

# Research status, hotspots and trends of acupuncture and moxibustion in the treatment of Alzheimer's disease

## A bibliometric analysis

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### Abstract

**Background:** Acupuncture and moxibustion (AM) are utilized to treat Alzheimer's disease (AD). However, no bibliometric analysis has explored this issue. Thus, this study investigated the status, hotspots and trends of AM in the treatment of AD.

**Methods:** CiteSpace and VOSviewer softwares were used to analyze the literature on the AM for AD in the Web of Science Core Collection database. We analyzed the data of countries/regions, institutions, journals, authors, keywords, and cited references.

**Results:** After removing duplicates, 193 articles were retrieved. The number of publications on this topic has increased gradually. The most productive and collaborative country was China (143 documents), followed by South Korea (19). The top 3 active academic institutions were Beijing University of Chinese Medicine, Capital Medicine University, and Guangzhou University of Chinese Medicine. The most productive journal was Evidence-based Complementary and Alternative Medicine (13 documents), followed by the Frontiers in Aging Neuroscience (10), Medicine (10), and Neural Regeneration Research (10). The top 3 co-cited journals were Evidence-based Complementary and Alternative Medicine (156 citations), Acupuncture Electro-therapeutics Research (152), and Acupuncture in Medicine (146). The research hotspots in this domain are dementia, memory, hippocampus, mouse models, and Parkinson's disease. Major frontiers are comparing the therapeutic effects of acupuncture and donepezil and electroacupuncture at different frequencies in this field.

**Conclusion:** This bibliometric study identified relevant hotspots and trends in research on AM in the treatment of AD, which can provide researchers with key information in this domain and help further explore new research directions.

**Abbreviations:** AD = Alzheimer's disease, AM = acupuncture and moxibustion, EA = electro-acupuncture, WOSCC = Web of Science Core Collection.

**Keywords:** acupuncture, Alzheimer's disease, bibliometric analysis, CiteSpace, moxibustion, Web of Science Core Collection

## 1. Introduction

Alzheimer's disease (AD) is the most common and prevalent neurodegenerative disorder among elderly population around the world.<sup>[1,2]</sup> It accounts for approximately 80% of all dementia cases. It is characterized by a progressive decline in memory and cognitive function, changes in personality and behavior, and other neuropsychiatric syndromes.<sup>[3-5]</sup> It was reported that

about 44 million population suffered from AD globally in 2015, with increase of prevalence in line with the aging population.<sup>[6-9]</sup> It has been estimated that about 65.7 million people will experience dementia by 2030, and 115.4 million in 2050 around the world.<sup>[7-10]</sup> Currently, it is a serious public health problem worldwide.<sup>[11]</sup>

Although a variety of studies have investigated AD, its pathogenesis and mechanisms are complicated and remain

JH-Y, X-LL, R-XG, and Q-HZ contributed equally to this work.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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largely unclear.<sup>[12]</sup> To date, there is no cure for AD. Although currently available treatments include gene therapy, immunotherapy, peptidomimetics, metal chelators, probiotics, and quantum dots, their efficacy remains limited.<sup>[13–20]</sup> Acupuncture and moxibustion (AM) have been widely used to ameliorate symptoms and improve the overall quality of life of patients with AD.<sup>[21–29]</sup> However, no study has explored the status, hotspots, and trends of AM in the treatment of AD. Therefore, this bibliometric analysis investigated the research status, hotspots, and trends of AM in the management of AD using VOSviewer and CiteSpace.

Vosviewer software is a visual bibliometric network software developed in 2009 by van Eck and Waltman at Leiden University in the Netherlands.<sup>[30]</sup> CiteSpace software is a visual information analysis software developed by Professor Chen Chaomei of Drexel University, which realizes multi-visual knowledge mapping in various research fields<sup>[31]</sup> and help scholars fully understand the research status, hotspots, and trends. To the best of our knowledge, no bibliometric study focusing on AM for AD management has been published. Therefore, based on the Web of Science Core Collection (WOSCC) database, this bibliometric analysis investigated the research status, hotspots, and trends of AM in the treatment of AD using VOSviewer and CiteSpace.

## 2. Methods

### 2.1. Ethic statement

This study did not require ethical approval because it was conducted based on the secondary literature analysis.

### 2.2. Data acquisition and retrieval strategy

Eligible publications related to AM for the treatment of AD were retrieved from the WOSCC database between 1900 and 2022. On May 25, 2022, we input search terms “Alzheimer’s disease”, “Alzheimer disease”, “Alzheimer Dementias”, “Senile Dementia”, “Acupuncture”, “Acupuncture Therapy”, “Acupuncture Treatment”, “Pharmacoacupuncture Treatment”, “acupuncture point”, “Acupotomy”, “electroacupuncture”, “electro-acupuncture”, “body acupuncture”, “Manual Acupuncture”, “auricular”, “Auricular Acupuncture”, “auricular needle”, “Ear Acupuncture”, “Moxibustion”, “Moxabustion”, “acupoint injection”, “catgut embedding”, “catgut implantation at acupoint”, “embedding thread”, and “Warm Acupuncture”. The search language was limited to English.

Two researchers (JH-Y and RH-G) independently carried out literature selection. Any disagreement was resolved by a third researcher (XL-L) through a discussion. In total, 203 studies were conducted. After eliminating 10 irrelevant search topics, 193 remaining publications, including articles (143) and reviews (50), were utilized for subsequent analysis. All selected records were exported in plain text format (Win, UTF-8) and analyzed using CiteSpace (5.8.R3) (Drexel University, Philadelphia, PA) and VOSviewer (1.6.17) (Leiden University, Leiden, Netherlands). A flowchart of the literature selection process is shown in Figure 1.

### 2.3. Statistical and analytical methods

Trends in the publications and types of articles were analyzed using Microsoft Excel 97. Tableau software (10.5) was used to

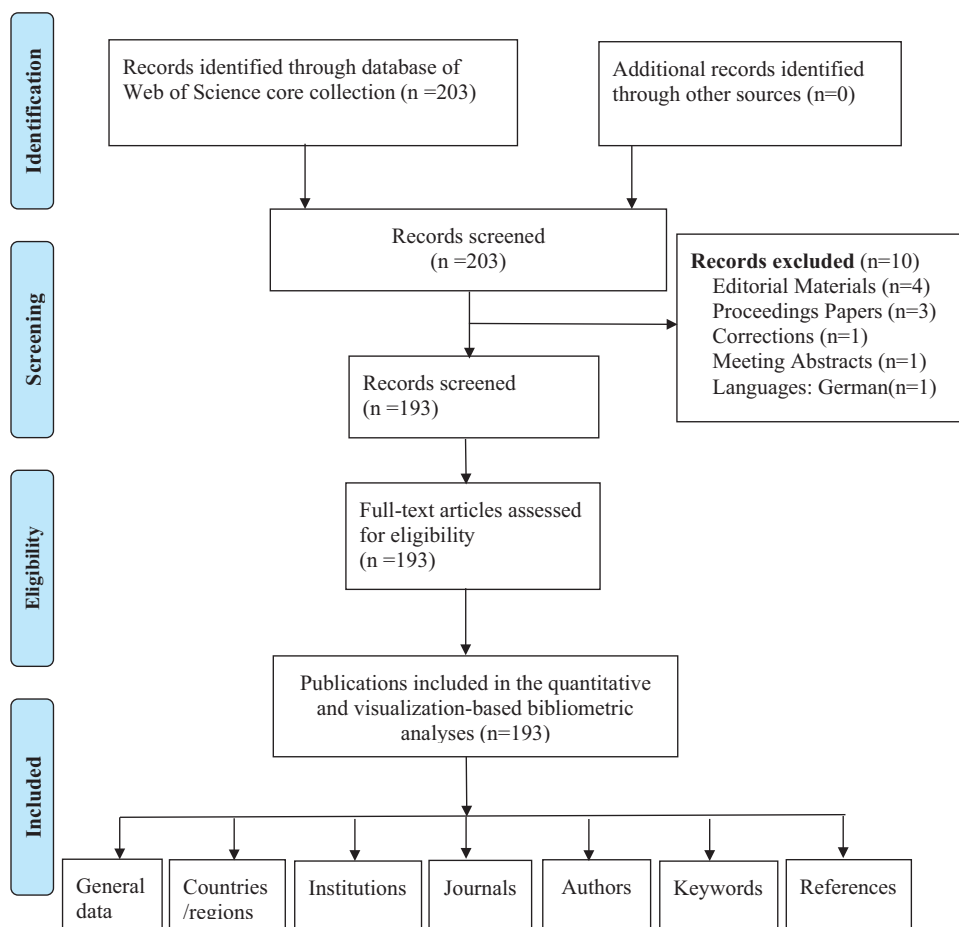


Figure 1. Procedure of study selection.

analyze the country/region global distribution maps. Vosviewer software (1.6.17) was employed to generate visual maps and conduct a bibliometric analysis of citations of countries/regions, institutions, authors, journals, references, and keywords. In the visual map, each node in the map represents the corresponding country/region, institution, author, journal, reference, and keyword. Links between nodes represent collaboration. CiteSpace was used to construct a dual-map overlay analysis for countries/regions, institutions, authors, keywords, co-cited references, and co-cited journals with nodes and links. The parameters of CiteSpace were set as follows: time span (1900–2022), years per slice (1); text processing: term source (title, abstract, author keywords, keywords plus); term type, links, and selection criteria default; node type (keyword and reference) for analysis; and pruning (pathfinder, pruning sliced networks, and pruning the merged network).

### 3. Results

#### 3.1. General description

After removing 10 irrelevant search records, a total of 193 publications related to AC for AD were identified in the WOSCC database from 1992 to 2022 and were included in the bibliometric analysis involving 20 countries/regions, 236 institutions, 89 journals and 911 authors. The types of included publications were as follows: articles (143), review articles (50), editorial materials (4), proceedings papers (3), corrections (1), and meeting abstracts (1). Articles and review articles accounted for 96% of the total publications (Fig. 2).

#### 3.2. Global publication trend

The number of publications on AM treatment for AD annually is shown in Figure 2. This number has increased annually since 2008, and its annual growth trend is in line with the fitting curve  $y = 1.6068x - 4.5425$ . Between 1992 and 2010, the

annual publications ranged from 0 to 3 articles, 12 articles in 18 years, and fewer than 1 article per year. Between 2012 and 2016, 6 to 11 articles were published annually, and 44 articles were published in 5 years, with an average of 8.8 articles per year. Between 2017 and 2021, there were more than 15 publications annually, with a total of 129 articles published in 5 years and an average of 45.8 articles published annually. Therefore, we divided the entire study period into 3 stages according to the number of annual publications: the initial stage (before 2010), transition stage (between 2012 and 2016), and rapid development stage (from 2017 to 2021) (Fig. 2). At initial stage, few studies were published, indicating a limited focus on the field. At the transition stage, more publications regarding AM in the treatment of AD have been published, exerting increasing attention to this issue. During the rapid development stage, increasing number of studies have been published. Since the date of search is up to May 25, 2022, the statistics of the literature in 2022 are not complete, but the fitting curve shows that the literature in the following years is increasing.

#### 3.3. Contribution of countries/regions

In this analysis, 20 countries/regions contributed to the research on AC for AD. A cooperative network for the countries/regions is illustrated by VOSviewer in Figure 3A and their distribution map is presented in Figure 3B. There were 11 nodes and 17 connections. Each node represents a country/region, and the connection between countries/regions indicates collaboration. The node sizes represent the number of publications, and connections between nodes represent collaboration, with a larger node suggesting more publications, a more connection indicating more collaborations, and a wider connection signifying a tighter collaboration. China has the largest number of nodes, followed by the USA and South Korea. China and the USA had the strongest collaborative networks with the greatest overall link strength (total link strength = 19), indicating the most active collaboration between the 2 countries.

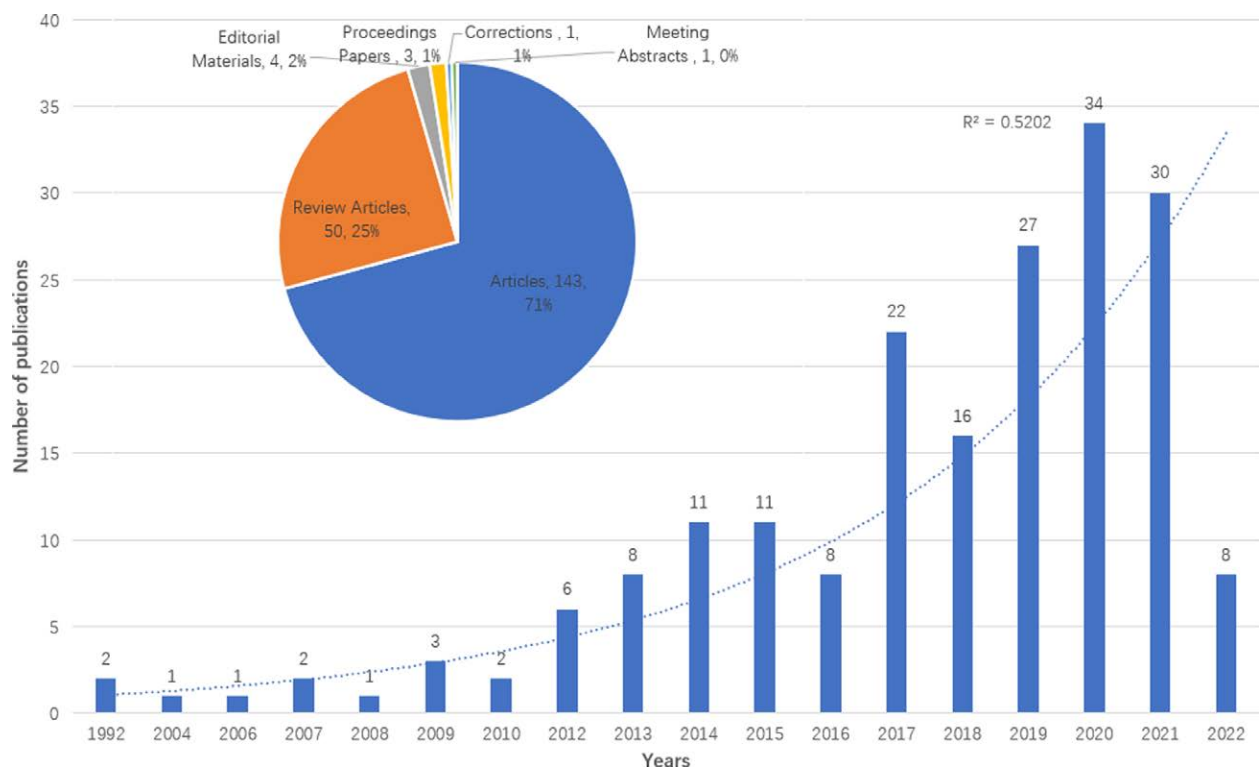


Figure 2. Number of annual publications.



**Figure 3.** (A) Cooperative network of countries/regions. (B) Distribution map of countries/regions.

The top 10 productive countries/regions are listed in Table 1. The most productive country/region was China (143 publications, 74.1% of all articles), followed by South Korea (19, 9.8%) and the USA (16, 8.3%). China had the most citations (1852 citations), followed by the USA (381), and South Korea (279).

### 3.4. Contribution of institutions

Cooperative network of institutions focusing on AC for AD was generated using VOSviewer (Fig. 4). There were 47 nodes and 112 connections. Each node represents an institution and its size corresponds to the number of publications. The connection between nodes represents cooperation, with a wider connection suggesting a tighter cooperation.

The top 10 institutions with the most publications are listed in Table 2. The most productive institution was Beijing University of Chinese Medicine (36 publications), followed by Capital Medicine University (23) and Guangzhou University of

Chinese Medicine (16). The highest average citation was Capital Medicine University (25.3) and the highest centrality (0.16), which indicated that it had a high influence and intermediary role.

### 3.5. Journal analysis

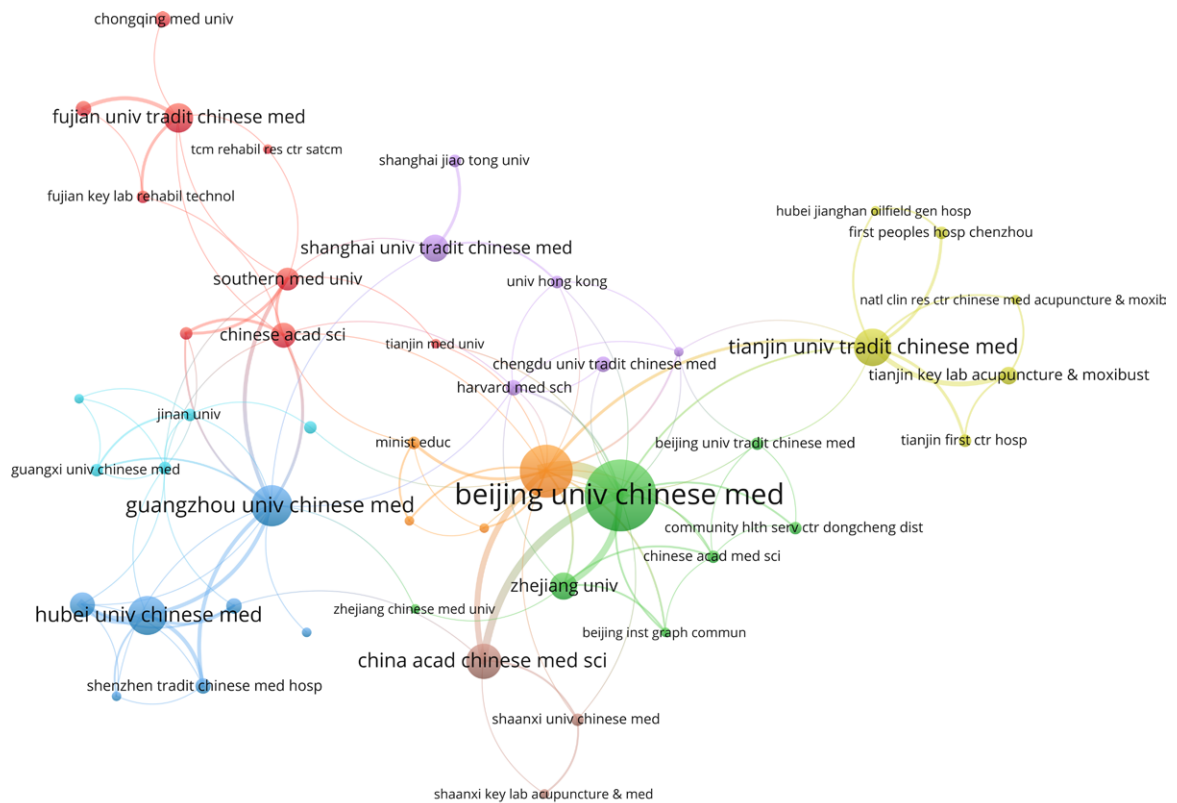
Cooperative network of journals on AC for AD was generated using VOSviewer (Fig. 5). There were 10 nodes and 38 links. Each node stands for a journal and its size corresponds to the number of publications in the journal. The link between nodes represents collaboration, with a wider link presenting a tighter collaboration.

The top 10 productive journals are listed in Table 3. In total, 193 articles were published in 89 journals. Of these, the most productive and cited journals were Evidence-based Complementary and Alternative Medicine (13 articles, 156 citations), followed by Frontiers in Aging Neuroscience (10, 118), Medicine (10, 128), and Neural Regeneration Research (10,

**Table 1**  
**Top 10 productive countries/regions.**

Ranking	Country/region	Documents	Total citations	Citations/paper
1	China	143	1852	13.0
2	South Korea	19	279	14.7
3	USA	16	381	3.7
4	Taiwan	12	104	8.7
5	Italy	4	54	13.5
6	UK	3	256	85.3
7	Germany	2	13	6.5
8	Australia	2	30	15.0
9	Ukraine	2	25	17.5
10	France	1	12	6.0

China = the People's Republic of China, UK = The United Kingdom of Great Britain and Northern Ireland, USA = United States of America.



**Figure 4.** Cooperative network of institution analysis.

9.5). It is suggested that these journals pay more attention to the research in the field of AM treatment for AD.

Other journals have published fewer than 10 articles on Acupuncture Electro-therapeutics Research. Although it published fewer than 10 articles, its average number of citations was the highest, indicating that more attention has been paid to the research results or research directions published in this journal. The top 10 publications were distributed in the first quartile (Q1, 2 articles), second quartile (Q2, 3 articles), third quartile (Q3, 2 articles), and fourth quartile (Q4, 3 articles), with an average impact factor of 3.011, implying that the quality of these journals is quite low.

**3.6. Contribution of authors**

A cooperative network of authors on AC for AD was created using VOSviewer (Fig. 6). There were 41 nodes and 170 links.

Each node represents an author and its size corresponds to the number of publications. The link between nodes signifies collaboration, with a wider link suggesting a closer collaboration.

The top 10 productive authors are listed in Table 4. All of them came from China, and the most productive authors were Zhi-gang Li (15 articles, 174 citations), followed by Jing Jiang (11, 110), and Chun-zhi Tang (9, 75), suggesting that these authors have performed much research in the field of AM treatment for AD. Lan Zhao published 7 articles with the highest average number of citations (15.1). This indicates that the author has received considerable attention in the field of AM treatment for AD.

**3.7. Keyword analysis**

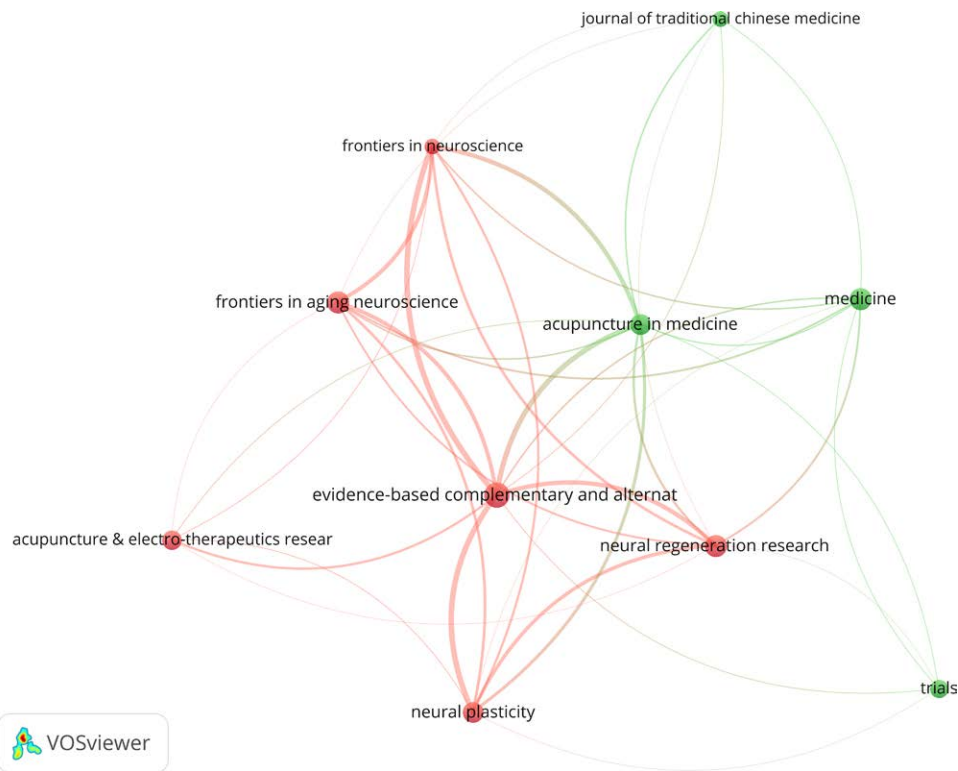
The keyword co-occurrence map of the AM treatment for AD is generated by CiteSpace in Figure 7A, involving 308 nodes and



**Table 2**  
**Top 10 productive institutions.**

Ranking	Institution	Documents	Total citations	Citations/paper	Centrality	Country
1	Beijing Univ Chinese Med	36	411	11.4	0.08	China
2	Capital Med Univ	23	581	25.3	0.16	China
3	Guangzhou Univ Chinese Med	16	84	5.3	0.11	China
4	Hubei Univ Chinese Med	15	115	7.7	0.01	China
5	Tianjin Univ Tradit Chinese Med	14	217	15.5	0.08	China
6	China Acad Chinese Med Sci	13	154	11.8	0.02	China
7	Fujian Univ Tradit Chinese Med	10	129	12.9	0.05	China
8	Korea Inst Oriental Med	9	107	11.9	0.01	Korea
9	China Med Univ	9	79	8.8	0.00	China
10	Zhejiang Univ	9	92	10.2	0.04	China

Acad = academic, China = The People's Republic of China, Med = medicine, Tradit = traditional, UK = The United Kingdom of Great Britain and Northern Ireland, Univ = University, USA = United States of America.



**Figure 5.** Cooperative network of journal analysis.

**Table 3**  
**Top 10 productive journals.**

Ranking	Journal	Documents	Citations	Citations/paper	IF* (Q)
1	Evidence-based Complementary and Alternative Medicine	13	156	12.0	2.630(Q2)
2	Frontiers in Aging Neuroscience	10	118	11.8	5.570(Q1)
3	Medicine	10	128	12.8	1.889(Q3)
4	Neural Regeneration Research	10	95	9.5	5.135(Q2)
5	Acupuncture in Medicine	9	146	16.2	2.267(Q2)
6	Neural Plasticity	9	34	3.8	3.599(Q3)
7	Acupuncture Electro-Therapeutics Research	8	152	19.0	0.143(Q4)
8	Trials	7	33	4.7	2.279(Q4)
9	Frontiers in Neuroscience	5	37	7.4	5.750(Q1)
10	Journal of Traditional Chinese Medicine	5	43	8.6	0.848(Q4)

IF = impact factor, Q = quartile category.

\*IF and Q in category according to Journal Citation Reports (2020).

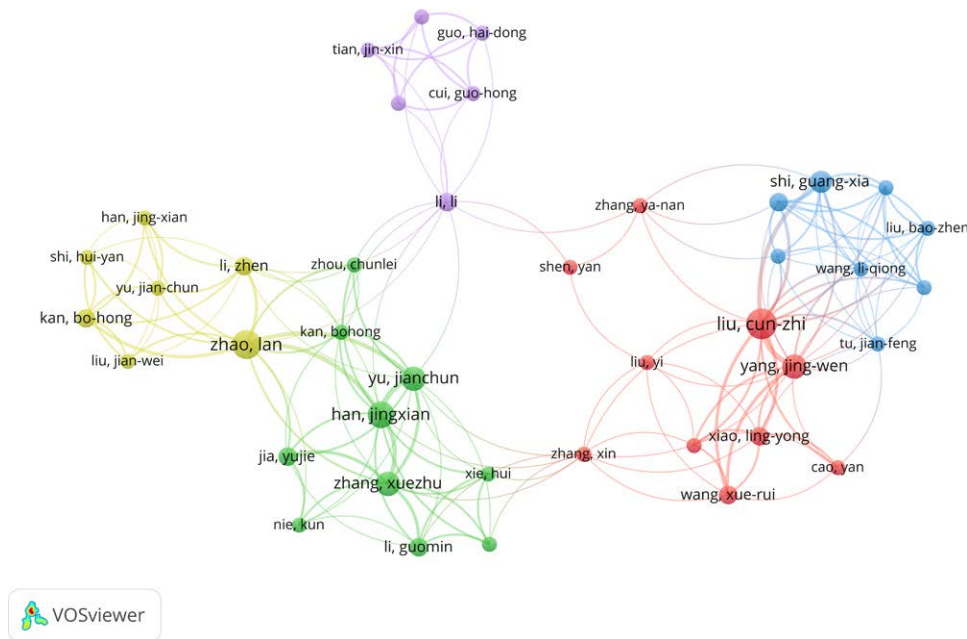


Figure 6. Cooperative network of author analysis.

**Table 4**  
Top 10 productive authors.

Ranking	Author	Documents	Citations	Citations/paper	Country
1	Li Zhigang	15	174	11.6	China
2	Jiang Jing	11	110	10.0	China
3	Tang Chunzhi	9	75	8.3	China
4	Kong Lihong	8	70	8.6	China
5	Liu Cunzhi	8	117	14.6	China
6	Tang Yinshan	7	92	13.1	China
7	Yu Chaochao	7	52	7.4	China
8	Zhao Lan	7	106	15.1	China
9	Tian Hailing	6	71	11.8	China
10	Xu Anping	6	30	5.0	China

1177 links. Each node represents keyword frequency and a link represents keyword co-occurrence, with a larger node denoting a higher frequency of keywords and a link representing co-occurrence between keywords.

The top 5 keyword co-occurrences and centrality are summarized in Table 5. The top frequency of keywords was AD (61), followed by acupuncture (39), dementia (36), memory (23), and the hippocampus (23). The keyword of high centrality indicates the hotspots and turning point of this field, and its value ranges from 0 to 1. A value of  $\geq 0.1$  shows higher centrality. The top 5 high centrality keywords were mouse model, AD, Parkinson’s disease, acupuncture, and dementia.

Keywords reflect the main research aims and objective of a study, and keywords clustering analysis represents the hot topics and research frontier in this field. A map of the keyword clustering analysis of AM treatment for AD is presented in Figure 7B.

This study had 9 major keywords clustering of “synaptic plasticity”, “fMRI”, “deficit”, “donepezil”, “herbal medicine”, “telomere”, “rat model”, “astrocyte”, and “randomized clinical trial”. As shown in Figure 7B from 1992 to 2022, there has been an increasing trend in research on AM treatment for AD since 2004. Mechanistic studies of AM, alone or in combination with donepezil and Chinese herbal medicine, to improve AD have been a research hotspot in this field, including research

on synaptic plasticity, astrocyte and telomere. Most studies are animal experiments and randomized controlled clinical trials, and fMRI is a major assessment tool.

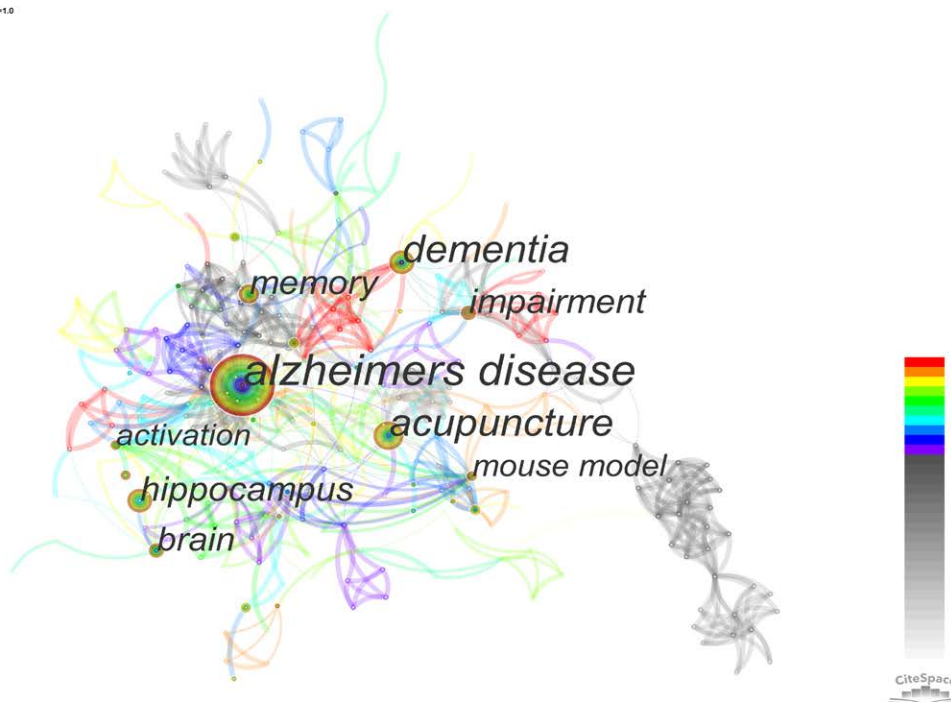
### 3.8. Co-cited reference analysis

A co-cited reference map was generated using CiteSpace (Fig. 8A), involving 529 nodes and 1564 links. Each node represents a co-cited reference, with a larger node indicating more frequent article citations. The link represents co-citation between studies, with a wider link suggesting a higher frequency of a co-cited reference.

The top 5 frequently co-cited references are listed in Table 6. The highest citation (34 citations) of co-cited references by Zhou, entitled “The effectiveness and safety of acupuncture for patients with Alzheimer disease: a systematic review and meta-analysis of randomized controlled trials” was published in *Medicine* in 2015.<sup>[25]</sup> This study provides high-level evidence of the efficacy and safety of AM in the treatment of AD.<sup>[25]</sup> The top centrality of the 5 co-cited references are presented in Table 7. The highest centrality (0.23) of co-cited reference with 2015 AD facts and figures was published by the Alzheimer’s Association in *Alzheimer’s & Dementia*.<sup>[32]</sup> This study discusses the incidence, prevalence, mortality, cost of care, and overall impact on nurses and society, and presents the current challenges in the diagnosis of AD.

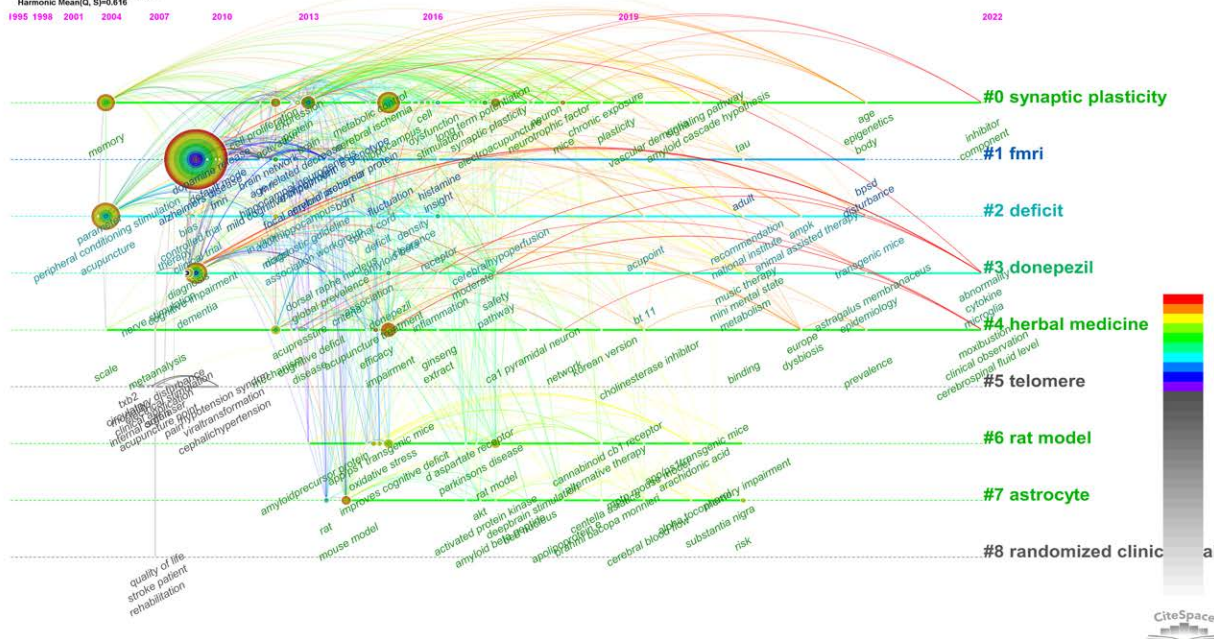
**A**

CiteSpace, v. 5.8.R3 (64-bit)  
 June 2, 2022 at 8:26:33 PM CST  
 Work: C:\Users\... (Desktop)\...  
 Timespan: 1992-2022 (Slice Length=1)  
 Selection Criteria: g-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0  
 Network: N=308, E=1497 (Density=0.0175)  
 Largest CC: 296 (96%)  
 Nodes Labeled: 1.0%  
 Pruning: Pathfinder  
 Modularity Q=0.9177  
 Weighted Mean Silhouette S=0.7977  
 Harmonic Mean(Q, S)=0.816



**B**

CiteSpace, v. 5.8.R3 (64-bit)  
 June 5, 2022 at 7:05:39 PM CST  
 Work: C:\Users\... (Desktop)\...  
 Timespan: 1992-2022 (Slice Length=1)  
 Selection Criteria: g-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0  
 Network: N=308, E=1497 (Density=0.0317)  
 Largest CC: 296 (96%)  
 Nodes Labeled: 1.0%  
 Pruning: None  
 Modularity Q=0.9177  
 Weighted Mean Silhouette S=0.7977  
 Harmonic Mean(Q, S)=0.816



**Figure 7.** (A) Keyword co-occurrence map. (B) Keyword clustering analysis.

Co-citation emergent analysis can reflect the research focus or trend of a research object in different periods. The blue line represents the period from 1992 to 2022, and the red line represents the period from appearance to the end of the cited references. Eleven emergent articles were obtained from Figure 8B with emergent intensity ranging from 3.69 to 6.08, all of which began to emerge after 2012 and lasted for 2 to 5 years. Li published

“Acupuncture improves cognitive deficits and increases neuron density of the hippocampus in middle-aged SAMP8 mice” in *Acupuncture Medicine* in 2012.<sup>[33]</sup> Wang published “Effect of acupuncture in mild cognitive impairment and AD: a functional MRI study” in *PloS One* in 2012,<sup>[34]</sup> which assessed the efficacy of acupuncture in the treatment of mild cognitive impairment and AD using fMRI. Both studies had the highest burst strength

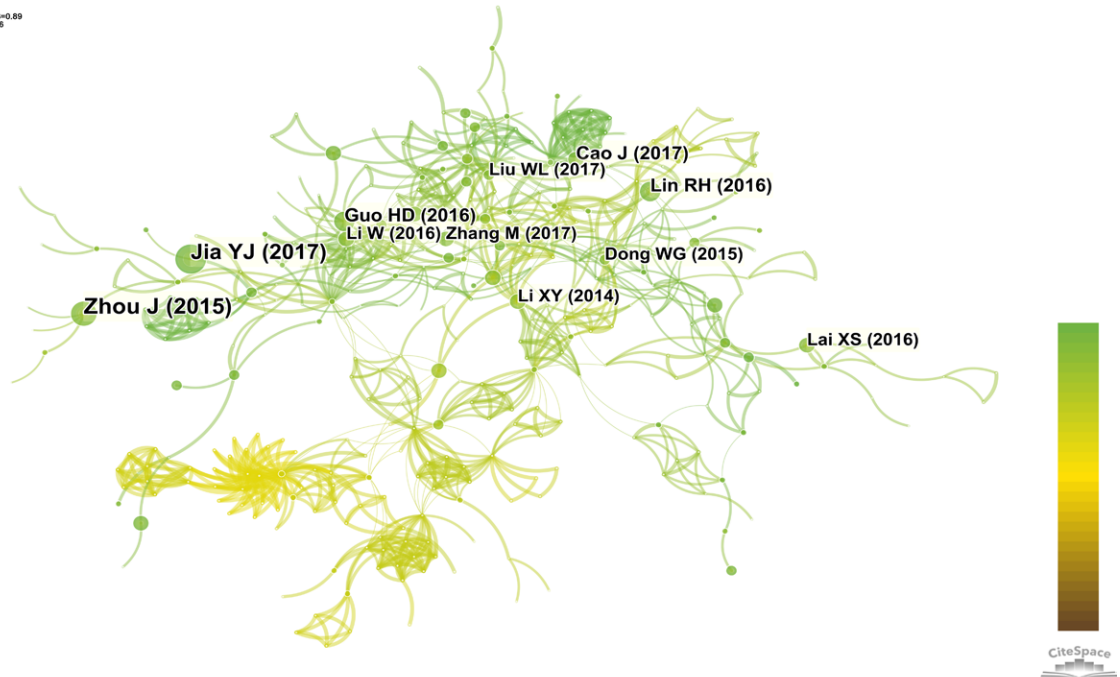


**Table 5**  
**Top 5 keyword co-occurrences and centrality.**

Ranking	Frequency	Keywords	Centrality	Ranking	Centrality	Keywords	Frequency
1	61	alzheimers disease	0.32	1	0.42	mouse model	16
2	39	acupuncture	0.25	2	0.32	alzheimers disease	61
3	36	dementia	0.25	3	0.26	parkinsons disease	6
4	23	memory	0.14	4	0.25	acupuncture	39
5	23	hippocampus	0.02	5	0.25	dementia	36

**A**

CiteSpace v. 5.8.R3 (64-bit)  
 June 2, 2022 at 8:07:08 PM CST  
 WoS: C:\Users\liuyujie\Desktop\科 医 研 究 阿 尔 茨 海 默 斯 数 据\data  
 Timespan: 1992-2022 (Slice Length=1)  
 Selection Criteria: g-index (k=25), LRF=3.0, L/N=10, LBY=5, e=1.0  
 Network: W=529, E=1379 (Density=0.0099)  
 Largest CC: 352 (66%)  
 Nodes Labeled: 1.0%  
 Pruning: Pathfinder  
 Modularity Q=0.929  
 Weighted Mean Silhouette S=0.89  
 Harmonic Mean(Q, S)=0.9216



**B Top 11 References with the Strongest Citation Bursts**

References	Year	Strength	Begin	End	1992 - 2022
Li GM, 2012, ACUPUNCT MED, V30, P339, DOI 10.1136/acupmed-2012-010180, DOI	2012	6.08	2013	2017	Horizontal bar chart showing citation burst from 2013 to 2017.
Wang ZQ, 2012, PLOS ONE, V7, P0, DOI 10.1371/journal.pone.0042730, DOI	2012	6.08	2013	2017	Horizontal bar chart showing citation burst from 2013 to 2017.
Li XY, 2014, BMC COMPLEMENT ALTERN M, V14, P0, DOI 10.1186/1472-6882-14-37, DOI	2014	4.65	2015	2019	Horizontal bar chart showing citation burst from 2015 to 2019.
Wang ZQ, 2014, PLOS ONE, V9, P0, DOI 10.1371/journal.pone.0091160, DOI	2014	4.25	2015	2018	Horizontal bar chart showing citation burst from 2015 to 2018.
Ballard C, 2011, LANCET, V377, P1019, DOI 10.1016/S0140-6736(10)61349-9, DOI	2011	3.73	2015	2016	Horizontal bar chart showing citation burst from 2015 to 2016.
Zhou J, 2015, MEDICINE, V94, P0, DOI 10.1097/MD.0000000000000933, DOI	2015	6.61	2017	2020	Horizontal bar chart showing citation burst from 2017 to 2020.
Lai XS, 2016, ACUPUNCT MED, V34, P215, DOI 10.1136/acupmed-2015-010865, DOI	2016	3.69	2017	2019	Horizontal bar chart showing citation burst from 2017 to 2019.
Zhang M, 2017, ACUPUNCT MED, V35, P0, DOI 10.1136/acupmed-2015-010972, DOI	2017	4.81	2019	2020	Horizontal bar chart showing citation burst from 2019 to 2020.
Zhou SM, 2017, AM J CHINESE MED, V45, P1327, DOI 10.1142/S0192415X17500732, DOI	2017	4.11	2019	2020	Horizontal bar chart showing citation burst from 2019 to 2020.
Jia YJ, 2017, BMC COMPLEMENT ALTERN M, V17, P0, DOI 10.1186/s12906-017-2064-x, DOI	2017	4.41	2020	2022	Horizontal bar chart showing citation burst from 2020 to 2022.
Yu CC, 2018, NEURAL REGEN RES, V13, P1833, DOI 10.4103/1673-5374.238620, DOI	2018	4.14	2020	2022	Horizontal bar chart showing citation burst from 2020 to 2022.

**Figure 8.** (A) Co-cited reference map. (B) References with strongest citation bursts.

of 6.08.<sup>[33,34]</sup> Jia Yujie published “Acupuncture for patients with mild to moderate AD: a randomized controlled trial” in BMC Complementary and Alternative Medicine in 2017.<sup>[35]</sup> Yu Chaochao published “High-frequency (50 Hz) electroacupuncture (EA) ameliorates cognitive impairment in rats with amyloid beta 1-42-induced AD” in Neural regeneration research in 2018.<sup>[36]</sup> Both studies have emerged since 2020 and up to the present,<sup>[35,36]</sup> which suggests that randomized controlled clinical trial of AM in improving cognitive impairment in AD and the

animal experimental study of high-frequency EA in improving amyloid β1-42-induced AD are the current research trends and hotspots.

**4. Discussion**

This study analyzed data from relevant studies on AM in the treatment of AD in the WOSCC database from 1992 to 2022. The related articles were systematically sorted by generating

**Table 6**  
**Top 5 frequently co-cited references.**

Ranking	Cited reference	Representative author	Frequency	Journal	Publication year
1	The effectiveness and safety of acupuncture for patients with Alzheimer disease: a systematic review and meta-analysis of randomized controlled trials <sup>[25]</sup>	Zhou, Jing	34	Medicine	2015
2	Acupuncture for patients with mild to moderate Alzheimer's disease: a randomized controlled trial <sup>[35]</sup>	Jia, Yujie	30	BMC Complementary and Alternative Medicine	2017
3	Electroacupuncture improves memory and protects neurons by regulation of the autophagy pathway in a rat model of Alzheimer's disease <sup>[54]</sup>	Guo, Haidong	18	Acupuncture Medicine	2016
4	Electroacupuncture at the Baihui acupoint alleviates cognitive impairment and exerts neuroprotective effects by modulating the expression and processing of brain-derived neurotrophic factor in APP/PS1 transgenic mice <sup>[55]</sup>	Lin, Ruhui	18	Molecular Medicine Reports	2016
5	Behavioral Changes and Hippocampus Glucose Metabolism in APP/PS1 Transgenic Mice via Electro-acupuncture at Governor Vessel Acupoints <sup>[40]</sup>	Cao, Jin	17	Frontiers in Aging Neuroscience	2017

**Table 7**  
**Top 5 co-cited references with high centrality.**

Ranking	Cited reference	Representative author	Centrality	Journal	Publication year
1	2015 Alzheimer's disease facts and figures <sup>[32]</sup>	Alzheimer's Association	0.23	Alzheimer's & Dementia	2015
2	Effect of acupuncture in mild cognitive impairment and Alzheimer disease: a functional MRI study <sup>[34]</sup>	Wang, Zhiquan	0.19	Plos One	2012
3	Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks <sup>[35]</sup>	Lijun Bai	0.14	Brain Research	2009
4	Effect of acupuncture given at the HT 7, ST 36, ST 40 and KI 3 acupoints on various parts of the brains of Alzheimer's disease patients <sup>[58]</sup>	Zhou, Youlong	0.12	Acupuncture Electro-Therapeutics Research	2008
5	Systemic oxidative stress in older patients with mild cognitive impairment or late onset Alzheimer's disease	Carlo Cervellati	0.12	Current Alzheimer research	2013

maps using Microsoft Excel, Tableau, VOSviewer, and CiteSpace software to investigate the general research status, hotspots, and trends in this field.

#### 4.1. General information for AM on AD

During the past 3 decades, the number of published articles on AM in AD has increased significantly. China has the most productive publications and citations, suggesting that it plays a leading role in AM research on AD in this field. The main research institutions were Beijing University of Chinese Medicine and Capital Medicine University. Among them, the most productive team by Zhi-gang Li and Jing Jiang was from the Beijing University of Chinese Medicine.

The team focused on the mechanisms of manual acupuncture or EA for enhancing behavior or cognition in mice model of AD, proposing that manual acupuncture could regulate cerebral blood flow<sup>[37]</sup> and pro-inflammatory protein expression in Samp8 mice.<sup>[38]</sup> In addition, EA could enhance the signal pathways of cerebral glucose metabolism,<sup>[39,40]</sup> A $\beta$  deposits in the hippocampus,<sup>[41]</sup> and Tau phosphorylation<sup>[42]</sup> in AD mice. The research results of Zhao Lan's team from the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine have received much attention and have demonstrated that acupuncture can promote nerve regeneration<sup>[43,44]</sup> and up-regulate g-protein coupling activity in SAMP8 mice.<sup>[45]</sup> Evidence-based Complementary and Alternative Medicine (impact factor of 2.630, Q2) was the most productive and cited journal. The most frequently cited journal was Acupuncture Electro-therapeutics Research (0.143, Q4). The research field was integrative

and complementary medicine and neuroscience and both of which have a general academic status and level of international influence. It is indicated that the depth of research on AM treatment in AD-related fields needs to be improved. From the visualization network in Figures 3, 4, and 6, we can see that there are fewer cooperative links among countries, institutions, and authors. It is suggested that long-term and stable collaboration should be established among countries/regions, institutions, and authors. In addition, university research institutes should strengthen their cooperation with medical and health institutions and enterprises to take advantage of their strengths and create excellent research conditions to further promote the improvement of technology in this field.

#### 4.2. Research hotspots and trends of AM on AD

This study investigated the research hotspots of AM on AD through keyword co-occurrence and time-line. The search keywords were "alzheimer's disease" and "acupuncture", and the other high-frequency keywords were "dementia", "memory" and "hippocampus". The keywords with high centrality usually represent the turning point of a knowledge map, which plays an effective role in supporting the research network in this field. High centrality keywords were "alzheimer's disease", "acupuncture", "dementia", "mouse model", and "Parkinson's disease", indicating research hotspots in this field. Keyword clustering is a kind of keyword with similar subject in the research field, which forms a network cluster and displays the keywords in the cluster according to the time distribution through the time line view to understand the evolution and phase characteristics of keyword

hotspots in this field. This study obtained 9 major keywords clustering of “synaptic plasticity”, “fMRI”, “deficit”, “donepezil”, “herbal medicine”, “telomere”, “rat model”, “astrocyte”, and “randomized clinical trial”.

This study summarizes research hotspots in 3 domains. First, mechanism of therapeutic action. The current mechanism of AM in AD includes the ability of acupuncture to modulate A $\beta$  metabolism, tau phosphorylation, neurotransmitters, neurogenesis, synapse and neuron function, autophagy, neuronal apoptosis, neuroinflammation, cerebral glucose metabolism, and brain responses.<sup>[46]</sup> Jiang et al<sup>[27]</sup> proposed that acupuncture as a therapeutic target for the treatment of mitochondrial dysfunction in AD, focusing on the mechanisms regulating mitochondrial dynamics, energy metabolism, calcium homeostasis, and apoptosis. Li et al<sup>[47]</sup> have proposed that EA ameliorates memory deficits and synaptic plasticity impairment by inhibiting NLRP3 inflammasome activation. Second, this study summarized animal studies and randomized controlled clinical trials. Lee et al<sup>[48]</sup> suggested that acupuncture in neurological disorder studies mostly suffers from rigorous methodology. More rigorous experimental studies are needed to determine the role of acupuncture in neurological disorder. In follow-up studies, animal experiments and randomized controlled clinical trials have become the focus of research in the field of AM for the treatment of AD. Studies on the therapeutic mechanisms of AM have mostly been conducted in AD mouse models.<sup>[49–51]</sup> Third, fMRI is an important modality for exploring brain functional connectivity in patients with AD. Wang et al<sup>[52]</sup> and Zheng et al<sup>[53]</sup> applied fMRI to elucidate the repair effect of acupuncture on hippocampal connections in AD patients, showing enhanced functional connectivity between the hippocampus and the anterior central gyrus in AD patients after acupuncture at Taichong (Liv3) and Hegu (LI 4).

This study explored the theoretical basis and research trends in the field of AM treatment for AD in accordance with the co-cited and emergent results of articles in this field. In co-cited references, studies on the efficacy and safety of AM in the treatment of AD<sup>[25,35]</sup> and animal experiments on the mechanism of action of EA in the treatment of AD<sup>[54–56]</sup> were co-cited with high frequency. Studies have reported that fMRI-based studies of AM in the treatment of AD<sup>[34,57,58]</sup> are co-cited as high centrality, which forms the theoretical basis for research in this field. Reference burst started from 2012 with trends having crossover and continuity. Emerging trends from 2013 to 2017, Li Guomin used the Maurice Water Maze test and the optical fractionator technique to assess the behavior and neuronal density in the hippocampus of SAMP8 mice, suggesting that AM can improve cognitive impairment and increase the density of hippocampal neurons in middle-aged SAMP8 mice.<sup>[33]</sup> According to the reference burst from 2015 to 2019, study published in *The Lancet* by the American Association of Neurological Surgeons summarized the latest evidence on the epidemiology, pathogenesis, diagnosis and treatment of AD, and methods to reduce the risk of AD.<sup>[59]</sup> Li et al<sup>[60]</sup> showed that EA decreases cognitive function, decreases A $\beta$  deposits, up-regulates BDNF expression, and promotes neurogenesis in APP/PS1 transgenic mice. Emerging trends from 2017 to 2020, Zhou et al<sup>[25]</sup> conducted a systematic review and meta-analysis of the efficacy and safety of AM in the treatment of AD. Lai et al<sup>[61]</sup> reported that acupuncture at Shenmen (HT7) could improve cerebral glucose metabolism in the hippocampus, thalamus, hypothalamus, frontal lobe/temporal lobe of AD rats and enhance memory ability through the modality of 18F-2-fluorodeoxy-d-glucose positron emission tomography. Zhang et al<sup>[62]</sup> suggested that acupuncture at Dazhui (GV20) and Shenshu (BL23) could improve cognitive impairment in AD rats by activating PPAR- $\gamma$  and inhibiting the expression of P-P38 MAPK. The therapeutic effect of decreasing A-B deposition and p-Tau SER404 protein concentration in the hippocampal CA1 region was observed. Emerging Trends from 2020 to 2022, a 28-week

clinical RCT by Jia et al<sup>[35]</sup> compared and evaluated the efficacy and safety of acupuncture plus Donepezil in patients with mild to moderate AD. Yu et al<sup>[36]</sup> showed that high frequency (50 Hz) EA was the most effective frequency for the treatment of  $\beta$ -42 amyloid-induced AD in rats.

## 5. Limitation

This study has several limitations. First, this study only collected and analyzed data from WOSCC alone because both CiteSpace and VOSviewer can not manage data from multiple databases simultaneously. It may result in losing some potential articles. Second, the search strategy of this study may not include all potential studies of AM on AD. Third, there may be unavailable information on shared first or last co-authorship because it is performed according to the author order listed in WOSCC. Finally, more broad evaluation on research capacity and power balances in the global health collaborations are encouraged to be utilized, because the only assessment is the bibliometric analysis of author order and citation rates in the current study, which maybe incomprehensive to address this issue.

## 6. Conclusion

This study summarizes the general research status, hotspots and trends of AM treatment in AD. The current research status shows that this field is in a rapid development stage, and countries/regions, institutions, and scholars need to strengthen cooperation to promote research progress. The research hotspots are mainly on changes in brain function and its mechanism of AM in improving cognition in AD. At present, the research frontier is the comparison of the therapeutic effects of AM with donepezil, and EA at different frequencies.

## Author contributions

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## References

- [1] Gale SA, Acar D, Daffner KR. Dementia. *Am J Med.* 2018;131:1161–9.
- [2] Scheltens P, Blennow K, Breteler MMB, et al. Alzheimer's disease. *Lancet.* 2016;388:505–17.
- [3] Joe E, Ringman JM. Cognitive symptoms of Alzheimer's disease: clinical management and prevention. *BMJ.* 2019;367:l6217.
- [4] Kim J, Jeong M, Stiles WR, Choi HS. Neuroimaging modalities in Alzheimer's disease: diagnosis and clinical features. *Int J Mol Sci.* 2022;23:6079.

- [5] Porsteinsson AP, Isaacson RS, Knox S, Sabbagh MN, Rubino I. Diagnosis of early Alzheimer's disease: clinical practice in 2021. *J Prev Alzheimers Dis.* 2021;1:8:371–86.
- [6] Yusuf M, Weyandt LL, Piryatinsky I. Alzheimer's disease and diet: a systematic review. *Int J Neurosci.* 2017;127:161–75.
- [7] Niu H, Álvarez-Álvarez I, Guillén-Grima F, Aguinaga-Ontoso I. Prevalence and incidence of Alzheimer's disease in Europe: a meta-analysis. *Neurologia.* 2017;32:523–32.
- [8] Jia J, Wang F, Wei C, et al. The prevalence of dementia in urban and rural areas of China. *Alzheimers Dement.* 2014;10:1–9.
- [9] Fiest KM, Roberts JL, Maxwell CJ, et al. The prevalence and incidence of dementia due to Alzheimer's disease: a systematic review and meta-analysis. *Can J Neurol Sci.* 2016;43:551–82.
- [10] Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement.* 2013;9:63–75.e2.
- [11] Alzheimer's Association. 2016 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2016;12:459–509.
- [12] Cummings JL, Tong G, Ballard C. Treatment combinations for Alzheimer's disease: current and future pharmacotherapy options. *J Alzheimers Dis.* 2019;67:779–94.
- [13] Serrano-Pozo A, Das S, Hyman BT. APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches. *Lancet Neurol.* 2021;20:68–80.
- [14] Wang S, Colonna M. Microglia in Alzheimer's disease: a target for immunotherapy. *J Leukoc Biol.* 2019;106:219–27.
- [15] Gorantla NV, Sunny LP, Rajasekhar K, et al. Amyloid- $\beta$ -derived peptidomimetics inhibits tau aggregation. *ACS Omega.* 2021;6:11131–8.
- [16] Kola A, Dudek D, Valensin D. Metal complexation mechanisms of polyphenols associated to Alzheimer's disease. *Curr Med Chem.* 2021;28:7278–94.
- [17] Kesika P, Suganthi N, Sivamaruthi BS, Chaiyasut C. Role of gut-brain axis, gut microbial composition, and probiotic intervention in Alzheimer's disease. *Life Sci.* 2021;264:118627.
- [18] Guo X, Lie Q, Liu Y, et al. Multifunctional selenium quantum dots for the treatment of Alzheimer's disease by reducing A $\beta$ -neurotoxicity and oxidative stress and alleviate neuroinflammation. *ACS Appl Mater Interfaces.* 2021;13:30261–73.
- [19] Briggs R, Kennelly SP, O'Neill D. Drug treatments in Alzheimer's disease. *Clin Med (Lond).* 2016;16:247–53.
- [20] Khan S, Barve KH, Kumar MS. Recent advancements in pathogenesis, diagnostics and treatment of Alzheimer's disease. *Curr Neuropharmacol.* 2020;18:1106–25.
- [21] Chen X, Liu F, Lin N, et al. Warming needle moxibustion for Alzheimer's disease: a systematic review of randomized controlled trials. *Geriatr Nurs.* 2022;43:219–26.
- [22] Du Y, Liu R, Sun G, Meng P, Song J. Pre-moxibustion and moxibustion prevent Alzheimer's disease. *Neural Regen Res.* 2013;8:2811–9.
- [23] Zhan Y, Fu Q, Pei J, et al. Modulation of brain activity and functional connectivity by acupuncture combined with donepezil on mild-to-moderate Alzheimer's disease: a neuroimaging pilot study. *Front Neurol.* 2022;13:912923.
- [24] Yin Z, Li X, Wang L, Sun M, Zhao L, Liang F. The comparative efficacy of multiple acupuncture for Alzheimer's disease: a Bayesian network meta-analysis. *Evid Based Complement Alternat Med.* 2022;2022:3288948.
- [25] Zhou J, Peng W, Xu M, Li W, Liu Z. The effectiveness and safety of acupuncture for patients with Alzheimer disease: a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltim).* 2015;94:e933.
- [26] Yu CC, Ma CY, Wang H, et al. Effects of acupuncture on Alzheimer's disease: evidence from neuroimaging studies. *Chin J Integr Med.* 2019;25:631–40.
- [27] Jiang YH, He JK, Li R, Chen ZH, Jia BH. Mechanisms of acupuncture in improving Alzheimer's disease caused by mitochondrial damage. *Chin J Integr Med.* 2022;28:272–80.
- [28] Ji S, Duan J, Hou X, et al. The role of acupuncture improving cognitive deficits due to Alzheimer's disease or vascular diseases through regulating neuroplasticity. *Neural Plast.* 2021;2021:16.
- [29] Yin W, Lv G, Li C, Sun J. Acupuncture therapy for Alzheimer's disease: The effectiveness and potential mechanisms. *Anat Rec (Hoboken).* 2021;304:2397–411.
- [30] van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics.* 2010;84:523–38.
- [31] Chen C. CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature. *J AM Soc Inf SCI Tec.* 2006;57:359–77.
- [32] Alzheimer's Association. 2015 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2015;11:332–84.
- [33] Li G, Zhang X, Cheng H, et al. Acupuncture improves cognitive deficits and increases neuron density of the hippocampus in middle-aged SAMP8 mice. *Acupunct Med.* 2012;30:339–45.
- [34] Wang Z, Nie B, Li D, et al. Effect of acupuncture in mild cognitive impairment and Alzheimer disease: a functional MRI study. *PLoS One.* 2012;7:e42730.
- [35] Jia Y, Zhang X, Yu J, et al. Acupuncture for patients with mild to moderate Alzheimer's disease: a randomized controlled trial. *BMC Complement Altern Med.* 2017;17:556.
- [36] Yu CC, Wang Y, Shen F, et al. High-frequency (50 Hz) electroacupuncture ameliorates cognitive impairment in rats with amyloid beta 1-42-induced Alzheimer's disease. *Neural Regen Res.* 2018;13:1833–41.
- [37] Ding N, Jiang J, Xu AP, Tang YS, Li ZG. Manual acupuncture regulates behavior and cerebral blood flow in the SAMP8 mouse model of Alzheimer's disease. *Front Neurosci.* 2019;13:37.
- [38] Ding N, Jiang J, Lu MH, et al. Manual acupuncture suppresses the expression of proinflammatory proteins associated with the NLRP3 inflammasome in the hippocampus of SAMP8 mice. *Evid Based Complement Alternat Med.* 2017;2017:3435891.
- [39] Jiang J, Gao K, Zhou Y, et al. Electroacupuncture treatment improves learning-memory ability and brain glucose metabolism in a mouse model of Alzheimer's Disease: using Morris water maze and MicroPET. *Evid Based Complement Alternat Med.* 2015;2015:142129.
- [40] Cao J, Tang YS, Li YJ, Gao K, Shi XD, Li ZG. Behavioral changes and hippocampus glucose metabolism in APP/PS1 transgenic mice via electro-acupuncture at governor vessel acupoints. *Front Aging Neurosci.* 2017;9:5.
- [41] Sun RQ, Wang ZD, Zhao J, et al. Improvement of electroacupuncture on APP/PS1 transgenic mice in behavioral probably due to reducing deposition of A beta in hippocampus. *Anat Rec (Hoboken).* 2021;304:2521–30.
- [42] Xu AP, Zeng QT, Tang YS, et al. Electroacupuncture protects cognition by regulating tau phosphorylation and glucose metabolism via the AKT/GSK3 beta signaling pathway in Alzheimer's disease model mice. *Front Neurosci.* 2020;14:585476.
- [43] Kan BH, Yu JC, Zhao L, et al. Acupuncture improves dendritic structure and spatial learning and memory ability of Alzheimer's disease mice. *Neural Regen Res.* 2018;13:1390–5.
- [44] Zhao L, Liu JW, Kan BH, Shi HY, Yang LP, Liu XY. Acupuncture accelerates neural regeneration and synaptophysin production after neural stem cells transplantation in mice. *World J Stem Cells.* 2020;12:1576–90.
- [45] Luo BH, Zhao L, Zhang XZ, et al. Acupuncture upregulates G protein coupled activity in SAMP8 mice. *Acupunct Med.* 2017;35:289–96.
- [46] Yu CC, Du YJ, Wang SQ, et al. Experimental evidence of the benefits of acupuncture for Alzheimer's disease: an updated review. *Front Neurosci.* 2020;14:549772.
- [47] Li K, Shi G, Zhao Y, et al. Electroacupuncture ameliorates neuroinflammation-mediated cognitive deficits through inhibition of NLRP3 in Presenilin1/2 conditional double knockout mice. *Neural Plast.* 2021;2021:8814616.
- [48] Lee H, Park HJ, Park J, et al. Acupuncture application for neurological disorders. *Neural Res.* 2007;29(Suppl 1):49–54.
- [49] Yang Q, Zhu S, Xu J, et al. Effect of the electro-acupuncture on senile plaques and its formation in APP(+)/PS1(+) double transgenic mice. *Genes Dis.* 2019;6:282–9.
- [50] Zhang J, Tang C, Liao W, Zhu M, Liu M, Sun N. The antiapoptotic and antioxidative stress effects of Zhisanzhen in the Alzheimer's disease model rat. *Neuroreport.* 2019;30:628–36.
- [51] Li L, Li L, Zhang J, et al. Disease stage-associated alterations in learning and memory through the electroacupuncture modulation of the cortical microglial M1/M2 polarization in mice with Alzheimer's disease. *Neural Plast.* 2020;2020:8836173.
- [52] Wang Z, Liang P, Zhao Z, et al. Acupuncture modulates resting state hippocampal functional connectivity in Alzheimer disease. *PLoS One.* 2014;9:e91160.
- [53] Zheng W, Su Z, Liu X, et al. Modulation of functional activity and connectivity by acupuncture in patients with Alzheimer disease as measured by resting-state fMRI. *PLoS One.* 2018;13:e0196933.
- [54] Guo HD, Zhu J, Tian JX, et al. Electroacupuncture improves memory and protects neurons by regulation of the autophagy pathway in a rat model of Alzheimer's disease. *Acupunct Med.* 2016;34:449–56.
- [55] Lin R, Chen J, Li X, et al. Electroacupuncture at the Baihui acupoint alleviates cognitive impairment and exerts neuroprotective effects by



- modulating the expression and processing of brain-derived neurotrophic factor in APP/PS1 transgenic mice. *Mol Med Rep.* 2016;13:1611–7.
- [56] Cao J, Tang Y, Li Y, Gao K, Shi X, Li Z. Behavioral changes and hippocampus glucose metabolism in APP/PS1 transgenic mice via electro-acupuncture at governor vessel acupoints. *Front Aging Neurosci.* 2017;9:5.
- [57] Bai L, Qin W, Tian J, et al. Acupuncture modulates spontaneous activities in the anticorrelated resting brain networks. *Brain Res.* 2009;1279:37–49.
- [58] Zhou Y, Jin J. Effect of acupuncture given at the HT 7, ST 36, ST 40 and KI 3 acupoints on various parts of the brains of Alzheimer's disease patients. *Acupunct Electrother Res.* 2008;33:9–17.
- [59] Sacks D, Baxter B, Campbell B, et al. Multisociety consensus quality improvement revised consensus statement for endovascular therapy of acute ischemic stroke. *Int J Stroke.* 2018;13:612–32.
- [60] Li X, Guo F, Zhang Q, et al. Electroacupuncture decreases cognitive impairment and promotes neurogenesis in the APP/PS1 transgenic mice. *BMC Complement Altern Med.* 2014;14:37.
- [61] Lai X, Ren J, Lu Y, et al. Effects of acupuncture at HT7 on glucose metabolism in a rat model of Alzheimer's disease: an 18F-FDG-PET study. *Acupunct Med.* 2016;34:215–22.
- [62] Zhang M, Xu GH, Wang WX, Meng DJ, Ji Y. Electroacupuncture improves cognitive deficits and activates PPAR- $\gamma$  in a rat model of Alzheimer's disease. *Acupunct Med.* 2017;35:44–51.