

A bibliometric analysis of mechanisms and linkage studies on neurological disorders and statins over the past 20 years

Shubin Feng^{a,1}, Juan Du^{b,1}, Xinru Xie^{c,1}, Yiru Li^c, Chuyuan Yu^c, Liling Cui^c, Mingcan Xue^c,
Chenxi Zhang^{c,*}

^a Department of Neurosurgery, the Fourth Hospital of Cangzhou City (Nanpi County People's Hospital), Hebei Province 061500, China

^b Department of Thoracic Surgery, Hebei Children's Hospital, 133 Jianhua South Street, Shijiazhuang, Hebei Province 050031, China

^c Tianjin Medical University, Tianjin, No. 22, Qixiangtai Road, Heping District, Tianjin 300070, China

ARTICLE INFO

Keywords:

Neurological disorders
Statins
Bibliometric studies
Alzheimer's disease
Multiple sclerosis
Cholesterol
Atorvastatin

ABSTRACT

Background: Neurological disorders are one of the major contributors to the burden of disease, affecting the quality of life of the global population. Statins, known for their cholesterol-lowering properties, have garnered substantial interest due to their potential neuroprotective effects and association with subjective cognitive decline. The study aims to provide a comprehensive bibliometric analysis of the literature on the nexus between neurological disorders and statins.

Methods: Using VOSviewer (1.6.20), CiteSpace (6.3.1 and 5.7.R2), and R (4.4.1), the systematic bibliometric analysis offers valuable insights into the research landscape of neurological disorders and statins from 2004 to 2024.

Results: The findings reveal a notable increase in scholarly output on neurological disorders and statins over the past two decades, with a particular emphasis on clinical trials and pharmacological mechanisms of statins. The remarkable multidisciplinary nature of the field is an important reason for its continued development. Compared to initial exploratory research, recent studies have placed increased emphasis on the neuroprotective roles of statins and their therapeutic potential in managing neurological disorders. Future research is anticipated to focus on precision medicine and personalized therapeutic strategies involving statins. The United States, China and Germany are leading the way in this field of research.

Conclusion: The study's findings are instrumental in informing future research directions and contribute to a broader understanding of the subject matter across various scientific disciplines. Statins have great potential in the treatment of neurological disorders and neuroprotection and are moving towards customized medicine and personalized therapy.

Introduction

Neurological disorders constitute a significant cause of global health burden, affecting over one-third of the world's population.¹ These disorders are characterized by a range of symptoms, including neurodevelopmental abnormalities, neurodegenerative processes in later life, and cognitive impairments. Additionally, they encompass conditions such as stroke, neonatal encephalopathy, migraine, Alzheimer's disease and other dementias, diabetic neuropathy, meningitis, epilepsy, neurological complications from preterm birth, autism spectrum disorders, and neurological cancers.^{2,3} According to the systematic analysis of the

Global Burden of Disease Study 2021 (GBD 2021), approximately 3.4 billion individuals worldwide were affected by neurological disorders in 2021, representing 43.1% of the global population, with the prevalence continuing to rise in recent years. Enhancing our understanding of these disorders, leveraging modern technologies such as metagenomic next-generation sequencing (mNGS) to improve early diagnosis, and standardizing clinical treatments in accordance with relevant guidelines and consensus are essential to increase cure rates,⁴ reduce mortality, and alleviate the disease burden.⁵

Statins primarily function in the prevention of cardiovascular diseases by inhibiting HMG-CoA reductase in the liver, thereby reducing

* Corresponding author.

E-mail address: 16622102356@163.com (C. Zhang).

¹ Shubin Feng, Juan Du and Xinru Xie contributed equally to this work.

cholesterol production and lowering blood levels of low-density lipoprotein cholesterol (LDL-C). Beyond their lipid-lowering effects,^{6,7} statins exhibit anti-inflammatory, antiplatelet, antioxidant, anti-proliferative,⁸ and immunosuppressive properties. And the most important thing is that studies have shown they have a protective effect on neuronal cells⁹ and have been linked to cognitive function.¹⁰ Statins can improve the survival environment of nerve cells through anti-inflammatory effects,¹¹ antioxidant effects, and also improve the function of neurotransmitters,¹² such as dopamine to treat neurological disorders.^{13,14} They also provides assistance in the treatment of neurological-related disorders due to their role in reducing beta-amyloid toxicity and regulating the activity of the transcription factor Nurr1.¹⁵ Given the substantial impact of neurological disorders on individuals and society, and considering the potential cytoprotective effects of statins on the nervous system and cognitive function,¹⁶ it is imperative to investigate the relationship between neurological disorders and statin use. The current fruitful and promising research on the role of statins in neurological disorders requires the analysis of hot spots and emerging trends.

Bibliometrics refers to the statistical analysis of data from scientific publications (e.g. articles and books), then assesses and reveals the structure, productivity, and trends of the research topic.¹⁷ The most apparent advantage of this method of analysis is the efficient review of publications with huge data on a specific topic or research area, which enables the identification of the most influential publications, as well as countries, authors, institutions, collaborations between active journals, popular keywords and research trends. As far as we know, there is only one bibliometric study which focus on the link between statins and dementia (a type of neurological disorders).¹⁸ However, this study's approach is single and was done through a website rather than specialized bibliometric software. While early publications provided insights into the link between dementia(a type of neurological disease) and statins, they were limited to only one neurological

disease, therefore we can enrich the field with a more comprehensive bibliometric analysis to elucidate the research themes that have attracted attention in the last decades.^{19,20} The convergence of visualization and data mining techniques has supported bibliometric approaches, but they have not yet been applied to the study of the relationship between neurological disorders and statins.

The aim of this study is to provide a comprehensive analysis and a clear overview of scientific articles on neurological disorders and statins from January 1, 2004 to June 1, 2024 by using state-of-the-art bibliometric methods, and to understand the patterns of research on neurological disorders and statins from several perspectives, such as the temporal evolution of scientific publications, major countries, institutions, authors, journals, and current trends in the research field.

Methods

Data collection

This study utilized the Pubmed Core Collection database with the following search strategy: TS= (("Alzheimer's disease" OR "Multiple sclerosis" OR "Parkinson's disease") AND "statin*") OR ("Nervous system" AND "statin*") OR (("Diseases of the nervous system" OR "Nervous system diseases") AND "statin*"). To minimize potential bias due to frequent database updates, we searched the literature from 2004 to 2024. And it is limited to English-language articles (Fig. 1). Data from PubMed articles were downloaded using the "Custom Selection" option, which selected all 29 fields to be customized in "plain text file" format to export.

Statistical analysis

Data analysis included information on authors, country, institution, year of publication, title, journal, references and keywords for

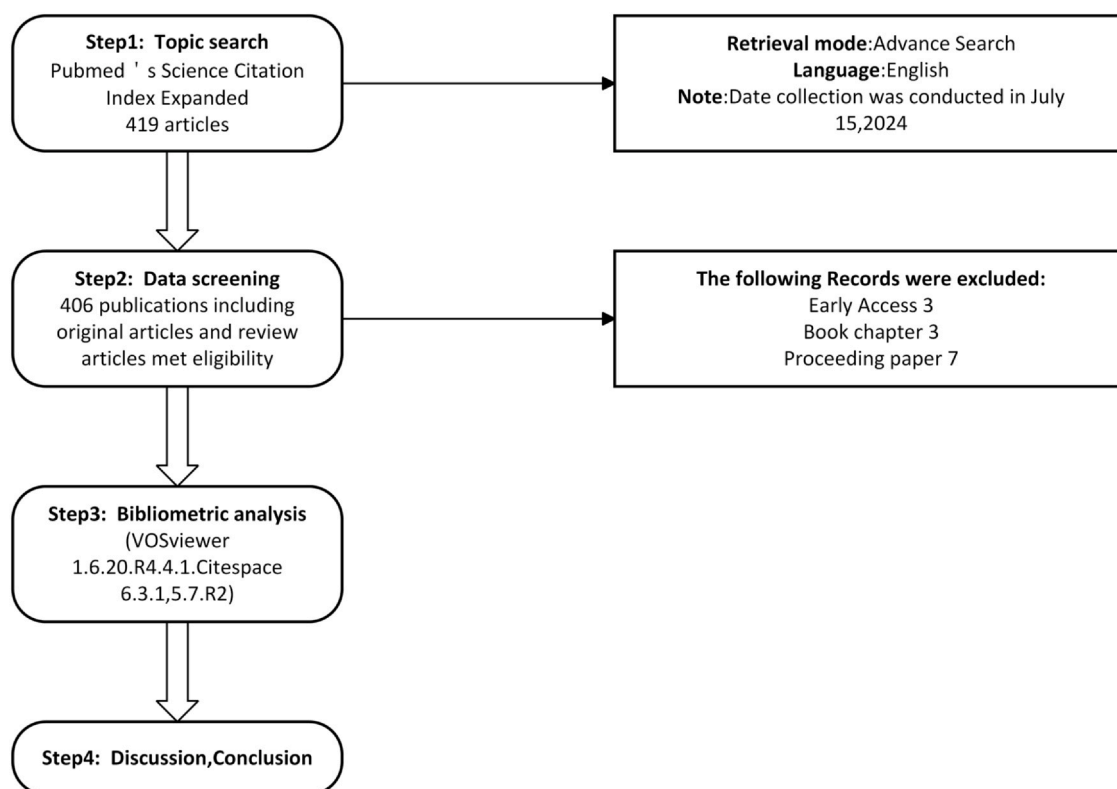


Fig. 1. Flow chart of the literature search and study process.

each article. Data such as number of articles, number of citations and journal impact factor were obtained through Pubmed. In this study, we used software such as VOSviewer (1.6.20), CiteSpace (6.3.1 and 5.7.R2), and R (4.4.1) to construct and visualize the co-authorship network of countries/regions, institutions, and authors, the co-citation network of authors and journals, and the keyword co-occurrence network.

Results

According to our search strategy, we can see that studies on traumatic brain injury and statins in PubMed have appeared since 1989 and have made great development after 2004, so we selected the period of 2004–2024 to conduct the study, which is a period of rapid development and high output of results. After sifting out the articles that are not too closely related to the topic, we finally got 406 studies that can be analyzed.

Analysis of trends in publications

The development of research findings on neurological disorders and statins has varied over time and regions, but there are certain patterns. We can know that academic research in this field was in a hot stage from 2006 to 2010, with a relatively large number of annual publications from the number of published papers. Since 2010, the number of publications show both an upward and a downward trend with a number of hot years, but the overall degree of hotness has declined slightly (Fig. 2A). It can also be seen that the year 2016 has the highest average number of citations, and the average total number of citations per paper reaches 5.3 citations per year. Citations in this area show a relatively stable trend, receiving sustained and widespread attention in recent years (Fig. 2B). The regional distribution of research results in this field is diversified, with a large number of countries making joint contributions (Fig. 2C). Nonetheless, it can still be judged that the United States is the regional leader, China is also very fruitful, and many other countries have a similar level of contribution.

If we link authors, keywords and journals, we can see that experimental neurology journal is the most prominent, which is closely related to keywords statins, neuroprotection, etc. From the perspective of key words, there are many related lines such as "statins" and "neuroprotection", indicating that research in this field is concentrating efforts on themes such as "the effects of statins on the nervous system (such as neuroprotection and intervention of related diseases)". From the perspective of journals, "experimental neurology" and "brain research" have rich connection lines, reflecting that these journals are the core platforms for the release of research results in this field, and have a high acceptance and publication volume of papers on related topics. From the perspective of the authors, some authors (such as "sahebkar a", etc.) have close associations with specific keywords and journals, reflecting their research expertise (focusing on neuro-related, statins, etc.) and preferences for the dissemination channels of achievements. (Fig. 3)

Journal and Co-citation analysis

The top three journals in terms of volume are journal of neurochemistry(8), experimental neurology(8), pharmacological research (7), glia(7), which have attained many achievements in the last two decades (Fig. 4A). In terms of citations, the top three journals are journal of neurochemistry(440), biomed research international(436), pharmacotherapy(324). These journals highlight important scholarly influences. The top three reference co-citations are yousef s, 2002, nature, v420, p78, doi 10.1038/nature01158 (73), vollmer t, 2004, lancet, v363, p1607, doi 10.1016/s0140-6736(04) 16205-3 (54), jick

h, 2000, lancet, v356, p1627, doi 10.1016/s0140-6736(00)03155-x (48) (Fig. 4B). These three articles have gained a high level of interest in the field.

Institutional and authors analysis

We have established strict inclusion criteria (screening institutions that have published more than three papers), aiming to reduce the complexity of interpretation caused by an excessive number of institutions and ensure the optimal focus on the topic (Fig. 5A). The research institutions are mainly concentrated in North America and Europe. Among them, univ calif san francisco ranked first in the world, Stanford univ ranked second in the world, boston univ, univ washington, etc. showed that the American institutions have the most achievements and the largest number of publications in the field (Fig. 5A). In terms of link strength, univ calif san francisco and Stanford univ collaborate most closely in this research. It may be owing to policy. Collaboration between authors in the same cluster is relatively closer. At the same time, ronaldson, patrick t. and singh, nderjit (Fig. 5B), who have a high number of publications, bring more international collaborations.

Keyword analysis

In this study, 1082 keywords (author's keywords) were extracted from 406 articles. According to the graphical analysis, the 10 most frequently used keywords are as follows: statins, alzheimer's disease, multiple sclerosis, cholesterol, atorvastatin, inflammation, neuroprotection, simvastatin, oxidative stress, apoptosis (Fig. 6). It is evident that neural related diseases and pathways are the focus of research. After superimposing the years, we can be found that the earliest keywords related to this field are traumatic brain injury, amyloid, eae, combination therapy, beta-amyloid, etc. As the research progresses, the keywords developed in this field are statins,²¹ multiple sclerosis, simvastatin,^{22,23} inflammation, etc. In recent years, the main keywords developed are autophagy, mevalonate pathway, prenylation, cognitive impairment, antioxidants, blood-brain barrier, pcsk9 and so on, revealing the research hotspots in recent years.

Here are the 33 most cited keywords (Fig. 7). In the early stage (around 2004–2007), keywords such as "experimental allergic encephalomyelitis" and "nitric oxide synthase" emerged suddenly, reflecting that the research at that time focused on the immune system of the nervous system and the basic molecular mechanisms. In the middle period (2010–2015), the popularity of "statin therapy", "neural control", etc. rose, reflecting the attention paid to the directions of clinical application and neural regulation. Recently (2020–2024), terms such as "inhibition", "blood-brain barrier", and "neurotrophic factor" have emerged as new hotspots, focusing on intervention mechanisms and the frontiers of brain science. Coa reductase inhibitor,²⁴ multiple sclerosis, nervous system,²⁵ indicating that the above directions are the key themes in this period. Expression,²⁶ lovastatin, oxidative stress, have longer duration (red length), some of them are from recent years and others are from earlier periods. There are long-lasting keywords during different periods in this field.

In terms of number of occurrences, central-nervous system²⁷ is leading broadly, followed by statins, and then nitric-oxide synthase, simvastatin, alzheimer disease, and so on (Fig. 8A,B). This indicates that these are the more popular research terms. The most popular of the latest keywords is inhibition. In this bibliometric study, the keywords amyloid precursor protein, cholesterol metabolism, oxysterols, alir-ocumab, pcsk9 were motifs, which means that they are well-developed and important motifs with a strong concentration and high density. In contrast, autophagy, cholesterol pathway, mitochondria,²⁸ epilepsy,²⁹ risk factors are basic themes, which are important to the field of study but undeveloped, meaning they have lower density, higher centrality

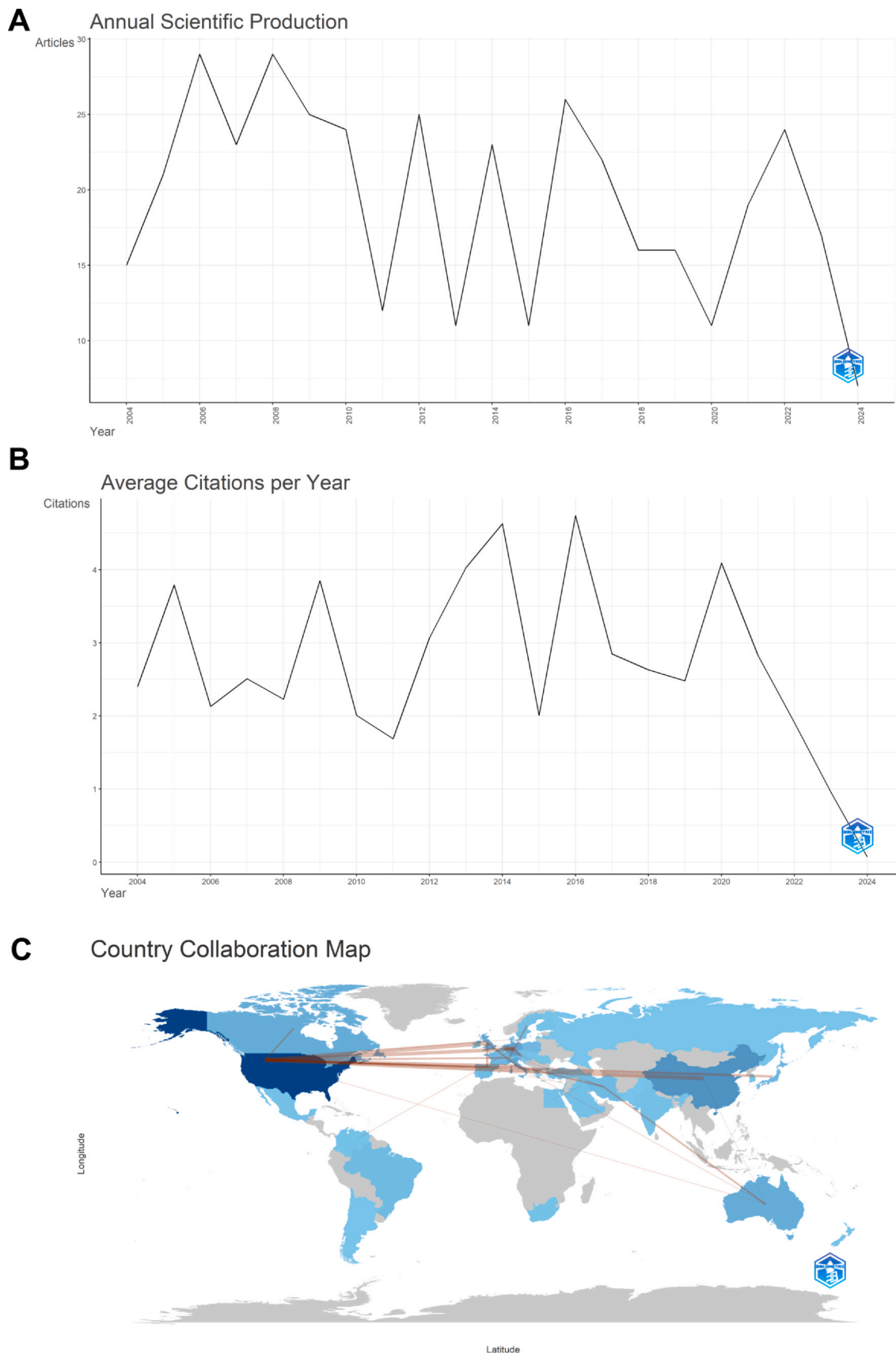


Fig. 2. Overview of trends in issuance. (A)The number of publications from 2004 to 2024. (B)The number of citations of papers from 2004 to 2024. (C)Regional overview of the volume of publications. The darker the color means the more papers published.

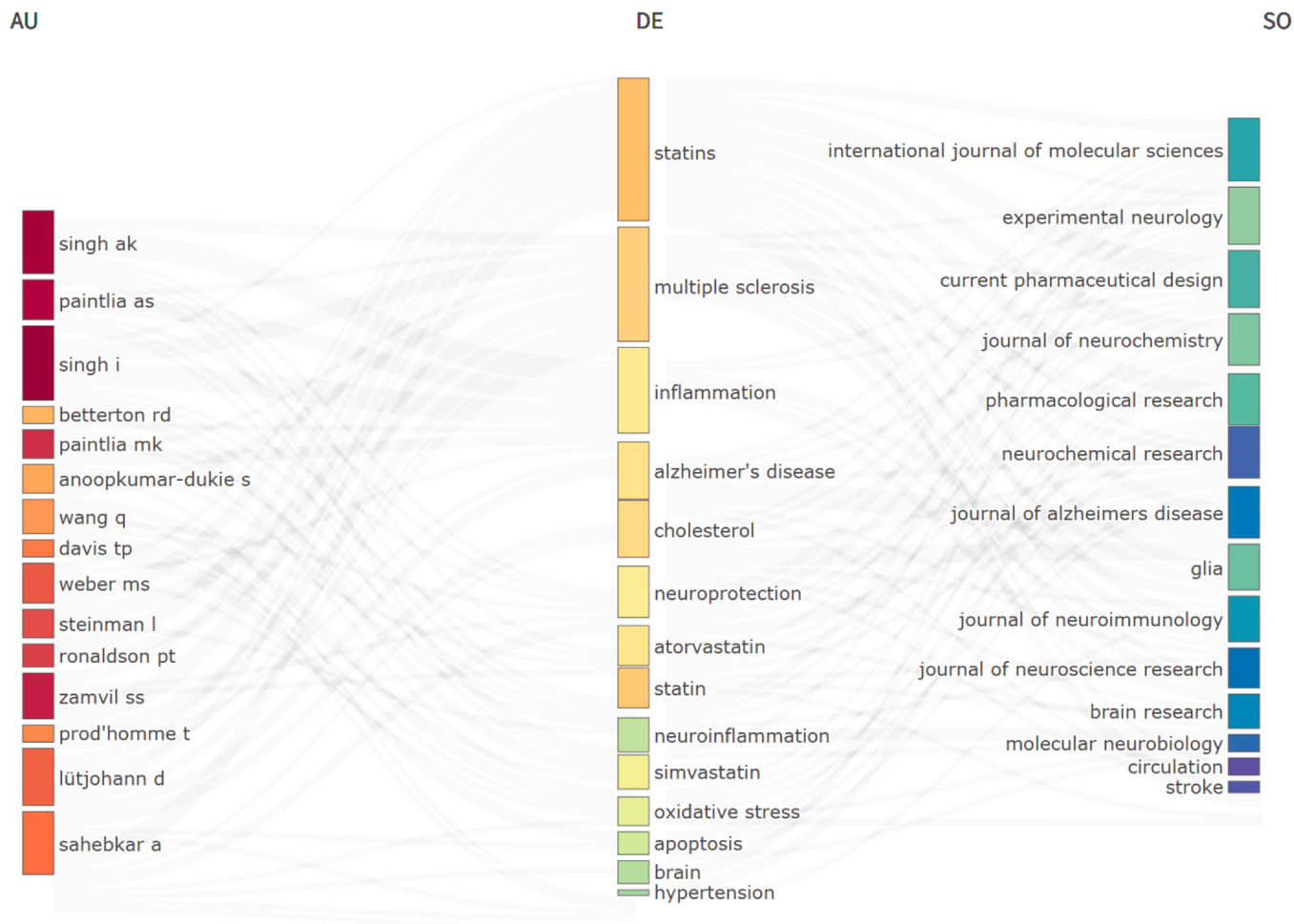


Fig. 3. The three field plot for author AU, keyword DE, and journal SO. The lines between the AU, DE, and SO identify the relationships and distributions among authors, keywords, and journals in the research field.

and require further research and analysis (Fig. 8C). Quadrant 4 themes are important to the field of study but they are underdeveloped and are generally concept-based, such as myopathy, neuropathy, hypertension etc.

Discussion

A review of neurological disorders and statin studies

This is a systematic and comprehensive bibliometric study to use a visualization tool to analyze trends in research on neurological disorders and statins. The number of publications and citations in this area is high, suggesting that there has been a high level of interest in research on neurological disorders and statins over the last 20 years.^{30,31} However, since 2004, there have been troughs between peaks in both the number of publications and citations with an overall slight downward trend in the number of publications and an overall mere upward trend in the number of citations.

Collaboration is a key feature of research on neurological disorders and statins, with an increasing number of countries and institutions collaborating with each other to drive development. USA, Peoples R China, Germany published the most literature on neurological disorders and statins. Among the most prolific and influential authors in the field, Ronaldson, Patrick T. and Singh, Inderjit who own higher number of publications have brought more international collaborations. The prevalence of interconnections between researchers suggests that

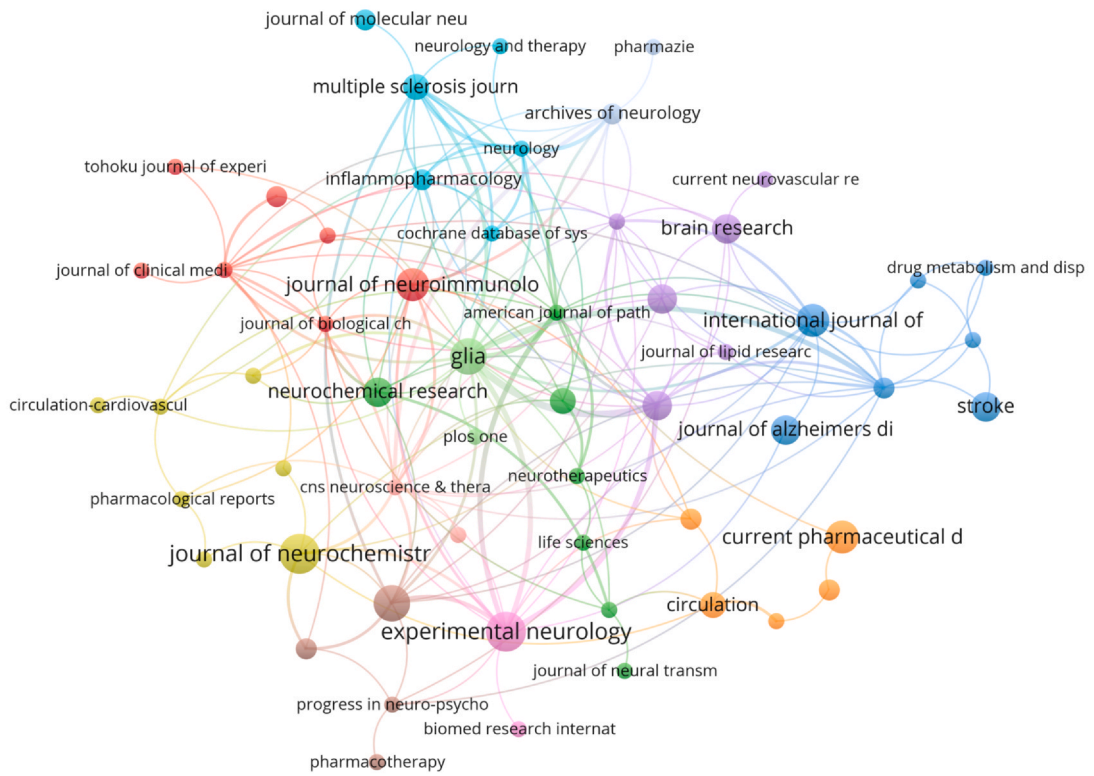
collaboration is widespread, which is consistent with previous research, however, international and large-scale academic collaboration may be lacking due to language barriers.

Researches about neurological disorders and statin has been recognized and disseminated by top journals such as journal of neurochemistry. A multidisciplinary approach is also important for neurological disease and statin research, as illustrated by the involvement of the fields of pharmacology,^{32,33} neuroscience³⁴ and clinical neurology.³⁵ Although the pace of development has slowed compared to the 20th century, this is still a steadily growing field that has been on a relatively high and stable trend. In addition, research related to individual specific diseases (e.g., Alzheimer's disease,³⁶ Parkinson's disease,^{37,38} eye diseases³⁹) is an integral and important part of neurological disease and statin research, and recent bibliometric studies have examined its impact over the past 20 years.

Research hotspots and frontiers in neurological disorders and statins

The analysis of the cited references reveals the most influential articles and provide a knowledge base for future research in the field. The most cited original research article is the 2016 paper by Thompson et al. on the topic of "statin side effects",⁴⁰ which may still be a hot topic nowadays. Role of inflammation, oxidative stress, and vascular dysfunction in hypertension in biomed research international by Dinh et al.'s in 2014, cholesterol in Alzheimer's disease in Lancet Neurology in

A



B

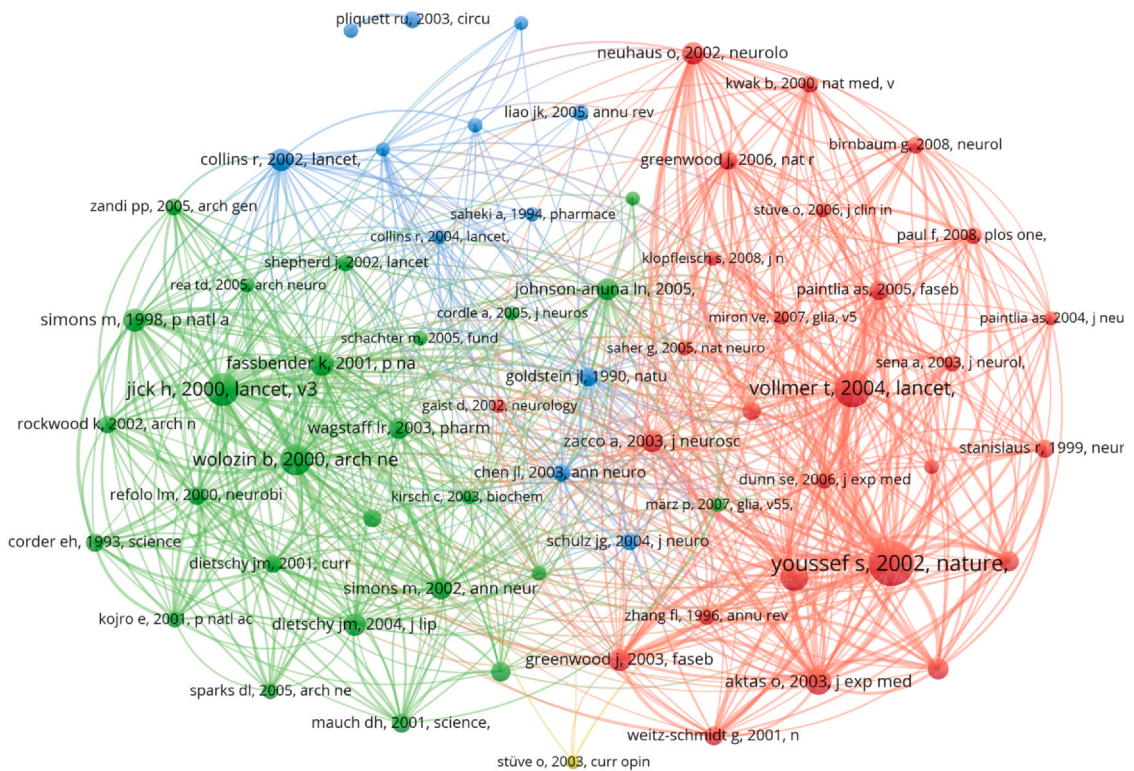


Fig. 4. Research linkages and citation mapping between journals. (A)The journal sources in this research area. (B)The co-citation analysis of the references. The size of the nodes represents the total number of articles in that journal, and the connecting lines' thickness indicate the degree of cross-referencing or strength of connection with other research outlets. The small red, green and blue dots respectively represent the classification of co-cited journals based on the source of the literature. The same color indicates journal groups with similar publication topics and close citation relationships.

Top 33 Keywords with the Strongest Citation Bursts

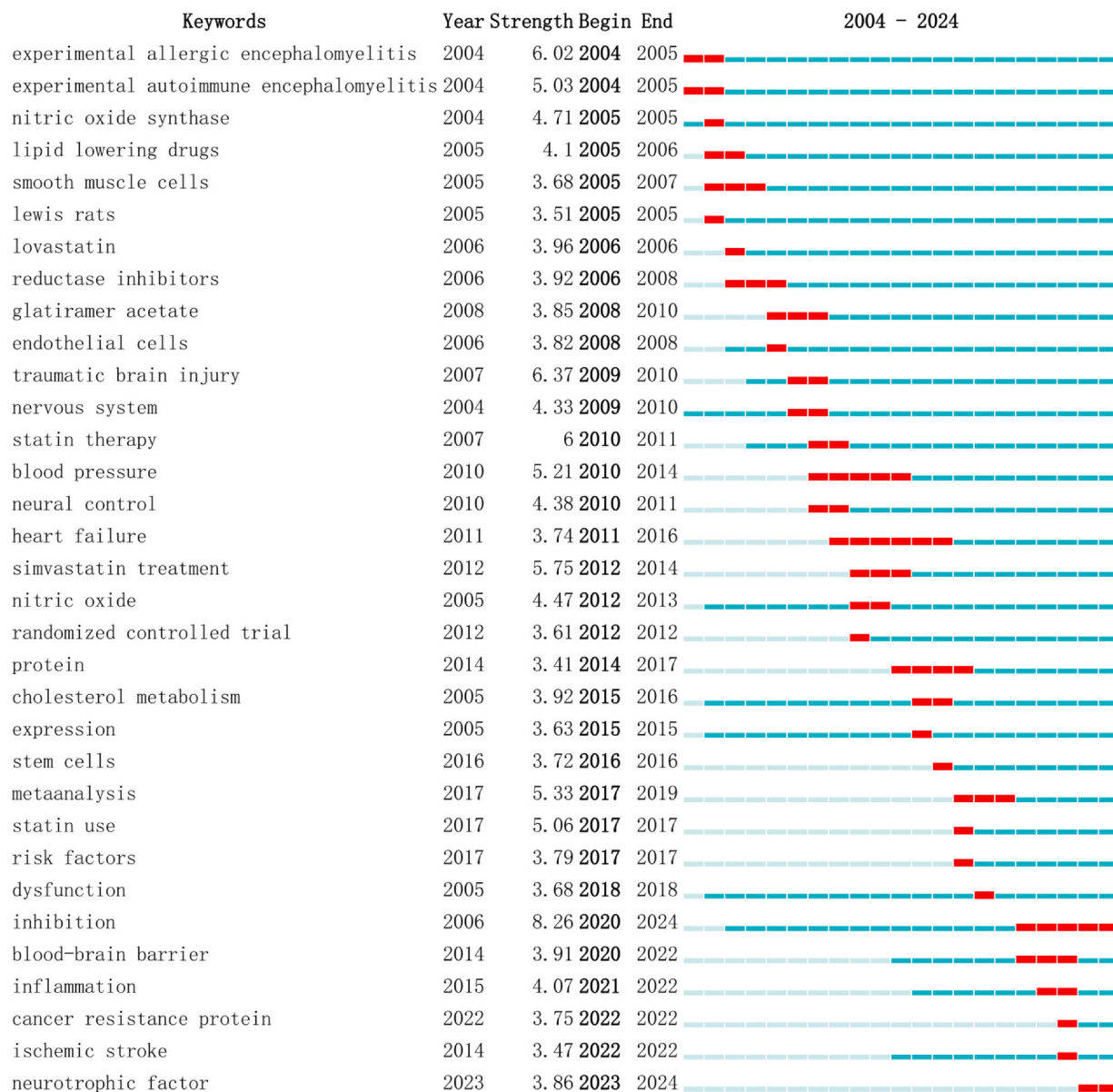


Fig. 7. Top 33 most frequently cited keywords. The blue length represents the existence time, and the red length represents the duration of the keywords with higher citation frequency (also called the emergence time, and the longer ones tend to represent the basic research in the field).

modulation of the inflammatory response and oxidative stress by statins and the impact of these effects on the course of neurological diseases is a major research interest. Cholesterol metabolism also plays a role in the pathogenesis of neurological disorders,^{57,58} and statins affect neurological disorders by modulating cholesterol metabolism. The main focus of research is on the mechanisms that statins treat neurological disorders by affecting these metabolic pathways. In addition, self-pharmacological mechanisms⁵⁹ and multiple drug associations (e.g., paclitaxel⁶⁰), associations with and effects on diabetes,⁶¹⁻⁶³ seizures⁶⁴ and high blood pressure,⁶⁵ specific molecular mechanisms,^{66,67} risk factors,⁶⁸ adverse events,⁶⁹ and caregiving⁷⁰ have been addressed, which can be very comprehensive.

A limitation of this study is that it does not include the WoS and Scopus databases. This decision was made because there is an imbalance in the coverage of the WoS database across disciplines that allows some disciplines to increase their relative weight in SSCI at the expense of others. The Scopus database, on the other hand, has a lower impact level and is not indexed in some journals. PubMed is considered a more reliable database. What's more, analyzing a large number of articles may experience duplicate inclusion when using multiple databases. Although this limitation is objective, the study has done as much elimination as possible. The bibliometric analysis is very comprehensive, which is unmatched by other literature studies.

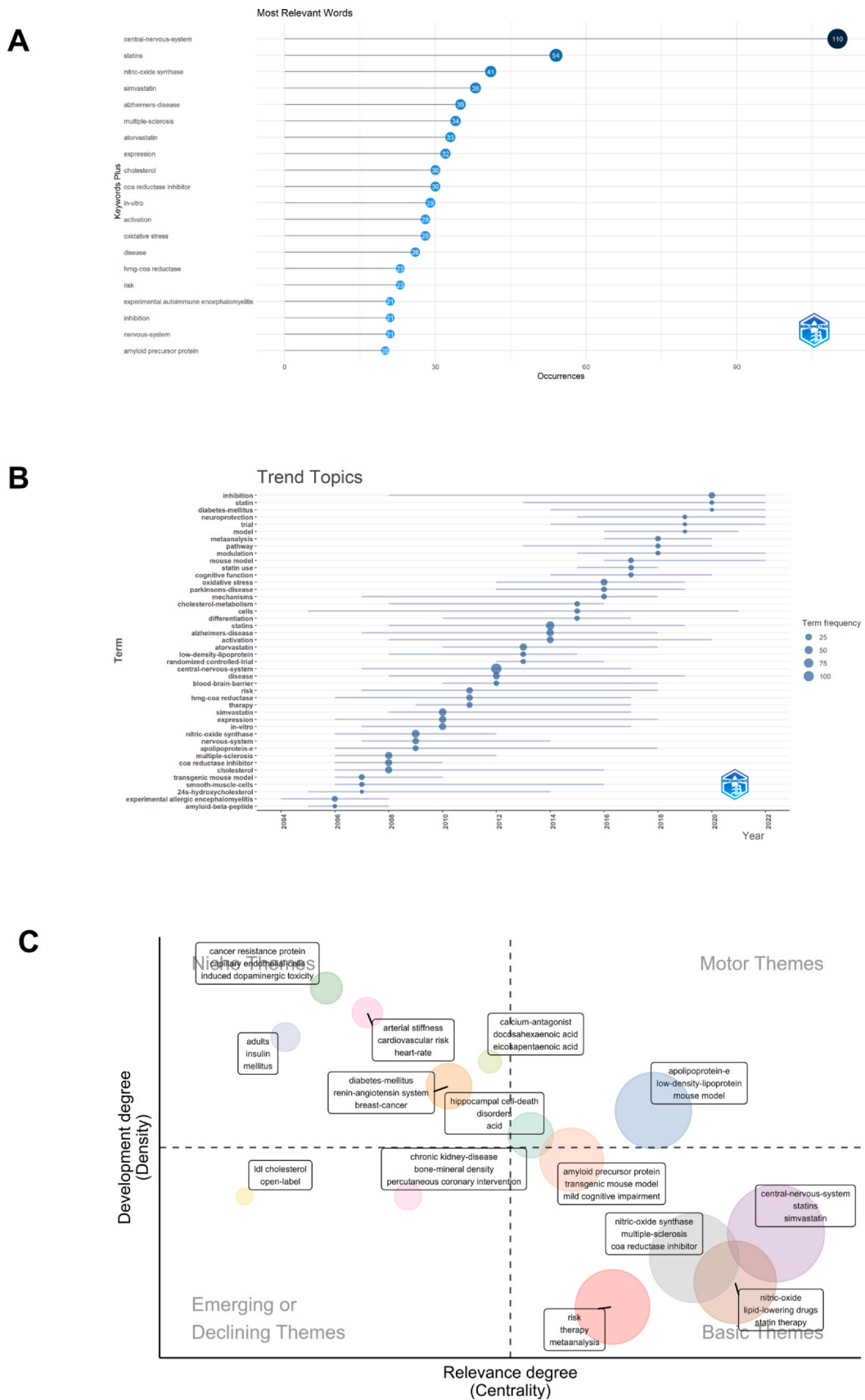


Fig. 8. (A) The analysis of the number of occurrences of the keywords. (B) The frequency of the keywords (by the size of the circle) and the time range of the occurrences (by the span of the horizontal line). (C) The thematic map grouping authors' keywords according to the relevance and degree of development.

Conclusion

This study systematically summarized articles on neurological disorders and statin research from 2004 to 2024 through a bibliometric analysis of visualization tools. The findings show a relatively stable focus on neurological disorders and statin research, and are conducted using a combined multidisciplinary approach. The United States, China, and Germany were identified as leaders in neurological disease and statin research. And univ calif san francisco play a central role in the research effort. Co-cited references mainly focus on statin-related side effects, and "inflammation" and "cholesterol in Alzheimer's disease" also have received special attention. The analysis also reveals popular research frontiers, including statins, Alzheimer's disease, multiple sclerosis, cholesterol, atorvastatin, inflammation, neuroprotection, simvastatin, oxidative stress, and apoptosis. By examining trends in neurological disorders and statins, the study provides valuable insights to better understand the current state of research and may inform future research directions for consideration. Recent studies have placed increased emphasis on the neuroprotective roles of statins and their therapeutic potential in managing neurological disorders. Future research is anticipated to focus on precision medicine and personalized therapeutic strategies involving statins, reflecting an ongoing shift towards tailored medical approaches.

Declarations

Not applicable.

Authors' contributions

Yiru Li: Writing – original draft. Chuyuan Yu: Visualization, Data curation. Liling Cui: Visualization, Data curation. Mingcan Xue: Visualization, Data curation. Chenxi Zhang: Writing – original draft, Data curation. Shubin Feng: Conceptualization. Juan Du: Conceptualization. Xinru Xie: Writing – review & editing, Visualization, Software, Formal analysis, Data curation, Conceptualization.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All the data can be downloaded from PubMed Core Collection.

Funding

This study was funded by the National Natural Science Foundation of China (No.82071390, 82001323, 82101434), Tianjin Key Medical Discipline (Specialty) Construction Project, and the Tianjin Haihe Scholar Health and Wellness Industry High-level Talent Selection and Training Project, Code: TJSHHYXXZ-D2–.

Data availability

All data will be made available on request to the corresponding author. Proposals will be reviewed and approved by the sponsor, investigator, and collaborators on the basis of scientific merit. After approval of a proposal, data will be shared through a secure online platform after the signing of a data access agreement.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to express our sincere gratitude to each author for their valuable contributions to this study.

Authors' other information

Not applicable.

References

- Chong PH, Boskovich A, Stevkovic N, et al. Statin-associated peripheral neuropathy: review of the literature. *Pharmacotherapy*. 2004;24(9):1194–1203. <https://doi.org/10.1592/phco.24.13.1194.38084>
- Umapathi T, Chaudhry V. Toxic neuropathy. *Curr Opin Neurol*. 2005;18(5):574–580. <https://doi.org/10.1097/01.wco.0000180158.34713.a>
- Morris G, Fernandes BS, Puri BK, et al. Leaky brain in neurological and psychiatric disorders: drivers and consequences. *Aust N Z J Psychiatry*. 2018;52(10):924–948. <https://doi.org/10.1177/0004867418796955>
- Peltier AC, Russell JW. Advances in understanding drug-induced neuropathies. *Drug Saf*. 2006;29(1):23–30. <https://doi.org/10.2165/00002018-200629010-00002>
- Weimer LH, Sachdev N. Update on medication-induced peripheral neuropathy. *Curr Neurol Neurosci Rep*. 2009;9(1):69–75. <https://doi.org/10.1007/s11910-009-0011-z>
- Fracassi A, Marangoni M, Rosso P, et al. Statins and the brain: more than lipid lowering agents. *Curr Neuropharmacol*. 2019;17(1):59–83. <https://doi.org/10.2174/1570159X15666170703101816>
- Zhang Q, Dong J, Yu Z. Pleiotropic use of statins as non-lipid-lowering drugs. *Int J Biol Sci*. 2020;16(14):2704–2711. <https://doi.org/10.7150/ijbs.42965>
- Chamani S, Mobasheri L, Zerehpooosh S, et al. The effect of statins on the differentiation and function of central nervous system cells. *Curr Med Chem*. 2024;31(11):1348–1360. <https://doi.org/10.2174/0929867330666230308121645>
- Kosowski M, Smolarczyk-Kosowska J, Hachula M, et al. The effects of statins on neurotransmission and their neuroprotective role in neurological and psychiatric disorders. *Molecules*. 2021;26(10) <https://doi.org/10.3390/molecules26102838>
- Malfitano AM, Marasco G, Proto MC, et al. Statins in neurological disorders: an overview and update. *Pharm Res*. 2014;38:74–83. <https://doi.org/10.1016/j.phrs.2014.06.007>
- Xu X, Gao W, Cheng S, et al. Anti-inflammatory and immunomodulatory mechanisms of atorvastatin in a murine model of traumatic brain injury. *J Neuroinflamm*. 2017;14(1):167. <https://doi.org/10.1186/s12974-017-0934-2>
- Wang M, Li M, Xie Y. The association between statins exposure and peripheral neuropathy risk: a meta-analysis. *J Clin Pharm Ther*. 2021;46(4):1046–1054. <https://doi.org/10.1111/jcpt.13393>
- Ling Q, Tejada-Simon MV. Statins and the brain: new perspective for old drugs. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;66:80–86. <https://doi.org/10.1016/j.pnpbp.2015.11.013>
- Svensden TK, Krøigård T, Wirefeldt M, et al. Statin use and peripheral nerve function-A prospective follow-up study. *Basic Clin Pharm Toxicol*. 2020;126(3):203–211. <https://doi.org/10.1111/bcpt.13320>
- Schmeer C, Kretz A, Isenmann S. Statin-mediated protective effects in the central nervous system: general mechanisms and putative role of stress proteins. *Restor Neurol Neurosci*. 2006;24(2):79–95.
- Orr JD. Statins in the spectrum of neurologic disease. *Curr Atheroscler Rep*. 2008;10(1):11–18. <https://doi.org/10.1007/s11883-008-0003-5>
- Ninkov A, Frank JR, Maggio LA. Bibliometrics: methods for studying academic publishing. *Perspect Med Educ*. 2022;11(3):173–176. <https://doi.org/10.1007/s40037-021-00695-4>
- Sang XZ, Chen W, Hou XX, et al. Association between statin use and dementia, and related mechanisms: a bibliometric analysis from 2007 to 2023. *J Alzheimers Dis*. 2024;101(3):847–876. <https://doi.org/10.3233/JAD-240270>
- Lei Q, Peng WN, You H, et al. Statins in nervous system-associated diseases: angels or devils. *Pharmazie*. 2014;69(6):448–454.
- Coulson WF. Statin neuropathy. *J Fam Pr*. 2011;60(4):182–184.
- Rajnikant GK, Zemke D, Kassab M, et al. The therapeutic potential of statins in neurological disorders. *Curr Med Chem*. 2007;14(1):103–112. <https://doi.org/10.2174/09298670779313462>
- Collins R, Armitage J, Parish S, et al. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high-risk conditions. *Lancet*. 2004;363(9411):757–767. [https://doi.org/10.1016/S0140-6736\(04\)15690-0](https://doi.org/10.1016/S0140-6736(04)15690-0)
- Mann CM, Lee JH, Hillyer J, et al. Lack of robust neurologic benefits with simvastatin or atorvastatin treatment after acute thoracic spinal cord contusion injury. *Exp Neurol*. 2010;221(2):285–295. <https://doi.org/10.1016/j.expneurol.2009.11.006>
- Reiss AB, Wirkowski E. Role of HMG-CoA reductase inhibitors in neurological disorders: progress to date. *Drugs*. 2007;67(15):2111–2120. <https://doi.org/10.2165/00003495-200767150-00001>

25. Otruba P, Kanovsky P, Hlustik P. Treatment with statins and peripheral neuropathy: results of 36-months a prospective clinical and neurophysiological follow-up. *Neuro Endocrinol Lett.* 2011;32(5):688–690.
26. Chun HJ, Kim DW, Yi HJ, et al. Effects of statin and deferoxamine administration on neurological outcomes in a rat model of intracerebral hemorrhage. *Neurol Sci.* 2012;33(2):289–296. <https://doi.org/10.1007/s10072-011-0733-y>
27. Weber MS, Youssef S, Dunn SE, et al. Statins in the treatment of central nervous system autoimmune disease. *J Neuroimmunol.* 2006;178(1-2):140–148. <https://doi.org/10.1016/j.jneuroim.2006.06.006>
28. Desai R, Campanella M. Exploring mitochondrial cholesterol signalling for therapeutic intervention in neurological conditions. *Br J Pharm.* 2019;176(22):4284–4292. <https://doi.org/10.1111/bph.14697>
29. Amanlou A, Nassireslami E, Dehpour AR, et al. Beneficial effects of statins on seizures independent of their Lipid-Lowering effect: a narrative review. *Iran J Med Sci.* 2023;48(1):13–25. <https://doi.org/10.30476/IJMS.2021.91645.2289>
30. Law M, Rudnicka AR. Statin safety: a systematic review. *Am J Cardiol.* 2006;97(8A) <https://doi.org/10.1016/j.amjcard.2005.12.010>
31. Bifulco M, Malfitano AM, Marasco G. Potential therapeutic role of statins in neurological disorders. *Expert Rev Neurother.* 2008;8(5):827–837. <https://doi.org/10.1586/14737175.8.5.827>
32. Zamami Y, Niimura T, Kawashiri T, et al. Identification of prophylactic drugs for oxaliplatin-induced peripheral neuropathy using big data. *Biomed Pharm.* 2022;148:112744. <https://doi.org/10.1016/j.biopha.2022.112744>
33. Menge T, Hartung HP, Stüve O. Statins—a cure-all for the brain. *Nat Rev Neurosci.* 2005;6(4):325–331. <https://doi.org/10.1038/nrn1652>
34. Hendrix S, Nitsch R. The role of t helper cells in neuroprotection and regeneration. *J Neuroimmunol.* 2007;184(1-2):100–112. <https://doi.org/10.1016/j.jneuroim.2006.11.019>
35. Pasha R, Azmi S, Ferdousi M, et al. Lipids, Lipid-Lowering therapy, and neuropathy: a narrative review. *Clin Ther.* 2022;44(7):1012–1025. <https://doi.org/10.1016/j.clinthera.2022.03.013>
36. Torrandell-Haro G, Branigan GL, Vitali F, et al. Statin therapy and risk of alzheimer's and age-related neurodegenerative diseases. *Alzheimers Dement.* 2020;6(1):e12108. <https://doi.org/10.1002/trc2.12108>
37. Jeong SH, Lee HS, Chung SJ, et al. Effects of statins on dopamine loss and prognosis in parkinson's disease. *Brain.* 2021;144(10):3191–3200. <https://doi.org/10.1093/brain/awab292>
38. Oveigharan S, Yu L, Barnes LL, et al. Association of statins with cerebral atherosclerosis and incident parkinsonism in older adults. *Neurology.* 2022;98(19):e1976–e1984. <https://doi.org/10.1212/WNL.000000000000200182>
39. Elsaïs A, Lund C, Kerty E. Ptosis, diplopia and statins: an association. *Eur J Neurol.* 2008;15(10):e92–e93. <https://doi.org/10.1111/j.1468-1331.2008.02234.x>
40. Thompson PD, Panza G, Zaleski A, et al. Statin-Associated side effects. *J Am Coll Cardiol.* 2016;67(20):2395–2410. <https://doi.org/10.1016/j.jacc.2016.02.071>
41. Vance JE. Dysregulation of cholesterol balance in the brain: contribution to neurodegenerative diseases. *Dis Model Mech.* 2012;5(6):746–755. <https://doi.org/10.1242/dmm.010124>
42. Ibáñez Pérez de la Blanca MA. Antithrombotic and risk of hemorrhagic complications in over-60-year-olds after mild-minimal traumatic brain injury. *Brain Inj.* 2023;37(12-14):1355–1361. <https://doi.org/10.1080/02699052.2023.2284907>
43. Brondino N, Emanuele E, Geroldi D. Caution on the potential usefulness of statins in neuropsychiatric diseases. *Med Hypotheses.* 2007;69(3):697. <https://doi.org/10.1016/j.mehy.2007.01.020>
44. Formaglio M, Vial C. Statin induced neuropathy: myth or reality? *Rev Neurol.* 2006;162(12):1286–1289. [https://doi.org/10.1016/s0035-3787\(06\)75148-7](https://doi.org/10.1016/s0035-3787(06)75148-7)
45. Lashgari NA, Roudsari NM, Zadeh S, et al. Statins block mammalian target of rapamycin pathway: a possible novel therapeutic strategy for inflammatory, malignant and neurodegenerative diseases. *Inflammopharmacology.* 2023;31(1):57–75. <https://doi.org/10.1007/s10787-022-01077-w>
46. Aizawa F, Kajimoto H, Okabayashi A, et al. Statins ameliorate oxaliplatin- and paclitaxel-induced peripheral neuropathy via glutathione S-transferase. *Neurochem Int.* 2024;180:105863. <https://doi.org/10.1016/j.neuint.2024.105863>
47. Nabavi SM, Ahmed T, Nawaz M, et al. Targeting STATs in neuroinflammation: the road less traveled. *Pharm Res.* 2019;141:73–84. <https://doi.org/10.1016/j.phrs.2018.12.004>
48. Fujimoto T, Morofuji Y, Kovac A, et al. Pitavastatin ameliorates Lipopolysaccharide-Induced Blood-Brain barrier dysfunction. *Biomedicines.* 2021;9(7) <https://doi.org/10.3390/biomedicines9070837>
49. Bifulco M, Malfitano AM, Marasco G. Potential therapeutic role of statins in neurological disorders. *Expert Rev Neurother.* 2008;8(5):827–837. <https://doi.org/10.1586/14737175.8.5.827>
50. Tierney EF, Thurman DJ, Beckles GL, et al. Association of statin use with peripheral neuropathy in the U.S. Population 40 years of age or older. *J Diabetes.* 2013;5(2):207–215. <https://doi.org/10.1111/1753-0407.12013>
51. Heyer EJ, Mergeche JL, Bruce SS, et al. Statins reduce neurologic injury in asymptomatic carotid endarterectomy patients. *Stroke.* 2013;44(4):1150–1152. <https://doi.org/10.1161/STROKEAHA.111.000362>
52. Petek B, Villa-Lopez M, Loera-Valencia R, et al. Connecting the brain cholesterol and renin-angiotensin systems: potential role of statins and RAS-modifying medications in dementia. *J Intern Med.* 2018;284(6):620–642. <https://doi.org/10.1111/joim.12838>
53. Carroll CB, Wyse R, Grosset DG. Statins and parkinson's: a complex interaction. *Mov Disord.* 2019;34(7):934–935. <https://doi.org/10.1002/mds.27721>
54. Komatsu R, Yilmaz HO, You J, et al. Lack of association between preoperative statin use and respiratory and neurologic complications after cardiac surgery. *Anesthesiology.* 2017;126(5):799–809. <https://doi.org/10.1097/ALN.0000000000001569>
55. Gluhovschi G, Gluhovschi C, Bob F, et al. Multiorgan-protective actions of blockers of the renin-angiotensin system, statins and erythropoietin: common pleiotropic effects in reno-, cardio- and neuroprotection. *Acta Clin Belg.* 2008;63(3):152–169. <https://doi.org/10.1179/acb.2008.026>
56. Wuerch E, Urgoitto GR, Yong VW. The promise of niacin in neurology. *Neurotherapeutics.* 2023;20(4):1037–1054. <https://doi.org/10.1007/s13311-023-01376-2>
57. Ravnskov U, Rosch PJ, Sutter MC, et al. Should we lower cholesterol as much as possible. *BMJ.* 2006;332(7553):1330–1332. <https://doi.org/10.1136/bmj.332.7553.1330>
58. Corrao G, Zambon A, Bertù L, et al. Lipid lowering drugs prescription and the risk of peripheral neuropathy: an exploratory case-control study using automated databases. *J Epidemiol Community Health.* 2004;58(12):1047–1051. <https://doi.org/10.1136/jech.2003.013409>
59. Brass LM, Alberts MJ, Sparks L, et al. An assessment of statin safety by neurologists. *Am J Cardiol.* 2006;97(8A) <https://doi.org/10.1016/j.amjcard.2005.12.017>
60. Catalano M, Ramello M, Conca R, et al. Risk factors for Nab-Paclitaxel and Gemcitabine-Induced peripheral neuropathy in patients with pancreatic cancer. *Oncology.* 2022;100(7):384–391. <https://doi.org/10.1159/000524868>
61. Brownrigg JR, de Lusignan S, McGovern A, et al. Peripheral neuropathy and the risk of cardiovascular events in type 2 diabetes mellitus. *Heart.* 2014;100(23):1837–1843. <https://doi.org/10.1136/heartjnl-2014-305657>
62. Davis TM, Yeap BB, Davis WA, et al. Lipid-lowering therapy and peripheral sensory neuropathy in type 2 diabetes: the fremantle diabetes study. *Diabetologia.* 2008;51(4):562–566. <https://doi.org/10.1007/s00125-007-0919-2>
63. Uwah AN, Ackler J, Leighton JC, et al. The effect of diabetes on oxaliplatin-induced peripheral neuropathy. *Clin Colorectal Cancer.* 2012;11(4):275–279. <https://doi.org/10.1016/j.clcc.2012.05.002>
64. Scicchitano F, Constanti A, Citraro R, et al. Statins and epilepsy: preclinical studies, clinical trials and statin-anticonvulsant drug interactions. *Curr Drug Targets.* 2015;16(7):747–756. <https://doi.org/10.2174/1389450116666150330114850>
65. Arjmand B, Dehghanbanadaki H, Yoosefi M, et al. Association of plasma acylcarnitines and amino acids with hypertension: a nationwide metabolomics study. *PLoS One.* 2023;18(1):e0279835. <https://doi.org/10.1371/journal.pone.0279835>
66. He J, Ren M, Li H, et al. Exosomal circular RNA as a biomarker platform for the early diagnosis of Immune-Mediated demyelinating disease. *Front Genet.* 2019;10:860. <https://doi.org/10.3389/fgene.2019.00860>
67. López-Farré AJ, Zamorano-León JJ, Segura A, et al. Plasma desmoplakin I biomarker of vascular recurrence after ischemic stroke. *J Neurochem.* 2012;121(2):314–325. <https://doi.org/10.1111/j.1471-4159.2012.07683.x>
68. Chen H, Clifford DB, Deng L, et al. Peripheral neuropathy in ART-experienced patients: prevalence and risk factors. *J Neurovirol.* 2013;19(6):557–564. <https://doi.org/10.1007/s13365-013-0216-4>
69. Harvey PD, Sabbagh MN, Harrison JE, et al. No evidence of neurocognitive adverse events associated with alirocumab treatment in 3340 patients from 14 randomized phase 2 and 3 controlled trials: a meta-analysis of individual patient data. *Eur Heart J.* 2018;39(5):374–381. <https://doi.org/10.1093/eurheartj/ehx661>
70. Keyrouz SG, Diringner MN. Year in review 2011. *Crit CareNeurocritical Care Crit Care.* 2012;16(6):245. <https://doi.org/10.1186/cc11825>