The global trends of migraine research from 2010 to 2019: a scientometric study

Tingting Lu[1,2#], Jieyun Li[2,3,4#], Jingwen Li[2,3,4], Meixuan Li[2,3,4], Lufang Feng[2,3,4], Xiuxia Li[2,3,4], Long Ge[2,3,4], Cuncun Lu[2,3,4,5], Kehu Yang[2,3,4]

[1]Institution of Clinical Research and Evidence Based Medicine, The Gansu Provincial Hospital, Lanzhou, China; [2]Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou, China; [3]Evidence-Based Social Science Center, School of Public Health, Lanzhou University, Lanzhou, China; [4]Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province, Lanzhou, China; [5]Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing, China

Contributions: (I) Conception and design: K Yang, C Lu; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: T Lu, J Li, J Li, M Li; (V) Data analysis and interpretation: T Lu, L Feng, X Li, L Ge; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Kehu Yang. Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou730000, China; Evidence-Based Social Science Center, School of Public Health, Lanzhou University, Lanzhou 730000, China; Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province, Lanzhou 730000, China. Email: kehuyangebm2006@126.com; Cuncun Lu. Evidence-Based Medicine Center, School of Basic Medical Sciences, Lanzhou University, Lanzhou730000, China; Evidence-Based Social Science Center, School of Public Health, Lanzhou University, Lanzhou 730000, China; Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province, Lanzhou 730000, China; Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing, China. Email: cuncunlu2017@163.com.

Abstract: In the recent years, migraine has been widely studied by scholars from all over the world. This study aimed to use scientometric methods to identify research frontiers and development trends in the field of migraine research. We used the Web of Science (WoS) core collection database to collect articles and reviews related to migraine published from 2010 to 2019 on March 25, 2020. VOSviewer, CiteSpace, and Excel were used for the scientometric analysis. A total of 6,357 publications (including 5,203 articles and 1,154 reviews) were identified. The United States published the most publications (n=2,151, 33.84%). Albert Einstein College of Medicine contributed the most publications (n=220, 3.46%). *Cephalalgia* was found to be the core journal with the most publications (n=766, impact factor 2019 =4.868) as well as the most co-citations (n=35,535). Lipton RB authored the most publications (n=159, 2.50%), while Silberstein SD received the most co-citations (n=4,215). The critical topics were causes and pathophysiological mechanisms, epidemiological characteristics, diagnostic criteria, treatment and prevention drugs, and migraine-related genes. Through the use of scientometric methods, this article has mapped the knowledge landscape of migraine research over the past decade. By showing the overall status of the field, it provides a useful reference for future research.

Keywords: Scientometrics; migraine; Web of Science (WoS); VOSviewer; CiteSpace

5768

Lu et al. Scientometric study of migraine research from 2010 to 2019

Introduction

Migraine is one of the most common headache disorders. The International Headache Society (IHS) differentiates migraine with and without aura. The main feature of migraine with aura is transient focal neurological symptoms, which typically precede or sometimes accompany headache (1). Migraine without aura is characterized by recurrent headaches lasting 4–72 hours accompanied by photophobia, phonophobia, nausea, and vomiting (1). According to a 2016 study, it was estimated that 1.04 billion people (95% UI 1.00–1.09) experienced migraine (2). Migraine causes 45.1 million [95% of uncertainty interval (UI) 29.0–62.8] years of life with disabilities (YLDs), ranking the second leading cause of YLDs globally (2). In the United States (USA) and Europe, the direct and indirect medical costs of migraine exceed $15 billion and €27 billion annually (3,4). The pathogenesis of migraine remains unclear, although studies have suggested roles of vascular and neuronal components (5). Although many treatments are currently available for migraine, including drugs [e.g., divalproex sodium, topiramate, metoprolol, propranolol, triptans, calcitonin gene-related peptide (CGRP) inhibitors] and non-drug therapies (e.g., acupuncture), these treatments relieve migraine symptoms rather than the underlying cause (6-8). In light of the many open questions in migraine research, the literature on migraine has increased significantly in recent years.

Scientometrics is a tool used for the statistical and quantitative analysis of research publications. As it can quantify the growth of literature in specific subjects and the impact of individual research results, scientometrics is considered an ideal methodological choice for evaluating research trends (9-12). Scientometrics has been widely used in various research fields (10-14). For example, scientometric analysis was used to analyze the knowledge base and emerging topics of drug liver injury in the past decade (11). Another study used scientometric methods to analyze the mTOR (mammalian target of rapamycin) signaling pathway in liver diseases (14). To our knowledge, scientometrics has not been applied to analyze the status and foci of global migraine research over the past decade. Therefore, this study aims to use scientometric methods to explore research patterns and frontiers in the field of migraine research. We hope that this scientometric analysis can provide migraine researchers with research directions, improving the quality of research, to ultimately benefit migraine patients.

Methods

Data source

We conducted a search for migraine-related literature using the Web of Science (WoS) core collection database on March 25, 2020. For this search, Science Citation Index-Expanded (SCIE) was the data source, the timespan was set from 2010 to 2019, and the publication type was limited to "article" or "review". The search strategy was as follows: (TI = migraine) OR (TS = "migraine disorder" OR "migraine disorders" OR "migraine with aura" OR "migraine without aura"). We completed all searches and downloaded the results within the same day to avoid the bias caused by daily database updates.

Statistical analysis

WoS database was used to identify the annual output (number of publications), publication language, and publication type of migraine research. We employed VOSviewer 1.6.14 (15) to identify authors/co-cited authors, journals/co-cited journals, countries (regions), institutions, and co-cited references. A related network map was established, in which bubbles represent elements such as countries and institutions, and the size of the bubbles represent the number or frequency, the larger bubbles indicate more publications or citations (16); the links between bubbles reflect co-authorship, co-occurrence, or co-citation relationships (10,11). The VOSviewer settings were as follows: counting method (full counting), thresholds (T) of elements (e.g., countries, institutions, authors, and references) adopted according to special situations. CiteSpace (5.6.R3) (16), a scientometric software tool, was used to depict dual-map overlays of journals and to identify references with a strong burst strength for exploring emerging topics (11,17). The key parameters of CiteSpace were as follows: link retaining factor (LRF =3), look back years (LBY =8), e for top N (e =2), time span (2010–2019), years per slice (1), links (strength: cosine, scope: within slices), selection criteria (top 50), and minimum duration (MD =4). Excel 2019 (Microsoft, Redmond, Washington, USA) was used to manage the data and create tables.

Results

Annual growth trends in publication output

A total of 6,357 publications related to migraine were

published between 2010 and 2019, including 5,203 articles and 1,154 reviews. Publications were in 14 languages, including English (n=6,156, 96.84%), Spanish (n=65, 1.02%), German (n=47, 0.74%), French (n=35, 0.55%), Turkish (n=18, 0.28%), and others. The annual output of migraine research showed a rising trend from 2010 to 2019 (*Figure 1*). The average annual output was 636 publications/year, there were 500+ publications/year in 2010–2012, 2014, and 2016, and 600+ publications/year in 2013, 2015, and 2017. The annual output exceeded 700 for the first time in 2018 (n=713, 11.22%) and peaked in 2019 (n=930, 14.63%).

Countries and institutions

A total of 92 countries/regions participated in migraine research. The top 10 countries are shown in *Table 1*. The USA published the most publications, accounting for
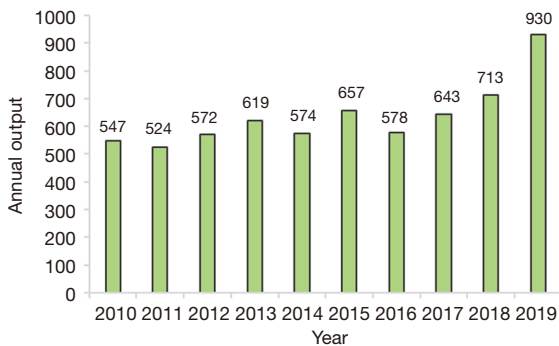
33.84% (n=2,151) of the included studies, followed by Italy (n=942, 14.82%), Germany (n=473, 7.44%), China (n=428, 6.73%), and England (n=426, 6.70%). Seven of the top 10 countries/regions belong to Europe. The remaining three countries belong to North America (USA), Eurasia (Turkey), and Asia (China). Countries/regions (n=21) with a number greater than or equal to 95 (T =95) were used to build the co-authorship network map (*Figure 2*). In this network map, the USA, Italy, and Germany have more publications. Collaboration is evident between several countries, e.g., the USA shows close cooperation with Germany, England, Italy, etc., and Germany shows close cooperation with France, USA, England, etc.

In total, 5,197 institutions contributed to migraine research publications. Among the top 10 institutions (*Table 1*), six are in the USA, and four are in European countries. Albert Einstein College of Medicine ranked first (n=220, 3.46%), followed by University of Copenhagen (n=208, 3.27%), Harvard University (n=167, 2.63%), Mayo Clinic (n=159, 2.50%) and Leiden University (n=157, 2.47%). The institutions (n=19) with publications greater than or equal to 65 (T =65) were used to build the co-authorship map (*Figure 2*). In this scientometric network, Albert Einstein College of Medicine, University of Copenhagen, and Harvard University have published more research. There are closed collaborations between institutions, such as, Albert Einstein College of Medicine shows close cooperation with Montefiore Headache Center, Montefiore Medical Center, and Mayo Clinic, etc., and King's College London shows close cooperation with University of California-San Francisco, University of

Figure 1 Annual output of migraine research.

Table 1 The top 10 countries and institutions involved in migraine research

| Rank	Country/region	Count	Institution	Count
1	USA (North America)	2,151	Albert Einstein College of Medicine (USA)	220
2	Italy (Europe)	942	University of Copenhagen (Denmark)	208
3	Germany (Europe)	473	Harvard University (USA)	167
4	China (Asia)	428	Mayo clinic (USA)	159
5	England (Europe)	426	Leiden University (The Netherlands)	157
6	Turkey (Eurasia)	378	King's College London (UK)	124
7	Denmark (Europe)	296	Harvard Medical School (USA)	116
8	The Netherlands (Europe)	266	University of California-San Francisco (USA)	110
9	Spain (Europe)	257	Thomas Jefferson University (USA)	104
10	France (Europe)	228	Sapienza University of Rome (Italy)	90
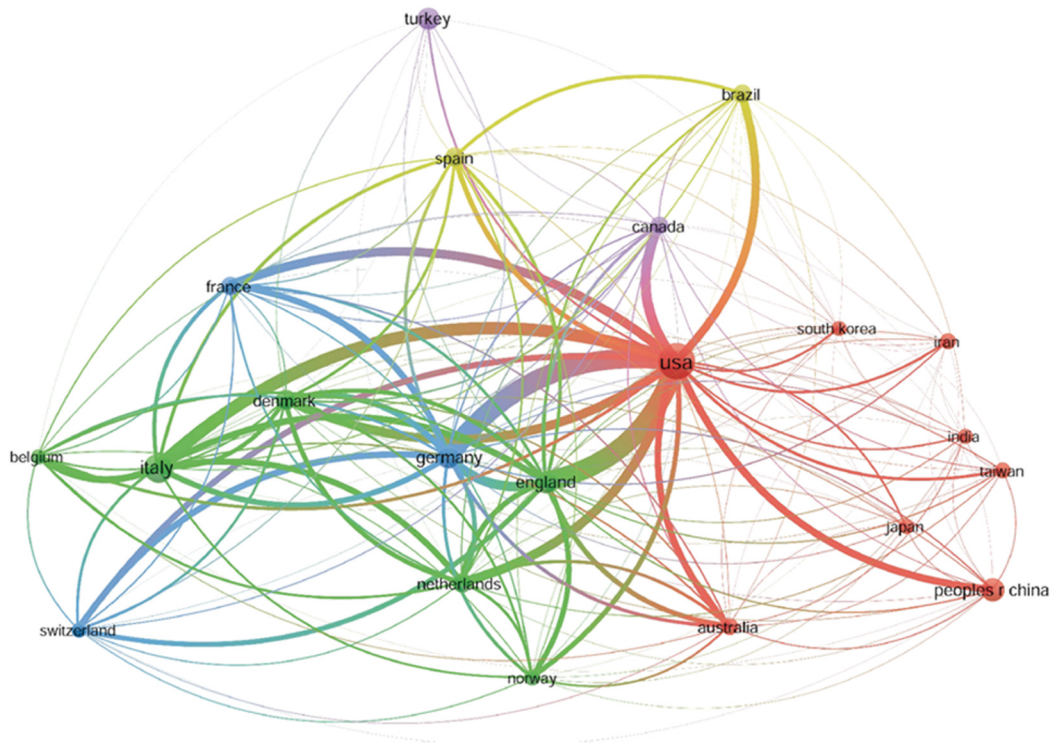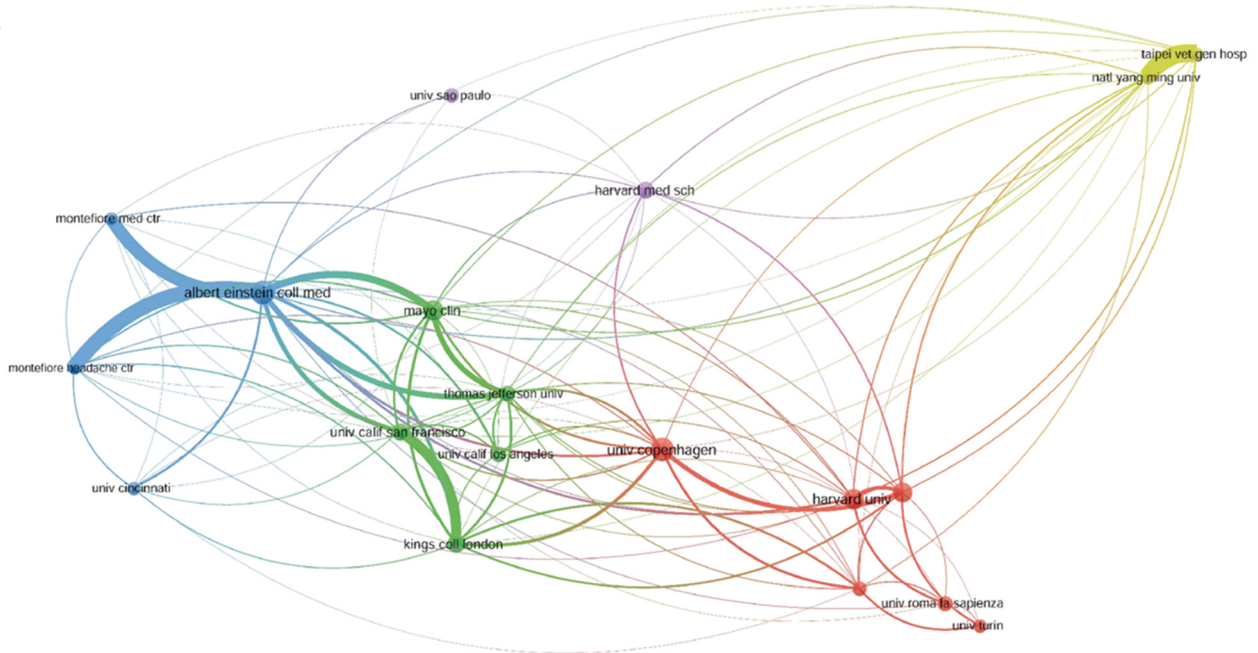
Figure 2 The network map of countries/regions (A, T =95) and institutions (B, T =65) participating in migraine research.

Table 2 The top 10 journals and co-cited journals in migraine research

Rank	Journal	Count	IF2019	Q	Co-cited journal	Co-citation	IF2019	Q
1	*Cephalalgia* (Norway)	766	4.868	Q1	*Cephalalgia* (Norway)	35,535	4.868	Q1
2	*Headache* (USA)	747	4.041	Q2	*Headache* (USA)	29,252	4.041	Q2
3	*Journal of Headache and Pain* (Italy)	434	4.797	Q1	*Neurology* (USA)	15,013	8.77	Q1
4	*Neurological Sciences* (Italy)	294	2.415	Q3	*Journal of Headache and Pain* (Italy)	7,527	4.797	Q1
5	*Current Pain and Headache Reports* (USA)	131	2.985	Q2	*Pain* (USA)	5,031	5.483	Q1
6	*Neurology* (USA)	109	8.77	Q1	*Annals of Neurology* (USA)	4,177	9.037	Q1
7	*Frontiers in Neurology* (Switzerland)	72	2.889	Q3	*Brain* (England)	4,136	11.337	Q1
8	*PLoS One* (USA)	62	2.74	Q2	*Journal of Neuroscience* (USA)	3,145	5.673	Q1
9	*European Journal of Neurology* (USA)	57	4.516	Q1	*Lancet Neurol* (England)	3,008	30.039	Q1
10	*Arquivos de Neuro-Psiquiatria* (Brazil)	47	1.008	Q4	*Lancet* (England)	2,937	60.392	Q1

IF, impact factor; Q, quartile in category.

Copenhagen, etc.

Journals and co-cited journals

A total of 6,357 papers were published in 986 journals. *Table 2* presents the top 10 productive journals in the field of migraine. According to the number of publications, *Cephalalgia* [n=766, 12.05%, IF (impact factor) 2019 =4.868, Q1] ranked first, followed by *Headache* (n=747, 11.75%, IF2019 =4.041, Q2), *Journal of Headache and Pain* (n=434, 6.83%, IF2019 =4.797, Q1), *Neurological Sciences* (n=294, 4.62%, IF2019 =2.415, Q3), and *Current Pain and Headache Reports* (n=131, 2.06%, IF2019 =2.985, Q2). Of these journals, five are published in the USA, one in Brazil, and the rest in European countries. Five journals (*Cephalalgia*, *Headache*, *Journal of Headache and Pain*, *Neurology*, *European Journal of Neurology*) have impact factors greater than 4; *Neurology*, issued by the USA, has the highest impact factor and 109 publications. Journals (n=19) with a number of publications greater than or equal to 35 (T =35) were used to construct the citation network (Figure S1A). *Cephalalgia*, *Headache*, *Journal of Headache and Pain*, and *Neurological Sciences* have more publications. *Cephalalgia* has a close citation relationship with *Headache*, *Journal of Headache and Pain*, etc.

When two journals are cited simultaneously by one or more identical publications, a co-citation relationship exists between the two journals (11). Five of the top 10 co-cited journals have impact factors greater than 8. The *Lancet*, which is issued by England, has the highest impact factor

(*Table 2*). Among the top 10 co-cited journals, *Cephalalgia* is the most co-cited (n=35,535, IF2019 =4.868, Q1), followed by *Headache* (n=29,252, IF2019 =4.041, Q2), *Neurology* (n=15,013, IF2019 =8.77, Q1), *Journal of Headache and Pain* (n=7,527, IF2019 =4.797, Q1) and *Pain* (n=5,031, IF2019 =5.483, Q1). Journals (n=21) with co-citations greater than or equal to 1500 (T =1500) were used to construct a co-citation map (Figure S1B). *Cephalalgia*, *Headache*, *Neurology*, and *Journal of Headache*, and *Pain* have more co-citations. *Cephalalgia* has a close co-citation relationship with *Headache*, *Neurology*, etc.

Figure 3 shows the dual-map overlay of journals. The left side represents the map of citing journals and the right side represents the map of cited journals (11,17). The labels represent the subject covered by the journal (18). Colored stripes represent the citation paths between publications in citing journals and publications in cited journals (19). The map has seven main citation paths: the orange paths (a, b) indicate that publications in Molecular/Biology/Immunology journals usually cite publications in Molecular/Biology/Genetics journals and Psychology/Education/Social journals. The green paths (c, d, e) represent that publications in Medicine/Medical/Clinical journals usually cite publications in Molecular/Biology/Genetics journals, Health/Nursing/Medicine journals, and Psychology/Education/Social journals. Of note, we found that some migraine publications in Neurology/Sports/Ophthalmology journals usually cite publications in Molecular/Biology/Genetics journals and Psychology/Education/Social journals, which are represented by the pink paths (f, g).
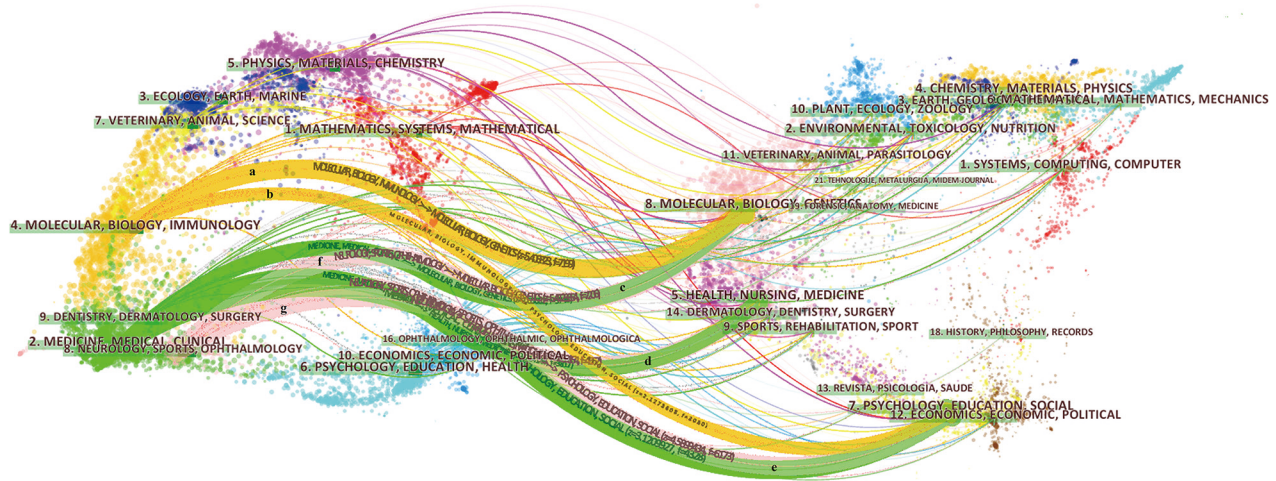
5772

Lu et al. Scientometric study of migraine research from 2010 to 2019

Figure 3 The dual-map overlay of journals related to migraine research.

Table 3 The top 10 authors and co-cited authors in migraine research

Rank	Author	Count	Co-cited author	Co-citation
1	Lipton RB	159	Silberstein SD	4,215
2	Goadsby PJ	129	Lipton RB	3,893
3	Ashina M	103	Bigal ME	2,632
4	Buse DC	89	Goadsby PJ	2,552
5	Ferrari MD	86	Bes A	1,775
6	Dodick DW	77	Olesen J	1,695
7	Olesen J	76	Diener HC	1,575
8	Silberstein SD	69	Stewart WF	1,318
9	Kurth T	62	Burstein R	1,116
10	Martelletti P	61	Dodick DW	1,081

Authors and co-cited authors

A total of 19,370 authors participated in migraine research. *Table 3* presents the top 10 productive authors. Lipton RB published the most papers (n=159, 2.50%), followed by Goadsby PJ (n=129, 2.03%), Ashina M (n=103, 1.62%), Buse DC (n = 89, 1.40%), and Ferrari MD (n=86, 1.35%). Authors (n=16) with a publication number greater than or equal to 45 (T =45) were used to construct the co-authorship map (Figure S2A). Lipton RB, Goadsby PJ, Ashina M, and Buse DC have more publications. There are close collaborations between Lipton RB and Buse DC, and

between Dodick DW and, Silberstein SD.

Co-cited authors can be defined as authors that are cited together (11,20). *Table 3* presents the top 10 co-cited authors. Silberstein SD has the most co-citations (n=4,215), followed by Lipton RB (n=3,893), Bigal ME (n=2,632), Goadsby PJ (n=2,552), and Bes A (n=1,775). Authors (n=25) with a co-citation number greater than or equal to 600 (T =600) were used to construct the co-authorship map (Figure S2B). Silberstein SD has the most co-citations, and has close co-citation relationships with Lipton RB, Bigal ME, Diener HC, Goadsby PJ, Olesen J, Dodick DW, etc.

Table 4 The top 10 co-cited references related to migraine research

Rank	Co-cited reference	Count
1	Silberstein SD, 2004. Migraine pathophysiology and its clinical implications. *Cephalalgia*, V24, P2 (5)	1,829
2	Bes A, 2013. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*, V33, P629 (1)	1,770
3	Lipton RB, 2007. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*, V68, P343 (21)	673
4	Lipton RB, 2001. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*, V41, P646 (22)	490
5	Stovner LJ, 2007. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia*, V27, P193 (23)	396
6	Goadsby PJ, 2002. Migraine—current understanding and treatment. *The New England Journal of Medicine*, V346, P257 (24)	325
7	Hadjikhani N, 2001. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. *Proceedings of the National Academy of Sciences of the United States of America*, V98, P4687 (25)	303
8	Olesen J, 2006. New appendix criteria open for a broader concept of chronic migraine. *Cephalalgia*, V26, P742 (26)	301
9	Sorge F, 1988. Flunarizine in prophylaxis of childhood migraine. A double-blind, placebo-controlled, crossover study. *Cephalalgia*, V8, P1 (27)	291
10	Diener HC, 2010. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. *Cephalalgia*, V30, P804 (28)	255

Co-cited references

Co-cited references are references that have been co-cited in a series of publications (11,17,20). A total of 94,610 references were co-cited by 6,357 publications. The top 10 co-cited references are shown in *Table 4*. The study entitled "Migraine pathophysiology and its clinical implications" by Silberstein *et al.* (5) in *Cephalalgia* with 1,829 co-citations ranked first, followed by Bes *et al.* (1) in *Cephalalgia* (n=1,770), Lipton *et al.* (21) in *Neurology* (n=673), and Lipton *et al.* (22) in *Headache* (n=490). The remaining six references had co-citations ranging from 255 to 396 (*Table 4*). References (n=27) with co-citations greater than or equal to 200 (T =200) were used to construct the co-citation map (Figure S3). "Silberstein SD, 2004, *Cephalalgia* (5)", "Bes A, 2013, *Cephalalgia* (1)", and "Lipton RB, 2007, *Neurology* (21)" have close co-cited relationships.

References with citation bursts

References with citation bursts are those that have a sudden increase in citations and receive widespread attention over a period of time (29,30). In CiteSpace, we set the threshold and minimum burst duration to 4 years. We detected 22 references with strong citation bursts (*Figure 4*). The blue line represents the time intervals and the red line represents the burst durations (19). The burst strengths ranged from 5.986 to 22.0083 and the burst durations ranged from 4 to 6 years. Eleven publications (6,31-40) had citation bursts ending in 2016 or later, six references (6,31-34,36) had citation bursts ending in 2016; two references (35,37) had bursts that ended in 2017, namely "Freilinger T, 2012, *Nature Genetics*, V44, P777", and "Natoli JL, 2010, *Cephalalgia*, V30, P599"; and three references (38-40) had bursts that ended in 2019, namely "Smitherman TA, 2013, *Headache*, V53, P427", "Noseda R, 2013, *Pain*, V154, P0", and "Maniyar FH, 2014, *Brain*, V137, P232". These publications with citation bursts may reflect the development frontiers of migraine research in recent years.

Discussion

General information

According to 2010–2019 data from SCIE in WoS, migraine research comprised a total of 6,357 items (5,203 articles and 1,154 reviews) published in 986 peer-reviewed journals with 94,610 co-cited references in 14 languages by 5,197 institutions from 92 countries/regions. The annual output of migraine related research showed a rising trend between 2010 and 2019. The USA occupies the leading position in migraine research, as it published the most research and has close collaborations with Germany and England.

Top 22 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2010 – 2019
Lipton RB, 2007, NEUROLOGY, V68, P343, DOI	2007	60.2589	2010	2015	
Olesen J, 2006, CEPHALALGIA, V26, P742, DOI	2006	59.1066	2010	2014	
Stovner LJ, 2007, CEPHALALGIA, V27, P193, DOI	2007	37.8215	2010	2015	
Dichgans M, 2005, LANCET, V366, P371, DOI	2005	32.7134	2010	2013	
Diamond S, 2007, HEADACHE, V47, P355, DOI	2007	27.3296	2010	2013	
Kurth T, 2006, JAMA-J AM MED ASSOC, V296, P283, DOI	2006	25.2357	2010	2014	
Scher AI, 2005, NEUROLOGY, V64, P614, DOI	2005	22.2976	2010	2013	
Ho TW, 2008, LANCET, V372, P2115, DOI	2008	17.6757	2010	2015	
Goadsby PJ, 2009, NEUROSCIENCE, V161, P327, DOI	2009	25.0292	2011	2014	
Kelman L, 2007, CEPHALALGIA, V27, P394, DOI	2007	23.3559	2011	2015	
Anttila V, 2010, NAT GENET, V42, P869, DOI	2010	20.0369	2011	2016	
Bigal ME, 2010, NEUROLOGY, V74, P628, DOI	2010	16.8358	2011	2016	
Bigal ME, 2008, NEUROLOGY, V71, P559, DOI	2008	16.2721	2011	2016	
Bigal ME, 2008, HEADACHE, V48, P1157, DOI	2008	22.0083	2012	2016	
Kruit MC, 2010, CEPHALALGIA, V30, P129, DOI	2010	11.3947	2012	2015	
Freilinger T, 2012, NAT GENET, V44, P777, DOI	2012	21.9416	2013	2017	
Silberstein SD, 2012, NEUROLOGY, V78, P1337, DOI	2012	7.6873	2013	2016	
Evers S, 2009, EUR J NEUROL, V16, P968, DOI	2009	6.5095	2013	2016	
Natoli JL, 2010, CEPHALALGIA, V30, P599, DOI	2010	5.986	2013	2017	
Smitherman TA, 2013, HEADACHE, V53, P427, DOI	2013	21.5006	2014	2019	
Noseda R, 2013, PAIN, V154, P0, DOI	2013	20.4609	2015	2019	
Maniyar FH, 2014, BRAIN, V137, P232, DOI	2014	16.4903	2015	2019	

Figure 4 Top 22 references with strong citation bursts (MD =4). MD, minimum duration.

Among the productive countries, China is the only Asian country, and the rest are European or American countries. Most productive institutions are located in the USA, among which the Albert Einstein College of Medicine has the most publications, ranking first. Albert Einstein College of Medicine has close collaborations with Montefiore Headache Center, which may be potential cooperation institutions for migraine researchers. *Cephalalgia*, published by Norway, published the most research and received the most co-citations, and thus it can be regarded as a core journal in the migraine field. The journals with the highest impact factors among the productive and co-cited journals are *Neurology* and *Lancet*, respectively. The dual-map overlay of journal analysis also provides indispensable references for future migraine research. In particular, we found that some publications in *Neurology* may be related to the pathogenesis of migraine (5,39). Among the authors, Lipton RB and Silberstein SD had the most publications and the most co-

citations, respectively. Lipton RB, Goadsby PJ, Dodick DW, Olesen J, and Silberstein SD are both productive and co-cited authors. Lipton RB, Bigal ME, and Silberstein SD showed close cooperation and were potential collaborators on migraine-related research. In summary, based on these findings, the field of migraine may have attracted more and more attention in recent years and will remain in a sustainable development stage.

Knowledge base

Co-cited references reveal how frequently two publications are cited together by other publications, which can be considered as the knowledge base of a specialized field (11,16). Therefore, in this scientometric study, we assess the knowledge base of migraine research in terms of the top 10 co-cited references. In 1988, Sorge *et al.* published a paper with 291 co-citations in *Cephalalgia*. This double-

blind crossover study showed that, compared to placebo, flunarizine could effectively treat childhood migraine without serious side effects (27). In 2001, the fourth most co-cited publication (490 co-citations) was published by Lipton *et al.* in *Headache*. This epidemiological study investigated the prevalence and burden of migraine in the USA from 1989 to 1999, showing that the prevalence and proportion of migraine have remained stable (22). In 2001, Hadjikhani *et al.* published a study with 303 co-citations in *Proceedings of the National Academy of Sciences of the United States of America* that used functional MRI (magnetic resonance imaging) to reveal that cortical spreading depression (CSD) can produce migraine visual aura in humans (25). In 2002, Goadsby *et al.* published the sixth most co-cited publication (325 co-citations) in The *New England Journal of Medicine*. The review describes the epidemiological characteristics, pathophysiological mechanisms, and critical symptomatic treatment of migraine, with the authors noting that more attention should be paid to triptans in drug therapy (24). In 2004, Silberstein *et al.* published the most co-cited publication (1,829 co-citations) in *Cephalalgia* that summarized the pathophysiology and clinical implications of migraine, describing how the vascular hypothesis of migraine has been replaced by a theory involving vascular and neuronal components and discussing the possible role of triptans (5). The phenomenon that this review received the most co-citations is consistent with previous scientometrics analyses that showed reviews always have higher citations than original studies (41). In 2006, Olesen *et al.* published a paper with 301 co-citations in Cephalalgia that provided new diagnostic criteria for chronic migraine based on clinical features and headache frequency (26). In 2007, Lipton *et al.* published the third most co-cited paper (673 co-citations) in *Neurology* (21). This paper found that the one-year prevalence of migraine was 11.7% (17.1% in women, 5.6% in men), with the highest prevalence among middle-aged people, and lowest among adolescents and people older than 60 (21). In 2007, Stovner *et al.* published "The global burden of headache: a documentation of headache prevalence and disability worldwide" in *Cephalalgia*, which was the fifth most co-cited publication (396 co-citations). The study showed that adults with closed headache disorders account for 46% of general headaches, and migraines account for 11%, ranking third among headache types (23). In 2010, Diener *et al.* published a clinical controlled trial, the tenth most co-cited publication, with 255 co-citations, in *Cephalalgia*, which evaluated the

safety and effectiveness of *OnabotulinumtoxinA* relative to placebo in the treatment of chronic migraine, showing that it can effectively prevent chronic migraine in adults (28). In 2013, the second most co-cited publication (1,770 co-citations) was published by Bes *et al.* in *Cephalalgia* (1). IHS provides diagnostic criteria for headaches in which migraine is classified as with aura (including sensory or other central nervous system symptoms usually associated with migraine) or without aura (with many symptoms such as nausea, photophobia, phonophobia) (1). In addition, we found an active co-citation relationship between the three papers that focus on epidemiological characteristics, pathophysiological mechanisms, and diagnostic criteria, respectively (1,5,21). We posit that they are often co-cited in the "Background" or "Introduction" sections during the of migraine related manuscripts. Overall, we found that the top co-cited publications mainly focused on etiology and pathophysiological mechanisms (e.g., cortical spreading depression, neuronal hyperexcitability, neurogenic inflammation), diagnostic criteria (diagnostic therapy criteria, migraine with and without aura), epidemiological characteristics (e.g., prevalence, age , and gender characteristics), disease burden, and treatment drugs (e.g., triptans, flunarizine, *OnabotulinumtoxinA*), which could be regarded as the research foundation of migraine.

Emerging topics

Papers with a high citation burst indicate the emerging trends and research frontiers in a specialized field within a period of time (3,16,29,30). The top 22 references with strong citation bursts were identified by CiteSpace. Here, we describe the 11 publications (6,31-40) with citation bursts ending in 2016 or later. As these publications may reflect the most recent topics in migraine research, they are included for in-depth analysis. The six publications (6,31-34,36) with citation bursts ending in 2016. In 2010, Anttila *et al.* published "Genome-wide association study of migraine implicates a common susceptibility variant on 8q22.1", which was the fifth strongest citation burst (n=20.0369) from 2011 to 2016 in *Nature Genetics*. This study identified *rs1835740* as the first genetic risk factor for migraine (31). The research team of Bigal ME were the authors of three (32-34). In 2010, Bigal *et al.* published a study with a burst strength of 16.8358 from 2011 to 2016 in *Neurology*. This population-based case-control study found that migraine with or without aura is related to cardiovascular diseases, e.g., stroke, myocardial infarction (32).

In 2008, "Chronic migraine in the population burden, diagnosis, and satisfaction with treatment", with a burst strength of 16.2721 from 2011 to 2016 published in *Neurology*, is an investigative study in which episodic migraine and chronic migraine are diagnosed using reliable questionnaires. Among 24,000 headache patients, 520 chronic migraine patients and 9,424 episodic migraine patients were identified. Most chronic migraine patients did not receive specific medication, and less than 48% of chronic migraine patients were satisfied with acute treatment (33). In 2008, "Acute Migraine Medications and Evolution from Episodic to Chronic Migraine: A Longitudinal Population-Based Study", which had the strongest citation burst (n=22.0083) from 2012 to 2016 and was published in *Headache* (34). The survey showed that the use of barbiturates and opioids increased the risk of transformed migraine, while the use of triptans did not (34). Furthermore, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) was protective or inductive depending on headache frequency. In 2012, Silberstein *et al.* published a study with a burst strength of 7.6873 from 2013 to 2016 in *Neurology*. This study reported updated pharmacologic treatment guidelines that divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, and timolol are effective in preventing migraine, and that frovatriptan is effective in preventing menstrual migraine; these drugs can be recommended for migraine patients, whereas, lamotrigine cannot be recommended (6). In 2009, Evers *et al.* published a study with a burst strength of 6.5095 from 2013 to 2016 in *European Journal of Neurology*. The European Federation of Neurological Societies has revised guideline for the treatment of migraine. Clinical practice guidelines recommend oral NSAIDs and triptans for acute treatment of migraine attacks. Beta-blockers (propranolol and metoprolol) flunarizine, valproic acid, and topiramate can also be used to prevent migraine (36). Two references (35,37) have citation bursts that ended in 2017. In 2012, Freilinger *et al.* published a study with the second strongest citation burst (n=21.9416) from 2013 to 2017 in *Nature Genetics*. The study analyzed the genome-wide association data of 2,326 migraine patients without aura and 4,580 population-matched controls, in order to determine the common genetic variants associated with migraine without aura. *MEF2D* (encoding myocyte enhancer factor 2D) and *TGFBR2* (encoding transforming growth factor β receptor 2) were found to have a credible association at the genome-wide level. The authors suggest that functional research is needed to

clarify a molecular mechanism and to discover potential therapeutic targets (35). In 2010, Natoli *et al.* published a paper with a burst strength of 5.986 from 2013 to 2017 in *Cephalalgia*. This study conducted a systematic review of the global prevalence of chronic migraine. The results of 12 studies showed that the prevalence of chronic migraine is 0–5.1% with an estimated range of 1.4–2.2% (37). Among the three references (38-40) with citation bursts ending in 2019, Smitherman *et al.* published "The prevalence, impact, and treatment of migraine and severe headaches in the USA: a review of statistics from national surveillance studies" in 2013, which had the third strongest citation burst (n=21.5006) from 2014 to 2019 in *Headache*. This review reported that migraine and other severe headaches are common public health problems, especially among women of childbearing age, whereas triptans are the most conventional analgesics for migraine (38). In 2013, Noseda *et al.* published the paper with fourth strongest citation burst (n=20.4609) from 2015 to 2019 in *Pain*. Their study analyzed the pathophysiology of migraine, which was mostly due to pain signals caused by peripheral intracranial nociceptors to activate trigeminal vascular pathways, and central nervous system structural dysfunction involving nerve excitability and pain regulation (39). In 2014, Maniyar *et al.* published "Brain activations in the premonitory phase of nitroglycerin-triggered migraine attacks" with a burst strength of 16.4903 from 2015 to 2019 in *Brain*. This functional neuroimaging study found that activation of the hypothalamus explained many premonitory symptoms of migraine, e.g., tiredness, nausea, photophobia (40). Overall, the current frontiers in the field of migraine research in recent years mainly include pathophysiological mechanisms (e.g., brain activation, sensitization of trigeminal vascular pathways), risk factors (e.g., drug-related, *rs1835740*), associations with other diseases (e.g., stroke, myocardial infarction), disease burden, epidemiological characteristics (e.g., prevalence), treatment and prevention (e.g., metoprolol, frovatriptan, NSAIDs), and migraine-related genes (e.g., *TGFBR2*, *MEF2D*).

Strengths and limitations

Our study has several strengths. First, it is the first scientometric analysis of migraine research and thus provides a comprehensive reference for researchers. Second, established scientometric software tools (VOSviewer, and CiteSpace) were employed to analyze related countries/regions, organizations, authors, journals, and references,

which clearly show the current status and frontiers of migraine research. Third, we searched the migraine-related literature based on the title, as a title-based search strategy ensures the accuracy of the data. However, this method may cause some important research to be missed. Thus, we also used common terms to conduct a topic search to ensure the comprehensiveness and accuracy of the included data. This study also has some limitations. First, we only searched WoS database and did not search other medical databases, since WoS is considered the most important database in scientometrics (11,17). Second, all data were extracted using scientometric tools, which differed from a systematic review or overview in which data were manually extracted by two or more reviewers (42-44); therefore, the data may be biased. With on-going development of the information science field and information visualization technology, we hope that these limitations will be solved by more advanced scientometric tools.

Conclusions

We employed WoS, VOSviewer, and CiteSpace to identify the knowledge base and research frontiers of the migraine field over the past decade. The number of migraine-related publications showed a rising trend from 2010 to 2019. During this period, the USA occupied the leading position in migraine research and Albert Einstein College of Medicine contributed the most publications. *Cephalalgia* was the core journal in the field of migraine. Lipton RB and Silberstein SD were the most productive and the most co-cited author, respectively, which may have an important influence on migraine research. Overall, the key research topics were identified as causes and risk factors, pathophysiological mechanisms, epidemiological characteristics, diagnostic criteria, treatment and prevention, and migraine-related targets. Investigating migraine disease burden, exploring pathophysiological mechanisms, and discovering effective treatments warrant further research attention. To our knowledge, this is the first scientometric study to use quantitative methods to provide a comprehensive view of migraine research over past decade. We hope that this analysis can guide migraine researchers and promote the quality of research to ultimately benefit migraine patients.

Acknowledgments

Footnote

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 2013;33:629-808.
2. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2018;17:954-76.
3. Hu XH, Markson LE, Lipton RB, et al. Burden of migraine in the United States: disability and economic costs. Arch Intern Med 1999;159:813-8.
4. De Hert M, Peuskens J. Cost of disorders of the brain in Europe. Eur J Neurol 2006;13:e7.
5. Silberstein SD. Migraine pathophysiology and its clinical implications. Cephalalgia 2004;24 Suppl 2:2-7.
6. Silberstein SD, Holland S, Freitag F, et al. Evidence-based

guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 2012;78:1337-45.

7. Wells RE, Bertisch SM, Buettner C, et al. Complementary and alternative medicine use among adults with migraines/severe headaches. Headache 2011;51:1087-97.

8. Zhao L, Chen J, Li Y, et al. The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial. JAMA Intern Med 2017;177:508-15.

9. Garas G, Cingolani I, Patel V, et al. Surgical Innovation in the Era of Global Surgery: A Network Analysis. Ann Surg 2020;271:868-74.

10. Lu C, Bing Z, Bi Z, et al. Top-100 Most Cited Publications Concerning Network Pharmacology: A Bibliometric Analysis. Evid Based Complement Alternat Med 2019;2019:1704816.

11. Ke L, Lu C, Shen R, et al. Knowledge Mapping of Drug-Induced Liver Injury: A Scientometric Investigation (2010-2019). Front Pharmacol 2020;11:842.

12. Chen H, Jiang W, Yang Y, et al. Global trends of municipal solid waste research from 1997 to 2014 using bibliometric analysis. J Air Waste Manag Assoc 2015;65:1161-70.

13. Ellegaard O, Wallin JA. The bibliometric analysis of scholarly production: How great is the impact? Scientometrics 2015;105:1809-31.

14. Fang J, Pan L, Gu QX, et al. Scientometric analysis of mTOR signaling pathway in liver disease. Ann Transl Med 2020;8:93.

15. van Eck NJ, Waltman L. Citation-based clustering of publications using CitNetExplorer and VOSviewer. Scientometrics 2017;111:1053-70.

16. Chen C. CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. J Am Soc Inf Sci 2006;57:359-77.

17. Lu C, Li X, Yang K. Trends in Shared Decision-Making Studies From 2009 to 2018: A Bibliometric Analysis. Front Public Health 2019;7:384.

18. Chen C, Leydesdorff L. Patterns of connections and movements in dual map overlays: A new method of publication portfolio analysis. J Assn Inf Sci Tec 2014;65:334-51.

19. Chen C, Dubin R, Kim MC. Emerging trends and new developments in regenerative medicine: a scientometric update (2000 - 2014). Expert Opin Biol Ther 2014;14:1295-317.

20. Liang YD, Li Y, Zhao J, et al. Study of acupuncture for

low back pain in recent 20 years: a bibliometric analysis via CiteSpace. J Pain Res 2017;10:951-64.

21. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007;68:343-9.

22. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache 2001;41:646-57.

23. Stovner LJ, Hagen K, Jensen R, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 2007;27:193-210.

24. Goadsby PJ, Lipton RB, Ferrari MD. Migraine--current understanding and treatment. N Engl J Med 2002;346:257-70.

25. Hadjikhani N, Sanchez Del Rio M, Wu O, et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. Proc Natl Acad Sci U S A 2001;98:4687-92.

26. Olesen J, Bousser MG, Diener HC, et al. New appendix criteria open for a broader concept of chronic migraine. Cephalalgia 2006;26:742-6.

27. Sorge F, De Simone R, Marano E, et al. Flunarizine in prophylaxis of childhood migraine. A double-blind, placebo-controlled, crossover study. Cephalalgia 1988;8:1-6.

28. Diener HC, Dodick DW, Aurora SK, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. Cephalalgia 2010;30:804-14.

29. Hou J, Yang X, Chen C. Emerging trends and new developments in information science: a document co-citation analysis (2009–2016). Scientometrics 2018;115:869-92.

30. Chen ML. A Data-Driven Critical Review of Second Language Acquisition in the Past 30 Years. Publications 2018;6:33.

31. Anttila V, Stefansson H, Kallela M, et al. Genome-wide association study of migraine implicates a common susceptibility variant on 8q22.1. Nat Genet 2010;42:869-73.

32. Bigal ME, Kurth T, Santanello N, et al. Migraine and cardiovascular disease: a population-based study. Neurology 2010;74:628-35.

33. Bigal ME, Serrano D, Reed M, et al. Chronic migraine in the population: burden, diagnosis, and satisfaction with treatment. Neurology 2008;71:559-66.

34. Bigal ME, Serrano D, Buse D, et al. Acute migraine

medications and evolution from episodic to chronic migraine: a longitudinal population-based study. Headache 2008;48:1157-68.

35. Freilinger T, Anttila V, de Vries B, et al. Genome-wide association analysis identifies susceptibility loci for migraine without aura. Nat Genet 2012;44:777-82.

36. Evers S, Afra J, Frese A, et al. EFNS guideline on the drug treatment of migraine--revised report of an EFNS task force. Eur J Neurol 2009;16:968-81.

37. Natoli JL, Manack A, Dean B, et al. Global prevalence of chronic migraine: a systematic review. Cephalalgia 2010;30:599-609.

38. Smitherman TA, Burch R, Sheikh H, et al. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. Headache 2013;53:427-36.

39. Noseda R, Burstein R. Migraine pathophysiology: anatomy of the trigeminovascular pathway and associated neurological symptoms, cortical spreading depression,

sensitization, and modulation of pain. Pain 2013;154 Suppl 1:S44-53.

40. Maniyar FH, Sprenger T, Monteith T, et al. Brain activations in the premonitory phase of nitroglycerin-triggered migraine attacks. Brain 2014;137:232-41.

41. Lei L. Should highly cited items be excluded in impact factor calculation? The effect of review articles on journal impact factor. Scientometrics 2020;122:1697-706.

42. Li X, Wei L, Shang W, et al. Trace and evaluation systems for health services quality in rural and remote areas: a systematic review. J Public Health 2018;26:127-35.

43. Li J, Gao W, Punja S, et al. Reporting quality of N-of-1 trials published between 1985 and 2013: a systematic review. J Clin Epidemiol 2016;76:57-64.

44. Huang D, Song X, Cui Q, et al. Is there an association between aircraft noise exposure and the incidence of hypertension? A meta-analysis of 16784 participants. Noise Health 2015;17:93-7.
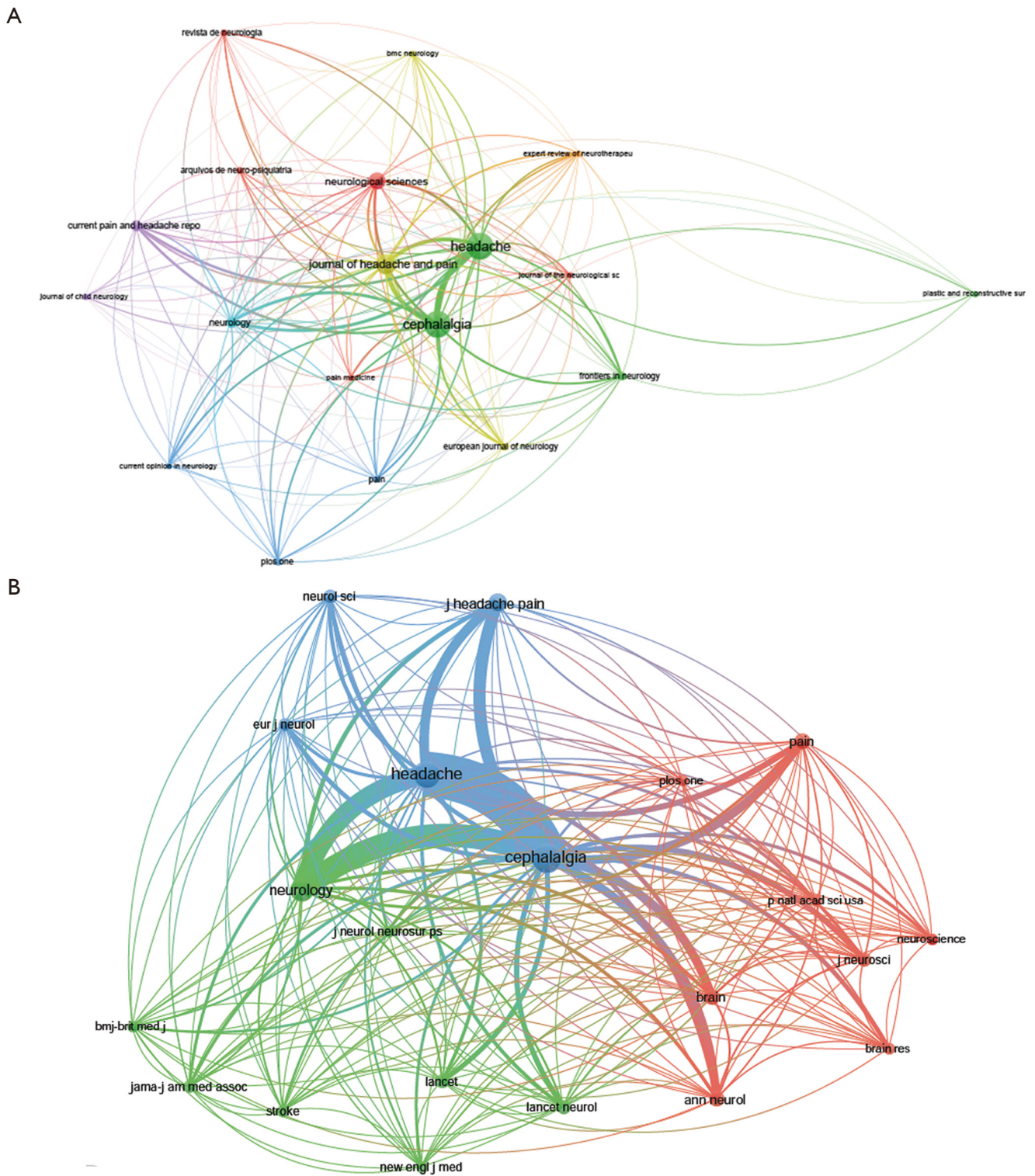
A

B

Figure S1 The network map of academic journals (A, T =35) and co-cited academic journals (B, T =1,500) for migraine research.

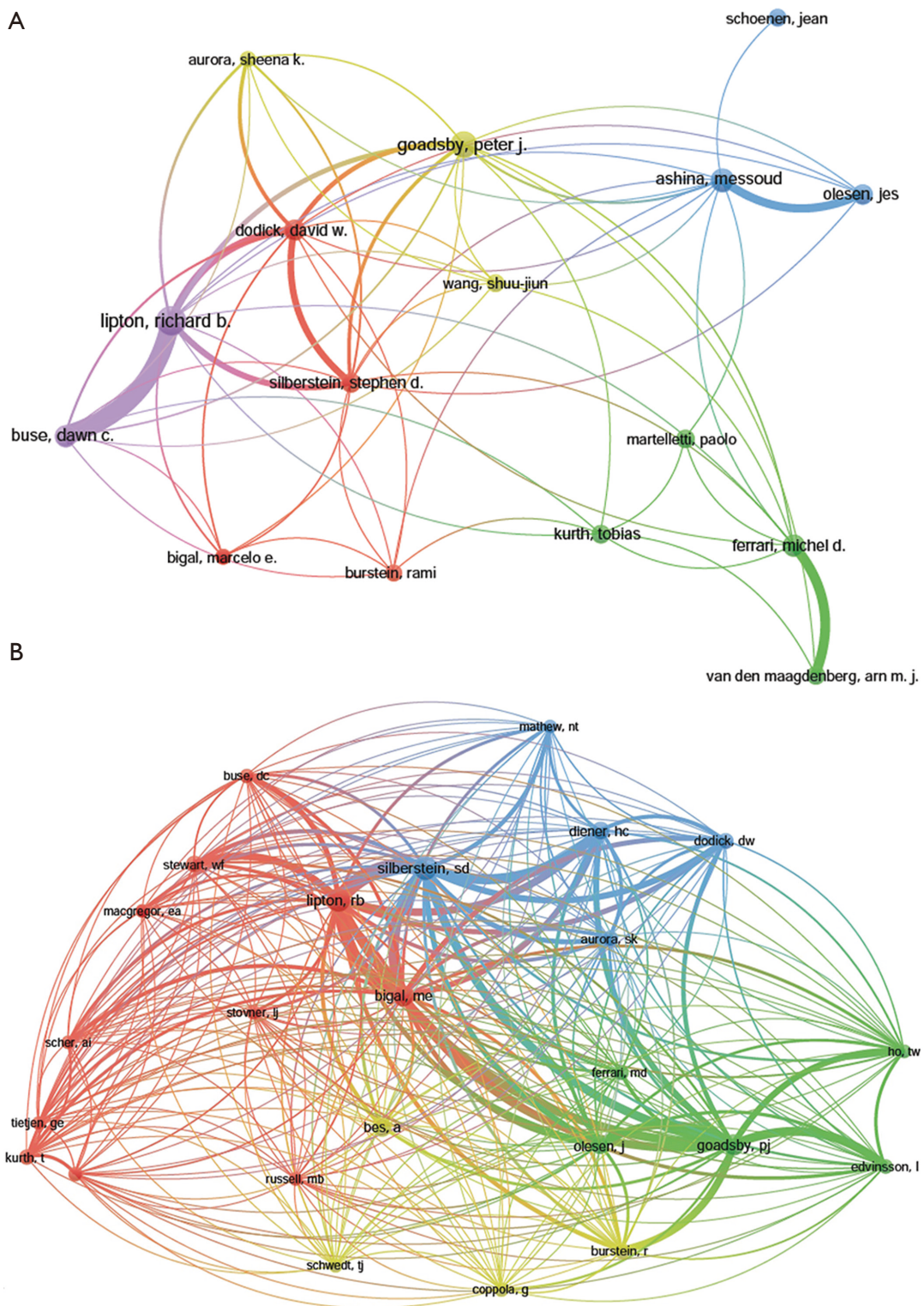http://dx.doi.org/10.21037/apm-20-2546

Figure S2 The network map of authors (A, T =45) and co-cited authors (B, T =600) related to migraine research.
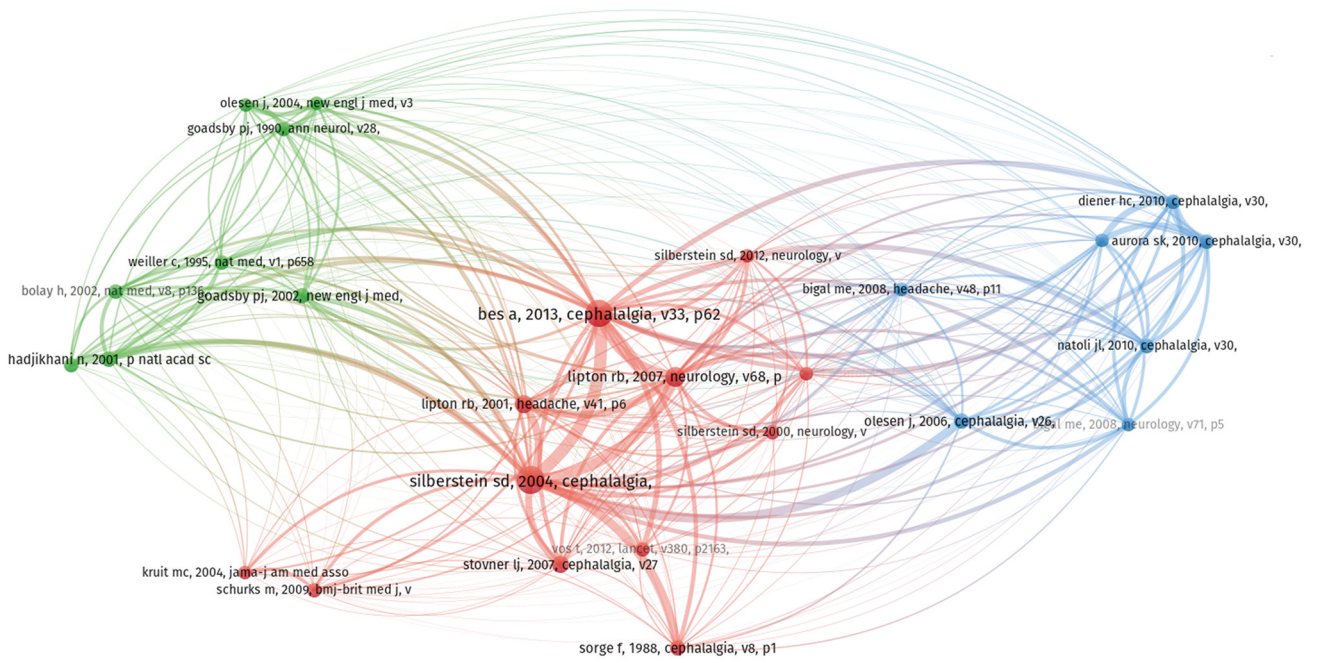
Figure S3 The network map of co-cited references for migraine research (T =200).