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REVIEW

Bibliometric Analysis of Functional Magnetic Resonance Imaging Studies on Manual Therapy Analgesia from 2002–2022

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Background: Research on the brain mechanisms underlying manual therapy (MT)-induced analgesia has been conducted worldwide. However, no bibliometric analysis has been performed on functional magnetic resonance imaging (fMRI) studies of MT analgesia. To provide a theoretical foundation for the practical application of MT analgesia, this study examined the current incarnation, hotspots, and frontiers of fMRI-based MT analgesia research over the previous 20 years.

Methods: All publications were obtained from the Science Citation Index-Expanded (SCI-E) of Web of Science Core Collection (WOSCC). We used CiteSpace 6.1.R3 to analyze publications, authors, cited authors, countries, institutions, cited journals, references, and keywords. We also evaluated keyword co-occurrences and timelines, and citation bursts. The search was conducted from 2002–2022 and was completed within one day on October 7, 2022.

Results: In total, 261 articles were retrieved. The total number of annual publications showed a fluctuating but overall increasing trend. Author B. Humphreys had the highest number of publications (eight articles) and J. E. Bialosky had the highest centrality (0.45). The United States of America (USA) was the country with the most publications (84 articles), accounting for 32.18% of all publications. Output institutions were mainly the University of Zurich, University of Switzerland, and the National University of Health Sciences of the USA. The Spine (118) and the Journal of Manipulative and Physiological Therapeutics (80) were most frequently cited. The four hot topics in fMRI studies on MT analgesia were "low back pain", "magnetic resonance imaging", "spinal manipulation", and "manual therapy." The frontier topics were "clinical impacts of pain disorders" and "cutting-edge technical capabilities offered by magnetic resonance imaging".

Conclusion: fMRI studies of MT analgesia have potential applications. fMRI studies of MT analgesia have linked several brain areas, with the default mode network (DMN) garnering the most attention. Future research should include international collaboration and RCTs on this topic.

Keywords: manual therapy, analgesia, functional magnetic resonance imaging, CiteSpace, bibliometric analysis, web of science

Introduction

Pain is among the most common reasons for medical care visits.[1] According to the pain matrix theory, pain consists of complex structures related to nociceptive processes, including physiological, emotional, and cognitive functions.[2,3] Consequently, pain is a multidimensional experience influenced by psychological and physiological factors. The prevalence of pain is high worldwide, with approximately 20% of the adult population suffering from it.[4–6] In clinical practice, multi-mode analgesic regimens (eg, medications[7] and analgesic injections[8]) are commonly used to relieve pain. However, because opioids are highly rewarding, long-term use may lead to opioid abuse and addiction.[9] In addition, nonsteroidal anti-inflammatory drugs (NSAIDs) can cause side

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effects such as nausea, peptic ulcers, gastrointestinal bleeding, and elevated blood pressure.[10] Therefore, as treatment duration increases, most patients find alternative therapies more appealing.

Manual therapy (MT) as an alternative therapy has sound effects on relieving pain, reducing chronic pain, improving sleep quality, increasing emotion, and reducing stress.[11,12] Broadly speaking, MT encompasses diverse techniques involving the manipulation of the affected pain site. Examples of such techniques include massage, chiropractic practices, mobilization, spinal manipulation, myofascial release, Tuina, and Shiatsu. In clinical practice, a variety of pain-related conditions are recommended to be treated first with MT, such as hip osteoarthritis,[13] subacromial pain,[14] low back pain,[15] neck pain,[16] and adhesive capsulitis.[17] However, the mechanisms have yet to be fully understood, and specifically, the underlying mechanisms in the brain remain unclear.

Functional magnetic resonance imaging (fMRI) is a non-invasive technique that has provided new insights into the brain structure and function.[18,19] By directly delving into the enigmatic realm of brain science within the living human body, fMRI circumvents the limitations posed by previous research predominantly reliant on animal models. As a result, the utilization of resting-state fMRI (rs-fMRI) to explore the intricate interplay between manipulation and the brain represents not only the forefront of this discipline but also commands unwavering attention both domestically and internationally. Consequently, it serves as a pivotal tool in unraveling the underlying mechanisms that underpin the analgesic effects of MT. MT affects numerous regions of the central nervous system (CNS) and exerts analgesic effects through neurotransmitters, signaling pathways, and immunological responses. Over the past few years, the central pain relief mechanism of MT has been increasingly explored.[20–22] Nevertheless, bibliometric analyses of fMRI studies in MT analgesia were not found in the literature review.

CiteSpace is one of the most popular bibliometric analysis software packages used for the statistical visualization of scientific literature across the globe.[23] The current study examined the status and trends of fMRI studies on MT analgesia over the previous 20 years (ie, 2002–2022) using CiteSpace software. Visualization and analysis were performed on the authors, cited authors, institutions, countries, cited journals, cited authors, and keywords. This study endeavors to delve into the developmental forefront of functional magnetic resonance imaging concerning MT analgesia, offering guidance to clinicians in managing and discerning MT strategies for patients experiencing pain, while also furnishing significant data to researchers within this domain.

Materials and Methods

Data Sources and Search Strategy

All data for this study were obtained from the Science Citation Index-Expanded (SCI-E) of Thomson Reuters' Web of Science Core Collection (WoSCC) because it is the most relevant online database. The data search strategy included the topics "manual therapy analgesia" and "functional Magnetic Resonance Imaging". The search was conducted to include publications from 2002–2022 and was completed within one day, October 7, 2022. Only English-language papers were included, and the country of publication and study type were not restricted. Duplicates and articles without the full text were excluded. The search strategies and results are listed in Table 1. A total of 261 articles were retrieved. Finally, we imported these articles into CiteSpace for deduplication, which revealed no duplicates.

Table 1 The Topic Search Query

Set	Results	Search Query
#1	60,680	TS=((Manual Therapy) OR (Massage) OR (Chiropractic) OR (Mobilization) OR (Spinal Manipulation) OR (Myofascial Release) OR (Tuina) OR Shiatsu))
#2	347,194	TS=((Functional Magnetic Resonance Imaging) OR (Magnetic Resonance Imaging) OR (Neuroimaging) OR (Functional MRI) OR (Positron-emission Tomography) OR (Electroencephalography) OR (Magnetoencephalography) OR (Functional Neuroimaging) OR (Resting State Functional Magnetic Resonance Imaging))
#3	414,057	TS=((Analgesia) OR (Manual Therapy Analgesia) OR (Anesthesia and Analgesia) OR (Pain) OR (Acute Pain) OR (Pain Measurement) OR (Breakthrough Pain) OR (Pelvic Girdle Pain) OR (Musculoskeletal Pain) OR (Chronic Pain) OR (Visceral Pain) OR (Nociceptive Pain) OR (Eye Pain) OR (Labor Pain) OR (Patellofemoral Pain Syndrome) OR (Flank Pain) OR (Complex Regional Pain Syndromes) OR (Shoulder Pain) OR (Neck Pain) OR (Pelvic Pain) OR (Back Pain))
#4	216	#1 AND #2 AND #3

Analysis Tool

The map generated using CiteSpace 6.1.R3 consisted of citation tree rings and lines. The occurrence and citation frequencies of the analyzed documents are shown by citation tree rings. The color of the citation tree rings corresponds to the citation time and the thickness reflects the volume of citations during that time. The color of the line connecting the points correlates with a given node's first co-occurrence time, whereas its thickness indicates the intensity of the co-occurrence relationship. The shift from cold to warm hues indicates the transition from past to present time. Network nodes are ranked according to their importance using the betweenness centrality index. CiteSpace employs this indication to determine and gauge the importance of literature and uses a purple circle to indicate key publications, authors, journals, and institutions. In particular, as an illustration: the author and co-author cartography may facilitate scholars in locating esteemed research institutions, prospective collaborators, and data regarding prolific writers. The nodes possessing significant centrality and frequent occurrence can be employed to probe significant quandaries and realms of investigation that hold distinct fascination for the discipline. Through executing a citation-based journal analysis, we ascertained the pivotal publications affiliated with fMRI studies on MT analgesia, thereby evaluating the adoption and impact of the articles disseminated within these periodicals. The chronological scrutiny of associated keywords serves to precisely identify the focal points of research and the projected trends in fMRI studies on MT analgesia.

The parameters of CiteSpace were as follows: the time slice was 2002–2022, the year per slice was one, the terms were selected as "Title", "Abstract", "Author Keywords", and "Keywords Plus"; the number of objects in each time slice was set to 50, and the minimum spanning tree algorithm was used.

Results

Annual Publications and Trends

After searching the databases, 261 articles matching this study were included. Figure 1 shows the number of articles published annually. The number of fMRI studies on manual treatment analgesia published between 2002 and 2022 exhibited a variable but overall upward trend. There were no fMRI studies on acupuncture analgesia between 2002 and 2007, indicating a lack of interest in this topic. Since 2008, the number of published articles has dramatically increased. The first significant increase in the number of publications occurred from 2008 to 2014, leading to the first peak in 2014, which demonstrated the growing recognition of the significance of fMRI research in MT analgesia. After a significant decline in 2015, volatility showed a second increase, peaking in 2019. In conclusion, fMRI research on manual analgesia has been conducted since 2008 and has gained increasing attention.

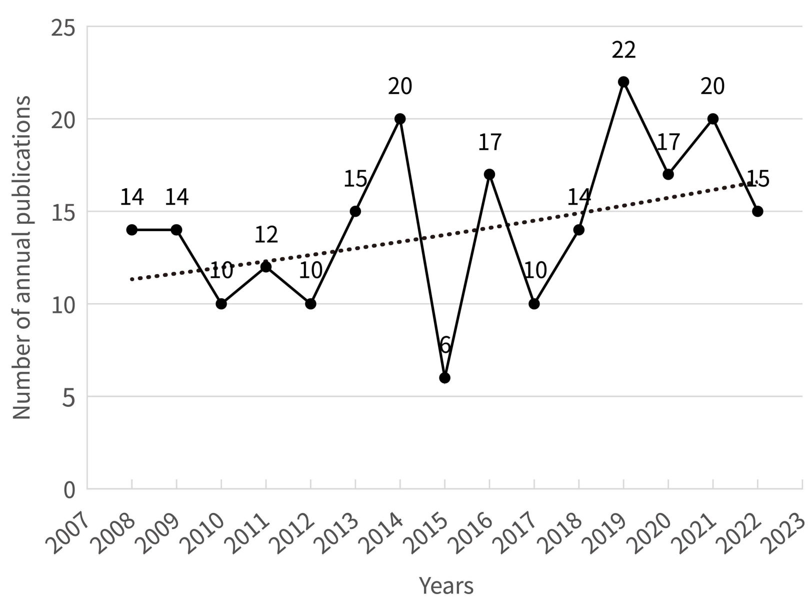

Figure 1 Map of annual publications related to fMRI studies on manual therapy analgesia.

Analysis of Authors and Cited Authors

The authors of the 261 publications were analyzed, resulting in 369 nodes (ie, 369 authors) with 453 links (Figure 2). Analysis of the study authors showed the top 10 authors were B. Humphreys (8 articles), B. Anklin (5), P. Beattie (5), J. Cantu (5), J. Cho (5), G. Cramer (5), S. Leemann (5), C. Peterson (5), D. Belavy (4), and K. Kim (4) (Table 2). Among them, the most prolific author was B. Humphreys with eight articles; he is from the Chiropractic Department at the University of Zürich and University Hospital Balgrist. In addition, seven of the top ten writers were from the United States of America (USA) and Switzerland, which confirms the findings of an examination of the contributions of nations and institutions. Based on the number of publications by high-impact authors, scientific studies can be analyzed in relation to their development and research paths.

The map of the cited authors comprises 480 nodes and 1458 links (Figure 3). J. E. Bialosky had the highest citation count (16 citations), followed by J. M. Fritz (13), J. D. Childs (13), J. A. Cleland (12), and M. N. Baliki (11) (Table 3). The top 10 centralities of the cited authors included J. E. Bialosky (0.45), M. A. Adams (0.23), J. A. Cleland (0.16), G. T. Allison (0.15), J. D. Cassidy (0.14), M. P. Jensen (0.13), B. Vicenzino (0.13), G. Bronfort (0.11), H. B. Albert (0.10), and M. N. Baliki (0.10) (Table 3). A comprehensive analysis found that J. E. Bialosky and M. A. Adams were professors in the field and had an important influence on the development of MT analgesia in fMRI.

Analysis of Countries and Institutions

Analysis of the country distribution revealed with 36 nodes and 49 links (Figure 4). The 261 references were published by researchers from 36 countries, and the top 10 countries for centrality (purple ring) were England (0.47), the USA (0.46), Germany (0.43), Canada (0.38), Australia (0.38), Spain (0.34), Norway (0.27), Denmark (0.17), Australia (0.17), and Italy (0.09). The top 10 countries in terms of publications are listed in Table 4. A total of 84 articles were published in the USA; this high rate may be related to the wide use of fMRI investigations on MT analgesia in the USA. China, South Korea, and Japan were the most productive countries in Asia, whereas the USA, Canada, and Switzerland were the most prolific countries in the West (Table 4).

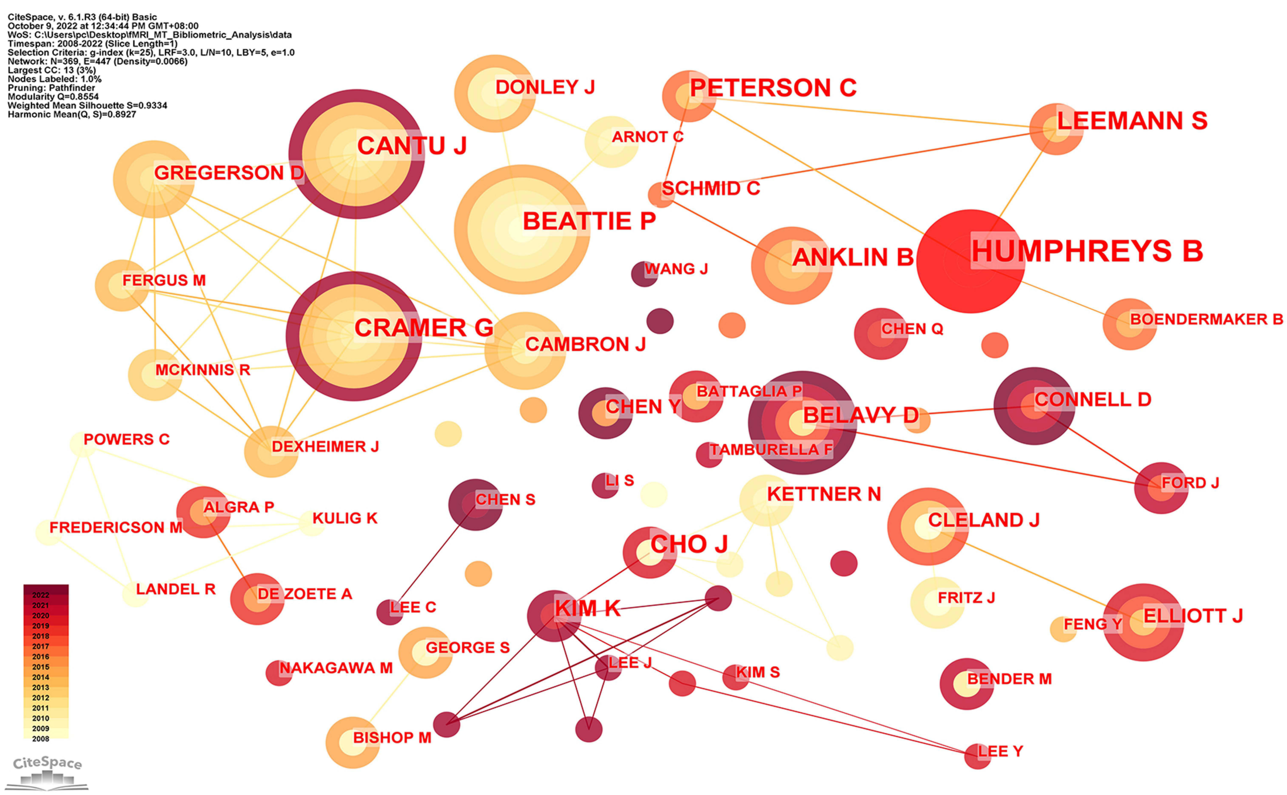

Figure 2 Map of authors related to fMRI studies on manual therapy analgesia.

Table 2 Top 10 Authors Who Performed fMRI Studies on Manual Therapy Analgesia

Rank	Author	Frequency	Year	Country
1	Humphreys B	8	2013	Switzerland
2	Anklin B	5	2013	Switzerland
3	Beattie P	5	2008	Columbia
4	Cantu J	5	2010	USA
5	Cho J	5	2009	USA
6	Cramer G	5	2010	USA
7	Leemann S	5	2013	Switzerland
8	Peterson C	5	2013	Switzerland
9	Belavy D	4	2011	Germany
10	Kim K	4	2019	Korea

The institution map consists of 318 nodes and 362 links (Figure 5). A total of 318 institutions were dedicated to the research of fMRI studies on MT analgesia; the top 10 institutions in terms of number of publications were Univ Zurich (8 articles), Natl Univ Hlth Sci (6), Canadian Mem Chiropract Coll (4), Harvard Med Sch (4), Kyung Hee Univ (4), La Trobe Univ (4), Logan Univ (4), Palmer Coll Chiropract (4), Aarhus Univ Hosp (3) and Adv HealthCare (3) (Table 5). The University of Zurich was most productive, and institutions generally did not work together closely.

Analysis of Cited Journals

Figure 6 and Table 6 show the co-citations of journals in the field of fMRI studies on MT analgesia over the last 20 years. *The Journal of Manipulative and Physiological Therapeutics* had the highest citation frequency and was a core journal and an important reference for fMRI studies on MT analgesia. *The American Journal of Roentgenology, Journal of Neurology, Neurosurgery and Psychiatry*, and *Brain Research* had the highest centrality, indicating that the articles published in these three journals were influential in the field of fMRI studies on MT analgesia.

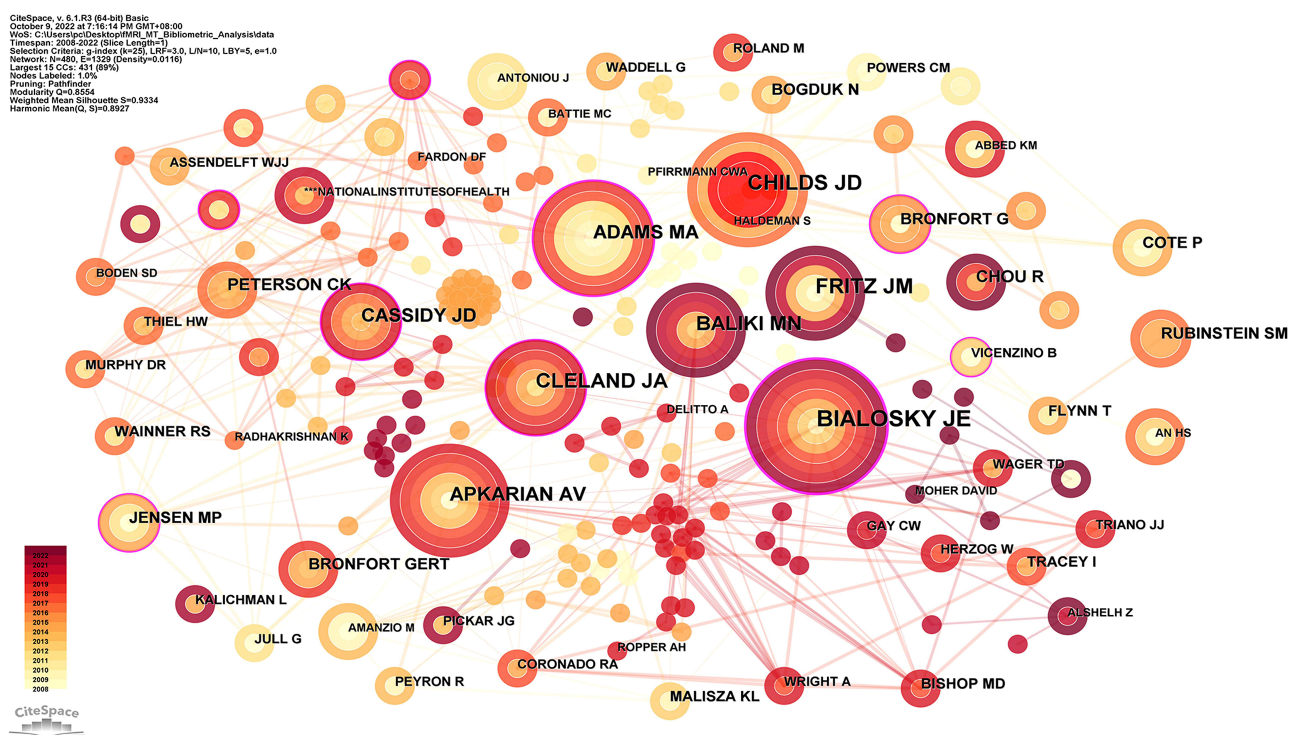

Figure 3 Map of cited authors related to fMRI studies on manual therapy analgesia.

Table 3 Top 10 Frequency and Centrality of Cited Authors Related to fMRI Studies on Manual Therapy Analgesia

Rank	Frequency	Author	Rank	Centrality	Author
1	16	Bialosky JE	1	0.45	Bialosky JE
2	13	Fritz JM	2	0.23	Adams MA
3	13	Childs JD	3	0.16	Cleland JA
4	12	Cleland JA	4	0.15	Allison GT
5	11	Baliki MN	5	0.14	Cassidy JD
6	10	Apkarian AV	6	0.13	Jensen MP
7	9	Adams MA	7	0.13	Vicenzino B
8	9	Cassidy JD	8	0.11	Bronfort G
9	8	Chou R	9	0.10	Albert HB
10	7	Peterson CK	10	0.10	Baliki MN

Figure 7 shows a dual map overlay of the references in the fMRI studies of MT analgesia. On the left are the citing journals and on the right are the referenced journals. The journals on the right side of the map are referenced by reference links that start with the journals on the left side of the map. The discipline of the source is indicated by the color of the links. The number of papers is represented by the vertical axis of the ellipse in the map, while the number of authors is shown by the horizontal axis. As shown in the map, the cited journals are mainly in the fields of neurology, sports, and ophthalmology, whereas the referenced journals are mainly in the fields of molecular biology, biology, and genetics. These findings suggest that future fMRI studies on MT analgesia are expected to cross-fertilize with these fields.

Keywords Co-Occurrence and Citation Burst Analysis

Analysis of the high-centrality and high-frequency keywords revealed with 371 nodes and 1234 lines (Figure 8). According to the frequency and centrality, we found the popular keywords were "low back pain", "magnetic resonance imaging", "management", "functional MRI", "pain", "neck pain", and "spinal manipulation" (Table 7).

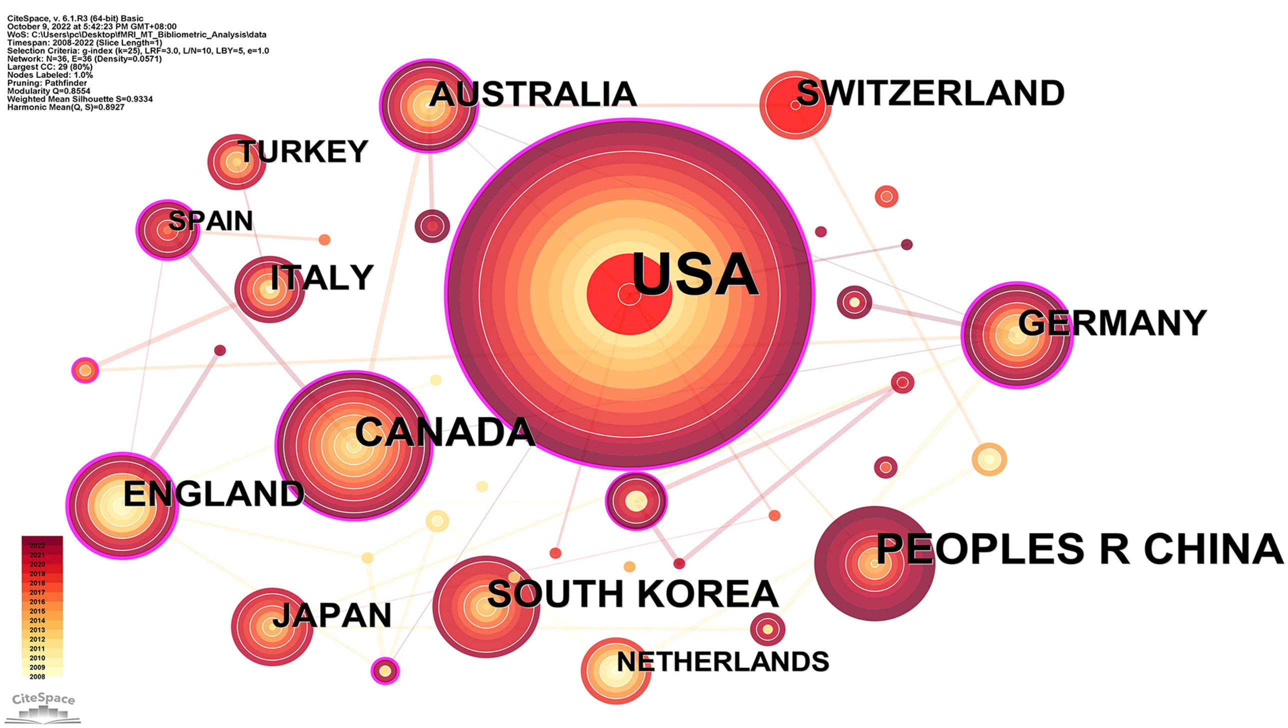

Figure 4 Map of countries related to fMRI studies on manual therapy analgesia.

Table 4 Top 10 Frequency and Centrality of Countries Related to fMRI Studies on Manual Therapy Analgesia

Rank	Frequency	Countries	Rank	Centrality	Countries
1	84	USA	1	0.47	England
2	21	Peoples R China	2	0.46	USA
3	18	Canada	3	0.43	Germany
4	14	South Korea	4	0.38	Canada
5	12	Switzerland	5	0.38	Australia
6	12	Germany	6	0.34	Spain
7	12	England	7	0.27	Norway
8	11	Italy	8	0.17	Denmark
9	11	Australia	9	0.17	Australia
10	10	Japan	10	0.09	Italy

The top 20 keywords with the strongest citation bursts from 2002 to 2022 are shown in Figure 9. In addition to the development patterns and research frontier, it identified the present research hotspots and priorities. The burst start and end times are denoted by "begin" and "end", respectively. Impact increases as "intensity" value increases. The light blue area represents the study period, whereas the red areas represent the beginning and end of a burst. Observing the citation bursts of keywords, we found that 'physical therapy' and 'chronic back pain' were the first keywords that appeared in 2008. The 'diagnosis' is the keyword with the most extended duration (seven years). The 'case report' has the highest intensity value of 3.81.

Keywords Timeline Analysis

Figure 10 presents a timeline review map of the seven distinct co-citation clusters (marked with numbers from 0 to 9) and their interrelationships. The timeline, from left to right, shows the times at which research keywords appeared and disappear from 2002 to 2022. It also displays the structural information of each cluster.

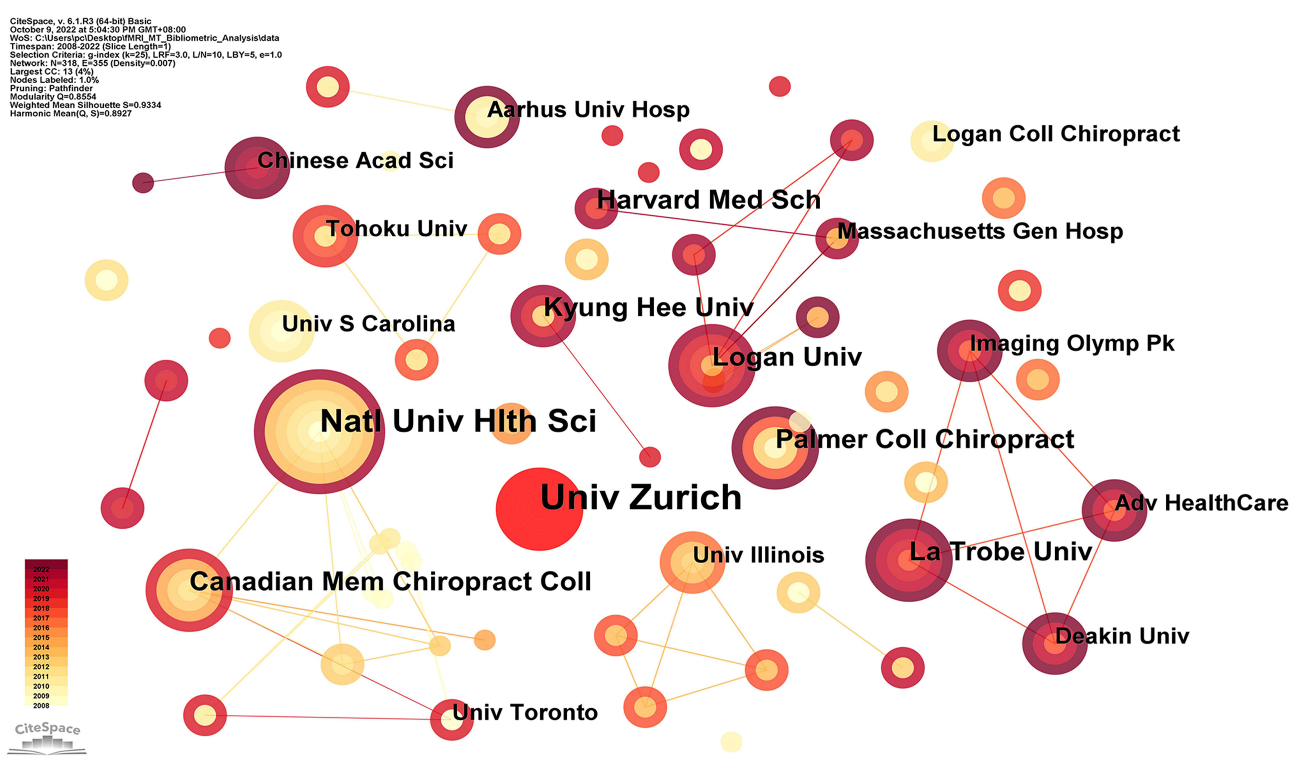

Figure 5 Map of institutions related to fMRI studies on manual therapy analgesia.

Table 5 Top 10 Publications and Centrality of Institutions Related to fMRI Studies on Manual Therapy Analgesia

Rank	Frequency	Year	Institutions
1	8	2013	Univ Zurich
2	6	2008	Natl Univ Hlth Sci
3	4	2011	Canadian Mem Chiropract Coll
4	4	2018	Harvard Med Sch
5	4	2012	Kyung Hee Univ
6	4	2017	La Trobe Univ
7	4	2014	Logan Univ
8	4	2009	Palmer Coll Chiropract
9	3	2009	Aarhus Univ Hosp
10	3	2017	Adv HealthCare

Figure 10 shows that the first cluster (#0), labeled as "shoulder pain", focused on diagnosis, management, classification, conservative treatment, cervical radiculopathy, burden, burst fracture, spinal cord, and case report. Cluster (#1), labeled as "lumbar vertebrae", focused on clinical trial, diurnal variation, chiropractic care, lumbar schwannoma, risk factor, correlate, brain activation pattern, muscle injury, breast magnetic resonance imaging (MRI), and knee osteoarthritis. Cluster (#2), labeled as "neuron" focused on low back pain, cross sectional area, lumbar spine, brain, chiropractic treatment, cortical reorganization, age related change, chronic sciatica, functional connectivity, and the USA. Cluster (#3), labeled as "cervical spine", focused on pain, controlled trial, activation, dissection, cerebral activation, abnormality, radiculopathy, and connectivity. Cluster (#4), labeled as "evidence-based medicine", focused on chronic neck pain, neck pain, cervical spine, Arnold-Chiari malformation, blood flow velocity, disk herniation, surgery, and neurogenic claudication. Cluster (#5), labeled as "radiology", focused on back pain, systematic review, follow up, back massage, cauda equina syndrome, bed rest, dynamic MRI, and complementary medicine. Cluster (#6), labeled as "randomized controlled

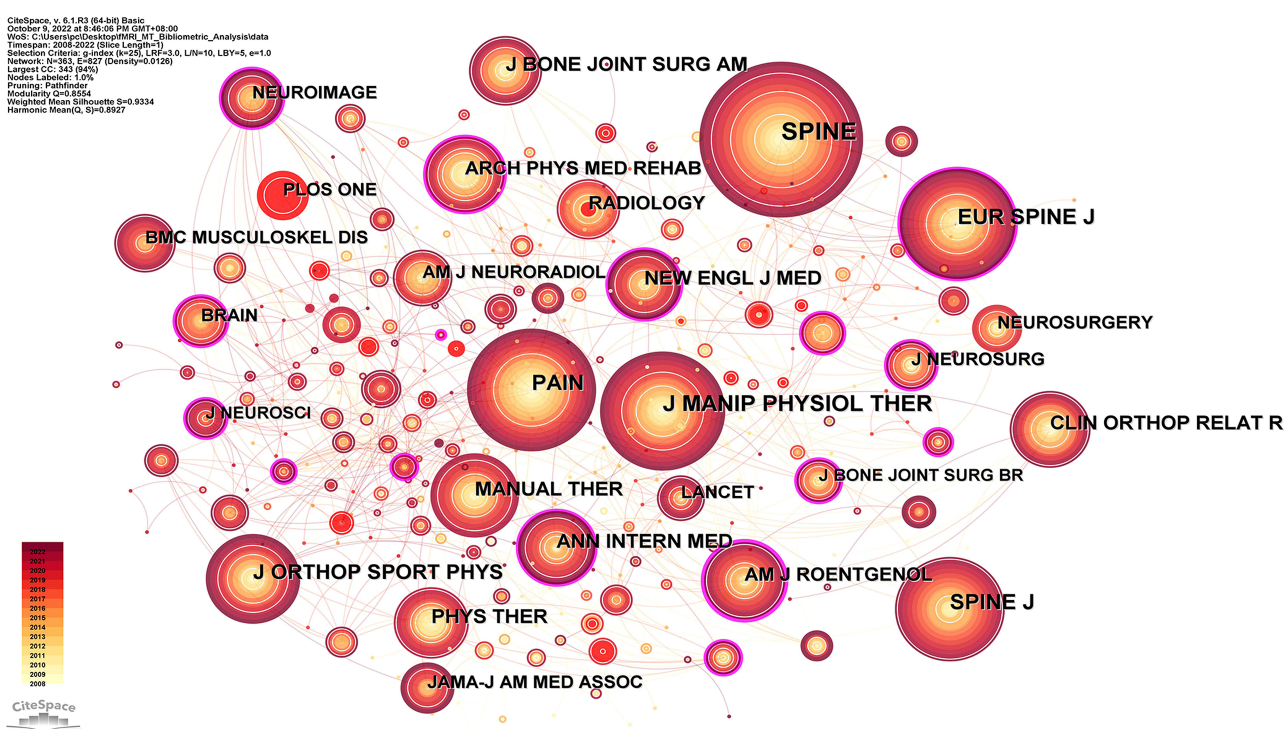

Figure 6 Map of cited journals related to fMRI studies on manual therapy analgesia.

Table 6 Top 10 Frequency and Centrality of Cited Journals Related to fMRI Studies on Manual Therapy Analgesia

Rank	Frequency	Cited Journals	Rank	Centrality	Cited Journals
1	118	Spine	1	0.20	Am J Roentgenol
2	80	J Manip Physiol Ther	2	0.19	J Neurol Neurosur Ps
3	69	Spine J	3	0.19	Brain Res
4	65	Eur Spine J	4	0.17	Eur Spine J
5	64	Pain	5	0.17	J Neurosurg
6	52	J Orthop Sport Phys	6	0.16	Arch Phys Med Rehab
7	47	Manual Ther	7	0.15	Neuroimage
8	46	Ann Intern Med	8	0.14	New Engl J Med
9	44	J Bone Joint Surg Am	9	0.14	Brain
10	43	Clin Orthop Relat R	10	0.13	Ann Intern Med

trial", focused on chiropractic management, drag, therapy, chronic pain, lumbar disc herniation, high velocity, chronic low back pain, thrust manipulation, intervertebral disc, and criterion related validity. Cluster (#7), labeled as "peroneal tendon", focused on MT, electrical stimulation exercise, manipulation, painful stimulation, chronic tennis elbow, electromyographic response, functional magnetic resonance imaging, and clinical pain. Cluster (#8), labeled as "velocity thrust manipulation", focused on MRI, ankle, facet joint, and decompression. Cluster (#9), labeled as "cerebral angiography", focused on computerized tomography angiography, blunt cerebrovascular injury, carotid artery dissection, gas bubble, chiropractic manipulation, and acupuncture.

Discussion

CiteSpace was used to conduct a bibliometric analysis of fMRI studies on MT analgesia from 2002 to 2022. We provided a summary of the overall data, hotspots, and trends in fMRI studies on MT analgesia.

General Information for fMRI Studies on MT Analgesia

As can be seen from the annual publication rate of fMRI studies on MT analgesia, it has been kept in a relatively stable state and has not made any significant advances in the past few years. This phenomenon may be related to the complexity

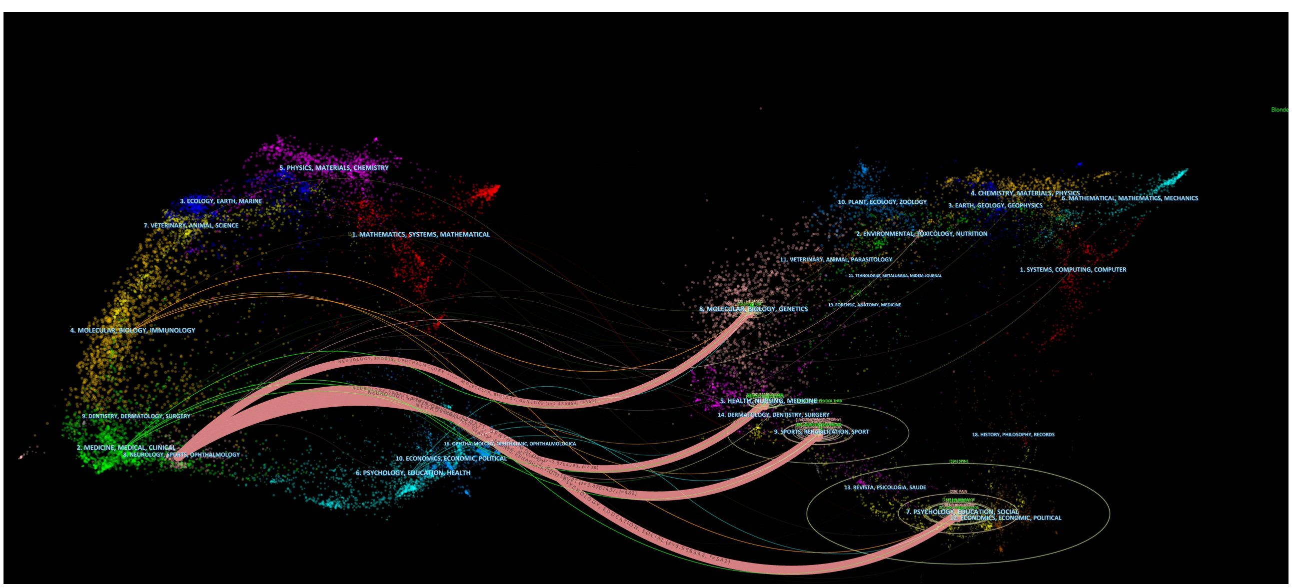

Figure 7 Dual_map_overlays related to fMRI studies on manual therapy analgesia.

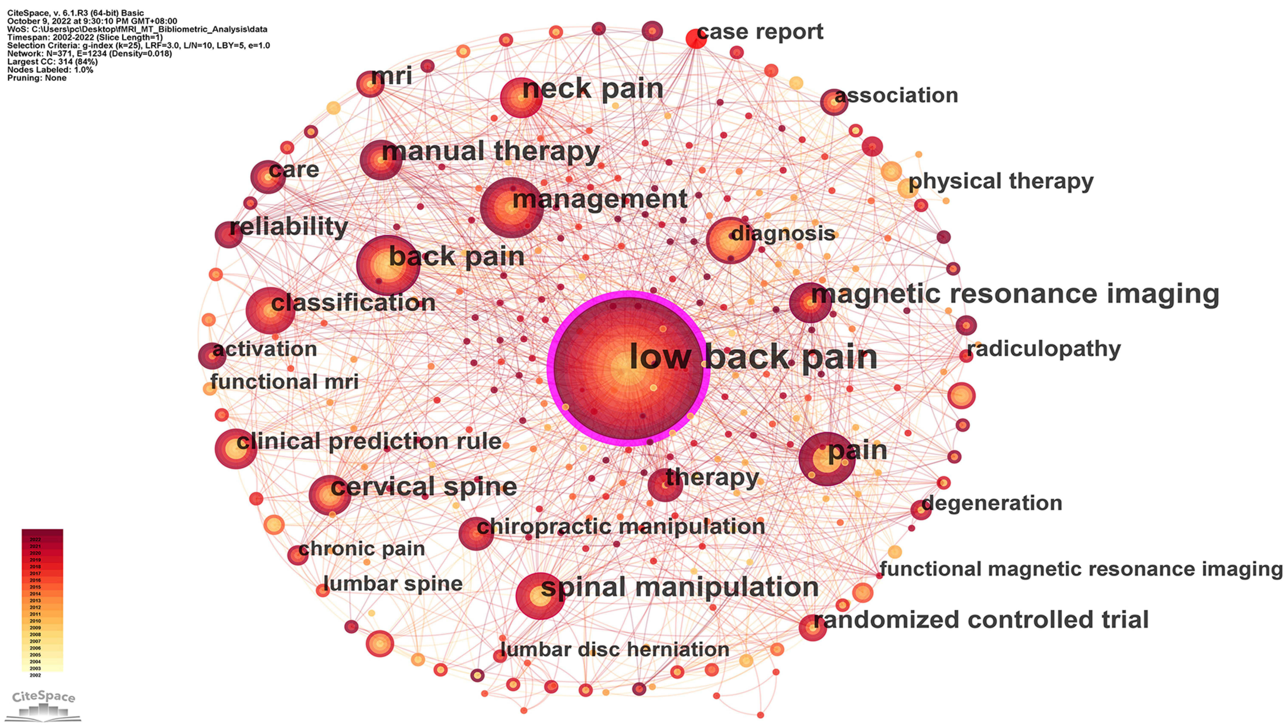

Figure 8 Map of keywords related to fMRI studies on manual therapy analgesia.

of MT analgesia, its interdisciplinary nature, or the fact that it is only used as a complementary therapy among other approaches; it also indicates great potential for the future.

The authors B. Humphreys, B. Anklin, P. Beattie, J. Cantu, J. Cho, G. Cramer, S. Leemann, C. Peterson, D. Belavy, and K. Kim published the most articles. The majority of them are chiropractors and/or possess educational backgrounds in psychology or fMRI. Furthermore, the linkages indicate that closer author collaboration is required in this field and it may be helpful in producing new high-quality articles. The most prolific author was Humphreys (eight articles); most of his articles focused on MT in treating low back pain and its related brain changes based on resting state-fMRI.[24–29] One of his studies, cited 30 times, reports that manual pressure can significantly reduce the extent of secondary sensory cortex (S2) activation.[24]

The USA (84 articles) and China (21 articles) were the largest producers. The USA was a key partner with other nations and published the most publications, accounting for 32.18% of all publications, as reflected by the highest

Table 7 Top 10 Frequency and Centrality of Keywords Related to fMRI Studies on Manual Therapy Analgesia

Rank	Frequency	Keywords	Rank	Centrality	Keywords
1	58	Low back pain	1	0.65	Low back pain
2	32	Magnetic resonance imaging	2	0.26	Magnetic resonance imaging
3	19	Management	3	0.13	Functional MRI
4	18	Pain	4	0.12	Spinal manipulation
5	17	Neck pain	5	0.11	Management
6	15	Spinal manipulation	6	0.10	Neck pain
7	14	Manual therapy	7	0.10	Cervical spine
8	12	Functional MRI	8	0.09	Pain
9	10	Therapy	9	0.08	Manual therapy
10	9	Cervical spine	10	0.07	Classification

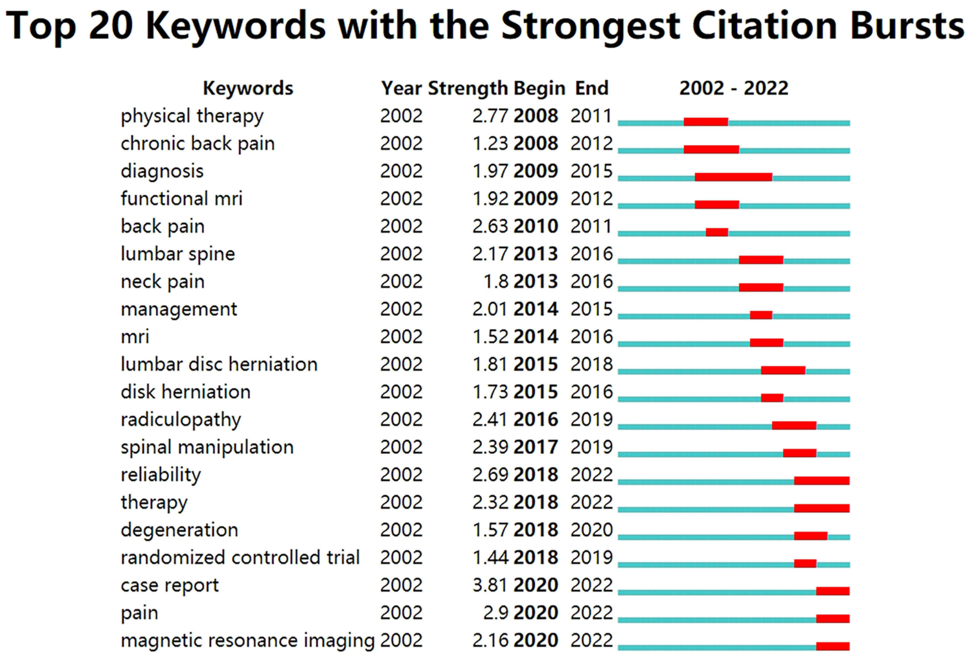

Figure 9 Top 20 keywords with the strongest citation bursts.

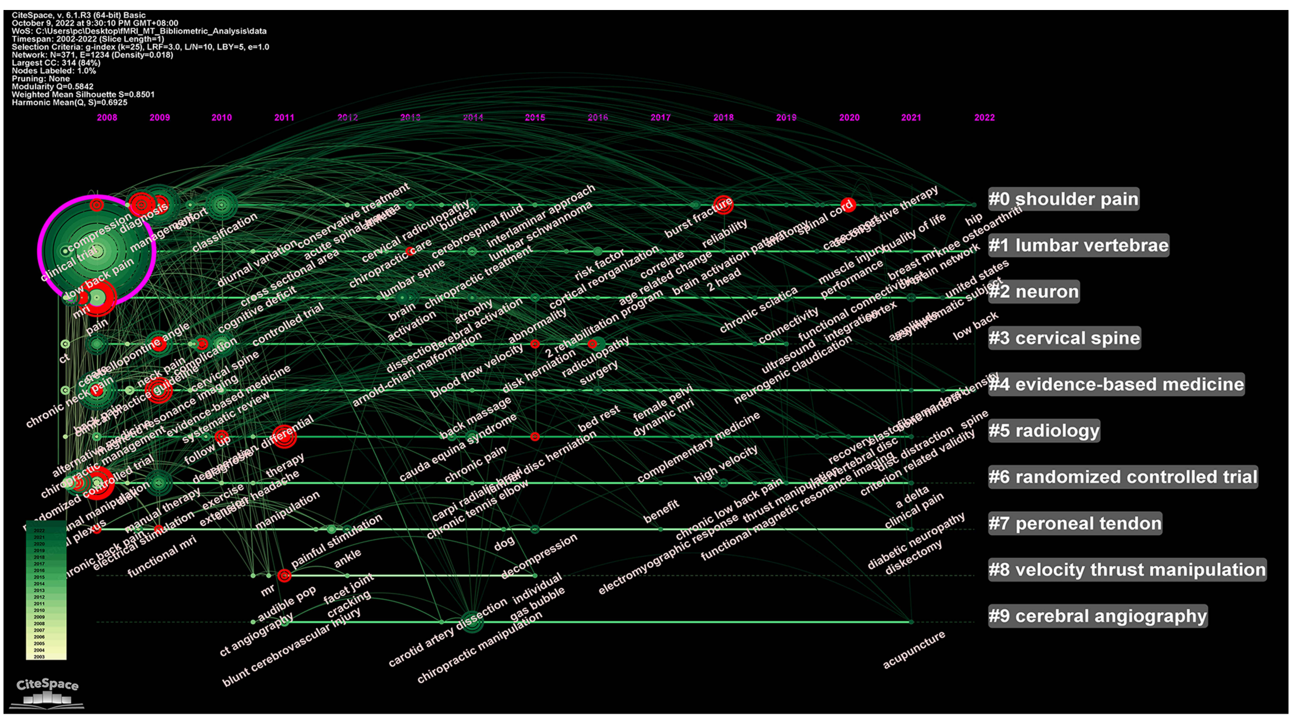

Figure 10 Map of keywords timeline related to fMRI studies on manual therapy analgesia.

centrality (0.46). This further demonstrates the close relationship between the economy and the advancement of science. China is the second-most-published country, which may be related to the wide use of fMRI investigations of MT analgesia. Additionally, the centrality and linkages of England, Germany, Canada, and Australia were strong, indicating that there has been development and some degree of steady expansion of international cooperation in fMRI studies on MT analgesia.

The main output institutions were the University of Zurich, Switzerland, and the National University of Health Sciences of the USA. These are closely related to the top authors, as many publications have already mentioned. An analysis of the colors of circles and lines showed that there were few institutional publications and minimal inter-institutional cooperation. This suggests a need for increased cooperative communication across institutions to advance fMRI studies of MT analgesia.

In the future, MT analgesia is expected to gain more acceptance. Research with a good design and quality control should be progressively published in high-quality journals because it is beneficial for the exchange of research findings of fMRI studies on MT analgesia.

Research Hotspots for fMRI Studies on MT Analgesia

Scientific problems and subjects that received considerable attention from researchers over a specific period are referred to as research hotspots. By analyzing cited authors, journals, and co-occurrence keywords, it is possible to identify frontiers and hotspots of fMRI studies in the MT analgesia field.[30,31]

Among the cited authors, Bialosky, with the highest frequency and highest centrality, focused on fMRI studies of MT analgesia. One of his studies reported that after the application of three different MT therapies in patients with low back pain, brain regions that process and regulate the pain experience (eg, somatosensory cortex, secondary somatosensory cortex, thalamus, anterior and posterior cingulate cortices, anterior and poster insula, and periaqueductal gray) were all altered to varying degrees in the functional connectivity between them.[32] In addition, J. M. Frizt,[33] J. D. Childs,[34] and J. A. Cleland[35] also occupy a crucial academic position in the field of fMRI studies on MT analgesia.

The top five most-cited journals were *Spine, The Journal of Manipulative and Physiological Therapeutics, Spine Journal, European Spine Journal*, and *Pain*. Most are associated with spinal-related pain, indicating that most fMRI research on MT analgesia focuses on degenerative sub-health diseases related to daily habits. One of the articles with the highest citations in *Spine* provided a model that enabled the visualization of the neurophysiological reaction cascades caused by the mechanical stresses of MT in the peripheral and central nervous systems.[36]

Based on the frequency and centrality of the co-occurrence keywords, “low back pain” accounted for 13.47% of all keywords and is the most frequent one in this field. Moreover, “magnetic resonance imaging”, “spinal manipulation”, and “manual therapy” also showed a high frequency and centrality. Over 70% of the population in developed countries experiences low back pain, and its prevalence is increasing in developing countries as well; this is why low back pain is a global problem.[37] Earlier this decade, both the public and professionals started to recognize the benefits of MT for low back pain.[38–40] However, the underlying mechanism remains unclear. In recent years, fMRI has become crucial for studying brain function.[41,42] Moreover, several studies have shown that the pain matrix, consisting of the cingulum_post, temporal_sup, precuneus, temporal_mid, occipital_sup, and occipital_mid, is variably activated after MT intervention in patients with spinal pain.[43–45]

Global Trend and Related-Brain Areas for fMRI Studies on MT Analgesia

The global trend for fMRI studies on MT analgesia was investigated from the strongest citation bursts and timeline of keywords.[46] Moreover, we can explore the crucial brain areas connected to MT analgesia through a thorough analysis of keywords.

Overall, the citation bursts and timelines of keywords in the first decade generally represented a focused discussion of conditions associated with spinal pain, fMRI techniques, and physical therapy. This finding suggests that fMRI research on physical therapy analgesia has attracted the attention of scientists for a considerable amount of time. In the last 10 years, physical therapy interventions using specific modalities and pain symptom reduction have received the most attention, and the number of randomized controlled trials (RCTs) has gradually increased. The keyword that lasted the longest (seven years) was “diagnosis”, highlighting a greater emphasis on the clinical impacts of pain disorders and the cutting-edge technical capabilities offered by MRI. In 1995, Biswal et al[47] pioneered resting-state fMRI, which led to clinical experimentation using noninvasive methods to assess the functional architecture of the brain. Since then, several studies have used fMRI to evaluate the changes in brain activity in pain-related diseases.[48–50] Over the past few decades, advances in fMRI have greatly enhanced our understanding of human brain cognition.

We explored keywords more deeply since the citation burst, and the timeline of the keywords could not visually identify the brain regions associated with MT analgesia. Previous studies have focused on the local impacts on brain regions and have produced a comprehensive evaluation of brain networks and connection effects between brain regions. One study showed the potential utility of the default mode network (DMN) as a neuroimaging biomarker for pain management in patients with chronic low back pain.[51] Another study also supported this result, and also reported reduced functional connectivity of the DMN with Precuneus_L and periaqueductal gray (PAG) as well as improved functional connectivity of the DMN with the frontal sup medial L and cingulum post_L.[52] A previous study showed that the DMN was activated during periods of wakeful rest and suppressed during cognitive stimulation, including performing complex tasks.[53] According to several studies, patients with acute and chronic pain situations show an altered DMN.[54–56]

Limitations

This study has several limitations. As CiteSpace cannot combine and evaluate the content of different databases, nor can it perform citation analysis on source material outside the WOSCC, only the WOSCC database was first examined. As CiteSpace is intended to detect and illustrate new trends and advancements in the field, this study also lacks a thorough and explicit discussion of the fundamental process behind MT analgesia. Through CiteSpace, we hope to showcase the advancements in research and the newest areas of study in the field of MT analgesia.

Conclusion

This study establishes a firm foundation for future research by supporting researchers in identifying the research progress and frontiers of fMRI studies on MT analgesia over the past 20 years. Through comprehensive analysis, we can see that: (1) although the number of studies on fMRI in MT analgesia is not yet abundant, there is great potential for development in this field. (2) fMRI studies of MT analgesia have linked several brain areas, with the DMN garnering the most attention. (3) Gaps in the literature include insufficient collaboration and lack of clarity regarding the central mechanisms of MT analgesia. (4) Future research should include international collaboration and RCTs on this topic.

Abbreviations

MT, manual therapy; fMRI, functional magnetic resonance imaging; CNS, central nervous system; WOSCC, Web of Science Core Collection; SCI-E, Science Citation Index-Expanded; NSAIDs, nonsteroidal anti-inflammatory drugs; S2, secondary sensory cortices; FC, functional connectivity; RCTs, randomized controlled trial; DMN, default mode network; PAG, periaqueductal gray.

Data Sharing Statement

The raw data can be directly obtained from the Web of Science Core Collection (WoSCC), and further inquiries can be directed at the corresponding author.

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Disclosure

The authors declare that they have no potential conflicts of interest in this study.

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