

# Research Hotspots and Trends on Acupuncture for Anti-Inflammation: A Bibliometric Analysis from 2011 to 2021

Bing Chen<sup>1,\*</sup>, Di Liu<sup>2,\*</sup>, Tao Li<sup>1</sup>, Lijiang Zheng<sup>1</sup>, Ling Lan<sup>1</sup>, Niu Yang<sup>1</sup>, Yinlan Huang<sup>1,3</sup>

<sup>1</sup>Ningxia Medical University, Yinchuan, People's Republic of China; <sup>2</sup>Traditional Chinese Medicine Orthopedics and Traumatology Department, General Hospital of Ningxia Medical University, Yinchuan, People's Republic of China; <sup>3</sup>Key Laboratory of Ningxia Ethnomedicine Modernization, Ministry of Education, Ningxia Medical University, Yinchuan, People's Republic of China

\*These authors contributed equally to this work

Correspondence: Yinlan Huang, Ningxia Medical University, No. 1160, Shengli Street, Xingqing District, Yinchuan, People's Republic of China, Tel +86 18209506917, Email lzdb@163.com

**Purpose:** We here explored the research status, research hotspots, and development trend of acupuncture against inflammation from both quantitative and qualitative aspects through bibliometrics.

**Methods:** We used CiteSpace and VOSviewer to analyze the literature about acupuncture against inflammation from 2011 to 2021 in the Web of Science Core Collection database by using a visual knowledge map.

**Results:** In total, 1479 articles were included, and the number of articles published each year exhibited an upward trend. The largest number of articles were published in China (661), followed by the United States (287) and South Korea (164). The most productive institution is Beijing University of Chinese Medicine (72), while the most influential institution is the Capital Medical University (0.28). *Evidence-based Complementary and Alternative Medicine* (131) is the journal that published most articles on the topic. Lin Yiwen is the most prolific author, and Borovikova L is the most influential co-cited author. The keywords that have burst in the last 2 years are inflammation and activation. The keywords with the highest frequency of use are electroacupuncture (EA), inflammation, and expression.

**Conclusion:** The number of publications on acupuncture for anti-inflammation research is rapidly increasing. China is a productive country, but the influence of centrality is poor. Research institutions are concentrated in universities, and the whole collaborative network needs to be strengthened. The anti-inflammatory mechanism of acupuncture is the main focus of research in this field. Regulation of immune cell balance by acupuncture may be a hot topic in mechanism research. At present, immune cells, vagus nerve, signal pathway, inflammatory corpuscles, cytokines and neurotransmitters are popular research topics. In the future, the basic research of acupuncture for anti-inflammation transformed into clinical practice may be a trend. EA and bee venom acupuncture may be promising research directions for acupuncture treatment for inflammatory diseases.

**Keywords:** acupuncture, anti-inflammation, bibliometric analysis, CiteSpace, VOSviewer

## Introduction

Inflammation is an important defense mechanism in humans triggered in response to external stimuli, and many diseases are clinically accompanied by inflammation. In the early disease stage, a moderate inflammatory reaction is a process of activating the autoimmune system and attaining body balance. When inflammation becomes unregulated, numerous tissues and cells die, resulting in abnormal changes in tissues and organs, and eventually organ failure.<sup>1,2</sup> According to statistics, 60% of chronic diseases that cause death worldwide are chronic inflammatory diseases,<sup>3</sup> which undoubtedly cause serious psychological and physiological harm to patients and their families, considerably affect their quality of life, and pose a heavy social and economic burden to medical systems globally. At present, no consensus exists on the best treatment for inflammatory diseases. Non-steroidal anti-inflammatory drugs, glucocorticoids and anti-cytokine antibodies

are often selected for drug therapy, and the mechanism underlying drug therapy is too complicated and is still under study.<sup>4</sup> Moreover, drug therapy offers only temporary relief from inflammatory reactions, and the long-term effect is not good and is accompanied by many adverse reactions. Anti-inflammatory treatment remains a huge challenge. Therefore, a safe and clinically effective non-drug treatment method must be urgently identified.

Acupuncture, a treasure of China, is one of the complementary alternative therapies, with simple operation and minimal side effects and its clinical anti-inflammatory effect has been unanimously recognized by doctors and patients globally. The World Health Organization recommends that acupuncture can treat various chronic inflammatory diseases.<sup>5</sup> Treatment of inflammatory diseases using acupuncture has been included in international guidelines, such as the National Guideline Clearinghouse of the USA. These guidelines recommend the treatment of allergic rhinitis and arthritis pain through acupuncture.<sup>6</sup> More and more evidence-based research and basic research have recently confirmed that acupuncture can effectively improve the inflammatory response in inflammatory diseases and chronic diseases, alleviate patients' symptoms, promote the recovery of body function, and improve patients' quality of life. These studies have not only evaluated the safety and effectiveness of acupuncture against inflammatory diseases but also revealed the anti-inflammatory mechanism of acupuncture from different angles and levels. Studies have shown that acupuncture can not only inhibit the activation and infiltration of inflammatory cytokines but also promote the expression of anti-inflammatory cytokines. It can balance the relationship between pro-inflammatory and anti-inflammatory cytokines and have a two-way regulatory effect on the body.<sup>7,8</sup> The anti-inflammatory mechanism of acupuncture in various non-infectious inflammatory diseases or chronic diseases with inflammatory reactions is found to be multi-channel and multi-target.<sup>1</sup> With the advancement of acupuncture, an increasing number of publications are related to acupuncture for inflammation treatment. However, visual analysis through bibliometrics is lacking. Therefore, quantitative and qualitative analyses of these documents should be conducted through bibliometrics and a macro overview of the current research status, hotspots, and future development direction should be taken. This will provide data support for acupuncture treatment of inflammatory diseases, better guide the clinical application of acupuncture, and relieve the pain for patients. Meanwhile, it will promote the better development of this research field at home and abroad.

In bibliometrics, information visualization technology is used to present the development history, research status, and development frontier of research topics in the form of knowledge maps.<sup>9</sup> CiteSpace is a software developed by Chen Chaomei, a Chinese American professor, and his team. It measures literature in a specific field through the theory of co-citation analysis and path-finding network algorithm.<sup>10</sup> VOSviewer is a JAVA-based visualization software developed in 2009 by Van Eck and Waltman of Leiden University, Netherlands. Its graphic display ability and versatility are strong. This software is suitable for analyzing large-scale data with different formats in various databases.<sup>11</sup> In this study, from the perspective of bibliometrics, CiteSpace and VOSviewer software were used for a systematic knowledge map analysis of the literature on acupuncture for anti-inflammation research in the Web of Science Core Collection database in the recent 11 years. The software aimed at scientifically and effectively excavating the research status, hotspots, and development frontiers in this field and providing references and ideas for follow-up research.

## Methods

### Literature Sources and Retrieval Methods

All data in this study came from the core collection of the Web of Science; all citation indices were selected, and advanced retrieval was conducted. The retrieval formula used was TS=(acupuncture OR acupuncture-moxibustion OR acupuncture therapy OR needle moxibustion OR acupuncture treatment OR manual acupuncture OR moxi-acupuncture OR acumoxi) AND TS=(inflammatory OR pro-inflammatory OR inflammation OR inflammatory state OR inflammatory reaction OR inflammatory process OR inflammatory response OR phlegmasia OR infection OR anti-inflammatory OR anti-inflammation OR anti-inflammatory effect OR anti-inflammatory activity OR anti-inflammatory effects OR anti-inflammatory response). The retrieval time was set from January 1, 2011, to December 31, 2021, and the language was limited to English. A total of 1497 pieces of data were retrieved, excluding the literature research types, such as conference summaries, letters, books, and news. The remaining 1479 pieces were removed after eliminating the duplicate records. All documents were exported in the

TXT format, with all records and cited references. In order to ensure the data reliability, two researchers from the research group verified the data after removing the duplicates, and, in case of any difference, negotiations were held with a third party.

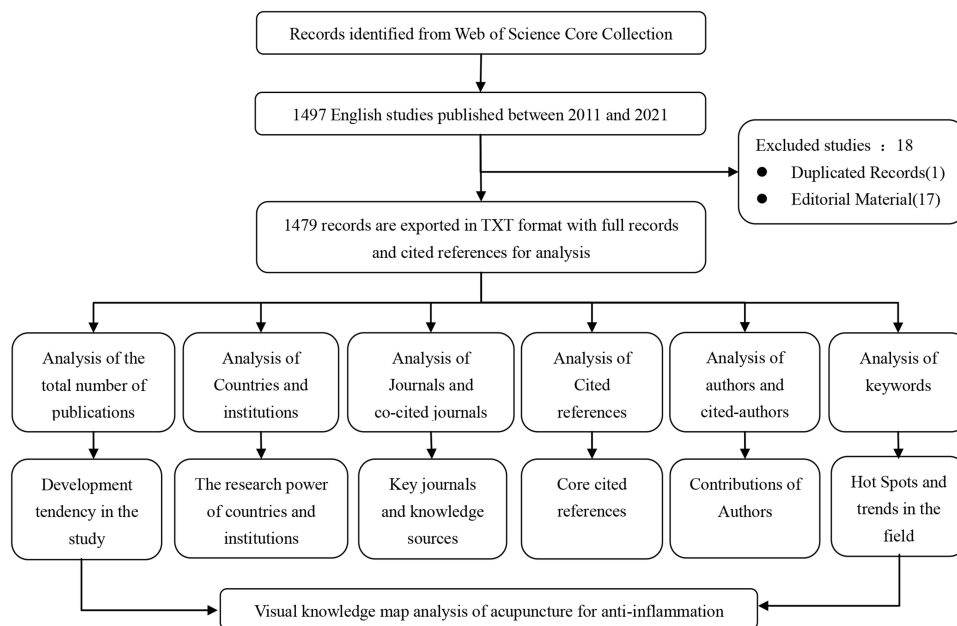
## Analysis Software

The visual knowledge map can reflect the overall research situation, the latest research progress, as well as the distribution of specific countries and institutions in the related research fields. It can also determine the mainstream academic groups, representatives, core technical fields, and hot issues, which is conducive to scientific research activities and academic exchanges. VOSviewer software was used to create a map based on bibliometrics. The maximum number of each document was set to 25, and the counting method used was Full counting. The type to be analyzed was selected to draw the knowledge map. CiteSpace's time partition was set from 2011 to 2021, and the time slice was set to "1". Set Top N = 50, TOP N% = 10%. For the cutting methods, Pathfinder and Pruning Sliced networks were used. The nodes were used to select countries, institutions, authors, and keywords. Based on the needs, a visual knowledge map was drawn. In the knowledge map, the node size indicates the frequency of co-occurrence or citation. The color of the nodes indicates the year, and the connection between nodes indicates cooperation, co-occurrence, or co-citation. The node with a high centrality serves as the key node in a specific field and as an important index to measure the extent of influence. Sudden detection indicated the burst of this research field in a specific period which is, the research hotspot at that time. In this paper, the CiteSpace and VOSviewer software were used to visually analyze the annual publication volume, countries, institutions, journals, cited references, authors, and keywords of acupuncture anti-inflammatory-related literature. The specific process is depicted in Figure 1.

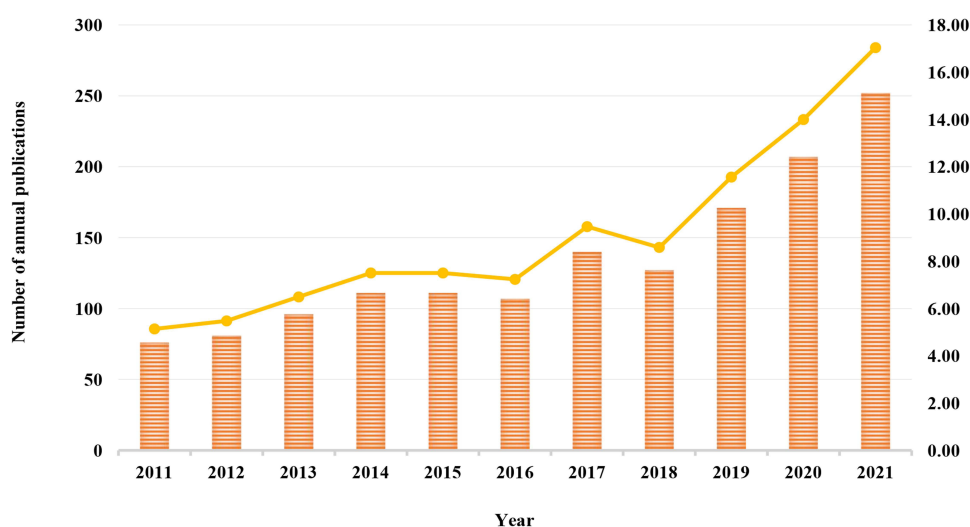
## Results

### Analysis of Annual Publications

In total, 1479 articles related to acupuncture for anti-inflammation research have been included, and the number of annual publications is increasing (Figure 2), which can be divided into three periods. Among them, from 2011 to 2015, research has shown a slow upward trend. Although the number of publications fluctuated from 2016 to 2018, the average number of publications in these 8 years was more than 100, which indicated that researchers extensively focused on this research field. From 2019 to 2021, the number of publications continued to increase rapidly, with the highest number reaching 252 in 2021 (17.04%). Among them, the most frequently cited article was



**Figure 1** Visual analysis flow chart of acupuncture for anti inflammation.



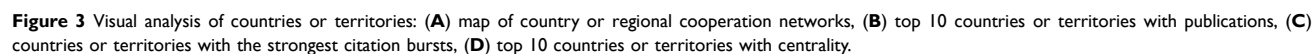
**Figure 2** Number of annual publications on acupuncture for anti-inflammation. (The bar chart represents the number of publications, and the line chart represents the proportion).

by Chen TY.<sup>12</sup> This study investigated whether acupuncture combined with frozen gel biomaterials could regulate the immune system and promote the healing of diabetic skin wounds. The underlying mechanism was that acupuncture activated C3a and C5a, promoted the secretion of cytokines SDF-1 and TGF  $\beta$ -1, and downregulated the expression of pro-inflammatory cytokines tumor necrosis factor (TNF)- $\alpha$  and interleukin (IL)-1 $\beta$ . Combined with frozen gel biomaterials, it produced a synergistic immunomodulatory effect. This thus provided a new method for accelerating tissue regeneration clinically. The latest research article on this topic was by Badakhsh.<sup>13</sup> This study systematically evaluated depression, anxiety, sleep quality, inflammatory factors, and quality of life of COVID-19 patients treated with different interventions of traditional Chinese medicine from the perspective of complementary alternative medicine. The role of acupuncture cannot be ignored, as it provides a new direction for COVID-19 treatment. Evidence shows that acupuncture, as a green anti-inflammatory treatment, is favored by people at home and abroad.

## Analysis of Countries

In total, 72 countries contributed articles on acupuncture anti-inflammation, with 105 cooperation lines (Figure 3A). Among them, countries with close cooperation were: Netherlands, Canada, and Japan, while China and the USA, which ranked in the top two in the number of published articles, had less cooperation. Table 1 presents the top 10 countries in terms of the number and centrality of articles published. China had the largest number of articles published (661), which is because China is the birthplace of acupuncture. The second is the United States (287), which indicates that the United States has made significant achievements in the acupuncture field. South Korea (164) ranks third, and the number of articles published in other countries is <100 (Figure 3B). According to the burst intensity value in Figure 3C, England, Netherlands, and South Korea are countries with the strongest burst, indicating that these countries were hot countries studying acupuncture for anti-inflammation at that time. From 2020 to 2021, Indonesia and Saudi Arabia had a burst, indicating that these countries have developed great potential in acupuncture for anti-inflammation research in the past 2 years. The top 10 countries in the center are shown in Figure 3D, and the top three countries are Netherlands, Canada, and France. Netherlands, Canada, and France are the most influential countries in this research field. To summarize, the regional distribution of this research is uneven, and the research strength is quite different. Although China ranked first in the number of publications, it ranked ninth in centrality and its cooperation was also very little. We should strengthen cooperation among countries, reinforce academic exchanges, and further enhance China's international influence in this research field.





In total, 385 institutions contributed 1479 articles, and 359 cooperation lines existed among institutions (Figure 4A). Figure 4B shows that the top three burst institutions were the University of Maryland (4.56), Nanjing University Chinese Medicine (3.95), and Shanghai Jiao Tong University (3.92). Among them, from 2011 to 2013, the University of Maryland was the research hotspot institution in this field, and from 2020 to 2021, Nanjing University of Chinese Medicine was the research hotspot institution. Figure 4C presents the top 10 institutions with published articles. Among

Rank	Country or Territory	Publications	Country or Territory	Centrality
1	China	661	Netherlands	0.59
2	USA	287	Canada	0.48
3	South Korea	164	France	0.38
4	Taiwan	85	England	0.36
5	Brazil	63	Norway	0.34

Journal of Pain Research 2023:16

Table 1 (Continued).

Rank	Country or Territory	Publications	Country or Territory	Centrality
6	Germany	57	Germany	0.29
7	Australia	51	USA	0.28
8	England	50	Italy	0.24
9	Italy	30	China	0.23
10	Canada	26	Sweden	0.22

them, the top three are the Beijing University of Chinese Medicine, China Medical University, and Shanghai University of Traditional Chinese Medicine. All of them are universities belonging to China. Figure 4D presents the top 10 institutions with centrality, with Capital Medical University demonstrating the highest centrality (0.28), indicating that Capital Medical University is the most influential institution in acupuncture against inflammation research, followed by the Beth Israel Deaconess Medical Center (0.19) and Shanghai University of Traditional Chinese Medicine (0.17). According to Table 2, most research institutions are located in China, and thus, China is currently the leading country in this research field. Except for the Chinese Academy of Medical Sciences, Korea Institute Oriental Medicine, and Beth

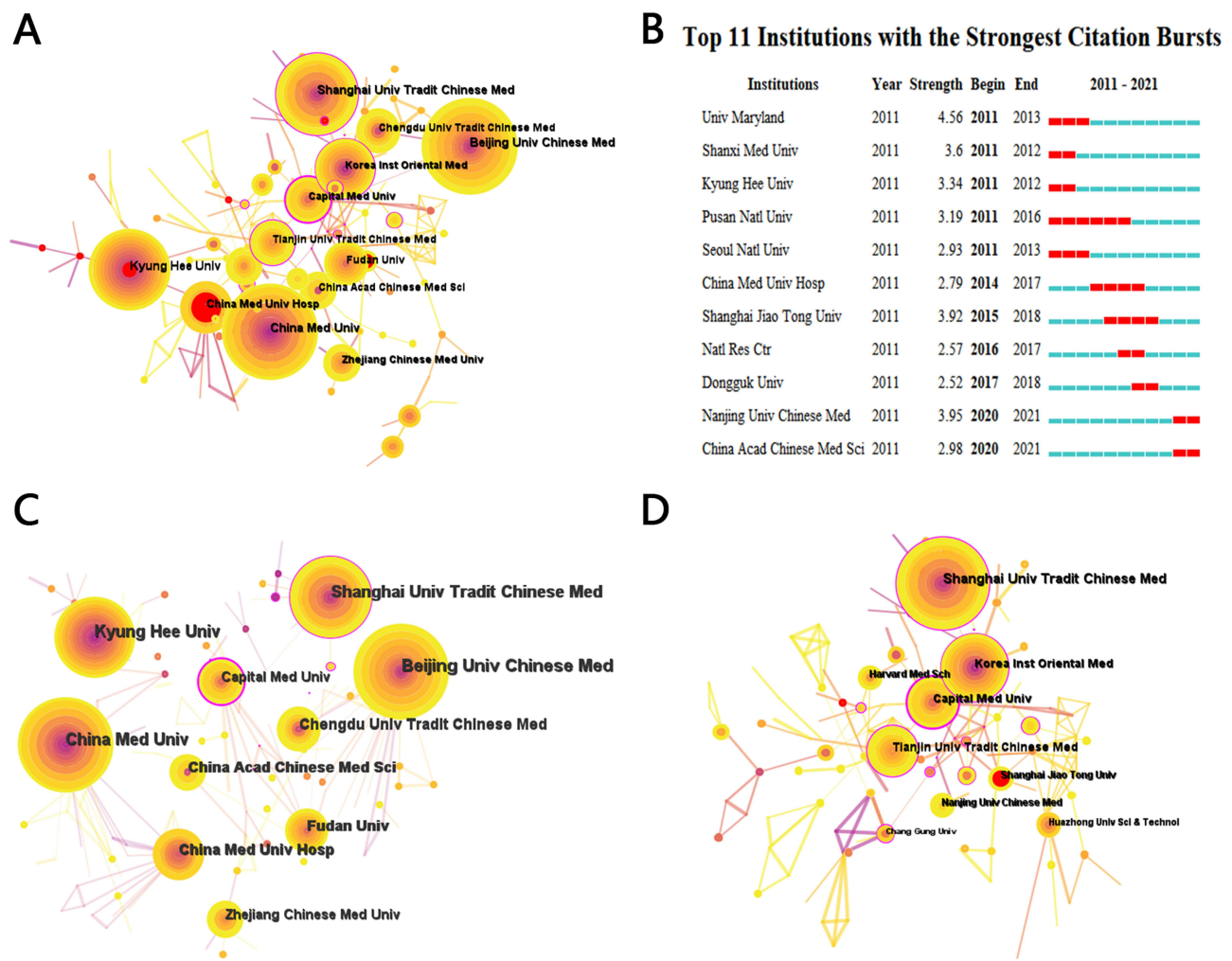


Figure 4 Visual analysis of institutions: (A) map of institutional cooperation network, (B) institutions with strongest citation bursts, (C) top 10 institutions in publications, (D) top 10 institutions in centrality.

**Table 2** Top 10 Institutions of Publications and Centrality on Acupuncture for Anti-Inflammation

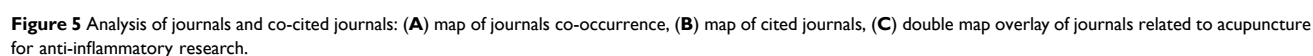
Rank	Institutions	Publications	Country	Institutions	Centrality	Country
1	Beijing University of Chinese Medicine	72	China	Capital Medical University	0.28	China
2	China Medical University	63	China	Beth Israel Deaconess Medical Center	0.19	USA
3	Shanghai University of Traditional Chinese Medicine	62	China	Shanghai University of Traditional Chinese Medicine	0.17	China
4	KyungHee University	60	South Korea	Chang Gung University	0.15	China
5	China Medical University	41	China	National Yang-Ming University	0.15	China
6	Chengdu University of Traditional Chinese Medicine	36	China	Tianjin University of Traditional Chinese Medicine	0.14	China
7	Fudan University	35	China	Korea Institute Oriental Medicine	0.13	South Korea
8	Chinese Academy of Medical Sciences	34	China	Southwest Medical University	0.13	China
9	Capital Medical University	32	China	University of Maryland	0.13	USA
10	Zhejiang Chinese Medical University	32	China	The University of Hong Kong	0.12	China

Israel Deaconess Medical Center, all other institutions are universities. Being the main front for training researchers, universities have the most scientific research output. In addition to the investment in scientific research in schools, we should also increase investment in research institutes, hospitals, and other institutions.

## Analysis of Journals and Co-Cited Journals

In this study, the number of journals included was 575, as shown in [Figure 5A](#). Among them, the journal *Evidence-based Complementary and Alternative Medicine* has the largest number of articles (131). [Table 3](#) lists the top five journals with published articles; most of these articles are published in the United States. Among them, *Evidence-based Complementary and Alternative Medicine* has the highest impact factor (IF) of 2.65, followed by *Acupuncture in Medicine*, which has an IF of 1.976. To summarize, the overall IF of journals was low, which indicates that the international acceptance of related literature on acupuncture treatment of inflammatory diseases is low. Analyzing co-cited journals would help understand the distribution of important knowledge sources in a specific field.<sup>14</sup> [Figure 5B](#) and [Table 3](#) show that the most frequently cited journals are *Evidence-based Complementary and Alternative Medicine*, with a citation frequency of 1512 times. Because acupuncture is an alternative therapy, most literature content related to acupuncture for anti-inflammation is on the mechanism of action, which is consistent with the contents of this journal. Second, *Pain* and *Acupuncture in Medicine* are in line with the research theme, because inflammation and pain often accompany each other, and the analgesic and anti-inflammatory effects of acupuncture on various diseases are obvious.

The double map superposition of journals is a new method for displaying the distribution, citation trajectory, gravity center shift, and other information of papers in this research field.<sup>15</sup> [Figure 5C](#) displays the double map superposition of journals related to acupuncture for anti-inflammation. The cited journal is on the left, the reference journal is on the right, and the link in the middle is the citation trail. The color of the link distinguishes the journal's discipline. The horizontal and vertical axes of the ellipse in the map indicate the number of authors and the number of papers, respectively. As shown in the figure, the journals with the most contributions are *Evidence-Based Complementary and Alternative Medicine*, *Pain*, *Acupuncture in Medicine*, and *Cochrane Database of Systematic Reviews*. The cited journals are mainly from the medicine, clinical, biology, immunology, and molecular science fields, and the reference journals are mainly from the fields of nutrition, health, medicine, psychology, biology, genes, and molecules. Literature and periodicals about





**Table 3** Top 5 Journals and Co-Cited Journals of Publications on Acupuncture for Anti-Inflammation

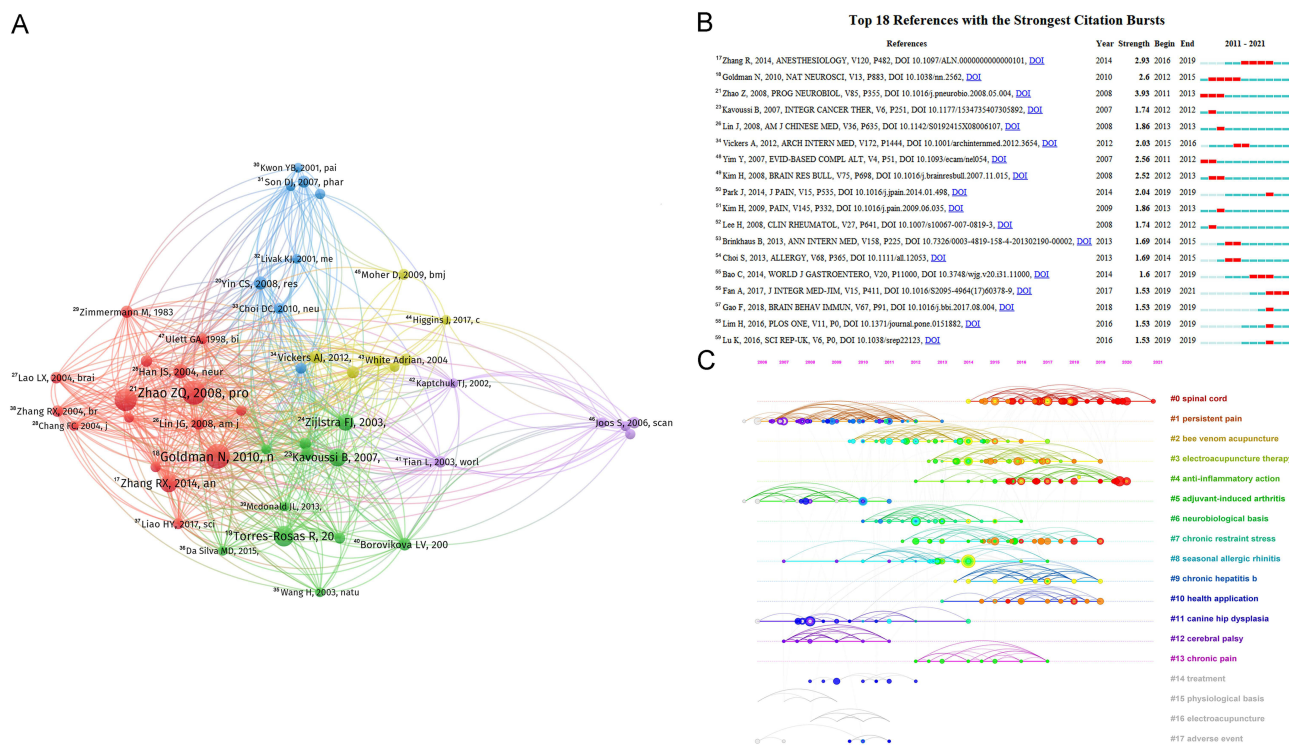
Rank	Journal	Pub	IF	Country	Co-Cited Journal	Pub	IF	Country
1	Evidence Based Complementary and Alternative Medicine	131	2.65	US	Evidence Based Complementary and Alternative Medicine	1512	2.65	US
2	Medicine	63	1.817	US	Pain	1119	7.926	US
3	Acupuncture in Medicine	55	1.976	England	Acupuncture in Medicine	850	1.976	England
4	Medical Acupuncture	41	\	US	Cochrane Database of Systematic Reviews	810	12.008	England
5	World Journal of Acupuncture-moxibustion	26	0.885	China	Plos one	774	3.752	US

**Abbreviations:** Pub, Publications; IF, Impact Factor; according to Journal Citation Reports (2021).

acupuncture treatment of inflammatory diseases have wide coverage, and their research contents are concentrated in the fields of medicine, biology, and molecules.

## Analysis of Co-Cited References

In total, 56,836 references were included in the study, and the literature with a citation frequency of >20 was displayed using a visual atlas, as shown in Figure 6A. Sigma value is calculated based on the centrality and the burstness, which can be used to identify innovative topics, with the calculation formula is as follows:  $\text{Sigma} = (\text{centrality} + 1) * \text{burstness}$ .<sup>16</sup> The literature with the largest sigma value in the figure is Zhang RX, 2014<sup>17</sup> (Sigma=3.428) and Goldman N, 2010<sup>18</sup> (Sigma=3.38). Both authors have studied the mechanism of acupuncture in treating inflammatory pain. Table 4 lists the top 10 cited references. Of them, 3 are research articles (Goldman N, 2010,<sup>18</sup> Torres-Rosas R, 2014,<sup>19</sup> Yin CS, 2008<sup>20</sup>) exploring the mediating factors and pathways of acupuncture-mediated anti-inflammatory and analgesic effects; 7 are reviews (Zhao ZQ, 2008,<sup>21</sup> Han JS, 2003,<sup>22</sup> Kavoussi B, 2007,<sup>23</sup> Zhang RX, 2014,<sup>17</sup> Zijlstra FJ, 2003,<sup>24</sup> Han JS, 2004,<sup>25</sup>



**Figure 6** Analysis of co-cited references: (A) map of the co-occurrence of co-cited references. (B) Map of co-cited references with the strongest citation bursts. (C) Timeline view of co-cited references.

**Table 4** Top 10 Co-Cited References on Acupuncture for Anti-Inflammation

Rank	Title	Fre	Author (Year)	Journal	IF
1	Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture	89	Goldman N (2010) <sup>18</sup>	Nature Neuroscience	28.771
2	Neural mechanism underlying acupuncture analgesia	84	Zhao ZQ(2008) <sup>21</sup>	Progress in Neurobiology	10.885
3	Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies	75	Han JS(2003) <sup>22</sup>	Trends in Neurosciences	16.978
4	Dopamine mediates vagal modulation of the immune system by electroacupuncture	64	Torres-Rosas R (2014) <sup>19</sup>	Nature Medicine	87.241
5	The neuroimmune basis of anti-inflammatory acupuncture	53	Kavoussi B (2007) <sup>23</sup>	Integrative Cancer Therapies	3.077
6	Mechanisms of Acupuncture-Electroacupuncture on Persistent Pain	51	Zhang RX(2014) <sup>17</sup>	Anesthesiology	8.986
7	Anti-inflammatory actions of acupuncture	49	Zijlstra FJ (2003) <sup>24</sup>	Mediators of Inflammation	4.529
8	Acupuncture and endorphins	37	Han JS(2004) <sup>25</sup>	Neuroscience Letters	3.197
9	A proposed transpositional acupoint system in a mouse and rat model	33	Yin CS(2008) <sup>20</sup>	Research in Veterinary Science	2.554
10	Acupuncture analgesia: A review of its mechanisms of actions	32	Lin JG(2008) <sup>26</sup>	American Journal of Chinese Medicine	6.005

**Abbreviations:** Fre, Frequency; IF, Impact Factor, according to Journal Citation Reports (2021).

Lin JG, 2008<sup>26</sup>) and summary of the clinical efficacy and mechanism of acupuncture for anti-inflammation and analgesia. Among them, the article of Torres-Rosas R was published in *Nature Medicine*, which has the highest IF.<sup>19</sup> This study investigated a new anti-inflammatory factor mediated by sciatic nerves. After EA stimulation, the vagus nerve was induced to activate aromatic L - amino acid decarboxylase, promote dopamine production, and achieve a good anti-inflammatory effect. The most frequently cited article was by Goldman N published in *Nature Neuroscience*.<sup>18</sup> This study investigated whether the anti-inflammatory and analgesic effects of acupuncture were mediated by acupuncture by activating the adenosine A1 receptor of the ascending nerve and expounded that interfering with the action of the adenosine A1 receptor or adenosine metabolites can prolong the clinical curative effect of acupuncture. The second most frequently cited article was by Zhao ZQ,<sup>21</sup> which was published in *Progress in Neurobiology* (IF 10.885). This article had the highest burst intensity value between 2011 and 2013, with a burst value of 3.93 (Figure 6B). This review expounded that the anti-inflammatory and analgesic mechanism of acupuncture is mainly reflected in the changes in different signal molecules and through functional brain imaging, including the mediation of opioid receptors, glutamate receptors, 5- hydroxytryptamine and CCK-8. The content of this article was a hot research topic at that time.

The reference that had a burst in recent years is Park JY, 2019.<sup>50</sup> This study proved that phosphorylation of extracellular signal-regulated kinase (ERK) after acupuncture is a marker of initiating the acupuncture effect, thereby providing new evidence for the mechanism underlying the anti-inflammatory and analgesic action of acupuncture. Another reference to the 2019 burst is Gao F.<sup>57</sup> This paper reveals that electroacupuncture (EA) inhibits the activation of NOD-like receptor thermal protein domain-associated protein 3(NLRP3) inflammatory bodies by stimulating CB2 receptors in inflammatory tissues, thus alleviating inflammatory pain. Lim HD,<sup>58</sup> through experimental studies, suggested that the anti-inflammatory effect of acupuncture may be mediated by the vagus nerve that regulates the inflammatory response in visceral organs. The article by Lu KW,<sup>59</sup> discussed the mechanism by which EA at the ipsilateral or contralateral acupoints ST36 and ST37 may change transient receptor potential vanilloid 1(TRPV1) and related signaling



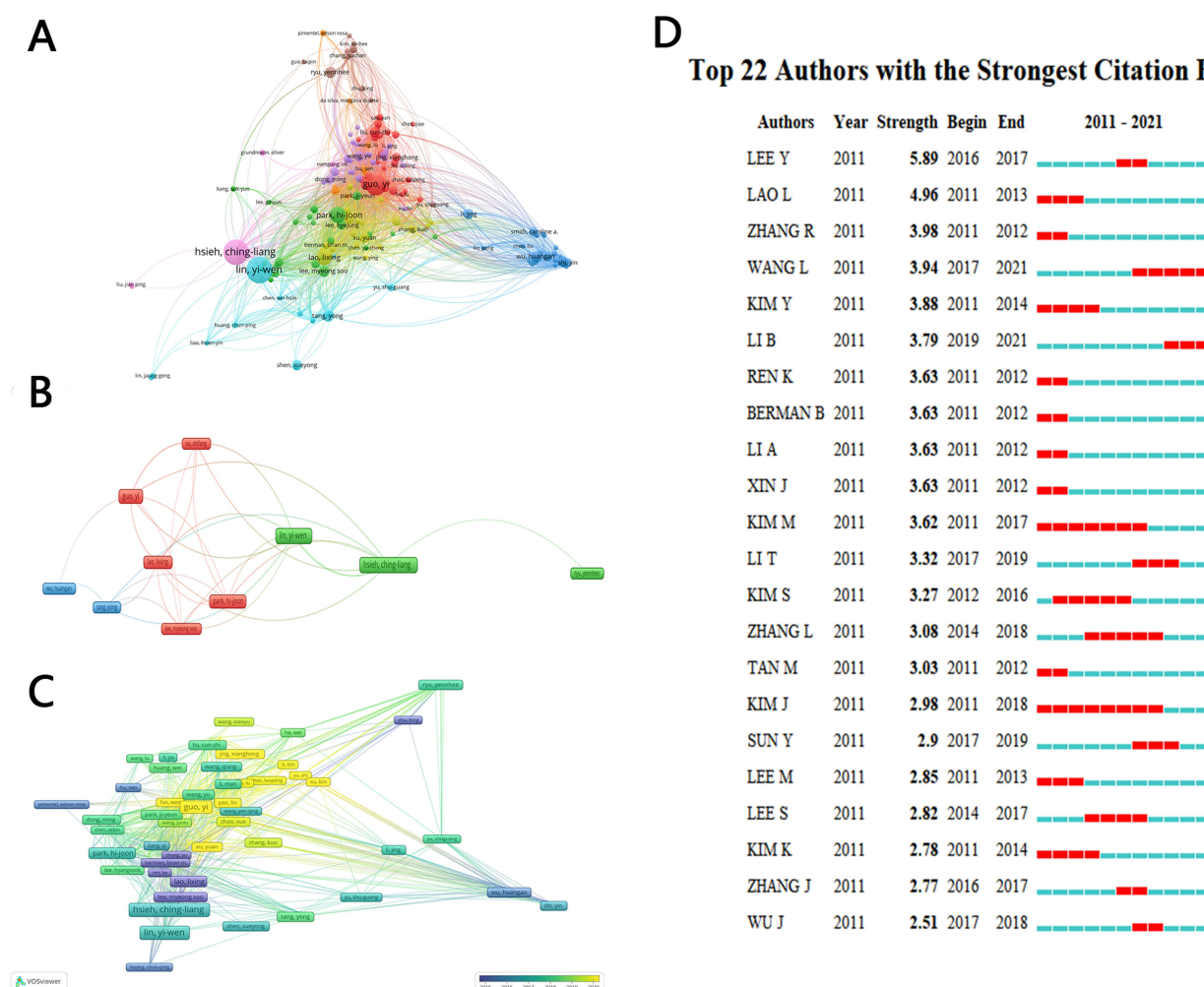
pathways to reduce inflammatory pain. Conclusively, these articles with strong bursts were the hotspots of research at that time and explored the anti-inflammatory mechanism of acupuncture from different angles.

The timeline chart of co-cited references (Figure 6C) is a view of a change in the clustering of co-cited references with time, which can reflect the evolution process of hot research topics. On the right is the clustering label, the horizontal axis represents the time, and the labels below the horizontal axis are the cited references. Among them, the Q value is the clustering module value. A Q value >0.3 indicates that clustering is significant. The S value is the average contour value of clustering, and the closer the S value is to 1, the higher the homogeneity is.<sup>60</sup> Eighteen clusters are present in the graph, Q = 0.8362, and S = 0.9363. The clustering results are reliable. The early research directions were # 1 persistent pain, # 5 adjuvant-induced arthritis, # 11 canine hip dysplasia and # 15 physiological basis and most of them were published before 2012. This was followed by # 2 bee venom acupuncture and #6 neurobiological basis, which mainly represent the research from 2010 to 2016; # 3 EA therapy, # 4 anti-infection action, # 7 chronological restraint stress, # 9 chronological therapy B, and # 10 health application, which represent the research conducted between 2013 and 2019 and finally, # 0 spinal cord which was the focus of research from 2014 to 2021. The hot topics studied in recent years are # 0 spinal cord and # 4 anti-infection action.

## Analysis of Authors and Co-Cited Authors

### Analysis of Authors

A total of 7225 authors contributed 1479 articles (Figure 7A). Figure 7B lists the top 10 authors with published articles. Including those listed in Table 5, most authors were from China, which indicates that China has conducted more research



**Figure 7** Analysis of authors: **(A)** map of author collaboration network, **(B)** top 10 authors in the number of published articles, **(C)** author map with more than 5 articles, **(D)** authors with the citation bursts.

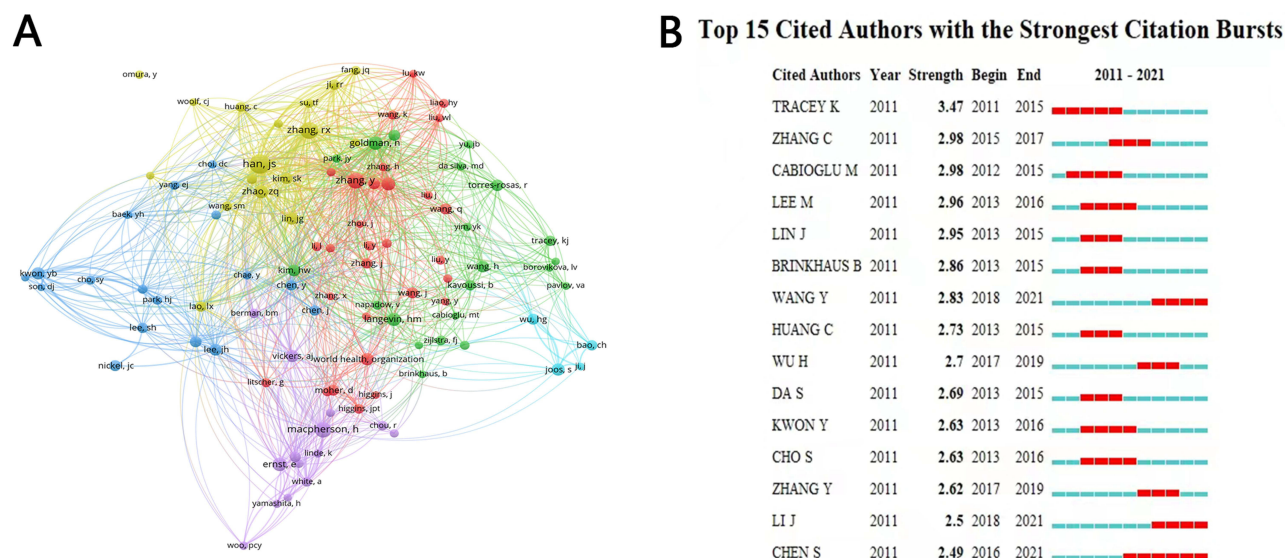
**Table 5** Top 10 Authors and Co-Cited Authors on Acupuncture for Anti-Inflammation

Rank	Author	Counts	Citations	Country or Territory	Co-Cited Author	Citations	Co-Cited Author	Centrality
1	Lin Yiwen	21	373	Taiwan	Han JS	176	Borovikova L	0.26
2	Hsieh Chingliang	20	369	Taiwan	Zhang RX	134	Choi S	0.22
3	Guo Yi	17	122	China	Macpherson H	120	Goldman N	0.20
4	Park Hijoon	13	129	South Korea	Zhang Y	115	Fang J	0.19
5	Lao Lixing	12	558	China	Goldman N	93	Huang Y	0.18
6	Lee Myeongsoo	9	318	South Korea	Ernst E	90	Belgrand M	0.18
7	Ryu Yeonhee	9	93	South Korea	Wang Y	84	Lee J	0.17
8	Tang Yong	9	113	China	Zhao ZQ	84	Chen J	0.17
9	Wu Huangang	9	129	China	Langevin HM	79	Li Y	0.14
10	Xu Zhifang	9	62	China	Kwon YB	77	Mcdonald J	0.14

in this field. The most prolific author is Lin Yiwen who studied the anti-inflammatory effects of different acupuncture types, such as EA,<sup>61</sup> ear acupuncture,<sup>62</sup> and bee venom acupuncture.<sup>63</sup> In addition, the anti-inflammatory mechanism of acupuncture was also revealed from different perspectives, such as the signaling pathway,<sup>64,65</sup> and nerve conduction.<sup>66</sup> Figure 7C lists the authors with more than five published articles; Of them, 93 authors were eligible. The colors of the nodes in the figure represent different years. Guo Yi and Xu Zhifang are active authors in the recent 2 years, with 17 and 9 published papers and their citation times being 122 and 62, respectively. The two authors have a close relationship and have jointly discussed that acupuncture in combination with bone marrow mesenchymal stem cell transplantation may become a new treatment method for spinal cord injury.<sup>67</sup> They also studied manual acupuncture, which can effectively stimulate innate immune cytokines and adaptive immune cytokines to reduce the inflammation and pain of infected joints. Thus, they provided the basis for the activation mechanism of manual acupuncture.<sup>68</sup> Figure 7D shows the author's burst in which the most burst is for Lee Y (5.89), followed by Lao L (4.96). Taken together, these authors are mainly exploring the anti-inflammatory mechanism of acupuncture, which may be the focus and hotspot of future research.

### Analysis of Co-Cited Authors

A total of 41,424 co-cited authors were included in this paper for visual analysis. Figure 8A shows the author's cooperation network with a co-cited frequency of >22. Table 5 lists the top 10 authors in terms of co-citations. Among them, Han JS was cited the most frequently, with the count reaching 176 times. His earliest exploration was the study of the relationship between acupuncture analgesia and central neurotransmitters.<sup>69</sup> However, the relationship between pain and inflammation is inextricably linked.<sup>70</sup> Borovikova L (0.26), Choi S (0.22), and Goldman N (0.20) ranked the top three in centrality. This finding shows that Borovikova L is the most influential co-cited author. In 2000, Borovikova L published an article in *Nature*, which first proposed the anti-inflammatory pathway of the parasympathetic nerve.<sup>40</sup> This article is also the most frequently cited. The most burst co-cited author is Tracey K (3.47) from 2011 to 2015, followed by Wang Y (2.83) and Li J (2.5) from 2018 to 2021 (Figure 8B). Wang Y reported that EA could reduce hypersensitivity injury by regulating JAK 2, STAT 3, and IL-6 expression in the spinal cord.<sup>71</sup> Li J evaluated the clinical effectiveness and safety of EA in knee osteoarthritis treatment. The results showed that EA provided better outcomes than western medicine.<sup>72</sup> The cited authors' research in this field mainly focused on the research of action mechanisms and clinical curative effect observation.



**Figure 8** Analysis of cited-authors: (A) map of cited author collaboration network, (B) cited authors with the strongest citation bursts.

## Analysis of Keywords

Keywords are standardized and professional terms that can comprehensively reflect the research topic. Visual analysis of high-frequency keywords can help better explore the research hotspots and directions in this field.<sup>73</sup> In total, 6062 keywords were included (Figure 9A). Figure 9B lists the top 10 keywords according to the frequency of occurrence, and the colors of nodes reflect different years. Inflammation and activation are popular keywords in recent years, which belong to the research content of the anti-inflammatory mechanism of acupuncture. This may be the research hotspot. Figure 9C shows the keywords with the strongest citation bursts. The top three keywords in terms of burst intensity values are double-blind (2011 to 2014), controlled trial (2011 to 2016), and osteoarthritis (2011 to 2013). This shows that double-blind, controlled trials and osteoarthritis had considerable influence then and attracted the attention of researchers. Acupuncture therapy, systematic review, and quality have recently burst, which shows that an increasing number of systematic review studies have been conducted on the topic of acupuncture against inflammation, and the quality requirements of these studies are also higher, which may be the future research trend.

Table 6 lists the top 10 keywords in terms of occurrence frequency and centrality. Among them, acupuncture (777) appeared the most frequently, followed by EA (283) and pain (237), which is in line with the research theme. The type of research on acupuncture against inflammation focuses on EA. In addition, the frequency of pain (166), expression (137), and activation (112) were all appeared more than 100 times, indicating that pain and inflammation are closely related. Inflammation may lead to pain, and pain may aggravate inflammation. The study on the mechanism of pain may be the key to exploring the anti-inflammatory mechanism of acupuncture; this needs further research to prove.<sup>74,75</sup> Table 6 also indicated that injection (0.28), impact (0.19), and messenger RNA (0.18) were the keywords with the highest centrality. Among them, “injection” was the most central keyword, which means that reagent injection has the greatest influence on animal experimental modeling in acupuncture and anti-inflammation research. We conducted log-likelihood ratio clustering on the included keywords and obtained a total of 17 clustering modules (Figure 9D). The top five refer to # 0 inflammatory disease, # 1 inflammatory pain, # 2 acupuncture, # 3 bee venom acupuncture, and # 4 pain. In the figure,  $Q = 0.7453$  and  $S = 0.8904$ , which indicates that the clustering results are convincing. Among them, the clusters closely related to acupuncture for inflammation treatment are as follows:

The largest clustering module was # 0, which contains 40 keywords with a silhouette of 0.878. Wang et al<sup>76</sup> concluded that the anti-inflammatory mechanism of acupuncture may be to regulate the secretion of related cytokines, thereby affecting the immune, endocrine, nervous, and other systems, or the polarization of T lymphocyte and cytokine





downregulation of pro-inflammatory factors (TNF- $\alpha$  and IL-1 $\beta$ ). This proved the precise effect of acupuncture in the treatment of inflammatory diseases.

The fourth clustering module was # 4, which contains 32 keywords and has a silhouette of 0.874. Jang et al<sup>81</sup> treated mice with Parkinson's disease and intestinal microbiota disorders by using acupuncture in ST36 and GB34. Acupuncture could restore the overexpression of the striatum and astrocytes and the conversion of Bax and Bcl-2 expression to block the inflammatory response and apoptosis. Moreover, acupuncture could regulate intestinal flora and enhance motor function. Abd El-Hameed et al<sup>82</sup> proved that bee venom acupuncture can effectively inhibit the high expression of pro-inflammatory cytokines, prevent the related damage caused by high levels of glutamate and dopamine in the hippocampus, and reduce the occurrence of pilocarpine-induced epilepsy in rats. Bee venom acupuncture can balance blood electrolytes and neurotransmitters and regulate the levels of pro-inflammatory and anti-inflammatory cytokines. Therefore, bee venom acupuncture can be used to prevent and treat various acute and chronic diseases, which may be the current research hotspot and the future development trend.

## Discussion

### Analysis of the Present Situation of Acupuncture Against Inflammation

In this study, the literature on acupuncture against inflammation published in the Web of Science Core Collection database from 2011 to 2021 was visually analyzed using bibliometrics. The number of publications related to this topic is increasing. This shows that this field has attracted considerable research attention. Inflammatory diseases are very common and are often accompanied by pain and other discomforts, which afflicts patients for a long time. Being among the main therapeutic methods of traditional Chinese medicine, acupuncture has a good clinical effect, particularly in the treatment of inflammatory bowel disease,<sup>83</sup> rheumatoid arthritis,<sup>84</sup> skin inflammation,<sup>85</sup> arteriosclerosis disease,<sup>86</sup> neuroinflammation,<sup>87</sup> postoperative sequelae,<sup>88</sup> and other diseases. Therefore, the number of publications in this research field is constantly increasing, and more research is expected in the future.

According to the country analysis, China has published the most articles, followed by the United States and South Korea. Although China contributes the most to this field and has a wide range of research, it has co-operated little with other countries and ranks ninth in centrality. It is necessary to strengthen the cooperation between countries, intensify in-depth research, promote academic exchanges, and enhance research influence in this field. This would lay the foundation for promoting acupuncture and its modernization and internationalization. Countries with the strongest citation bursts in the recent 2 years are Indonesia and Saudi Arabia, illustrating the huge potential for acupuncture and anti-inflammation research in these two countries.

**Table 6** Top 10 Keywords in Frequency and Centrality on Acupuncture for Anti-Inflammation

Rank	Keywords	Frequency	Keywords	Centrality
1	Acupuncture	777	Injection	0.28
2	Electroacupuncture	283	Impact	0.19
3	Inflammation	237	Messenger RNA	0.18
4	Pain	166	Fos expression	0.17
5	Expression	137	Infection	0.17
6	Activation	112	Adult	0.15
7	Management	111	Mice	0.15
8	Double-blind	91	Postoperative pain	0.15
9	Stimulation	91	Inflammatory pain	0.13
10	Mechanisms	89	Sepsis	0.13

Among the institutions, Beijing University of Chinese Medicine has the largest number of publications, and Capital Medical University has the largest centrality influence. This indicates that China occupies the main position of this research, which is consistent with the national analysis results. Most institutions are universities. This shows that a huge power gap exists in this field, because of an imbalance in research investment or because other institutions have not paid sufficient attention to this topic. Therefore, investment in research institutions, talent introduction, and academic exchange should increase.

The impact factors of cited journals are generally low, which indicates that the influence of and attention on this research field is insufficient. The main journal and most cited journal is *Evidence Based Complementary and Alternative Medicine*, which mainly focuses on evidence-based traditional medicine. Therefore, extensive literature is available on the anti-inflammatory mechanism of acupuncture.

The results of the author's analysis showed that Lin Yiwen is the author who publishes the most articles, followed by Hsieh Chingliang. Moreover, they closely co-operation for research on this topic. They mostly studied the mechanism of EA in treating various inflammatory diseases. They also expounded that acupoint injection of bee venom has anti-inflammatory, anti-apoptotic, and analgesic effects. Thus, bee venom acupuncture may be a hot research topic in recent years. Recently, the cooperative teams of Guo Yi and Xu Zhifang are more active. The team suggested that inhibiting macrophage polarization in arthritis may be among the key mechanisms of anti-inflammation. Joint injury and inflammation are mainly caused by the infiltration of inflammatory factors, including IL, interferon, TNF. Acupuncture can adjust the aforementioned inflammatory factors in two directions so that the body is in a balanced state.

## Analysis of Hotspots and Frontiers in Acupuncture for Inflammation Treatment

Among the 56,836 co-cited references, most of the high-frequency cited references are reviews, with relatively few research articles being published. The contents of the co-cited references reflect that the research on the anti-inflammatory effect of acupuncture mainly focuses on the discussion of the mechanism of action, and many animal experimental models also exist. The co-cited literature reveals that the most studied mechanisms in recent years are as follows: acupuncture stimulates the phosphorylation of protease ERK, inhibits the activation of NLRP3 inflammatory bodies, regulates CB2 receptors, and modifies the TRPV1 signaling pathway. The mechanism of the aforementioned hotspots is related to the immune cells of the immune system. During the development of many inflammatory diseases, the infiltration of multiple immune cells and the imbalance of immune polarization are the keys to inflammation. Regulating the immune cell balance may be the core action mechanism of acupuncture against inflammation and has been a hot research topic in recent years. Furthermore, the anti-inflammatory mechanism of acupuncture is multi-channel and multi-target. The mechanism is relatively complex and needs to be further studied in the future. This will help us to better find the key targets for treating inflammatory diseases, which will be the trend of future research.

The timeline chart of co-citation references shows that the co-citation of acupuncture against inflammation literature involves many disciplines and has rich topics. The three biggest topics studied are # 0 spinal cord, # 1 persistent pain, and # 2 bee venom acupuncture. The most popular topics in recent years are # 0 spinal cord and # 4 anti-inflammatory action, which may provide a direction for follow-up research. We classified the contents of the co-cited documents, involving obstetrics and gynecology, urology, dermatology, internal medicine, orthopedics, neurology, cell biology, psychiatry, anesthesiology, biophysics, and other disciplines. Acupuncture treatment for inflammation may be one of the universal ways to treat many diseases in many disciplines.

After visual analysis of keywords, we noted that among the literature on the anti-inflammatory effect of acupuncture, the most common types of acupuncture are EA, ear acupuncture, manual acupuncture, and bee venom acupuncture. Among them, EA is the most studied and may be the future research trend. According to the top 10 keywords in terms of frequency of use, inflammation, activation, expression, stimulation, and mechanisms all belong to the category of mechanism research. The literature on the anti-inflammatory effect of acupuncture mainly focuses on the exploration of the anti-inflammatory mechanism. According to its contents, acupuncture's anti-inflammatory is mainly achieved through the following pathways: 1. The most classic anti-inflammatory pathway is the HPA, and acupuncture can adjust the balance of this axis in both directions. On the one hand, acupuncture can directly activate HPA for anti-inflammation. Acupuncture can also promote the secretion of adrenocortical hormone and cortisol, thus controlling inflammation.<sup>89</sup> On



the other hand, acupuncture can downregulate the adrenocortical hormone, inhibit HPA hyperactivity, and reduce the sensitivity of the glucocorticoid receptor, thus achieving anti-inflammatory effects. 2. Sympathetic anti-inflammatory pathway: Acupuncture stimulation intensity can regulate the sympathetic nerve to activate adrenaline and release neurotransmitters such as catecholamine, ATP, and neuropeptide Y, thus regulating the inflammatory response of the body. Moreover, macrophages and T lymphocytes mediate the local anti-inflammatory effects of many sympathetic nerves. 3. Vagus nerve anti-inflammatory pathway: Acupuncture stimulates acupoints, and sensory nerves transmit information into the spinal cord and project them to many parts of the brain, such as the nucleus tractus solitarius, dorsal nucleus of the vagus nerve, and hypothalamus. After brain integration, the nerve–endocrine–immune network can be activated for triggering the anti-inflammatory effect. For example, acupuncture at Zusanli can improve the brain function of Parkinson's disease, regulate intestinal flora disorder, and control the inflammatory reaction and apoptosis.<sup>81</sup> 4. Anti-inflammatory pathway to regulate the immune cell balance: Acupuncture can regulate the balance of immune cells (macrophages, granulocytes, lymphocytes, etc.) to resist inflammation. For example, after acupuncture, macrophages are transformed from the M1 pro-inflammatory type to the M2 anti-inflammatory type.<sup>90</sup> It can also inhibit the expression of pro-inflammatory cytokines (TNF- $\alpha$ , IL-1, IL-6, etc.) or promote the release of anti-inflammatory and tissue repair factors (IL-10 and TGF- $\beta$ ) to regulate body inflammation.<sup>91</sup>

In a word, most research on the anti-inflammatory mechanism of acupuncture focuses on the aforementioned four anti-inflammatory pathways, which is consistent with the results of Li, N.<sup>1</sup> The anti-inflammatory mechanism of acupuncture is multi-channel and multi-target and there may be intersections in different anti-inflammatory channels. Inflammation is an important initial link in the development of various diseases. To a large extent, acupuncture can control various kinds of inflammation in the disease. Therefore, studying the anti-inflammatory effect of acupuncture is helpful to better find the key target of treating inflammatory diseases. Among them, the anti-inflammatory pathway of acupuncture that regulates the immune cell balance may be a research hotspot in recent years. Currently, immune cells, vagus nerve, signal pathway, inflammatory corpuscles, cytokines, and neurotransmitters are hot topics, and may also be the future development trend. Moreover, the top keywords “injection” and “mice” showed that most research on the anti-inflammatory mechanism of acupuncture is basic research conducted using animal models, which can provide data support for clinical practice. However, clinical research on this topic and its verification are lacking, and there is no better transformation from basic research to clinical practice. The investment in clinical research should be increased, and experimental design and quality control must be strictly monitored. The key targets of acupuncture against inflammation should be verified from a large number of basic data. Furthermore, we should summarize the anti-inflammatory laws of acupuncture and the clinically dominant diseases, evaluate the effectiveness and safety of acupuncture, and promote the predictive research work of acupuncture in treating inflammatory diseases. This may be the future research trend.

The advantage of this study is that it evaluates the global trend of acupuncture against inflammation research from 2011 to 2021 using the bibliometric method. The research data comes from English articles available in the Web of Science Core Collection database, which has high credibility and reliability. However, we did not search and analyze other databases, which may have resulted in research bias. In addition, acupuncture originated in China, and records in Chinese cannot be ignored, which may have led to language bias. We look forward to more comprehensive and detailed research in the future.

## Conclusion

In this study, bibliometrics was used to systematically categorize and objectively analyze the literature on acupuncture for anti-inflammation in the last 11 years. The research status, research hotspots and future development trend are preliminarily expounded, which is consistent with the results of acupuncture against inflammation research at present.<sup>92,93</sup> The research results may offer some value for acupuncture in treating inflammatory diseases. The number of publications in this research field is increasing, which reflects that use of acupuncture for inflammation treatment is a hot research topic for scholars. Regarding research trends, understanding the action mechanism of acupuncture against inflammation is the main focus of this field. The anti-inflammatory pathway of acupuncture that regulates immune cell balance may be extensively studied in mechanism research. Immune cells, vagus nerve, signal pathways, inflammatory corpuscles, cytokines, and neurotransmitters are popular research topics at present. However, a large number of high-

quality clinical research and verification is lacking; therefore, transforming the basic research of acupuncture against inflammation into clinical practice may be the trend of future research. In addition, EA and bee venom acupuncture are playing increasingly crucial roles in the treatment of inflammatory diseases, and may be a promising research direction.

## Data Sharing Statement

The data used to support the present findings are available from the corresponding author upon a reasonable request.

## Funding

This study was supported by the key project of the Key Laboratory of Ningxia Ethnomedicine Modernization, Ministry of Education (Project No. XZ 2021008) and the Natural Science Foundation of Ningxia (Project No. 2020 AAC 03173).

## Disclosure

Bing Chen and Di Liu are co-first authors for this study. The authors declare no conflicts of interest in this work.

## References

- Li N, Guo Y, Gong Y, et al. The Anti-inflammatory actions and mechanisms of acupuncture from acupoint to target organs via neuro-immune regulation. *J Inflamm Res.* 2021;14:7191–7224. doi:10.2147/JIR.S341581
- Kohandel Z, Farkhondeh T, Aschner M, et al. Anti-inflammatory action of astaxanthin and its use in the treatment of various diseases. *Biomed Pharmacother.* 2022;145:112179. doi:10.1016/j.biopha.2021.112179
- Khumalo GP, Van Wyk BE, Feng Y, et al. A review of the traditional use of Southern African medicinal plants for the treatment of inflammation and inflammatory pain. *J Ethnopharmacol.* 2022;283(114436):114436. doi:10.1016/j.jep.2021.114436
- Dinareello CA. Anti-inflammatory agents: present and future. *Cell.* 2010;140(6):935–950. doi:10.1016/j.cell.2010.02.043
- Dou B, Li Y, Ma J, et al. Role of neuroimmune crosstalk in mediating the anti-inflammatory and analgesic effects of acupuncture on inflammatory pain. *Front Neurosci.* 2021;15. doi:10.3389/fnins.2021.695670
- Yun-zhi Z, Bo C, Meng-dan LI, et al. The including and recommendation of acupuncture in NGC and NICE. *Zhongguo Zhen Jiu.* 2019;39(4):423–427. doi:10.13703/j.0255-2930.2019.04.020
- Yang F, Gong Y, Yu N, et al. ST36 Acupuncture Alleviates the Inflammation of Adjuvant-Induced Arthritic Rats by Targeting Monocyte/Macrophage Modulation. *Evid Based Complement Alternat Med.* 2021;2021:1–14. doi:10.1155/2021/9430501
- Zhi H, Wang Y, Chang S, et al. Acupuncture can regulate the distribution of lymphocyte subsets and the levels of inflammatory cytokines in patients with mild to moderate vascular dementia. *Front Aging Neurosci.* 2021;13. doi:10.3389/fnagi.2021.747673
- Ninkov A, Frank JR, Maggio LA. Bibliometrics: methods for studying academic publishing. *Perspect Med Educ.* 2022;11(3):173–176. doi:10.1007/s40037-021-00695-4
- Wu M, Wu D, Hu C, et al. Studies on children with developmental coordination disorder in the past 20 years: a bibliometric analysis via CiteSpace. *Front Psychiatry.* 2021;12. doi:10.3389/fpsy.2021.776883
- Van Eck NJ, Waltman L. Software survey: vOSviewer, a computer program for bibliometric mapping. *Scientometrics.* 2010;84(2):523–538. doi:10.1007/s11192-009-0146-3
- Chen T, Wen T, Dai N, et al. Cryogel/hydrogel biomaterials and acupuncture combined to promote diabetic skin wound healing through immunomodulation. *Biomaterials.* 2021;269(120608):120608. doi:10.1016/j.biomaterials.2020.120608
- Badakhsh M, Dastras M, Sarchahi Z, et al. Complementary and alternative medicine therapies and COVID-19: a systematic review. *Rev Environ Health.* 2021;36(3):443–450. doi:10.1515/revheh-2021-0012
- Li F, Wang S, Yao Y, et al. Visual analysis on the research of monocarboxylate transporters based on CiteSpace. *Medicine.* 2021;100(44):e27466. doi:10.1097/MD.00000000000027466
- Shi Y, Wei W, Li L, et al. The global status of research in breast cancer liver metastasis: a bibliometric and visualized analysis. *Bioengineered.* 2021;12(2):12246–12262. doi:10.1080/21655979.2021.2006552
- Wang K, Zhang H, Li X, et al. Bibliometric analysis of global research trends on small-cell lung cancer (2012–2021). *Front Oncol.* 2022;12. doi:10.3389/fonc.2022.955259
- Zhang RX, Lao L, Ren K, et al. Mechanisms of acupuncture–electroacupuncture on persistent pain. *Anesthesiology.* 2014;120(2):482–503. doi:10.1097/ALN.0000000000000101
- Goldman N, Chen M, Fujita T, et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nat Neurosci.* 2010;13(7):883–888. doi:10.1038/nn.2562
- Torres-Rosas R, Yehia G, Peña G, et al. Dopamine mediates vagal modulation of the immune system by electroacupuncture. *Nat Med.* 2014;20(3):291–295. doi:10.1038/nm.3479
- Yin CS, Jeong H, Park H, et al. A proposed transpositional acupoint system in a mouse and rat model. *Res Vet Sci.* 2008;84(2):159–165. doi:10.1016/j.rvsc.2007.04.004
- Zhao ZQ. Neural mechanism underlying acupuncture analgesia. *Prog Neurobiol.* 2008;85(4):355–375. doi:10.1016/j.pneurobio.2008.05.004
- Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci.* 2003;26:17–22. doi:10.1016/s0166-2236(02)00006-1
- Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. *Integr Cancer Ther.* 2007;6(3):251–257. doi:10.1177/1534735407305892

24. Zijlstra FJ, van den Berg-de Lange I, Huygen F, et al. Anti-inflammatory actions of acupuncture. *Mediators Inflamm.* 2003;12(2):59–69. doi:10.1080/0962935031000114943
25. Han JS. Acupuncture and endorphins. *Neurosci Lett.* 2004;361(1–3):258–261. doi:10.1016/j.neulet.2003.12.019
26. Lin JG, Chen W. Acupuncture analgesia: a review of its mechanisms of actions. *Am J Chin Med.* 2008;36(4):635–645. doi:10.1142/s0192415x08006107
27. Lao L, Zhang RX, Zhang G, et al. A parametric study of electroacupuncture on persistent hyperalgesia and Fos protein expression in rats. *Brain Res.* 2004;1020(1–2):18–29. doi:10.1016/j.brainres.2004.01.092
28. Chang FC, Tsai HY, Yu MC, et al. The central serotonergic system mediates the analgesic effect of electroacupuncture on ZUSANLI (ST36) acupoints. *J Biomed Sci.* 2004;11(2):179–185. doi:10.1007/BF02256561
29. Zimmermann M. Ethical guidelines for investigations of experimental pain in conscious animals. *Pain.* 1983;16(2):109–110. doi:10.1016/0304-3959(83)90201-4
30. Kwon YB, Lee JD, Lee HJ, et al. Bee venom injection into an acupuncture point reduces arthritis associated edema and nociceptive responses. *Pain.* 2001;90(3):271–280. doi:10.1016/S0304-3959(00)00412-7
31. Son DJ, Lee JW, Lee YH, et al. Therapeutic application of anti-arthritis, pain-releasing, and anti-cancer effects of bee venom and its constituent compounds. *Pharmacol Ther.* 2007;115(2):246–270. doi:10.1016/j.pharmthera.2007.04.004
32. Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) method. *Methods.* 2001;25(4):402–408. doi:10.1006/meth.2001.1262
33. Choi DC, Lee JY, Moon YJ, et al. Acupuncture-mediated inhibition of inflammation facilitates significant functional recovery after spinal cord injury. *Neurobiol Dis.* 2010;39(3):272–282. doi:10.1016/j.nbd.2010.04.003
34. Vickers AJ, Cronin AM, Maschino AC, et al. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med.* 2012;172(19):1444–1453. doi:10.1001/archinternmed.2012.3654
35. Wang H, Yu M, Ochani M, et al. Nicotinic acetylcholine receptor alpha7 subunit is an essential regulator of inflammation. *Nature.* 2003;421(6921):384–388. doi:10.1038/nature01339
36. Da Silva MD, Bobinski F, Sato KL, et al. IL-10 cytokine released from M2 macrophages is crucial for analgesic and anti-inflammatory effects of acupuncture in a model of inflammatory muscle pain. *Mol Neurobiol.* 2015;51(1):19–31. doi:10.1007/s12035-014-8790-x
37. Liao HY, Hsieh CL, Huang CP, et al. Electroacupuncture attenuates CFA-induced inflammatory pain by suppressing Nav1.8 through S100B, TRPV1, opioid, and adenosine pathways in mice. *Sci Rep.* 2017;7:42531. doi:10.1038/srep42531
38. Zhang RX, Lao L, Wang L, et al. Involvement of opioid receptors in electroacupuncture-produced anti-hyperalgesia in rats with peripheral inflammation. *Brain Res.* 2004;1020(1–2):12–17. doi:10.1016/j.brainres.2004.05.067
39. McDonald JL, Cripps AW, Smith PK, et al. The anti-inflammatory effects of acupuncture and their relevance to allergic rhinitis: a narrative review and proposed model. *Evid Based Complement Alternat Med.* 2013;2013:591796. doi:10.1155/2013/591796
40. Borovikova LV, Ivanova S, Zhang M, et al. Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin. *Nature.* 2000;405(6785):458–462. doi:10.1038/35013070
41. Tian L, Huang YX, Tian M, et al. Downregulation of electroacupuncture at ST36 on TNF-alpha in rats with ulcerative colitis. *World J Gastroenterol.* 2003;9(5):1028–1033. doi:10.3748/wjg.v9.i5.1028
42. Kaptchuk TJ. Acupuncture: theory, efficacy, and practice. *Ann Intern Med.* 2002;136(5):374–383. doi:10.7326/0003-4819-136-5-200203050-00010
43. White A. Writing case reports--author guidelines for acupuncture in medicine. *Acupunct Med.* 2004;22(2):83–86. doi:10.1136/aim.22.2.83
44. Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions version 5.2.0. *Cochrane Collab.* 2017;8:01–7.
45. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ.* 2009;339:b2535. doi:10.1136/bmj.b2535
46. Joos S, Wildau N, Kohlen R, et al. Acupuncture and moxibustion in the treatment of ulcerative colitis: a randomized controlled study. *Scand J Gastroenterol.* 2006;41(9):1056–1063. doi:10.1080/00365520600580688
47. Ulett GA, Han S, Han JS. Electroacupuncture: mechanisms and clinical application. *Biol Psychiatry.* 1998;44(2):129–138. doi:10.1016/s0006-3223(97)00394-6
48. Yim YK, Lee H, Hong KE, et al. Electro-acupuncture at acupoint ST36 reduces inflammation and regulates immune activity in Collagen-Induced Arthritic Mice. *Evid Based Complement Alternat Med.* 2007;4(1):51–57. doi:10.1093/ecam/nel054
49. Kim HW, Uh DK, Yoon SY, et al. Low-frequency electroacupuncture suppresses carrageenan-induced paw inflammation in mice via sympathetic post-ganglionic neurons, while high-frequency EA suppression is mediated by the sympathoadrenal medullary axis. *Brain Res Bull.* 2008;75(5):698–705. doi:10.1016/j.brainresbull.2007.11.015
50. Park JY, Park JJ, Jeon S, et al. From peripheral to central: the role of ERK signaling pathway in acupuncture analgesia. *J Pain.* 2014;15(5):535–549. doi:10.1016/j.jpain.2014.01.498
51. Kim HY, Wang J, Lee I, et al. Electroacupuncture suppresses capsaicin-induced secondary hyperalgesia through an endogenous spinal opioid mechanism. *Pain.* 2009;145(3):332–340. doi:10.1016/j.pain.2009.06.035
52. Lee H, Lee JY, Kim YJ, et al. Acupuncture for symptom management of rheumatoid arthritis: a pilot study. *Clin Rheumatol.* 2008;27(5):641–645. doi:10.1007/s10067-007-0819-3
53. Brinkhaus B, Ortiz M, Witt CM, et al. Acupuncture in patients with seasonal allergic rhinitis: a randomized trial. *Ann Intern Med.* 2013;158(4):225–234. doi:10.7326/0003-4819-158-4-201302190-00002
54. Choi SM, Park JE, Li SS, et al. A multicenter, randomized, controlled trial testing the effects of acupuncture on allergic rhinitis. *Allergy.* 2013;68(3):365–374. doi:10.1111/all.12053
55. Bao CH, Zhao JM, Liu HR, et al. Randomized controlled trial: moxibustion and acupuncture for the treatment of Crohn's disease. *World J Gastroenterol.* 2014;20(31):11000–11011. doi:10.3748/wjg.v20.i31.11000
56. Fan AY, Miller DW, Bolash B, et al. Acupuncture's role in solving the opioid epidemic: evidence, cost-effectiveness, and care availability for acupuncture as a primary, non-pharmacologic method for pain relief and management-white paper 2017. *J Integr Med.* 2017;15(6):411–425. doi:10.1016/S2095-4964(17)60378-9
57. Gao F, Xiang HC, Li HP, et al. Electroacupuncture inhibits NLRP3 inflammasome activation through CB2 receptors in inflammatory pain. *Brain Behav Immun.* 2018;67:91–100. doi:10.1016/j.bbi.2017.08.004

58. Lim HD, Kim MH, Lee CY, Namgung U. Anti-inflammatory effects of acupuncture stimulation via the vagus nerve. *PLoS One*. 2016;11(3):e0151882. doi:10.1371/journal.pone.0151882
59. Lu KW, Hsu CK, Hsieh CL, et al. Probing the effects and mechanisms of electroacupuncture at ipsilateral or contralateral ST36-ST37 acupoints on CFA-induced inflammatory pain. *Sci Rep*. 2016;6:22123. doi:10.1038/srep22123
60. Yang Q, Yang D, Li P, et al. A bibliometric and visual analysis of global community resilience research. *Int J Environ Res Public Health*. 2021;18(20):10857. doi:10.3390/ijerph182010857
61. Liao E, Tang N, Lin Y, et al. Long-term electrical stimulation at ear and electro-acupuncture at ST36-ST37 attenuated COX-2 in the CA1 of hippocampus in kainic acid-induced epileptic seizure rats. *Sci Rep*. 2017;7(472). doi:10.1038/s41598-017-00601-1
62. Kuo C, Lin Y, Tang N, et al. Electric stimulation of the ears ameliorated learning and memory impairment in rats with cerebral ischemia-reperfusion injury. *Sci Rep*. 2016;6(1). doi:10.1038/srep20381
63. Tsai L, Lin Y, Hsieh C. Effects of bee venom injections at acupoints on neurologic dysfunction induced by thoracolumbar intervertebral disc disorders in canines: a randomized, controlled prospective study. *Biomed Res Int*. 2015;2015(363801):1–7. doi:10.1155/2015/363801
64. Huang H, Liao H, Lin Y. Effects and mechanisms of electroacupuncture on chronic inflammatory pain and depression comorbidity in mice. *Evid Based Complement Alternat Med*. 2020;2020:1–10. doi:10.1155/2020/4951591
65. Lu K, Hsu C, Hsieh C, et al. Probing the effects and mechanisms of electroacupuncture at ipsilateral or contralateral ST36–ST37 acupoints on CFA-induced inflammatory pain. *Sci Rep*. 2016;6(1). doi:10.1038/srep22123
66. Huang C, Chen H, Su H, et al. Electroacupuncture reduces carrageenan- and CFA-induced inflammatory pain accompanied by changing the expression of Nav1.7 and Nav1.8, rather than Nav1.9, in mice dorsal root ganglia. *Evid Based Complement Alternat Med*. 2013;2013:1–8. doi:10.1155/2013/312184
67. Tang H, Guo Y, Zhao Y, et al. Effects and mechanisms of acupuncture combined with mesenchymal stem cell transplantation on neural recovery after spinal cord injury: progress and prospects. *Neural Plast*. 2020;2020:8890655. doi:10.1155/2020/8890655
68. Xu Y, Hong S, Zhao X, et al. Acupuncture alleviates rheumatoid arthritis by immune-network modulation. *Am J Chin Med*. 2018;46(5):997–1019. doi:10.1142/S0192415X18500520
69. Han JS, Tang J, Ren MF, et al. Central neurotransmitters and acupuncture analgesia. *Am J Chin Med*. 1980;8(4):331–348. doi:10.1097/ALN.00000000000002130
70. Ji R, Nackley A, Huh Y, et al. Neuroinflammation and central sensitization in chronic and widespread pain. *Anesthesiology*. 2018;129(2):343–366. doi:10.1097/ALN.00000000000002130
71. Wang Y, Xia Y, Xue M, et al. Electroacupuncture ameliorates mechanical hypersensitivity by down-regulating spinal Janus kinase 2/signal transducer and activation of transcription 3 and interleukin 6 in rats with spared nerve injury. *Acupunct Med*. 2021;39(4):358–366. doi:10.1177/0964528420938376
72. Li J, Li Y, Luo L, et al. The effectiveness and safety of acupuncture for knee osteoarthritis. *Medicine*. 2019;98(28):e16301. doi:10.1097/MD.00000000000016301
73. Yu T, Yang H, Luo X, et al. Scientometric analysis of disaster risk perception: 2000–2020. *Int J Environ Res Public Health*. 2021;18(24):13003. doi:10.3390/ijerph182413003
74. Zhou WBS, Meng J, Zhang J. Does low grade systemic inflammation have a role in chronic pain? *Front Mol Neurosci*. 2021;14. doi:10.3389/fnmol.2021.785214
75. Dainese P, Wyngaert KV, De Mits S, et al. Association between knee inflammation and knee pain in patients with knee osteoarthritis: a systematic review. *Osteoarthritis Cartilage*. 2022;30(4):516–534. doi:10.1016/j.joca.2021.12.003
76. Wang J, Lu S, Yang F, et al. The role of macrophage polarization and associated mechanisms in regulating the anti-inflammatory action of acupuncture: a literature review and perspectives. *Chin Med*. 2021;16(1). doi:10.1186/s13020-021-00466-7
77. Ren W, Fu J, Yin H, et al. CBS-induced H2S generation in hippocampus inhibits EA-induced analgesia. *Evid Based Complement Alternat Med*. 2020;2020:1–10. doi:10.1155/2020/5917910
78. Cai W, Ma W, Wang G, et al. Antidepressant, anti-inflammatory, and antioxidant effects of electroacupuncture through sonic hedgehog–signaling pathway in a rat model of poststroke depression. *Neuropsychiatr Dis Treat*. 2019;15:1403–1411. doi:10.2147/NDT.S205033
79. Yu M, Wei R, Zhang T, et al. Electroacupuncture relieves pain and attenuates inflammation progression through inducing IL-10 production in CFA-induced mice. *Inflammation*. 2020;43(4):1233–1245. doi:10.1007/s10753-020-01203-2
80. Liu P, Zhou Y, Zhang Y, et al. Electroacupuncture alleviates surgery-induced cognitive dysfunction by increasing alpha 7-nAChR expression and inhibiting inflammatory pathway in aged rats. *Neurosci Lett*. 2017;659:1–6. doi:10.1016/j.neulet.2017.08.043
81. Jang J, Yeom M, Ahn S, et al. Acupuncture inhibits neuroinflammation and gut microbial dysbiosis in a mouse model of Parkinson's disease. *Brain Behav Immun*. 2020;89:641–655. doi:10.1016/j.bbi.2020.08.015
82. Abd El-Hameed AM, Abuelsaad ASA, Khalil A. Bee venom acupuncture therapy ameliorates neuroinflammatory alterations in a pilocarpine-induced epilepticus model. *Metab Brain Dis*. 2021;36(7):2047–2058. doi:10.1007/s11011-021-00766-9
83. Li Y, Zhang H, Yang J, et al. P2Y12 receptor as a new target for electroacupuncture relieving comorbidity of visceral pain and depression of inflammatory bowel disease. *Chin Med*. 2021;16(1). doi:10.1186/s13020-021-00553-9
84. Li H, Man S, Zhang L, et al. Clinical efficacy of acupuncture for the treatment of rheumatoid arthritis: meta-analysis of randomized clinical trials. *Evid Based Complement Alternat Med*. 2022;2022:1–12. doi:10.1155/2022/5264977
85. Zhao B, Chen Y, Liao S, et al. Successfully treated recalcitrant atopic eczema with acupoint autohemotherapy: a case report and hypothesized mechanism of the therapy. *J Integr Med*. 2022;20(2):182–186. doi:10.1016/j.joim.2022.01.003
86. Wu X, Mo Q, Yang Z, et al. Comparative efficacy of different types of acupuncture as adjuvant therapy on carotid atherosclerosis: a protocol for systematic review and network meta-analysis. *BMJ Open*. 2022;12(4):e49778. doi:10.1136/bmjopen-2021-049778
87. Xin Y, Wang J, Xu A. Electroacupuncture ameliorates neuroinflammation in animal models. *Acupunct Med*. 2022;40(5):474–483. doi:10.1177/09645284221076515
88. Tang Y, Wang T, Yang L, et al. Acupuncture for post-operative cognitive dysfunction: a systematic review and meta-analysis of randomized controlled trials. *Acupunct Med*. 2021;39(5):423–431. doi:10.1177/0964528420961393
89. Ulloa L, Quiroz-Gonzalez S, Torres-Rosas R. Nerve stimulation: immunomodulation and control of inflammation. *Trends Mol Med*. 2017;23(12):1103–1120. doi:10.1016/j.molmed.2017.10.006

90. Xu Z, Hong S, Wang S, et al. Neuroendocrine-immune regulating mechanisms for the anti-inflammatory and analgesic actions of acupuncture. *World J Tradit Chin Med.* 2020;6(4):384–392. doi:10.4103/wjtc.wjtc\_41\_20
91. Ouyang B, Gao J, Che J, et al. Effect of electro-acupuncture on tumor necrosis factor- $\alpha$  and vascular endothelial growth factor in peripheral blood and joint synovia of patients with rheumatoid arthritis. *Chin J Integr Med.* 2011;17(7):505–509. doi:10.1007/s11655-011-0783-2
92. Cao B, Tan F, Zhan J, et al. Mechanism underlying treatment of ischemic stroke using acupuncture: transmission and regulation. *Neural Regen Res.* 2021;16(5):944. doi:10.4103/1673-5374.297061
93. Na-na Y, Chun-xia T, Yue-jie LI, et al. Research progress of acupuncture for peripheral inflammatory response. *Zhongguo Zhen Jiu.* 2022;42(9):1078–1082. doi:10.13703/j.0255-2930.20211028-0003

### Journal of Pain Research

Dovepress

### Publish your work in this journal

The Journal of Pain Research is an international, peer reviewed, open access, online journal that welcomes laboratory and clinical findings in the fields of pain research and the prevention and management of pain. Original research, reviews, symposium reports, hypothesis formation and commentaries are all considered for publication. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-pain-research-journal>