to conduct visualization analysis of publication volume, countries, authors, institutions, keywords, and co-citation networks. Results A total of 3,189 publications were included. Since 2004, the number of publications on AI application in AD has increased steadily, entering a phase of rapid growth from 2015 and peaking at over 600 publications. A total of 94 countries, 3,930 institutions, 13,563 authors, and 52,019 cited authors contributed to this research. Among them, the United States and China are in a leading position in this field; Korea University ranked first in publication volume. Additionally, ZHANG DAOQIAG, LIU MINGXIA, SUK HEUNG-IL, and CLIFFFORD R. JACK JR are not only prolific authors but also the most-cited authors. According to visualization analysis of keywords and citation results, it was found that AD diagnosis and disease stage classification, and predicting risk factors for AD are current research hotspots, while task analysis represents a future research trend for AI application in AD. Conclusion The application of artificial intelligence to AD has attracted widespread attention from researchers worldwide. AD diagnosis and disease stage classification, and predicting risk factors for AD are current research hotspots, while assistance in drug development, personalized treatment and care, and improving AI algorithm performance within task analysis may become future research trends.

Full Text

The Hotspots and Frontier Trends of Artificial Intelligence in the Clinical Diagnosis and Treatment of Alzheimer's Disease: Bibliometric Analysis of the Past 20 Years

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Abstract

Background: Currently, the number of research papers on the application of artificial intelligence (AI) to Alzheimer's disease (AD) has increased significantly, making it important to clarify the latest research hotspots and future development trends in this field. **Objective:** To summarize relevant research on AI applications in AD through bibliometric analysis and identify research hotspots and trends from 2004 to 2023. **Method:** Literature on AI applications in AD from January 2004 to June 2023 was searched in the Web of Science Core Collection database. Microsoft Office Excel, CiteSpace, and VOSviewer software were used to visually analyze publication volumes, countries, authors, institutions, keywords, and co-citation networks. **Results:** Ultimately, 3,189 articles were included. The number of publications on AI applications in AD has steadily increased since 2004 and entered a rapid growth phase after 2015, with annual outputs exceeding 600 articles at its peak. A total of 94 countries, 3,930 institutions, 13,563 authors, and 52,019 cited authors contributed to this research. Among them, the United States and China lead the field; South Korean universities ranked first in publication output; additionally, ZHANG DAOQIANG, LIU MINGXIA, SUK HEUNG-IL, and CLIFFORD R. JACK JR were not only highly productive authors but also the most frequently cited. Visualization analysis of keywords and citations revealed that AD diagnosis and disease staging, as well as prediction of AD risk factors, are current research hotspots, while task analysis represents a future trend in AI applications for AD. **Conclusion:** AI applications in AD have attracted widespread attention from researchers worldwide. AD diagnosis and disease staging, along with prediction of AD risk factors, are current research hotspots, while auxiliary drug

development, personalized treatment and care, and improvement of AI algorithm performance in task analysis may become future research trends.

Key words: Alzheimer disease; Dementia; Artificial intelligence; CiteSpace; VOSviewer; Bibliometrics

Alzheimer's disease (AD) is the most common type of dementia in older adults, clinically characterized by progressive decline in memory, language, and other cognitive functions. Its pathological features primarily include amyloid plaques, phosphorylated tau protein tangles, and neurodegeneration [?, ?]. As global population aging intensifies, the prevalence of AD is expected to increase exponentially in the coming years, making it one of the most impactful and costly diseases of this century [?]. Unfortunately, due to the clinical heterogeneity and pathological complexity of AD, no effective treatment currently exists, and existing therapeutic approaches can only delay disease progression [?]. Therefore, early screening and treatment are crucial for AD prevention and control. However, medical data from AD patients is characterized by complexity and vastness, posing significant challenges for analysis using traditional computational tools [?]. In recent years, artificial intelligence has developed rapidly, achieving major advances in AD diagnosis, prediction, disease staging, detection, and personalized treatment and care [?, ?, ?, ?]. By efficiently and accurately analyzing complex and large-scale medical data, AI can reduce the burden on healthcare workers. Nevertheless, with the dramatic increase in relevant publications on AI applications in AD, researchers face difficulty identifying the latest research hotspots and future development trends. This study employs bibliometric methods to conduct an in-depth analysis of research on AI applications in AD from 2004 to 2023, aiming to reveal research hotspots and development trends from a visual perspective, thereby providing new ideas and clues for future research.

1.1 Literature Sources and Search Strategy

The Web of Science Core Collection (WOSCC) database was systematically searched, with citation indexes including Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), Current Chemical Reactions Expanded (CCR-EXPAND), and Index Chemicus (IC). The search timeframe covered January 2004 to June 2023. Inclusion criteria were: (1) relevance to AD and AI themes; (2) English language; (3) article type as Article or Review. Exclusion criteria were: (1) irrelevant to research themes or content; (2) duplicate publications; (3) unknown author or affiliation information.

The initial search yielded 11,864 articles. After screening by three researchers based on titles, abstracts, and full texts, 3,189 articles were ultimately included, comprising 2,964 Articles (92.94%) and 225 Review Articles (7.06%). The search terms and strategy are detailed in Table 1 and Figure 1 [FIGURE:1].

Table 1 Search terms for artificial intelligence applications in the field of AD from 2004 to 2023

Category	Search Terms
AD-related	dementia; Alzheimer Disease; Alzheimer's Disease
AI-related	artificial intelligence; machine intelligence; computational intelligence; intelligent learning; machine learning; deep learning; neural learning; feature* learning; supervised learning; neural network*; unsupervised clustering; feature* mining; data mining; deep network*; image* segmentation; graph mining; feature* selection; data clustering; semantic segmentation; knowledge graph; feature* extraction; big data; expert* system*; bayes* network; neural nets model

1.2 Statistical Methods

Microsoft Office Excel 2019, CiteSpace (version 6.2.R6), and VOSviewer (version 1.6.19) were used to visually analyze publication volumes, countries, authors, institutions, keywords, and co-citation networks. Microsoft Office Excel 2019 was used for statistical analysis of annual, institutional, and author frequencies. CiteSpace was employed for keyword co-occurrence and burst detection analyses. VOSviewer was utilized for network analysis of countries, institutions, authors, and co-cited literature.

2.1 Annual Publication Volume Analysis

From 2004 to 2023, the annual publication volume of AI applications in AD showed an overall growth trend according to curve fitting analysis ($R^2 = 0.9679$). Based on this growth pattern, two phases can be identified: 2004–2014 represents a slow growth phase, with annual publications consistently below 100, indicating the field was in its infancy; while 2015–2023 represents a rapid growth phase, with annual publications exceeding 600 at its peak (Figure 2 [FIGURE:2]).

2.2 Country/Region Analysis

A total of 94 countries published research articles on AI applications in AD. The United States ranked first globally in publication output (876 articles, 27.47% of total), followed by China (845 articles, 26.50%). The combined output of these two countries accounted for over half of global publications. However, in terms of total citations, the United States (n = 33,613) surpassed China (n = 15,172).

2.3 Institution Analysis

Globally, 3,930 institutions contributed to AI research in AD, but only four institutions published more than 50 articles. South Korean universities had the highest publication count (80 articles), followed by the University of North Carolina, USA (69 articles) and the Chinese Academy of Sciences (61 articles). In terms of total citations, the University of North Carolina ranked first (4,954 citations), followed by South Korean universities (4,833 citations) and University College London (2,660 citations). Regarding collaboration, South Korean universities and the University of North Carolina demonstrated particularly close cooperative relationships, while collaboration among other high-output institutions remains to be strengthened (Figure 3

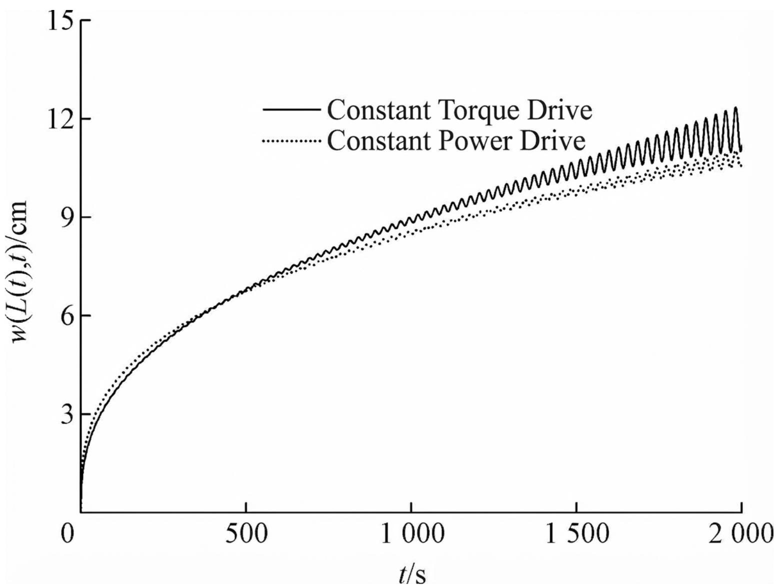

Figure 1: Figure 3

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2.4 Author Analysis

A total of 13,563 authors contributed to AI applications in AD research. The top three authors by publication volume were SHEN DINGGANG (72 articles), ZHANG DAOQIANG (32 articles), and LIU MINGXIA (30 articles) (Table 2). Additionally, these highly productive authors maintained close collaborative relationships (Figure 4

), particularly among authors within the same cluster, such as the top three authors and the network formed among THOMPSON PAUL M, WANG YALIN, and YE JIEPING.

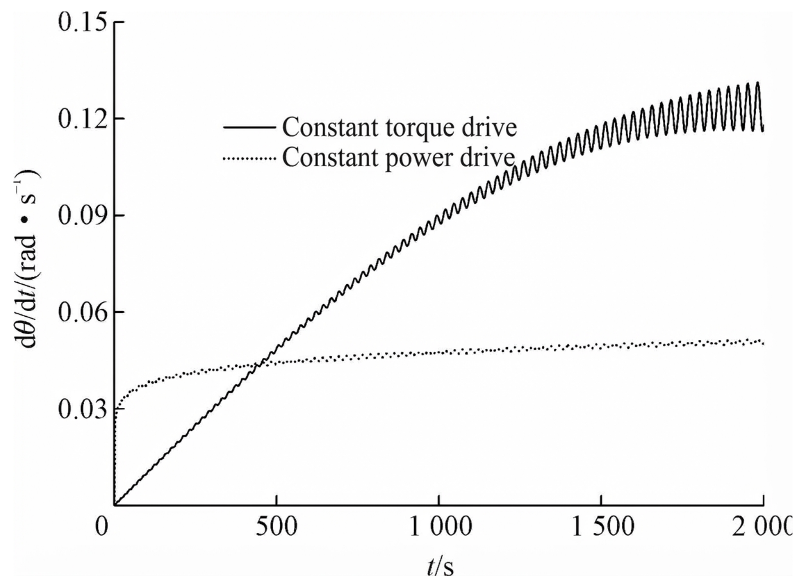

Figure 2: Figure 4

Table 2 Top 10 authors by publication volume

Author	Publications
SHEN DINGGANG	72
ZHANG DAOQIAG	32
LIU MINGXIA	30
THOMPSON PAUL M	28
SUK HEUNG-IL	27
WANG LEI	26
LEE KUN HO	25
WESTMAN ERIC	24
HAMPEL HARALD	23
CLIFFFORD R. JACK JR	22

2.5.1 Cited Author Analysis

A total of 52,019 cited authors contributed to AI applications in AD research, with 39 authors cited more than 200 times. The top three most frequently cited authors were CLIFFFORD R. JACK JR (1,388 citations), PETERSEN RONALD C (808 citations), and ZHANG DAOQIANG (600 citations) (Table 3). Combined with Table 2 analysis, ZHANG DAOQIAG, LIU MINGXIA, SUK HEUNG-IL, and CLIFFFORD R. JACK JR were not only highly productive but also highly cited authors.

Table 3 Top 10 authors by co-citation frequency

Co-cited Author	Citations
CLIFFFORD R. JACK JR	1,388
PETERSEN RONALD C	808
ZHANG DAOQIANG	600
SUK HEUNG-IL	588
FISCHL BRUCE	456
ASHBURNER JOHN	398
BRAAK HEIKO	367
LIU MANHUA	298
LIU MINGXIA	287
DUBOIS BRUNO	265

2.5.2 Cited Literature Analysis

Cited literature represents an important indicator for evaluating current research hotspots. All articles in this study cited a total of 87,819 references, with Figure 5 [FIGURE:5] showing the network analysis of the top 10 co-cited articles. The most frequently co-cited article was "Hierarchical feature representation and multimodal fusion with deep learning for AD/MCI diagnosis" by SUK et al. [**?**], published in *NeuroImage*, which proposed a novel method for advanced latent and shared feature representation from neuroimaging modalities to improve AD and mild cognitive impairment (MCI) diagnosis accuracy. The second most cited was "Machine learning framework for early MRI-based Alzheimer's conversion prediction in MCI subjects" by MORADI et al. [**?**], which used supervised learning to construct a novel MRI-based framework for predicting MCI-to-AD conversion. The third most cited was "Multimodal Neuroimaging Feature Learning for Multiclass Diagnosis of Alzheimer's Disease" by LIU et al. [**?**], which designed a diagnostic framework with deep learning architecture that extracts information from multiple data modalities, achieving performance improvements in AD data classification. These findings indicate that AI applications in AD primarily focus on diagnosis, disease staging, and prediction.

2.6.1 Keyword Co-occurrence Analysis: 2004–2014

Keyword co-occurrence analysis reflects research hotspots in an academic field. Based on overall publication trends, this study conducted separate co-occurrence analyses for 2004–2014 and 2015–2023. Using CiteSpace for keyword co-occurrence mapping of 2004–2014, 107 nodes and 279 links were generated with a network density of 0.0242 (Figure 6 [FIGURE:6]). Excluding terms similar to AD, the central keywords during this period were classification, diagnosis, MRI, atrophy, segmentation, brain, pattern, and support vector machine, indicating that research focused on using MRI, segmentation techniques, brain patterns, and support vector machine classification models for AD disease staging and diagnosis.

2.6.2 Keyword Co-occurrence Analysis: 2015–2023

CiteSpace analysis of 2015–2023 keywords generated 182 nodes and 550 links with a network density of 0.0118 (Figure 7 [FIGURE:7]). During this period, keywords such as machine learning, deep learning, prediction, feature selection, biomarker, segmentation, conversion, convolutional neural network, and risk emerged with dramatically increased frequency, particularly machine learning and deep learning with 460 and 322 occurrences respectively, indicating that research emphasis shifted to improving algorithm performance to assist AD diagnosis and disease staging, with greater attention to predicting AD risk factors.

Additionally, based on AI models used and their functions in AD, keywords were categorized into two groups (Table 4). The top five AI models were machine learning, deep learning, convolutional neural network, neural network, and support vector machine; the top five functions were classification, diagnosis, risk prediction, feature extraction, and image segmentation.

Table 4 Hot keywords from 2015 to 2023

Category	Keyword	Frequency
AI Models	machine learning (机器学习)	460
	deep learning (深度学习)	322
	convolutional neural network (卷积神经网络)	215
	neural network (神经网络)	198
	support vector machine (支持向量机)	156
Functions	classification (分类)	398
	diagnosis (诊断)	367
	prediction (预测)	289
	feature selection (特征提取)	234
	Segmentation (分割)	198

2.6.3 Keyword Burst Analysis

Keyword burst refers to keywords frequently cited within a specific period, which can explore development trends in a field. CiteSpace identified the top 25 most emergent keywords (Figure 8 [FIGURE:8]). In the early stage, segmentation (2007–2017) and voxel-based morphometry (2008–2018) showed long burst durations, indicating their significant influence on the field. Since 2016, keywords such as computer-aided diagnosis, big data, and feature representation have increased, demonstrating growing exploration of the field with deepening research methods (2016–2023). Furthermore, keywords artificial intelligence, deep learning, and task analysis have continued to burst until present. Further analysis revealed that task analysis includes auxiliary drug development, personalized treatment and care, and improving AI algorithm performance, which may become future research hotspots.

3.1 Research Status Analysis

The results show that literature on AI applications in AD has steadily increased, likely due to rapid AI development providing unprecedented possibilities for disease prediction, diagnosis, and classification [?]. According to curve fitting predictions, more countries and researchers will engage in AD AI research in the future. Based on country analysis, the United States and China lead the field; however, China lags behind the United States in citation frequency. Therefore, China should focus more on improving academic quality to advance research. Regarding institutions, although domestic renowned universities such as Shanghai Jiao Tong University and University of Chinese Academy of Sciences have published multiple high-impact papers, collaboration with other institutions remains insufficient. The collaboration networks among countries, institutions, and authors appear relatively sparse, lacking extensive domestic and international cooperation. This suggests China should actively recruit and cultivate talented individuals to strengthen cooperation and exchange among authors, institutions, and countries to advance AI development in AD.

3.2 Current Research Hotspots

Based on cited literature and keyword co-occurrence analyses, this study identified research hotspots in AI applications for AD, primarily categorized into:

3.2.1 AD Diagnosis and Disease Staging Currently, neuroimaging is a critical tool for diagnosing and staging neurodegenerative diseases like AD [?]. However, analyzing and interpreting large volumes of brain imaging data presents challenges [?]. Consequently, AI combined with multi-feature neuroimaging data for AD diagnosis and staging has attracted researchers' attention [?, ?, ?]. ZHANG et al. [?] were among the early researchers to propose using machine learning models for AD diagnosis, achieving 93.2% accuracy using a linear support vector machine classifier with three biomarkers to classify and diagnose normal subjects versus AD. However, machine learning models require cumbersome and time-consuming steps including feature extraction, selection, and dimensionality reduction, which deep learning overcomes [?]. Some researchers [?] introduced a CNN-based deep learning model using 2D brain MRI images as input, demonstrating diagnostic accuracy comparable to AD specialists. Notably, beyond brain imaging for AD diagnosis, CHEUNG et al. [?] recently developed a novel deep learning model based on retinal imaging for AD diagnosis and classification, achieving 79.6%–92.1% accuracy in test datasets. Future advances in AI and neuroimaging promise more accurate and efficient diagnostic and classification tools to improve AD diagnosis.

3.2.2 Prediction of AD Risk Factors Pathological changes in AD patients are often insidious before diagnosis, necessitating early and precise prediction for high-risk populations. However, traditional risk prediction models had high error rates for personalized AD risk assessment [?], which AI has improved. In a cohort study, YOU et al. [?] developed a machine learning model for multi-factor AD prediction including age, ApoE 4, leg fat percentage, and medication frequency as 10 conventional and novel predictors, demonstrating precise prediction of high-risk individuals for AD within 5, 10, or more years. To better understand disease-related genetic risks, ZHOU et al. [?] used deep learning to develop an effective model for predicting polygenic risk. Additionally, identifying predictors for MCI-to-AD conversion represents an important research area [?, ?]. LIN et al. [?] developed an AI grading method that effectively fused multimodal data to precisely predict MCI-to-AD conversion within 3 years. Deep learning combined with neuroimaging data achieved up to 84.2% accuracy for predicting MCI-to-AD conversion [?]. Unlike previous studies, recent research [?, ?] predicted AD risk by combining vocal features and chromatic pupillometry with AI. In summary, AI applications show enormous potential for AD risk prediction, improving prediction accuracy and enabling more comprehensive risk assessment through multimodal data integration.

3.3 Future Research Trends

Based on keyword burst analysis, task analysis in AI represents a future development trend, specifically including auxiliary drug development, personalized treatment and care, and improving AI algorithm performance.

3.3.1 Auxiliary Drug Development The drug development process for neurological diseases like AD generates massive and complex data, making effective integration, correlation, and analysis of large-scale data a core challenge [?]. The rise of AI technology provides possibilities for deep mining of valuable new information. Recent studies have applied AI to AD drug development, including target identification, virtual screening, and drug repurposing prediction. For example, TSUJI et al. [?] developed a deep learning-based computational framework that successfully predicted potential novel drug targets for AD, identifying key genes (such as spleen tyrosine kinase and epidermal growth factor receptor) as new therapeutic targets. Additionally, DAS et al. [?] used fully automated AI-assisted ligand screening tools during virtual screening to successfully identify compounds that may inhibit tau protein aggregation from vast compound libraries. For AD drug repurposing, FANG et al. [?] proposed a network-based AI method that successfully identified pioglitazone as a potentially effective AD drug by integrating multi-omics data and drug target networks with diverse information. Thus, AI holds promise for advancing AD drug development.

3.3.2 Personalized Treatment and Care With rapid AI development, researchers have begun applying this advanced technology to provide personalized treatment and care for AD patients, demonstrating effectiveness and feasibility

[?]. One study designed a computer-based intervention management system for dementia patients that analyzes individual needs to generate personalized treatment task lists, helping healthcare workers better manage and care for dementia patients to alleviate symptoms and improve quality of life [?]. Additionally, research teams developed digital reminiscence therapy applications using AI technology to generate nostalgic images or videos by analyzing AD patient information, thereby stimulating patient memory [?]. Using this program effectively reduced depressive symptoms in AD patients and increased their enthusiasm for social interaction. These findings suggest that AI technology can help better understand individual patient differences and provide personalized treatment and care plans.

3.3.3 Improving AI Algorithm Performance As algorithm models mature and develop, AI demonstrates enormous potential in AD clinical diagnosis and treatment. However, AI algorithms face many technical challenges, including poor generalization performance—for example, machine learning models can accurately classify schizophrenia patients from specific hospitals but show poor generalization when applied to samples from other hospitals [?]. Additionally, AI algorithm models often lack transparency, making it difficult to directly explain their prediction results and decision-making processes [?], which may lead to researcher distrust in AI systems. Recently, scholars have suggested that future improvements could combine deep learning with ensemble learning or merge other hybrid data types (such as omics data) to enhance model performance and transparency [?, ?]. Meanwhile, AI algorithms rely on large datasets for training, but predictions may be erroneous if data are non-standard or sample sizes are small. Therefore, improving dataset sample size, quality, and standardization represents an important challenge for AI clinical applications. In summary, researchers need to enhance algorithm performance to promote AI development and application in AD clinical diagnosis and treatment.

4 Research Limitations

This study comprehensively analyzed literature on AI applications in AD using bibliometric methods. However, several limitations should be considered for future research. First, this study only collected data from WOSCC, potentially overlooking representative literature from other databases. Second, the study included only English-language literature, omitting publications in other languages. Finally, recently published high-quality articles may not yet have been identified due to low citation frequencies.

5 Summary and Outlook

In summary, this study conducted an in-depth analysis of literature on AI applications in AD through bibliometrics. The results reveal that AI has been widely applied in AD, with current research hotspots focusing on AD diagnosis and disease staging, prediction of AD risk factors, while auxiliary drug development, personalized patient treatment and care, and improvement of AI algorithm performance may become future trends. Additionally, China and the USA lead this field, demonstrating their academic influence. However, urgent need exists to strengthen cooperation among countries, institutions, and authors to advance the field and enable more AD patients to benefit.

Author Contributions: YU Ruxia and JIANG Jing conceived the research and constructed the overall study design, responsible for manuscript writing and revision; WANG Qiucheng and WANG Yue collected, screened, and organized research data for analysis and reproducibility; ZHAO Xiaoyue formatted figures and revised text.

Conflicts of Interest: None declared.

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