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Global Trends and Research Frontiers in Ischemic Stroke and Inflammation: A Bibliometric Analysis from 2015 to 2025

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Abstract

Background

This study aimed to provide a bibliometric overview of ischemic stroke (IS) and inflammation, summarize recent advances, identify research hotspots, and highlight potential directions for inflammation-targeted therapeutic strategies.

Methods

Publications on IS and inflammation from 2015 to 2025 were retrieved from the Web of Science Core Collection. Bibliometrix, VOSviewer, and CiteSpace were used to analyze and visualize countries/regions, institutions, authors, journals, cited references, and keyword networks.

Results

A total of 7,338 publications from 1,287 sources were included. Scientific output increased substantially over the past decade. China and the USA were the leading contributors. China ranked first in publication output and total citations, whereas the USA showed a higher average citation rate and broader international collaboration. Major universities and medical research centers, including Capital Medical University, Zhejiang University, and Harvard University, made substantial contributions and formed active collaboration networks. The International Journal of Molecular Sciences was the most productive journal, while the Journal of Neuroinflammation had the highest impact factor among the top 10 source journals. Keyword and cluster analyses identified oxidative stress, reperfusion injury, blood-brain barrier dysfunction, microglial activation, autophagy, pyroptosis, gut microbiota, network pharmacology, and stem cell-related research as major hotspots and emerging frontiers.

Conclusion

This bibliometric analysis mapped the knowledge structure and research trends of IS and inflammation from 2015 to 2025. The findings suggest rapid growth in this field, with increasing emphasis on microglia-centered mechanisms, regulated cell death, neurovascular injury, gut microbiota, and translational therapeutic strategies.

Clinical Trial Registration

Not applicable.

1. Introduction

Stroke, a prevalent cerebrovascular disease, significantly impacts global health due to its high morbidity and mortality rates[1]. ischemic stroke (IS) representing 75–80% of all stroke cases, and is characterized by the sudden interruption of blood flow to localized brain tissues, resulting in either acute or subacute brain damage[2,3]. This disruption often leads to varying degrees of language, motor; and sensory dysfunction, profoundly affecting the quality of life for patients[3]. Intravenous tissue-type plasminogen activator remains a cornerstone in the management of acute IS, recommended within 4.5 hours from symptom onset[3,4]. Advanced imaging techniques are now essential in guiding the selection of patients for interventions such as thrombectomy, ensuring that even those with large core infarcts[5], who were — previously considered less likely to benefit — are accurately identified and treated. However, the utility of these treatments is limited by this narrow therapeutic window, and they do not directly address the long term cellular damage that follows reperfusion. These limitations underscore the critical need for a deeper understanding of the molecular and cellular modifications that ensure after stroke in order to pave the way for innovative therapeutic strategies.

Intense and prolonged inflammatory responses significantly exacerbate brain damage following a stroke. Extensive research has demonstrated that post-stroke inflammation contributes to the breakdown of the blood-brain barrier (BBB), the development of vasogenic edema, hemorrhagic transformation, and the potential recovery of neurological functions[6–8]. Neuroinflammation, a consistent feature associated with all stages of IS, is triggered by the release of damage-associated molecular patterns (DAMPs) from injured and dying cells[7,9]. These DAMPs, such as adenosine, heat shock proteins, high mobility group box 1, and interleukin-33, activate immune cells and initiate various signaling pathways[7,10]. Recent studies employing meta-analyses and Mendelian randomization indicate that inflammatory markers like IL-6 and high-sensitive CRP (hs-CRP) can be biomarkers to predict the recurrence and severity of IS, suggesting their potential in guiding anti-inflammatory treatment strategies[11]. Consequently, targeting neuroinflammatory pathways offers promising therapeutic avenues for both treating and even preventing IS. Despite extensive research, there is still a shortage of comprehensive data synthesizing the volume of literature, the contributing countries, institutions, journals, and leading researchers in the field of IS and inflammation.

Bibliometrics, widely used to analyze scholarly publications, use databases like the Web of Science (WOS) to organize and evaluate empirical contributions, thus clarifying complex research landscapes[12]. This method is increasingly being applied across various disciplines, proving particularly effective for science mapping, which is — a crucial tool in an era characterized by voluminous, fragmented, and sometimes contentious studies. Bibliometrics integrates quantitative and qualitative analyses to reveal various facets of publications, such as identifying the contributing countries, journals, authors, and institutions. It highlights commonly cited studies and prevalent keywords, and delineates the collaboration networks among nations, institutions, and researchers within specific scientific domains. Additionally, bibliometrics studies can offer newcomers a comprehensive overview of the evolution and developmental frontiers of a specific research area[13]. While several bibliometric analyses have explored

IS or inflammation-related topics individually[14–16], a comprehensive overview of the research landscape at the intersection of these two areas remains limited. This study seeks to address this gap by constructing a global map of scientific publications on IS and inflammation, offering new insights into the combined development and emerging trends of these fields.

2. Methods

This manuscript does not contain any animal or individualized patient information, nor does it include potentially identifiable human images or data. Consequently, ethical approval was not required for this work.

2.1 Data source and Search Strategy

For our bibliometric study, we accessed the Web of Science Core Collection (WOSCC), renowned for its comprehensive inclusion of over 12,000 influential journals across multiple disciplines. The WOSCC database suite includes the Science Citation Index Expanded (SCI-expanded), Social Sciences Citation Index (SSCI), and other relevant indexes tailored to our interdisciplinary focus. on March 15, 2026, we conducted a search specifically designed to gather literature on IS and neuroinflammation. Our search string was meticulously crafted to capture all pertinent studies: ((TS= (“ischemic stroke” OR “cerebral ischemia” OR “ischaemic stroke” OR “brain ischemia” OR “cerebral ischaemia” OR “cerebral infarction” OR “brain ischaemia” OR “brain infarction”)) AND TS=(inflammation OR inflammations OR inflammatory)) AND TS=(mechanism*). This query was limited to articles published between January 1, 2015, to December 31, 2025, focusing on ‘regular articles’ and ‘reviews’ to ensure the inclusion of all comprehensive studies and critical analyses relevant to our objectives.

We retrieved the “complete record” from the WOS database, including 7,338 publications from 1,287 sources, with no duplicated or invalid records identified during data screening. These records, containing details including authors, source, title, publication data, abstract, keywords, addresses, references, and grants, were exported in plain text format and they were labeled “download_xx” for use with bibliometric tools. The final dataset included 11,490 author keywords and 310,651 cited references. The WOS Citation Report showed that the publications from 2015 to 2025 had a total of 231,138 citations, with these publications being cited by 136,905 articles, an h-index of 170, and an average citation rate of 31.67 per item. In addition, our dataset meets the minimum sample size threshold for bibliometric analysis (at least 200 papers), as recommended by previous studies[17].

2.2 Bibliometric analysis

For bibliometric analysis, the latest versions of several bibliometric tools were utilized including: the “Bibliometrix” R package[18], VOSviewer software (Version 1.6.20)[19], and CiteSpace software (Version 6.3.R2 Advanced)[20]. The global annual publication volume and trend maps were constructed using CiteSpace, with the data de-duplicated annually and imported into Microsoft Excel (Version 2024) for chart insertion. The exponential growth trend and its fit were analyzed using Excel to assess overall

trends. Bibliometrix R package includes a range of functions for scientometric quantitative research. In this study, it was employed to: 1) summarize the volume of publications and citations among countries, institutions, journals, and authors 2) identify the cumulative occurrences of keywords and 3) to visualize country cooperation networks and generate Sankey diagrams mapping the flow of authors, keywords and institutions. VOSviewer, a free Java-based software, is a distance-based bibliometric tool that focuses on visualizing bibliometric networks[21] and it was employed to visualize the cooperation networks among countries and authors. CiteSpace is a Java application that focuses on dynamic visualizations, reflecting the evolution of bibliometric networks over time[22] and it was used to visualize the country cooperation network, keywords with the strongest citation bursts, and the timeline distribution of keyword clusters.

3. Results

3.1 Annual publication trends and country/region distribution

As shown in Fig. 1A, the annual number of publications showed a sustained upward trend over the past decade, increasing from approximately 350 publications in 2015 to more than 1,100 publications in 2025. Exponential fitting demonstrated a strong goodness of fit, with an R^2 value of 0.9343, indicating a consistent growth pattern in this research field. Although a slight decrease was observed in 2023, the publication output increased again in 2024 and reached its highest level in 2025.

3.2 Country/region contributions, citation impact, and collaboration networks

Figure 1B and Tables 1 and 2 provide a comprehensive overview of global research outputs and citation metrics in IS and inflammation from 2015 to 2025. The country-wise distribution of publications showed that China had a substantial lead in publication output, followed by the USA, Germany, Korea, India, Iran, Japan, Italy, the United Kingdom, and Canada. It is important to note that this analysis accounts for contributions from multiple authors per article, which may result in country-specific output counts exceeding the total number of published articles.

As shown in Table 1, China ranked first in global citations, with 119,974 citations and an average of 27 citations per article, indicating both high productivity and substantial academic influence. The USA ranked second in total citations, with 40,319 citations, and showed a higher average citation rate of 52.9 citations per article, suggesting strong international recognition of its research output. Germany, Italy, and the United Kingdom also demonstrated considerable citation impact, with the United Kingdom showing the highest average article citation rate among the top 10 countries at 60.8 citations per article. Other countries, including Korea, India, Canada, Iran, and Japan, also made notable contributions to the field, reflecting the broad international interest in IS and inflammation research.

Table 1
Citation metrics of the top 10 contributing countries/regions in research on ischemic stroke and inflammation.

Rank	Country	Global Citations	Average Article Citations
1	CHINA	119974	27
2	USA	40319	52.9
3	GERMANY	8835	48
4	ITALY	5542	44
5	UNITED KINGDOM	5533	60.8
6	KOREA	5112	27.8
7	INDIA	4313	24
8	CANADA	4106	47.7
9	IRAN	3903	22.6
10	JAPAN	3710	26.1

Table 2 further summarizes the top 10 countries by publication output. China contributed 4,442 articles, accounting for 60.53% of the total publications, followed by the USA with 762 articles, accounting for 10.38%. Germany and Korea each published 184 articles, followed by India, Iran, Japan, Italy, the United Kingdom, and Canada. In terms of international collaboration, Germany had the highest proportion of multiple-country publications among the top 10 countries, with an MCP percentage of 44.57%, followed by the United Kingdom at 39.56% and the USA at 27.30%. In contrast, China had a relatively lower MCP percentage of 9.82%, indicating that although China had the highest publication output, a large proportion of its publications were single-country publications.

Table 2
Top 10 countries/regions by publication output in research on ischemic stroke and inflammation.

Rank	Country	Articles	Articles %	SCP	MCP	MCP %
1	CHINA	4442	60.53	4006	436	9.82
2	USA	762	10.38	554	208	27.30
3	GERMANY	184	2.51	102	82	44.57
4	KOREA	184	2.51	160	24	13.04
5	INDIA	180	2.45	131	49	27.22
6	IRAN	173	2.36	130	43	24.86
7	JAPAN	142	1.94	126	16	11.27
8	ITALY	126	1.72	92	34	26.98
9	UNITED KINGDOM	91	1.24	55	36	39.56
10	CANADA	86	1.17	65	21	24.42
SCP, Single Country Publications; MCP, Multiple Country Publications						

The combined insights from Figs. 2A, 2B, and 2C, together with the data in Table 2, highlight the extensive scope of global collaboration in the field of IS and inflammation. Each figure, generated using distinct bibliometric tools, provides a complementary view of the international research landscape. Figure 2A, produced using Bibliometrix, maps the global network of research collaborations and shows that China, the USA, and several European countries are major contributors to international cooperation. Figure 2B, created with VOSviewer, illustrates country collaboration clusters based on co-authorship relationships. The USA showed extensive international links, while China had prominent collaborative connections with the USA and several Asian and European countries. The color-coded clusters indicate different collaborative communities within the global research network. Figure 2C, generated by CiteSpace, further depicts the temporal evolution of country-level collaboration from 2015 to 2025, with node size representing publication volume and connecting lines indicating collaborative relationships. Overall, these findings suggest that research on IS and inflammation has developed into a globally collaborative field, with China and the USA serving as the leading contributors in both publication output and international research connections.

3.3 Institutional contributions and collaboration analysis

Up to 3,144 institutions are reported to have contributed to research on IS and inflammation. Figure 3A highlights the ten institutions with the highest number of publications in this domain. Capital Medical University leads with 487 articles, followed by Zhejiang University and Harvard University, with 273 and 261 articles, respectively. Other highly productive institutions include Shanghai Jiao Tong University with

252 articles, Soochow University with 246 articles, Wuhan University with 232 articles, Wenzhou Medical University with 228 articles, Nanjing Medical University with 220 articles, Fudan University with 204 articles, and Harvard University Medical Affiliates with 202 articles. These data underline the concentrated research efforts of leading academic institutions in this field.

Figure 3B, which utilizes VOSviewer for analysis, illustrates the intricate network of interactions among these institutions. The network map reveals that a substantial portion of collaborations was concentrated among Chinese institutions. Notably, major nodes such as Capital Medical University, Zhejiang University, Shanghai Jiao Tong University, Soochow University, Wuhan University, Wenzhou Medical University, Nanjing Medical University, and Fudan University are prominently represented and closely interconnected, indicating a strong domestic collaboration network within China. The size of each node corresponds to the institution's publication volume, while the color gradient, from darker to lighter shades, marks the timeline of publication activities, with earlier works shown in darker tones and more recent works in lighter tones. This visualization not only underscores the pivotal role of Chinese institutions in spearheading research in this field but also shows how these domestic collaborations were augmented by international partnerships. For example, Harvard University and Harvard University Medical Affiliates, despite being based in the USA, feature prominently within the network, highlighting the global dimension of institutional contributions and collaborations in IS and inflammation research.

3.4 Source journal analysis

Research on IS and inflammation is widely disseminated across a diverse array of scientific journals. Table 3 displays the top 10 journals with the most published articles in this domain, alongside their respective impact factors (IFs) for 2024. According to the Journal Citation Reports (JCR), these journals are predominantly ranked in the first quartile (Q1), with others categorized in the second (Q2) and third quartiles (Q3), showcasing a spectrum of influence within the academic community. Geographically, the distribution of these publishers is primarily concentrated in Europe, with journals based in Switzerland, England, Ireland, and the Netherlands, while also featuring contributions from the USA and China. This geographic distribution emphasizes the international extent and cooperative nature of research within this field.

Table 3
Top 10 source journals by publication output in research on ischemic stroke and inflammation.

Rank	Sources	Articles	Country	IF	JCR-c
1	International Journal of Molecular Sciences	187	Switzerland	4.9	Q1
2	Frontiers in Pharmacology	175	Switzerland	4.8	Q1
3	Molecular Neurobiology	146	USA	4.3	Q1
4	Journal of Neuroinflammation	123	ENGLAND	10.1	Q1
5	Frontiers in Neurology	112	Switzerland	2.8	Q2
6	Journal of Ethnopharmacology	108	Ireland	5.4	Q1
7	Neural Regeneration Research	94	China	6.7	Q2
8	International Immunopharmacology	91	Netherlands	4.7	Q1
9	Frontiers in Immunology	89	Switzerland	5.9	Q1
10	Journal of Stroke & Cerebrovascular Diseases	85	USA	1.8	Q3

IF, Impact Factor (2024); JCR-C, Journal Citation Reports Category (2024).

3.5 Author productivity and collaboration analysis

Bibliometrix and VOSviewer were employed to generate visualization networks of authors and co-cited authors with respect to research on IS and inflammation. A significant number of 25,929 authors have contributed to research in this area. As illustrated in Table 4, among these authors, Ying Wang was a highly influential researcher, having published 154 articles with an h-index of 39, reflecting a substantial impact in the field. Following closely were Lu Wang and Jin Wang, with 96 and 124 publications and h-indices of 35 and 34, respectively. Yun Zhang, Yang Li, Jun Chen, Xue Li, Lin Zhang, Jie Li, and Gao Chen also featured prominently, with high h-indices and substantial publication counts, indicating their significant contributions to the research community.

Table 4
Top 10 influential authors in research on ischemic stroke and inflammation.

Rank	Author	Articles	H-index
1	Ying Wang	154	39
2	Lu Wang	96	35
3	Jin Wang	124	34
4	Yun Zhang	163	34
5	Yang Li	134	33
6	Jun Chen	65	31
7	Xue Li	96	29
8	Lin Zhang	96	29
9	Jie Li	83	28
10	Gao Chen	52	27

The co-citation network (Fig. 4A) delineates clusters of authors who have been particularly impactful in this field of research. This illustrates the complex web of co-authorship, with nodes representing individual researchers and links showing their collaborative interactions. The node size corresponds to each author's publication output, and the thickness of the links indicates the strength of their collaborative ties. This mapping reveals several densely connected clusters centered on prolific authors, while also pointing out less connected groups, highlighting opportunities for enhanced collaboration.

Figure 4B provides a visual account of the publication output of these leading researchers over time, displaying not only their productivity but also the trajectory of their influence in the research community. For instance, authors such as Ying Wang, Yun Zhang, Yang Li, Jin Wang, Lu Wang, Xue Li, Lin Zhang, Jie Li, Jun Chen, and Gao Chen contributed consistently to the field, with several showing sustained or increasing publication activity in recent years.

3.6 Highly cited references analysis

To highlight the most impactful research within the specialized area of IS and inflammation, we have compiled a list of reports that have received the highest local citations, emphasizing their significance over general global citation metrics. This methodical approach is particularly beneficial for new scholars in the field, enabling them to effectively identify foundational and influential research. The research compiled on inflammation in IS referenced 310,651 cited references, with the top 10 most locally cited works detailed in Table 5.

The table displays a variety of critical studies, demonstrating the depth and breadth of research in IS and inflammation. For instance, the work “Functions and mechanisms of microglia/macrophages in neuroinflammation and neurogenesis after stroke” by Xiong XY, published in Progress in Neurobiology in 2016, has garnered 165 local citations and 593 global citations, establishing its key role in post-stroke neuroinflammation and neurogenesis research. Following closely, “Global brain inflammation in stroke” by Shi KB, published in Lancet Neurology in 2019, has accumulated 161 local citations and 740 global citations, greatly enhancing our understanding of global inflammatory responses after stroke. Further, the paper by Jiang XY, “Blood-brain barrier dysfunction and recovery after ischemic stroke,” published in Progress in Neurobiology in 2018, received 158 local citations and 770 global citations, emphasizing the importance of blood-brain barrier dysfunction and recovery in ischemic stroke pathology. Moreover, Iadecola C’s article titled “Immune responses to stroke: mechanisms, modulation, and therapeutic potential,” published in Journal of Clinical Investigation in 2020, received 149 local citations and 606 global citations, highlighting the mechanisms, modulation, and therapeutic potential of immune responses in stroke.

Table 5
Top 10 locally cited references in research on ischemic stroke and inflammation.

Rank	References	Local Citations	Global Citations	Author	Journal	Year
1	Functions and mechanisms of microglia/macrophages in neuroinflammation and neurogenesis after stroke	165	593	XIONG XY	PROG NEUROBIOL	2016
2	Global brain inflammation in stroke	161	740	SHI KB	LANCET NEUROL	2019
3	Blood-brain barrier dysfunction and recovery after ischemic stroke	158	770	JIANG XY	PROG NEUROBIOL	2018
4	Pathogenic mechanisms following ischemic stroke	151	530	KHOSHNAM SE	NEUROL SCI	2017
5	Immune responses to stroke: mechanisms, modulation, and therapeutic potential	149	606	IADECOLA C	J CLIN INVEST	2020
6	Glial Cells: Role of the Immune Response in Ischemic Stroke	147	492	XU SB	FRONT IMMUNOL	2020
7	Neuroinflammation, Stroke, Blood-Brain Barrier Dysfunction, and Imaging Modalities	137	663	CANDELARIO-JALIL E	STROKE	2022
8	Dual Functions of Microglia in Ischemic Stroke	134	445	QIN C	NEUROSCI BULL	2019
9	Neuroinflammatory Mechanisms in Ischemic Stroke: Focus on Cardioembolic Stroke, Background, and Therapeutic Approaches	124	487	MAIDA CD	INT J MOL SCI	2020
10	The NLRP3 inflammasome drives inflammation in ischemia/reperfusion injury after transient middle cerebral artery occlusion in mice	101	315	FRANKE M	BRAIN BEHAV IMMUN	2021

3.7 Research keywords and frontier analysis

Keywords in scientific articles often reflect the main research topics and can reveal emerging trends within a specific field. Considering that the search strategy already included terms related to ischemic stroke, inflammation, and mechanisms, these search-defined terms were not overinterpreted as independent research hotspots. Instead, the interpretation focused on non-search-defined keywords that reflected specific biological processes, pathological mechanisms, therapeutic strategies, and emerging research directions. By using Bibliometrix analysis of keyword co-occurrence in IS and inflammation research, and merging terms with similar meanings, Fig. 5A displays a keyword frequency map from 2015 to 2025. Beyond the search-related terms, frequently occurring keywords included “oxidative stress,” “reperfusion injury,” “microglia,” “activation,” “apoptosis,” “expression,” “neuroprotection,” and “blood-brain barrier,” suggesting that oxidative injury, ischemia-reperfusion damage, microglial activation, cell death pathways, and neurovascular unit dysfunction are major thematic areas in this field.

Based on the keyword co-occurrence network according to CiteSpace, we conducted an emergent word detection analysis to identify the top 25 keywords with the strongest citation bursts in IS and inflammation research. As depicted in Fig. 5B, the timeline, shown as a blue line, features red segments indicating the duration of citation bursts for each keyword. Earlier burst keywords were mainly related to experimental ischemia models and inflammatory signaling, including “rat brain,” “tumor necrosis factor,” “intercellular adhesion molecule-1,” “toll-like receptors,” and “middle cerebral artery.” In contrast, more recent burst keywords included terms related to regulatory mechanisms, vascular injury, and translational research, such as “microRNAs,” “blood-brain barrier,” “cell migration,” and “vascular dementia,” indicating a gradual shift from classical inflammatory pathways toward molecular regulation and vascular-neuroimmune interactions.

The timeline viewer effectively illustrates the dynamic evolution of research hotspots in IS and inflammation through keyword representation. It explores temporal characteristics of research fields and the rise and fall of key terms within clusters. Documents within the same cluster are aligned horizontally, indicating chronological progression from left to right. The number of documents in each cluster underscores the depth and impact of research achievements in those areas. The CiteSpace timeline visualization identified major clusters including “acute ischemic stroke,” “cerebral ischemia-reperfusion injury,” “network pharmacology,” “Alzheimer’s disease,” “stem cells,” “cerebral ischemia,” “hemorrhagic transformation,” “vascular dementia,” “gut microbiota,” and “subarachnoid hemorrhage” (Fig. 5C). After accounting for the search-defined terms, the timeline analysis suggests that the field has evolved from classical ischemia-reperfusion injury and inflammatory signaling toward more diversified topics, including network pharmacology, stem cell-related repair, gut microbiota, vascular cognitive impairment, and neurovascular complications.

The Sankey diagram effectively illustrates the relationships among leading authors, their affiliated institutions, and frequently occurring keywords within the field of IS and inflammation. In this diagram, the rectangles are proportionally scaled to represent the frequency of occurrences of authors, affiliations, and keywords within the dataset. The thickness of the lines between nodes reflects the volume of connections, thereby illustrating the intensity of associations among the entities represented.

The diagram created by Bibliometrix highlights a dense network of interactions, particularly involving major institutions such as Capital Medical University, Zhejiang University, Wuhan University, Wenzhou Medical University, Fudan University, Shanghai Jiao Tong University, Nanjing Medical University, Harvard University, and Soochow University. After accounting for search-defined terms, the keyword component further suggests that topics such as oxidative stress, microglia, autophagy, pyroptosis, blood-brain barrier, and neuroprotection were closely connected with major authors and institutions in this field (Fig. 6).

4. Discussion

With the rapid development in big data science and visualization technology, scientometric maps have become a crucial tool for quickly identifying research hotspots and potential future research directions. This bibliometric analysis, utilizing various tools, provides an in-depth exploration of the dynamics and advancements in research on inflammatory mechanisms of IS from 2015 to 2025. The results showed that scientific output in this field has increased substantially over the past decade. China and the USA are the major contributors in this field, although they show distinct contribution patterns. China ranked first in both publication output and total global citations, whereas the USA showed a higher average citation rate and more extensive international collaborations, indicating its strong global academic influence. At the institutional level, major universities and medical research centers, particularly Capital Medical University, Zhejiang University, Harvard University, and several other leading Chinese institutions, made substantial contributions and formed active collaboration networks. Among the 10 most productive journals, the Journal of Neuroinflammation had the highest IF, while the International Journal of Molecular Sciences was the most prolific journal, and the distribution of these publishers was primarily concentrated in Europe. Furthermore, based on keywords with the strongest citation bursts and cluster analysis of co-occurring keywords, we identified several important hotspots and emerging frontiers in this field. These can be broadly classified into pathophysiological mechanisms, such as oxidative stress, reperfusion injury, and blood-brain barrier dysfunction; cellular-level research, particularly microglial activation and polarization; regulated cell death and inflammatory pathways, including autophagy and pyroptosis; and translational frontiers, such as gut microbiota, network pharmacology, and stem cell-related research. These topics highlight crucial areas of ongoing and future investigations that bridge basic and translational sciences in IS and inflammation.

In this bibliometric analysis, the reasons behind the significant contributions of China and the United States in IS and inflammation research merit deeper analysis. Similar patterns have been observed in bibliometric studies of other biomedical fields, including Parkinson's disease[23], Alzheimer's dementia[24], and myasthenia gravis [25]. Academic productivity is closely associated with national research capacity, which is often shaped by economic strength, research infrastructure, and long-term funding support[26]. In the present study, China ranked first in both publication output and total global citations, reflecting its rapidly expanding research capacity and increasing academic influence in this field. This may be partly attributable to China's large stroke burden, sustained investment in biomedical research, and the

concentration of research activity in major universities and medical institutions. In parallel, China's rapid economic growth has been accompanied by a marked expansion in scientific productivity[26]. China has also been reported to have surpassed the United States as the world's largest producer of scholarly publications, while its R&D expenditure has approached that of the United States in recent years[27]. In contrast, although the United States contributed fewer publications than China in the present analysis, it showed a higher average citation rate and a higher proportion of multiple-country publications, indicating stronger international visibility and collaboration intensity. These observations suggest that the leading positions of China and the United States are underpinned not only by academic activity itself, but also by broader national investment in biomedical science, public health priorities, and international research collaboration.

Building on foundational investments and strategic policies that enhance scientific output, international collaboration also plays a crucial role in strengthening a country's global leadership in scientific research. A further point of discussion is that high MCP percentages were not restricted to the largest producers. Countries such as Germany, the United Kingdom, and India also demonstrated relatively high proportions of multiple-country publications compared with China (Table 2). This indicates that smaller or mid-sized research systems may rely more heavily on international partnerships to enhance visibility, access expertise, and increase competitiveness. Such a pattern suggests that collaboration may serve different functions in different national contexts: for large scientific systems, it may enhance academic influence and translational reach; for smaller systems, it may represent an important mechanism for capacity building and international relevance [26]. These findings indicate that international collaboration provides an important complementary dimension for understanding academic influence beyond publication volume alone.

Extending this interpretation from national and institutional contributions to the knowledge base of the field, the author productivity and highly cited reference analyses provide a deeper understanding of how historical foundations and current research activity intersect to shape IS and inflammation research. The locally cited reference analysis showed that the most influential works were mainly concerned with microglia/macrophage function[28], global brain inflammation after stroke[29], blood-brain barrier dysfunction and recovery[30], immune responses to stroke[31], glial-cell involvement[32], and neuroinflammatory mechanisms in different stroke contexts[6] (Table 5). These studies have collectively established the conceptual foundation of this field by emphasizing post-stroke neuroinflammation, microglial activation, immune-cell infiltration, blood-brain barrier injury, and inflammatory signaling as central mechanisms of ischemic brain injury and repair. Continuing this intellectual foundation, the author analysis showed that 25,929 authors have contributed to this research area, with several leading authors demonstrating both high publication output and considerable h-index values (Table 4). The cooperation network map further revealed densely connected author clusters, indicating that sustained collaboration among productive research groups has played an important role in advancing this field (Fig. 4A and 4B). Taken together, these findings suggest that the development of IS and inflammation

research has been driven by both the lasting influence of foundational mechanistic studies and the concentrated contributions of active author networks.

Keywords in scientific research serve as crucial indicators that reflect the core content of studies, helping to identify pivotal themes and frontier directions in specific areas of research. Analyzing the frequency and co-occurrence of keywords reveals that terms related to IS and inflammation often focus on potential mechanisms involving microglia, highlighting microglia as a major cellular-level hotspot in this field and a central component of neuroinflammatory responses. Microglia are the principal immune cells within the CNS and play pivotal roles in the pathophysiology of IS. They phagocytose cellular debris, release neurotrophic factors and reactive oxygen species, and regulate synaptic pruning controlled by the complement system. Furthermore, microglia engage in complex interactions with various neuronal and non-neuronal cell types, such as astrocytes[33]. Following ischemic events, microglia are activated, releasing pro-inflammatory cytokines that enhance phagocytosis and exhibit antigen-presenting capabilities[34]. Microglial activation plays a beneficial role in clearing dead cells and tissue debris and in promoting the release of growth factors, but it can also exacerbate brain tissue damage through the release of pro-inflammatory cytokines and oxidants[33,35,36]. This dual role highlights the complexity and significance of microglial function, which is also a critical determinant of neuronal death following cerebral ischemia.

The most locally cited reference in the present analysis was Xiong et al.'s 2016 review, "Functions and mechanisms of microglia/macrophages in neuroinflammation and neurogenesis after stroke," which emphasized the dual roles of microglia/macrophages in brain injury, repair, and regeneration after stroke. This raises a pertinent question: are microglia/macrophages friend or foe in IS? Polarization describes the process by which microglia/macrophages adopt various phenotypes in response to stimuli, timing, and microenvironmental context[37]. This adaptive capability underlies microglial functional diversity in pathophysiological conditions, critically influencing the progression and resolution of neuroinflammation. The patterns of microglial activation vary substantially between the infarcted core and peri-infarcted areas[38]. Traditionally, microglial activation has been categorized into two primary phenotypes: classical activation (M1) and alternative activation (M2)[39]. Regulating microglial polarization may offer a promising strategy for improving stroke outcomes. For instance, after an IS episode, oxidative stress can activate the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, which promotes the polarization of microglia towards the anti-inflammatory M2 phenotype[40]. In addition, findings from our keyword and cluster analyses indicate that inflammatory pathways and regulated cell-death processes, particularly autophagy and pyroptosis, are closely connected with microglial function[41]. Autophagy may interact with ischemic inflammation by regulating microglial activation, as stroke-induced PARP14 has been shown to restrict post-stroke microglial activation and promote functional recovery through microglial autophagy modulation[42], whereas NLRP3 inflammasome activation can promote caspase-1-dependent pyroptosis and amplify post-ischemic inflammatory injury[43].

IS initiates an inflammatory cascade that leads to microglial activation and the recruitment of peripheral immune cells to the ischemic hemisphere [44]. Studies have shown that some of these immune cells originate from the intestine and they are influenced by the gut microbiota[45,46]. Functionally, the microbiome is vital for the maturation and functioning of the host's immune system, influencing the balance between pro-inflammatory and anti-inflammatory responses[47]. Additionally, gut bacteria are critical for the maturation and function of microglia under both steady-state conditions and following pathological disturbances. For instance, mice raised in germ-free environments, which lack all commensal bacteria, display an immature microglial phenotype[48]. As the gut microbiota becomes increasingly central in biomedical research, a better understanding of the gut–brain axis is driving the development of innovative research strategies aimed at reducing stroke severity and enhancing neurological recovery.

This study has several limitations. Firstly, only the WOSCC database was utilized for literature retrieval. Although WOSCC is often recommended as the most reliable database for bibliometric studies, some articles may still be missed, and citation counts may be underestimated, and potentially not reflecting the current status of all research in the field of inflammation in IS accurately. Secondly, the use of various tools without standardized parameter settings can introduce variability, leading to differing analysis results. Thirdly, bibliometric analysis cannot assess the quality of individual studies because citation metrics are time-dependent, meaning recent articles may have fewer citations compared to older articles due to their later publication dates. In addition, total citations can be misleading as some controversial studies can often be cited extensively for the wrong reasons.

5. Conclusions

This study conducted a detailed bibliometric analysis of research on inflammation and IS from 2015 to 2025, evaluating the literature contributions from various countries, institutions, authors, and journals. Based on 7,338 publications retrieved from the WOSCC database, our findings showed that scientific output in this field has increased substantially over the past decade. China and the USA were the leading contributors, with China ranking first in publication output and total global citations, while the USA showed stronger average citation impact and international collaboration. We also examined the evolution of research themes and identified several important hotspots, including oxidative stress, reperfusion injury, blood-brain barrier dysfunction, microglial activation, autophagy, pyroptosis, gut microbiota, network pharmacology, and stem cell-related repair. These findings provide useful information on the current research landscape and may help guide future mechanistic and translational studies on inflammation-targeted strategies for IS.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

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Data Availability

The bibliographic data analyzed during this study were retrieved from the Web of Science Core Collection. The processed data are available from the corresponding author upon reasonable request.

Consent to Publish

Not applicable.

Clinical Trial Registration

Not applicable.

Conflict of Interest

The authors declare that they have no competing interests.

Author Contribution

Conceptualization: B.L., C.T.O., and C.J.; Methodology: B.L. and D.L.; Data Curation: B.L., D.L., J.M., and X.L.; Formal Analysis: B.L. and D.L.; Visualization: B.L.; Writing—Original Draft Preparation: B.L.; Writing—Review and Editing: D.L., J.M., X.L., C.T.O., and C.J.; Supervision: C.T.O. and C.J.; Funding Acquisition: B.L. All authors have read and agreed to the published version of the manuscript.

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Figures

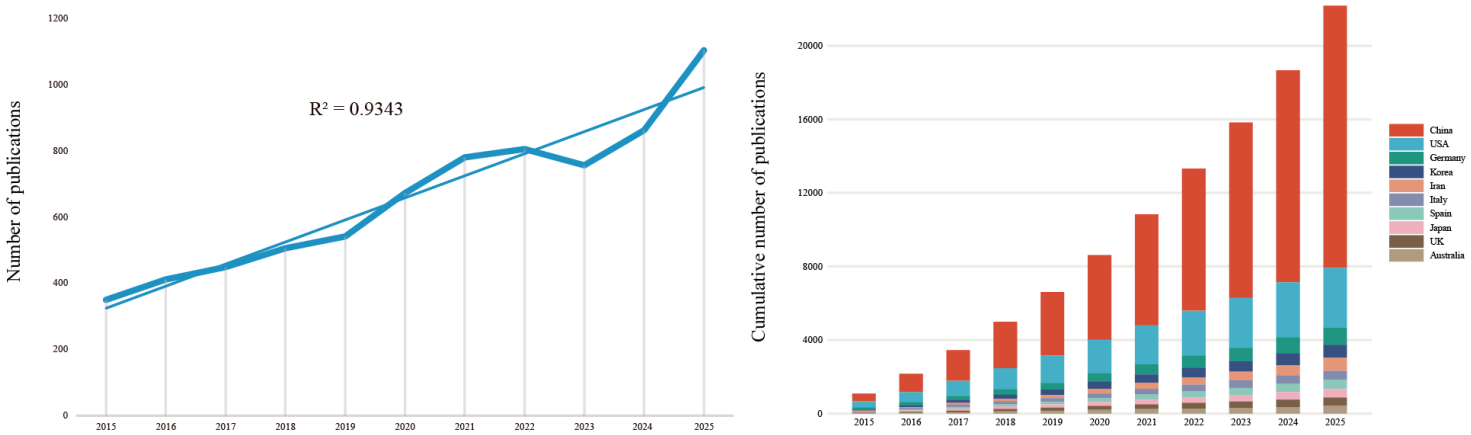


Figure 1

Trends in global research output on ischemic stroke and inflammation. (A) Annual publication output from 2015 to 2025 with exponential growth fitting. (B) Country-wise distribution of publications among the top contributing countries.

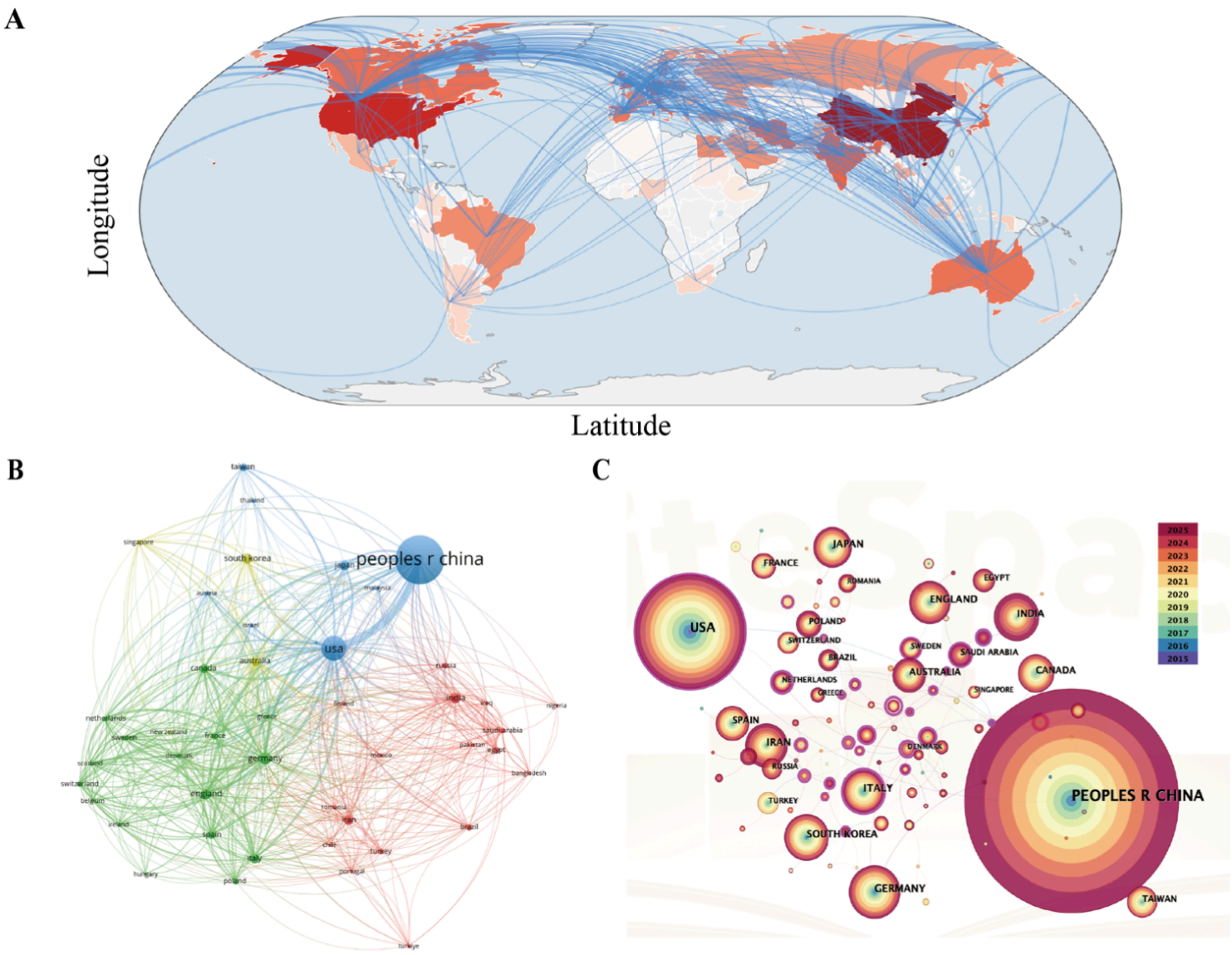


Figure 2

Country/region collaboration networks in research on ischemic stroke and inflammation. (A) Global collaboration map generated using Bibliometrix. (B) Country/region collaboration network generated using VOSviewer. (C) Country/region collaboration network generated using CiteSpace.

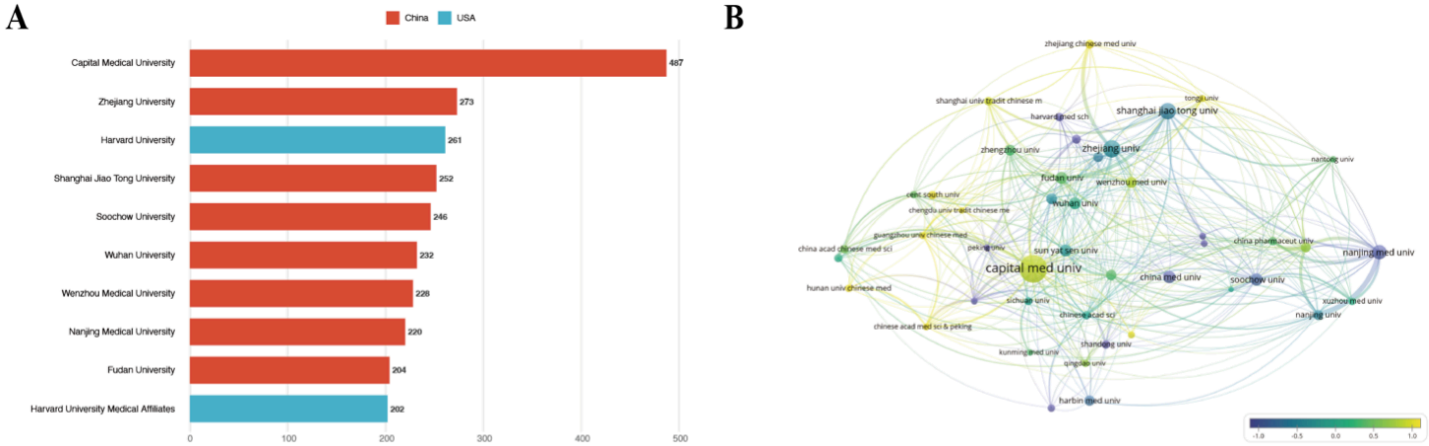


Figure 3

Key institutions in ischemic stroke and inflammation research. (A) Top 10 institutions ranked by number of publications. (B) Visualization of the global institutional co-authorship network.

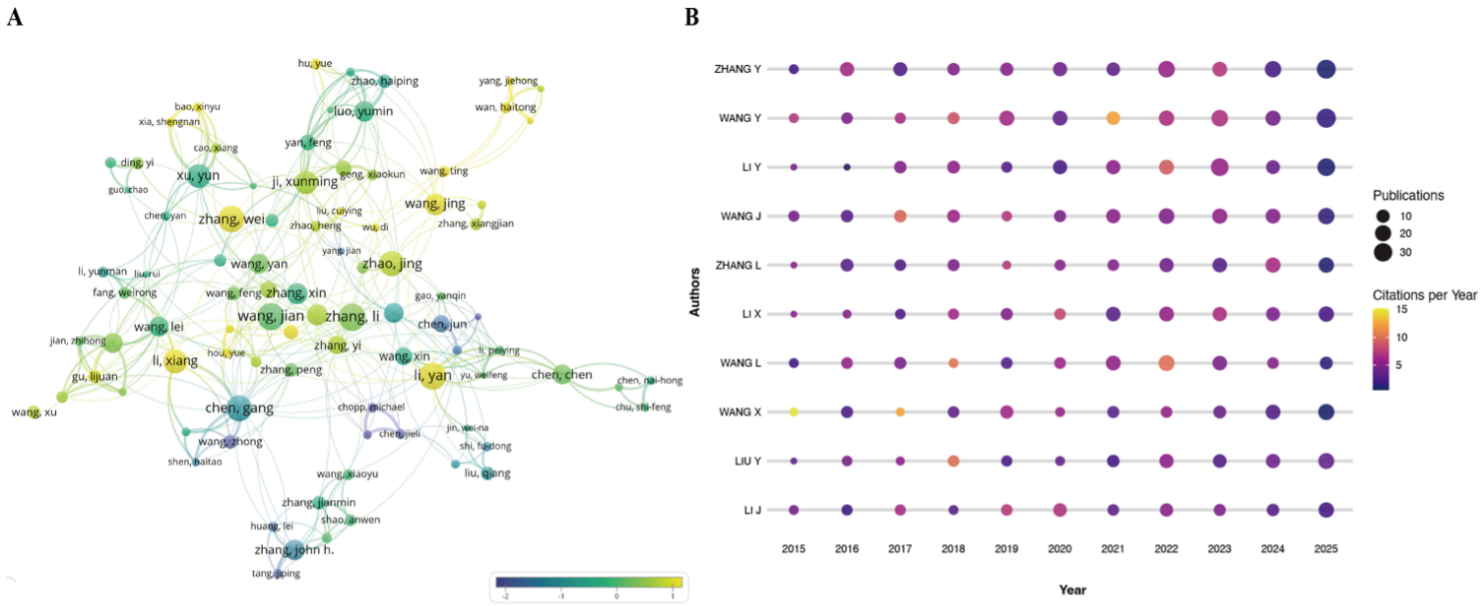


Figure 4

Visual atlas of influential authors in research on ischemic stroke and inflammation. (A) Author collaboration network map. (B) Authors' production over time.

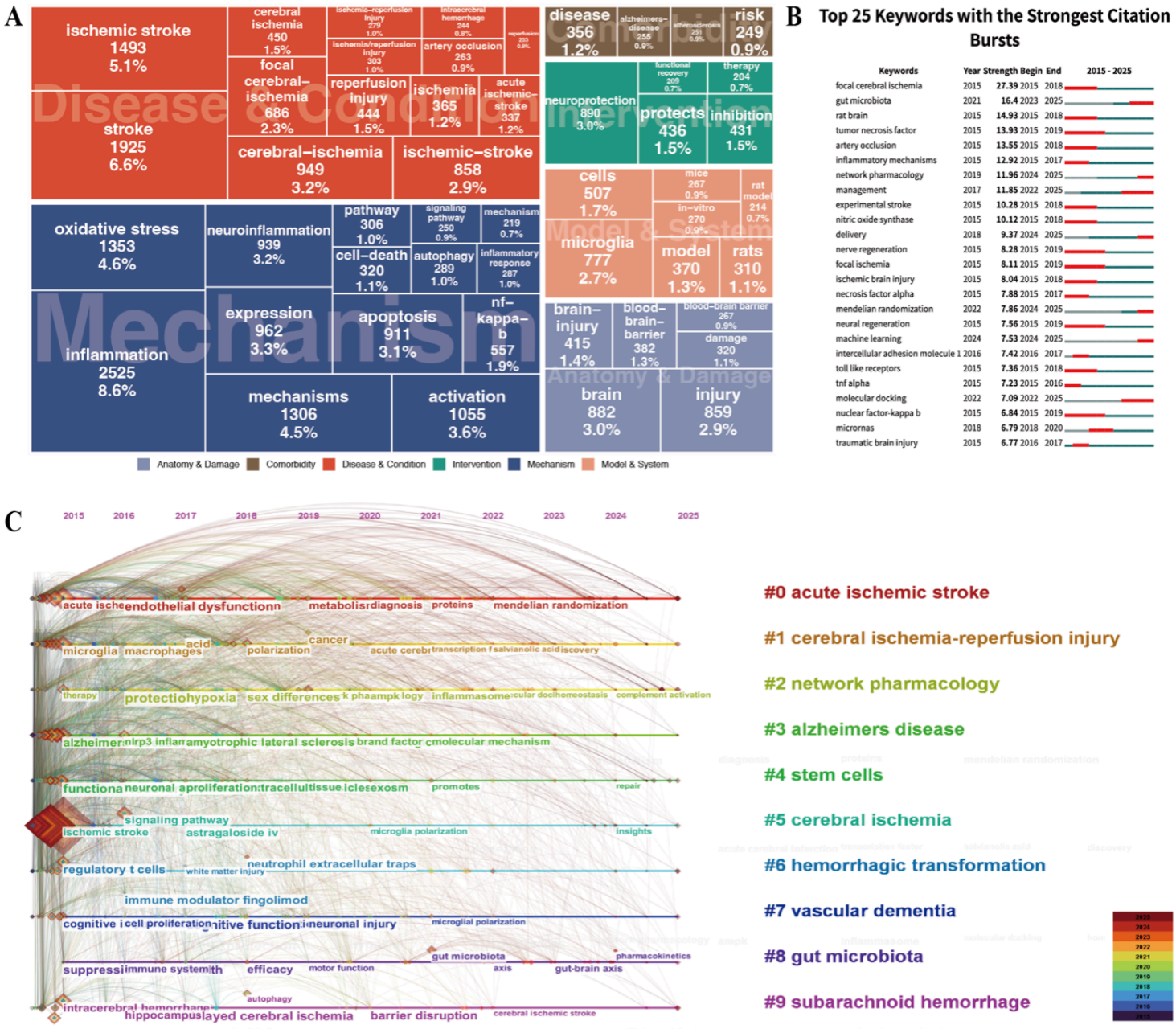


Figure 5

Visualization of research hotspots and frontiers in ischemic stroke and inflammation. (A) Treemap of keyword frequencies. (B) Top 25 keywords with the strongest citation bursts. (C) Timeline distribution of keyword clusters.

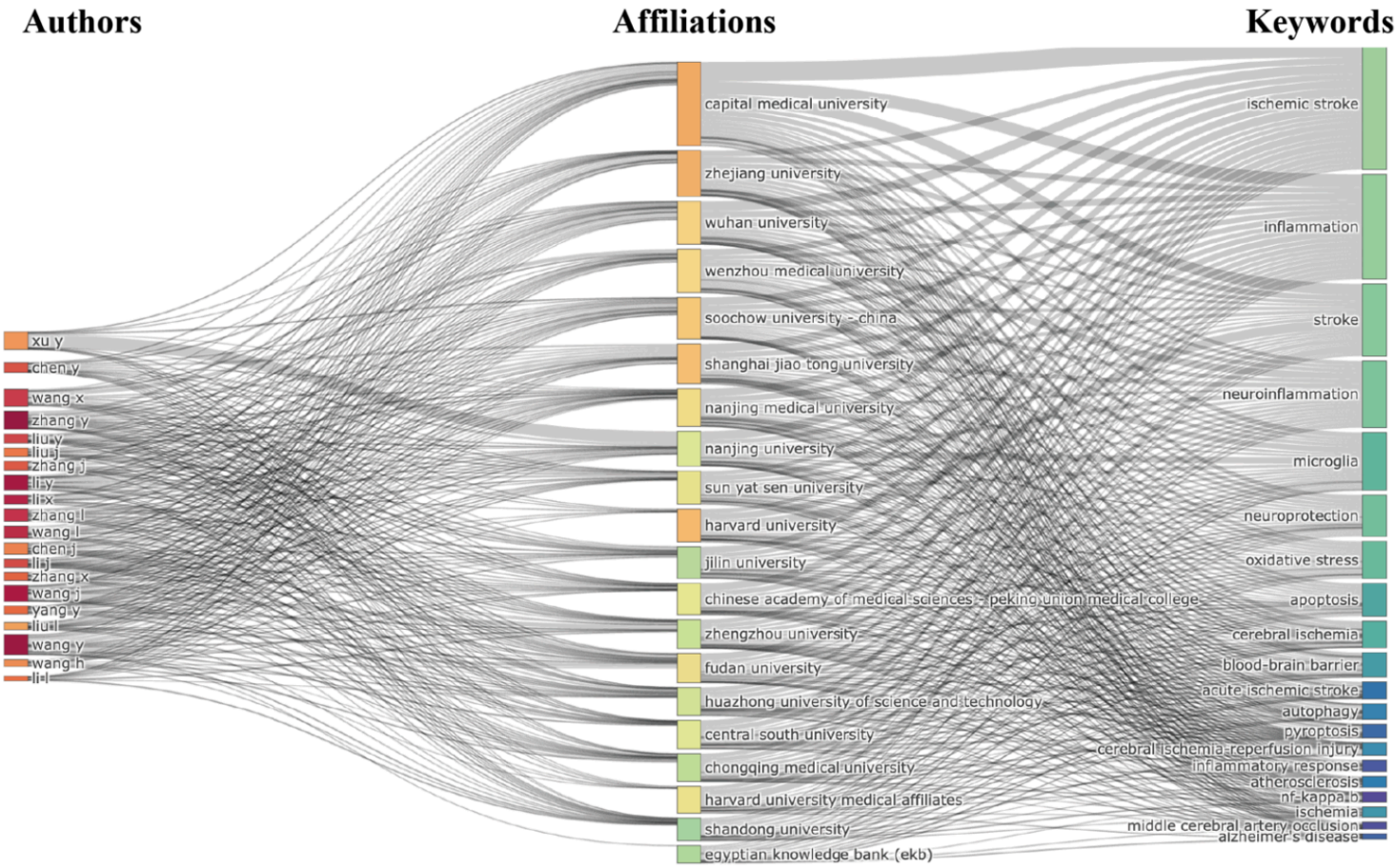


Figure 6

Three-field Sankey diagram of authors, affiliations, and keywords in ischemic stroke and inflammation research.