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ORIGINAL RESEARCH

Central Nervous System Involvement in Inflammatory Bowel Disease: A Bibliometric Analysis of Collaboration, Hotspots, and Research Trends

Jingwen Li[1], Wen Ru[2], Yan Zhao[3], Chen Liu[2]

[1]7T Magnetic Resonance Imaging Translational Medical Center, Department of Gastroenterology, Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing, People's Republic of China; [2]7T Magnetic Resonance Imaging Translational Medical Center, Department of Radiology, Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing, People's Republic of China; [3]Army Medical University Library, Army Medical University (Third Military Medical University), Chongqing, People's Republic of China

Correspondence: Chen Liu, 7T Magnetic Resonance Imaging Translational Medical Center, Department of Radiology, Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing, People's Republic of China, Email liuchen@aifmri.com

Purpose: Research on central nervous system (CNS) involvement in inflammatory bowel disease (IBD) has expanded rapidly, reflecting growing interest in the interaction between intestinal inflammation and brain-related disorders. This study aimed to systematically map the research landscape of IBD-related CNS involvement and to identify major research hotspots, intellectual structures, and emerging frontiers using bibliometric approaches.

Methods: Publications related to IBD and CNS disorders were retrieved from the Web of Science Core Collection, between January 1, 2005, and December 31, 2024. Bibliometric and visualization analyses were conducted utilizing CiteSpace, VOSviewer, and Bibliometrix to evaluate publication trends, collaboration patterns, thematic evolution and historical development.

Results: A total of 2,429 publications were included. The annual number of publications increased steadily from 2005 to 2024, with a marked acceleration after 2021, indicating increasing scholarly interest in this interdisciplinary field. Sixty-two countries/regions, 2,774 institutions, and 12,399 researchers have contributed to this field. The United States and China emerged as prominent contributors, with Mayo Clinic and Harvard Medical School recognized as central institutional centers. Thematic and keyword-based analyses revealed that research hotspots have evolved along three interrelated dimensions: a sustained focus on the gut-brain axis as the core mechanistic axis; an expansion of phenotypic profiling from general neurological involvement to a stratified central nervous system (CNS) phenotype spectrum; and a translational progression from descriptive correlations to precise predictions and targeted intervention.

Conclusion: By integrating multiple bibliometric indicators, this study provides the developmental trajectory and thematic structure of IBD-related CNS research. The findings highlight that gut microbiota and gut-brain axis mechanisms as prominent emerging hotspot, while neurodegenerative disorders represent an expanding clinical frontier. Future studies should strengthen interdisciplinary collaboration, longitudinal cohort design, multimodal phenotyping, and mechanism-informed translational research.

Keywords: inflammatory bowel disease, brain, visualization, bibliometric analysis

Introduction

Inflammatory bowel disease (IBD) is a chronic, immune-mediated disorder of the gastrointestinal tract, including ulcerative colitis (UC) and Crohn's disease (CD).[1,2] It poses a high disease burden worldwide, and more than 10 million new IBD cases are predicted by 2050 in newly industrialized countries such as Asia, the Middle East and South America with a varying and sometimes severe disease course.[3,4] The primary clinical symptoms include bloody or purulent stool, recurrent diarrhea, rectal bleeding, weight loss and abdominal pain.[5,6] Bowel perforation, septic shock, and various other serious complications can happen in severe situations. At present, there is no cure available.[7,8] The

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rapid changes in lifestyle, diet and environment may be important contributors to the rising incidence of IBD.[9,10] The etiology of IBD has not yet been fully elucidated, and its pathogenetic repercussions are thought to be a complex interplay of genetic, environmental, dietary, infectious, psychological, and other factors.[11]

Beyond these gastrointestinal manifestations, up to 50% of patients experience at least one extra-intestinal manifestation in the course of IBD.[12] Psychiatric comorbidity, including depression, anxiety, and bipolar disorder (BD), is well known to be more prevalent in IBD.[13,14] Many previous research on brain disorders among IBD patients has focused primarily on depression and anxiety.[15,16] Of further note, increasing research shows that IBD has been associated with a higher risk of neurodegenerative diseases such as stroke or cerebrovascular accident, dementia, Parkinson's disease (PD), multiple sclerosis (MS), and peripheral neuropathy.[17,18] This evidence has indicated a complex relationship between intestinal inflammation and central nervous system disorders. Growing attention has therefore been directed toward the gut–brain axis, with gut microbiota, microbial metabolites, neuroinflammation, and barrier dysfunction being considered key mechanisms connecting intestinal and brain pathology.[19–21] However, the directionality, causality, and overall knowledge structure of these associations remain insufficiently clarified.

Bibliometric analysis can effectively process large amounts of literature, assess the present research status, and predict future research hotspots.[22,23] Although a few previous bibliometric studies on the IBD–brain axis have mainly focused on psychiatric comorbidities,[24,25] and some reviews have separately addressed neurodegenerative diseases in IBD,[17,26] a comprehensive bibliometric analysis covering the broader spectrum of central nervous system (CNS) disorders in IBD is still lacking. To address this gap, the present study provides a unified, macro-level mapping of the IBD–brain research landscape from 2005 to 2024, identifying not only the evolution of research output and collaboration patterns, but also emerging hotspots such as gut microbiota, gut–brain axis, and neurodegeneration. This broader perspective offers new insight into how the field is shifting from a predominantly psychiatric focus toward a more integrated neurological framework and may help guide future mechanistic and translational studies.

Methods

Data Source and Search Strategy

Relevant publications on inflammatory bowel disease and neurological aspects from January 1, 2005, to December 31, 2024, were retrieved from the Web of Science Core Collection (WoSCC) database on January 31, 2025. The search strategy was designed to achieve high sensitivity for studies concerning inflammatory bowel disease and its neurological or brain-related manifestations.

Based on the theme of the present study, the search terms were developed and refined with input from Yan Zhao an information specialist from the Army Medical University Library, to balance comprehensiveness and relevance. The topic search was performed using the following formula: TS = ((“inflammatory bowel disease” OR “ulcerative colitis” OR “Crohn disease”) AND (“brain” OR “gut-brain axis” OR “central nervous system” OR “cerebral” OR “neurolog”)) **Two types of papers, articles and reviews in English language solely, were chosen. To ensure the relevance and quality of the included literature, two senior physicians (Dr. Jingwen Li and Dr. Ru Wen) specializing in gastroenterology independently reviewed the titles and abstracts of the retrieved articles. Duplicate records (if any) resulting from internal database indexing overlaps were systematically eliminated utilizing the automated deduplication algorithms inherent within the bibliometrix R package, followed by a secondary manual screening phase. Studies were excluded if they: (1) Focused on IBD but did not examine CNS disorders; (2) Investigated CNS disorders in contexts unrelated to IBD; (3) Discussed IBD without meaningful connection to CNS disorders. In cases of disagreement, a senior professor (Pro. Liu) served as an arbitrator to make the final inclusion decision.

A flow diagram illustrating the selection process is presented in Figure 1A. As a result, 2,429 relevant literatures were chosen and saved in plain .txt format, and complete records and cited references also included. The WoSCC database search results were used for further analysis, covering bibliographical profiles, citation trends, collaboration information, and other retrieved publications.

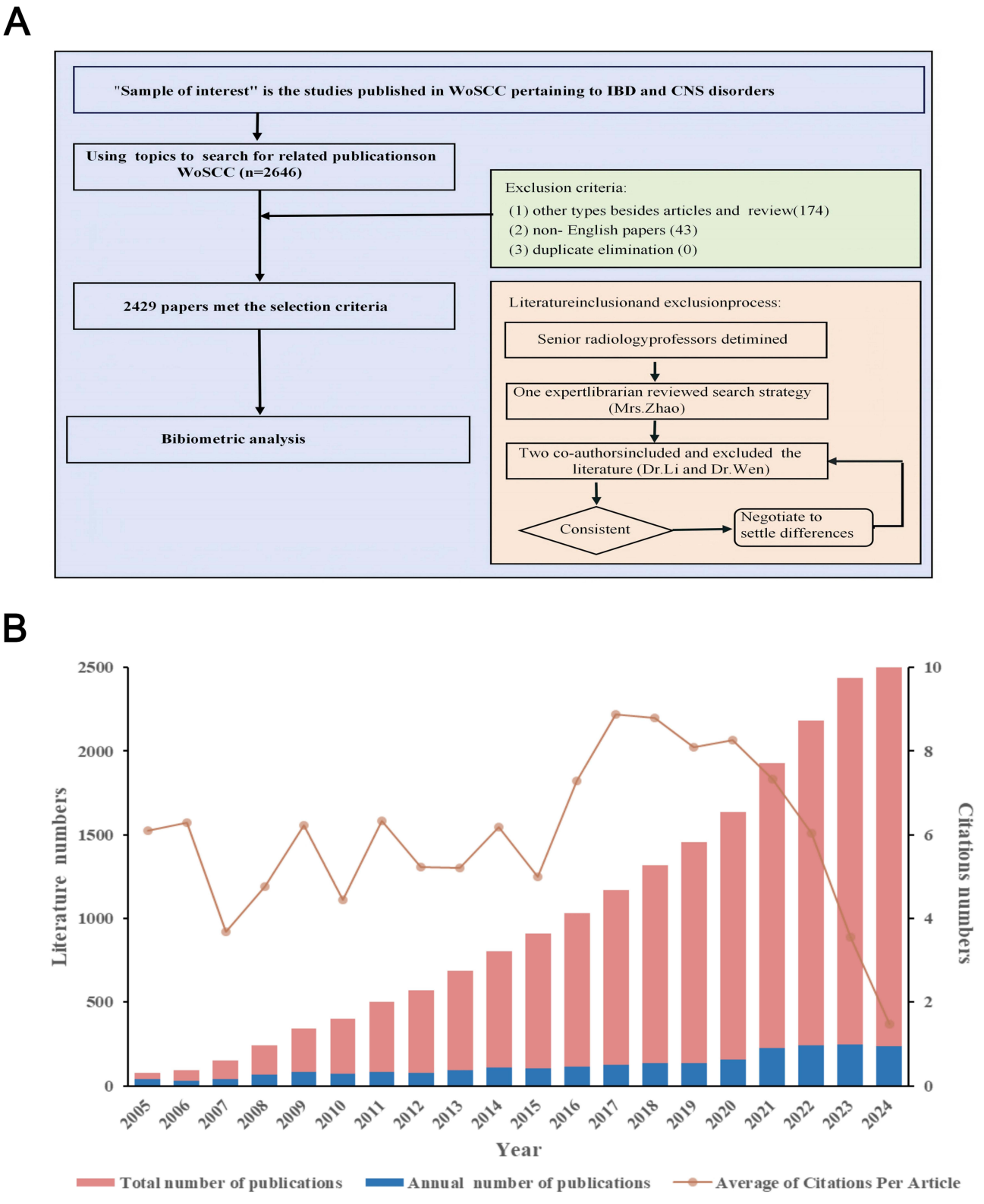

Figure 1 (**A**) Flow chart illustrating the process in this study. (**B**) Global trends in the number of published articles related to cerebral implications for IBD from 2005 to 2024.

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Analysis Methods

Data analysis utilized VOSviewer (v1.6.17), CiteSpace (v6.1.R6) and the Bibliometrix R package to comprehensively investigate the structural characteristics and developmental trends within the research domain.[27] Firstly, VOSviewer was utilized to construct and visualize collaborative networks among countries, institutions, journals, authors, and keywords. In these visualizations, node sizes correspond to their respective weights, while the thickness of the connecting lines indicates the strength of collaboration, co-citation, or co-occurrence relationships. Secondly. CiteSpace was employed to perform analyses of citation bursts, reference co-citation, and keyword timelines, facilitating the identification of pivotal literature and the evolution of research topics. For cluster analysis, we assessed the capabilities of clustering using modularity (Q value) and silhouette (S value) metrics. A Q value greater than 0.3 suggests a significant clustering structure, while an S value exceeding 0.5 indicates that the clusters are reasonably homogeneous and well-separated.

Besides, CiteSpace demonstrated citation relationships across different disciplines and helped to identify research hotspots and emerging themes by making dual-map overlays. Finally, Bibliometrix was used to analyze publication counts, reference analysis, national distribution, collaboration patterns, thematic evolution analysis and historical analysis. This tool allows raw data from Web of Science databases, and supports descriptive statistical analysis, thereby elevating the systematic and reproducible nature of the study. The raw data utilized in this study are publicly accessible, eliminating the requirement for an ethical review. The flowchart for this research study was shown in Figure 1A.

Results

Annual Publications and General Characteristics

Totally, 2,429 publications on the relationship between inflammatory bowel disease and the brain (published 2005–2024) were identified for analysis (Figure 1A). Global trends in the field were shown in Figure 1B. The annual number of publications rose steadily over this period, from 38 in 2005 to nearly 250 in 2024, a seven-fold increase, with the sharpest surge occurring after 2021. The number of articles on IBD and CNS diseases had a significant raise. This suggested that worldwide research teams showed active interest in the past three years.

Analysis of Cooperation Condition

Countries/Regions

Relevant research spanned 62 countries; the USA (588; 24.2%) and China (379; 15.6%) jointly accounted for >40% of output (Figure 2A). The top 10 countries published 1777 articles, constituting nearly 73.2% of the total publications. Network analysis (Figure 2B) showed intensive bilateral links—particularly USA–China—plus an active "second ring" of UK, Germany and Canada. The collaboration network maps (Figure 2B) indicated active cooperation among countries. The extensive collaborations between 30 most productive countries were shown in Figure 2B. Countries with high productivity tended to have more collaboration, the United States and China were the two main contributors and their cooperation was far more common than that of other countries. The cooperation between the other countries such as the United Kingdom, Germany, and Canada was relatively frequent.

Institutions

Research on IBD and CNS disorders was conducted at 2774 institutions globally, with Table 1 highlighting the top 10 institutions. Harvard University (138 papers) and the University of California system (>130) spearhead output (Table 1). The close collaborative relationships between different institutions in this field were illustrated in Figure 2C. The analysis of institutional co-occurrence revealed that institutions with high publication volumes tend to maintain close collaborative relationships, with domestic partnerships being more prevalent than international ones. The cooperation was more common among top institutions and countries.

Authors

Totally, over 12399 researchers participated in research about IBD and CNS diseases. Bruno Bonaz from France had the highest number of publications (n = 19), followed by Charles N Bernstein (n = 16) (Table 2). The author co-occurrence analysis revealed multiple research groups and collaborations among researchers in this field (Figure 2D). Nodes

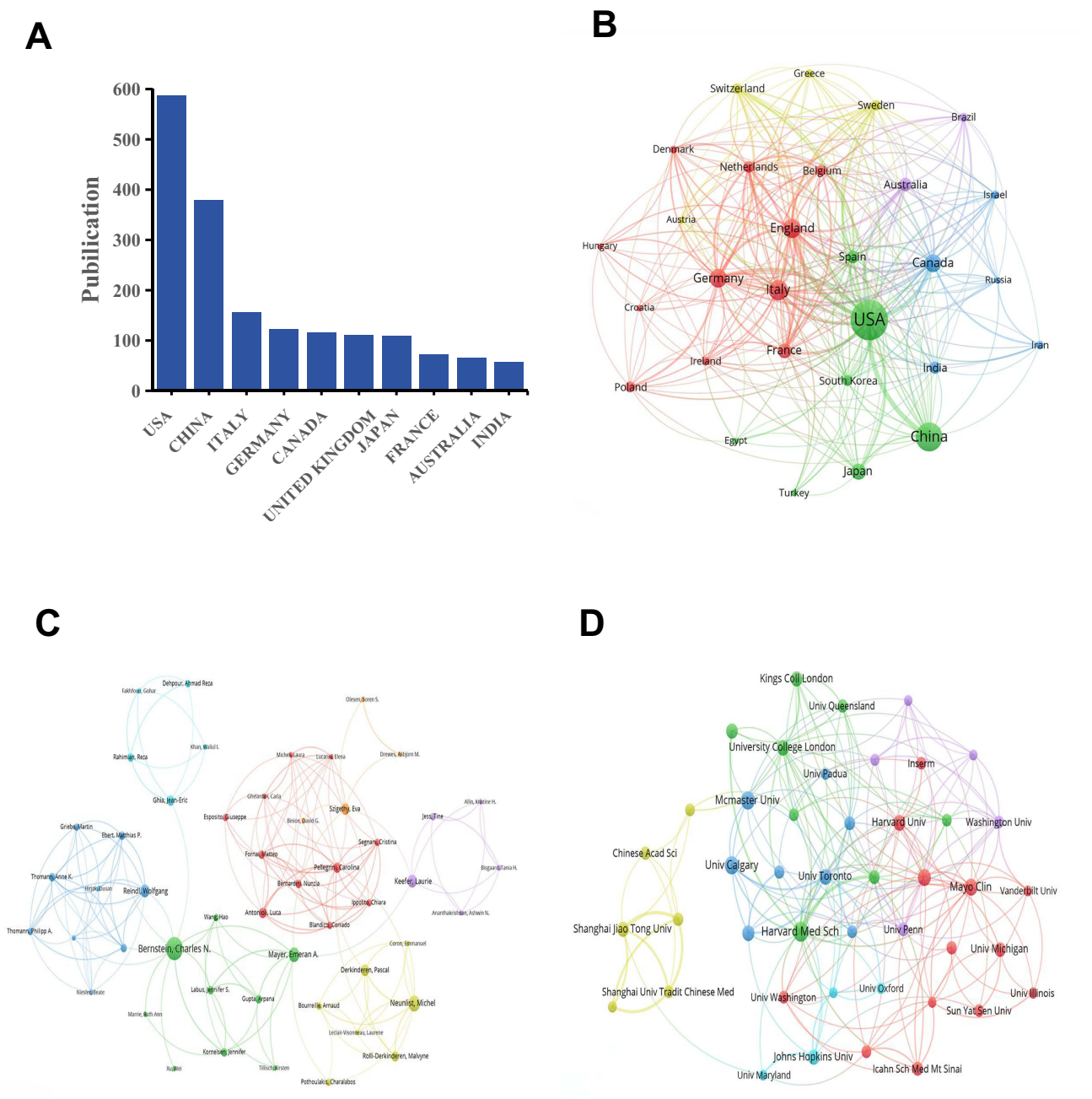

Figure 2 (**A**) The ten most productive countries. The network maps showing countries/regions (**B**), authors (**C**) and institutions (**D**) involved in the research on cerebral implications for IBD.

represented authors, with node size positively correlated to the authors' publication numbers. Lines represented the cooperation between authors, and line thickness indicated the frequency of cooperation.

Analysis of Journals

Up to the end of 2024, 942 SCI journals published articles about IBD and brain. Table 3 listed the top 10 journals actively publishing articles. Among them, the INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES had the highest number of publications (n=69) and citations (2713). FRONTIERS IN IMMUNOLOGY was the second published journal (n=49) with 1719 citations in total. The dual-map overlay of journals (Figure 3) illustrated the disciplinary spread of the IBD–brain literature. Research on this topic was published primarily in journals in the medical and life sciences (depicted

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Table 1 The Top 10 Prolific Institutions

Institutions	Publications
Harvard University	138
University of California System	130
University of London	100
Harvard University Medical Affiliates	94
University of California Los Angeles	86
University of Calgary	77
Harvard Medical School	75
Institute National De La Sante Et De La Recherche Medicale (Inserm)	74
University College London	58
Free University of Berlin	50

Table 2 The Top 10 Prolific Authors

Name	Country	Publications	Total Citations	Per Citations
Bruno Bonaz	France	19	2790	146.84
Charles N Bernstein	Canade	16	987	61.69
Sonia Pellissier	France	15	2352	156.80
Sven Seiwerth	Croatia	15	625	41.67
Predrag Sikiric	Croatia	15	625	41.67
Keith A Sharkey	Canade	14	629	44.93
Emeran A Mayer	USA	13	2436	187.38
Yi Wang	China	12	726	60.50
Jakub Fichna	Poland	12	443	36.92
Li, Lu	China	12	422	35.17

Table 3 The Top 10 Journals of Publications on Cerebral Implications for IBD (Sorted by Total Citations)

Journal	Impact Factor (2024)	Total Publications	Total Citations
International Journal of Molecular Sciences	4.9	69	2713
Frontiers In Immunology	5.7	49	1719
Neurogastroenterology and Motility	3.5	44	2015
World Journal of Gastroenterology	4.3	43	2080
Plos One	2.9	35	1902
Inflammatory Bowel Diseases	4.5	34	1483
Frontiers In Neuroscience	3.2	31	1341
Scientific Reports	3.8	28	875
Journal of Neuroinflammation	9.3	20	1498
Nutrients	4.8	20	581

on the left side of the dual-map), while the references cited by these articles were largely found in journals of neurology and immunology (right side). This suggested that the field draws on knowledge from neuroscience and immunology even as it remains rooted in the medical literatures.

Analysis of Co-Cited References

Co-cited references are those references, which are cited together by other publications integrated into study. We constructed a co-citation network of references, aiming to explore the knowledge base of IBD and brain. Figure 4A

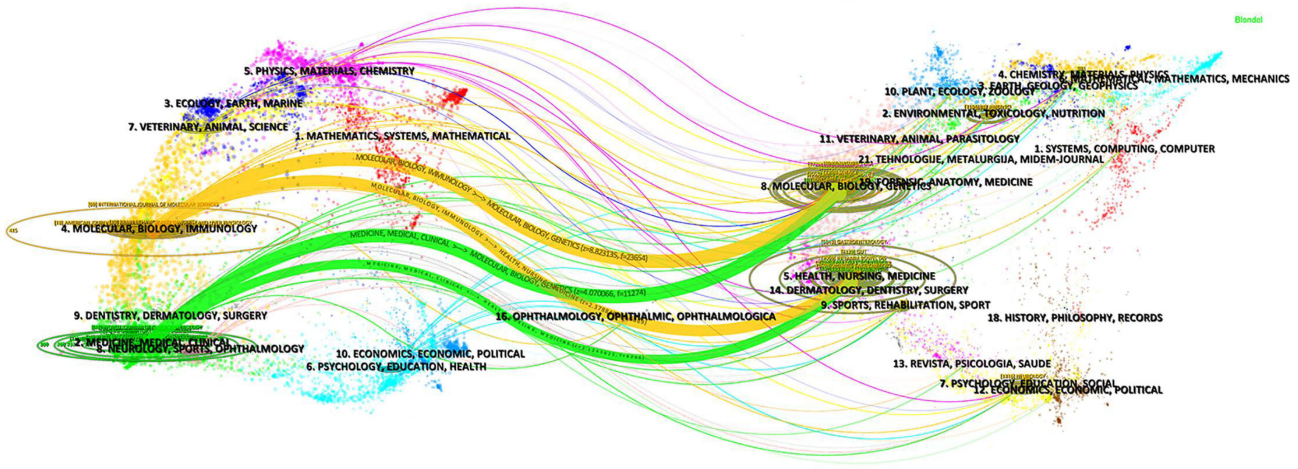

Figure 3 Dual-map overlay of journals, illustrating cross-disciplinary citation flows. Left: citing journals; Right: cited journals. Colored paths represent citation relationships.

illustrated the co-cited reference distribution network from 2005 to 2024, highlighting references cited more than 27 times. The lighter the color of the node indicated later citation.

The citation impact of publications is considered a crucial metric for evaluating scientific documents, despite being influenced by various factors. Table 4 presented the top 10 most frequently cited references. The article "Brain-gut interactions in inflammatory bowel disease," published in GASTROENTEROLOGY, was the most frequently cited with 123 citations. The paper titled 'Ingestion of Lactobacillus Strain Regulates Emotional Behavior and Central GABA Receptor Expression in Mice via the Vagus Nerve' ranked second (n=106). The most cited articles in this field were published in leading journals. Among the top 10 co-cited references, all but one (Sudo N et al) were published after 2010, with approximately half published in the past ten years.

Based on CiteSpace's clustering of the reference co-citation network, 20 clusters were recognized totally and the ten largest clusters were shown in Figure 4B. In the timeline map, nodes of different colors on the same line represented different years of references in a cluster, the older references were nearly closer to the left. Modularity Q (0.8697) was greater than 0.3, and Mean Silhouette (0.9472) values was greater than 0.7, indicating that the clustering structure was convincing. The ten largest clusters were as follows: "t cells" (cluster #0), "depression" (cluster #1), "crohns disease" (cluster #2), "inflammatory bowel disease" (cluster #3), "functional magnetic resonance imaging" (cluster #4), "natalizumab" (cluster #5), "parkinsons disease" (cluster #6), "thromboembolism" (cluster #7), "autism" (cluster #8), "ileum" (cluster #9), and "phosphorylation" (cluster #10). The timeline view of co-cited clusters showed the evolution of these research themes, with some clusters-notably those related to gut–brain axis mechanisms and microbiome interactions-emerging more prominently in recent years.

Citation bursts highlight references that receive notable citations during a specific timeframe. Figure 5 showed the top 20 articles with the strongest citation bursts, red bars indicated high citation frequency and green bars indicated low citation frequency. Many of these high-impact papers were published in the last decade (for instance, around 2015–2018) and correspond to breakthrough findings related to the gut–brain axis and IBD, such as the reference "Brain-Gut Interactions in Inflammatory Bowel Disease" by Bonaz BL with the highest burst strength (21.62). The presence of multiple recent citation bursts suggested rapidly growing interest in these novel topics.

Analysis of Keywords

Keyword co-occurrence analysis is used to explore the hot topics in the research field. We extracted and clustered the 100 most frequent keywords, with every keyword appearing at least 40 times. The different colored dots illustrated four clusters, containing 31, 30, 26, and 13 keywords, respectively. Cluster 1 (red) primarily related to possible cerebral implications in IBD, with keywords such as "inflammation", "brain", "pain", and "Parkinson's disease". Cluster 2 (green) contained keywords related to emotional symptoms and survival of IBD, such as "stress", "depression", "pain" and

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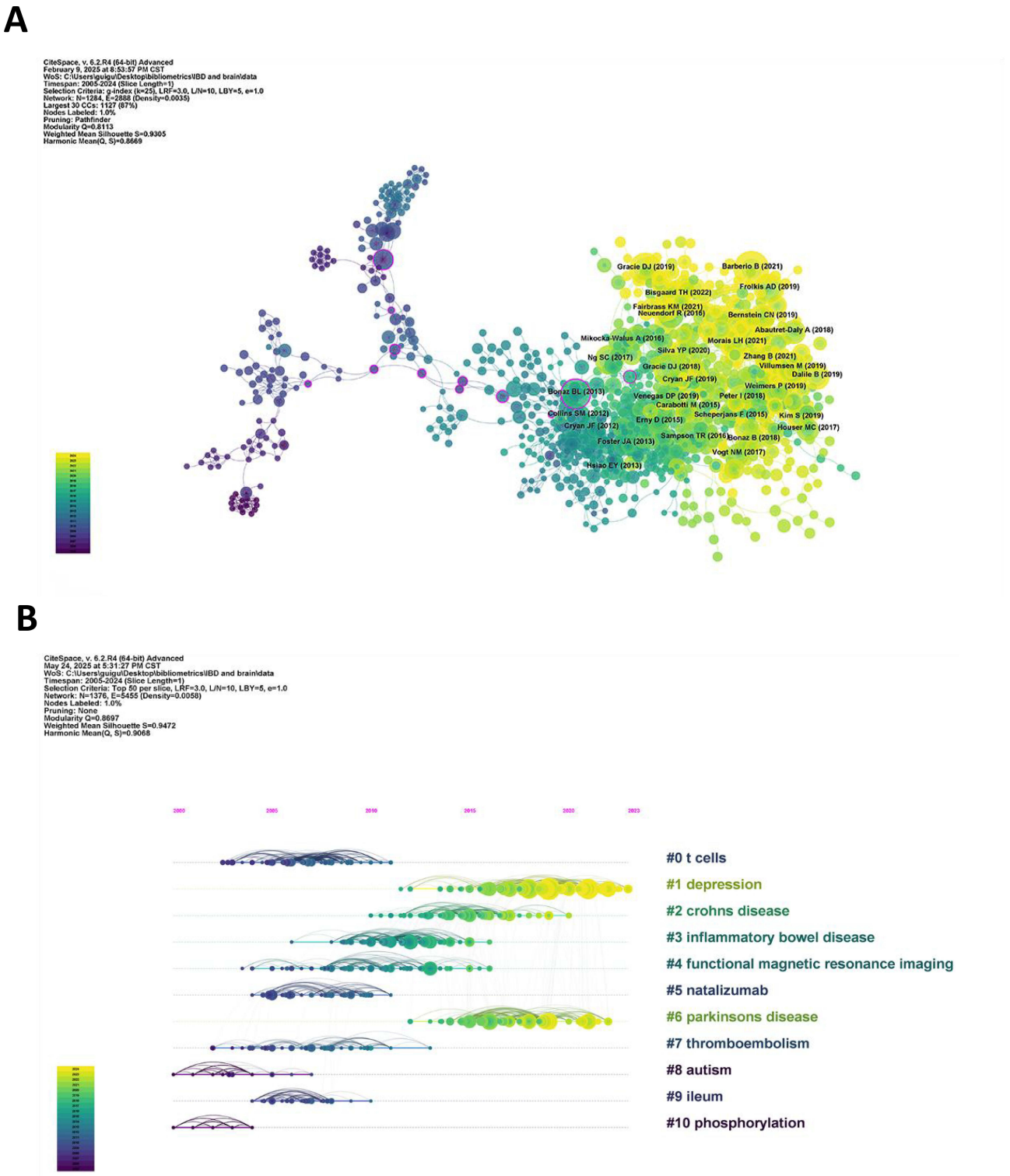

Figure 4 (**A**) The map of the co-cited references clusters. Node size represents publication output, with colors denoting distinct collaborative modules. (**B**) Timeline view of co-cited references clusters.

"quality of life". Cluster 3 (blue) and Cluster 4 (yellow) focused on potential mechanisms and gut microbiota, respectively (Figure 6A). The keyword burst detection (Figure 6B) further showed that terms like "gut–brain axis," "gut microbiota," and "metabolism" had strong citation bursts in recent years. These ongoing bursts indicated that these

Table 4 The Top 10 High-Cited reference

Author	Year	Journal	Title	Co-Citations
Bonaz BL, et al[28]	2013	Gastroenterology	Brain-gut interactions in inflammatory bowel disease	123
Bravo JA, et al[29]	2011	Proc Natl Acad Sci U S A	Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve	106
Carabotti M et al[30]	2015	Ann Gastroenterol	The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems	98
Cryan JF, et al[31]	2012	Nat Rev Neurosci	Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour	98
Erny D, et al[32]	2015	Nat Neurosci	Host microbiota constantly control maturation and function of microglia in the CNS	86
Heijtza RD, et al[33]	2011	Proc Natl Acad Sci U S A	Normal gut microbiota modulates brain development and behavior	86
Sudo N, et al[34]	2004	J Physiol	Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice	85
Cryan JF, et al[35]	2019	Physiol Rev	The Microbiota-Gut-Brain Axis	84
Sampson TR, et al[36]	2016	CELL	Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease	83
Gracie DJ, et al[37]	2018	Gastroenterology	Bi-directionality of Brain-Gut Interactions in Patients with Inflammatory Bowel Disease	77

topics are current hotspots and are likely to remain focal points of future research. A marked growth in IBD–brain research indicated that the gut microbiota and gut–brain axis as prominent emerging themes in this field.

Thematic Evolution Analysis

To comprehensively identify research priorities in this field, we performed thematic evolution analysis. In all the published literature, thematic evolution has gradually developed from inflammation, tight junction, microbiome, and vagus nerve in 2005–2019 to infliximab, chronic pain, gut microbiota, diagnosis, magnetic resonance imaging, and epidemiology in 2020–2024 (Figure 7A). In the thematic map of all articles, a four themes quadrant is provided based on the centrality and density along the x-axis and y-axis, the four quadrants of the map (counterclockwise) represent motor

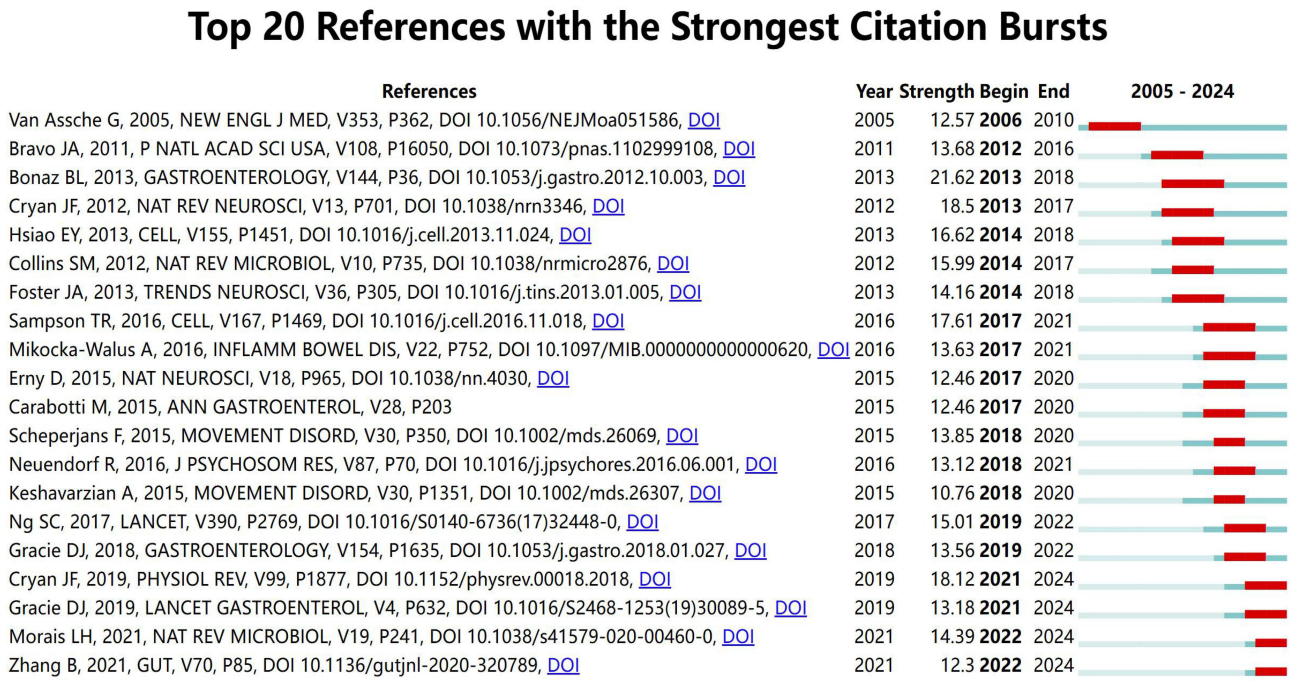

Figure 5 Visual analysis of references with the strongest citation bursts, highlighting the top 20 references with the strongest burst strengths. This figure is a CiteSpace-generated citation-burst visualization based on the analyzed WoSCC dataset; the displayed records represent bibliometric source records rather than all references directly cited in the manuscript text.

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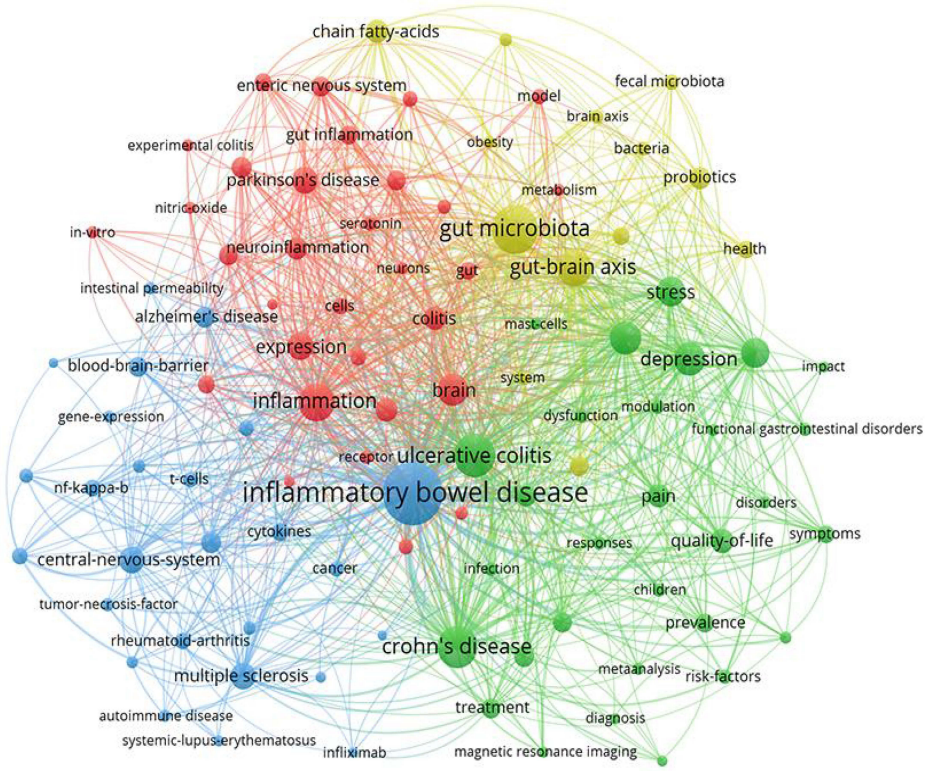
A



B

Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2005 - 2024
tnf alpha	2005	17.98	**2005**	2014	
systemic lupus erythematosus	2005	9.91	**2005**	2015	
multiple sclerosis	2005	9.48	**2005**	2014	
nitric oxide	2005	7.82	**2005**	2014	
blood brain barrier	2005	7.26	**2005**	2011	
progressive multifocal leukoencephalopathy	2006	8.25	**2006**	2010	
rheumatoid arthritis	2007	10.36	**2007**	2015	
collagen induced arthritis	2007	8.46	**2007**	2013	
corticotropin releasing factor	2007	5.84	**2007**	2015	
gene related peptide	2007	5.82	**2007**	2016	
central nervous system	2005	21.3	**2008**	2012	
experimental autoimmune encephalomyelitis	2006	8.98	**2008**	2018	
cerebral venous thrombosis	2008	7.74	**2008**	2014	
growth factor beta	2008	6.61	**2008**	2012	
intestinal epithelial cells	2011	5.64	**2011**	2018	
heart rate variability	2012	6.91	**2012**	2018	
white matter lesions	2012	5.94	**2012**	2014	
traumatic brain injury	2010	5.91	**2014**	2016	
chain fatty acids	2014	8.21	**2019**	2022	
alpha synuclein	2016	6.33	**2019**	2024	
gut brain axis	2018	8.28	**2021**	2022	
gut microbiota	2009	8.06	**2021**	2022	
barrier	2021	5.62	**2021**	2024	
metabolism	2009	6.29	**2022**	2024	
ibd	2020	5.81	**2022**	2024	

Figure 6 (**A**) Network map of the top 100 keywords organized into five distinct clusters. (**B**) Keywords with the strongest citation bursts on cerebral implications of IBD.

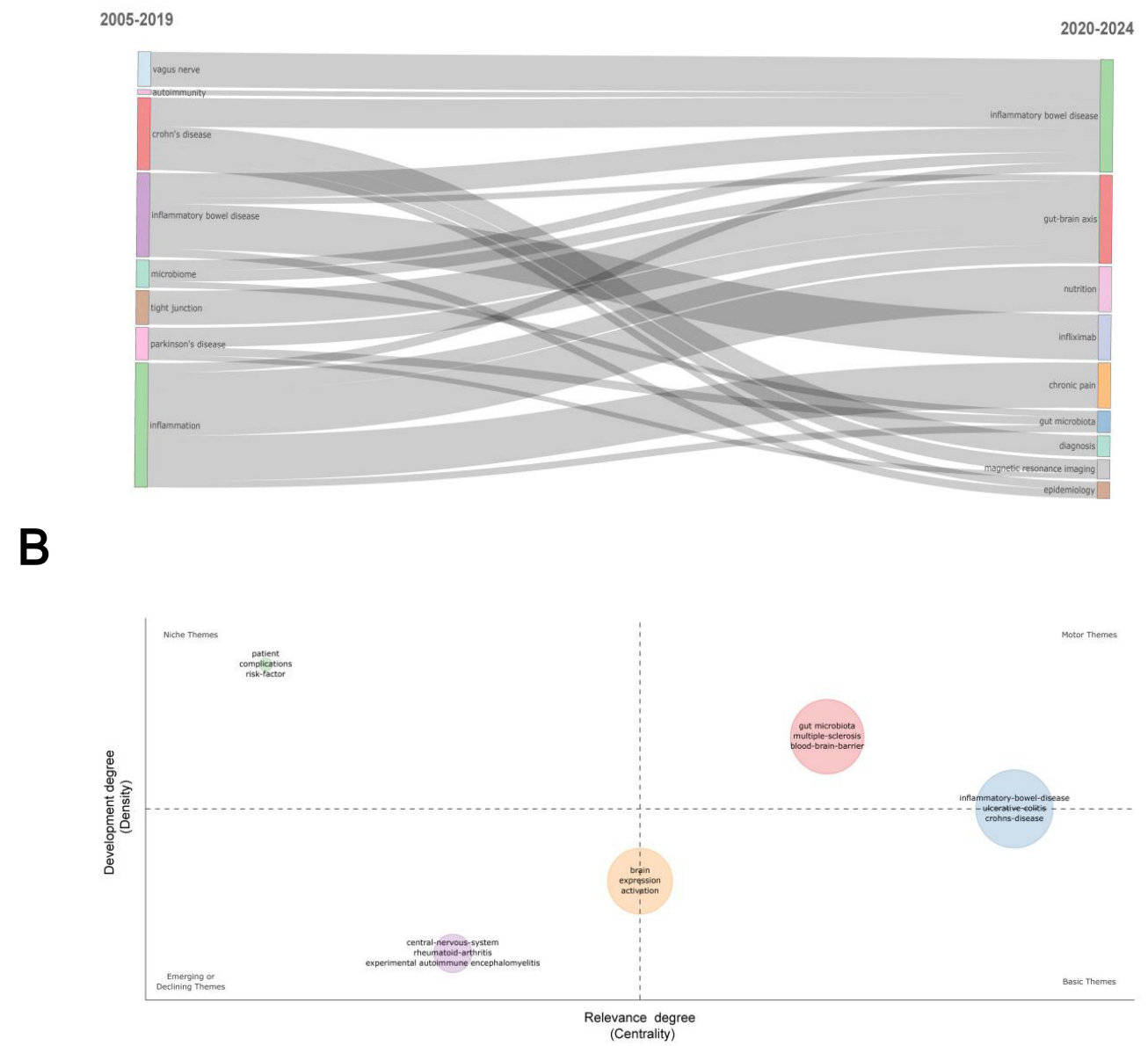


Figure 7 Theme changes and trend of published articles related to CNS disorders from 2005 to 2024. (**A**) thematic evolution of total published articles; (**B**) thematic map of total published articles.

themes (first quadrant), highly specialised themes (second), emerging or disappearing themes (third), and core themes (fourth). The themes in first quadrant are "gut micribiota" "multiple scierosis" "blood brain barrier", all of which are relevant and well-developed for the structuring of this research field, in second quadrant are "patient", "complications" and "risk factor", in third quadrant are "central nervous system", "rheumatoid arthritis" and "experimental autoimmune encephalomyelitis", themes between the third and fourth quadrants were "brain" "expression" and "activation", in the fourth are "inflammatory bowel disease" ulcerative colitis, "crohn's disease" (Figure 7B). Overall, the thematic map indicates that the knowledge structure of this field is centered on IBD-related topics, and gut microbiota-related research representing a prominent theme.

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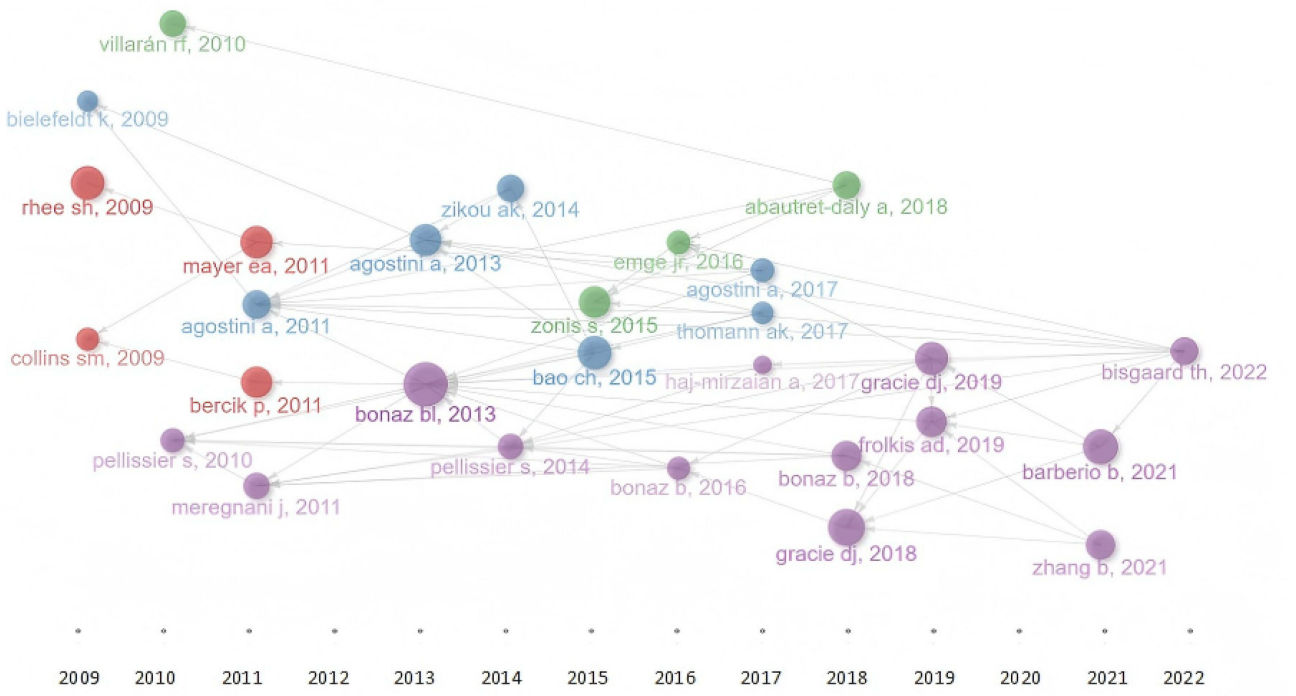

Figure 8 Historiograph of IBD and CNS disorders research.

Historical Analysis of IBD and CNS Disorders Research

We further analyzed the historiograph of IBD and CNS disorders research in order to understand the publications that were important in the history of the discipline (Figure 8), which are also shown in Table 5. Early highly cited publications were mainly concentrated on the brain-gut-enteric microbiota axis, gut-brain communication, and experimental investigations concerning vagus nerve stimulation, microbiota, and CNS injury. Subsequent research expanded toward brain

Table 5 Historiograph of IBD and CNS Orders

Title	Journal	Years	LCS	GCS
Principles and clinical implications of the brain-gut-enteric microbiota axis[38]	Nat Rev Gastroenterol Hepatol.	2009	62	918
Gut feelings: the emerging biology of gut-brain communication[39]	Nat Rev Neurosci.	2011	56	1080
Ulcerative colitis exacerbates lipopolysaccharide-induced damage to the nigral dopaminergic system: potential risk factor in parkinson's disease[40]	J Neurochem.	2010	38	152
Anti-inflammatory effect of vagus nerve stimulation in a rat model of inflammatory bowel disease[41]	Auton Neurosci	2011	38	199
The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice[42]	Gastroenterology	2011	52	1224
Brain functional changes in patients with ulcerative colitis: a functional magnetic resonance imaging study on emotional processing[43]	Inflamm Bowel Dis.	2011	43	63
New insights into the brain involvement in patients with crohn's disease: a voxel-based morphometry study[44]	Neurogastroenterol Motil.	2013	54	87
Brain-gut interactions in inflammatory bowel disease[28]	Gastroenterology.	2013	123	461
Brain involvement in patients with inflammatory bowel disease: a voxel-based morphometry and diffusion tensor imaging study[45]	Eur Radiol.	2014	40	54
Alterations in brain grey matter structures in patients with crohn's disease and their correlation with psychological distress[46]	J Crohns Colitis.	2014	62	72

functional alterations,structural alterations, and the interactions between the brain and IBDin IBD patients. Numerous publications from the period 2013 to 2015 held pivotal roles within the citation network, serving as critical links between earlier studies and subsequent research. In Table 5, brain–gut interactions in inflammatory bowel disease (2013) had the highest LCS, while the intestinal microbiota affect central levels of brain-derived neurotrophic factor and behavior in mice (2011) had the highest GCS.

Discussion

IBD has become a globally health challenge impairing millions of patients, imposing a rising burden on healthcare systems significantly.[2] In this context, research on neurological implications in IBD has expanded substantially over the past two decades. Our bibliometric analysis of 2,429 publications shows sustained growth in scientific attention, with especially rapid expansion between 2021 and 2024. The United States and China were the major contributors, and international collaboration networks were centered around institutions such as Mayo Clinic and Harvard Medical School. Although broad multidisciplinary journals published the largest number of papers, specialty journals such as Gastroenterology retained strong structural influence in the co-citation network. Compared with previous bibliometric studies that focused mainly on anxiety, depression, or emotional factors in IBD,[24,25] the present analysis maps a broader spectrum of CNS disorders and suggests that the field is moving toward a more integrated neurological and microbiota-oriented framework.

Emerging Hotspots and Future Trend

Integrating co-citation analysis, citation burst detection, keyword co-occurrence, thematic mapping, and intellectual historiography, reveals a clear conceptual shift in the field. Earlier studies were largely framed within a conventional inflammation- and immune-centered model, emphasizing TNF-α, T-cell responses, blood-brain barrier dysfunction, and autoimmune mechanisms.[5,47,48] In contrast, recent high-intensity bursts for terms such as gut-brain axis, metabolism, and neurodegeneration suggest a transition toward a more integrated framework centered on gut microbiota and microbially mediated signaling pathways. Overall, the main focus areas and emerging directions in IBD-related CNS disorders can be summarized from three aspects: molecular mechanisms, phenotypic change and disease relevance with translational applications. Importantly, these observations reflect patterns of scholarly attention rather than definitive biological hierarchies.

Mechanistically: From Traditional Inflammation to Intestinal-Brain Axis

Early high-frequency keywords and citation bursts were largely focused on inflammatory mediators, autoimmune overlap, and experimental evidence of CNS immune activation. It reflects an initial effort to explain the interrelationship of intestinal and neurological pathology through shared immunopathogenic mechanisms. In recent years, subsequent shifts in keyword importance indicate a growing expansion of research attention toward to brain–gut axis, especially that gut microbiota. The keyword network depicted in Figure 6A and the thematic map presented in Figure 7B further reveal that, the entities that have assumed a central role include gut microbiota, the gut-brain axis, neuroinflammation, the enteric nervous system, metabolism, chain fatty acids, and the barrier dysfunction. Research increasingly focuses on dysbiosis, loss of short-chain-fatty-acid-producing bacteria, altered bile acid and other microbial metabolite pathways, barrier dysfunction, and neuroimmune activation as candidate links between intestinal inflammation and CNS abnormalities.[35,49–55] These observations support microbiota-centered gut-brain mechanisms as the most prominent emerging hotspot in the current IBD-CNS research landscape. Also, it indicates that the field moves the discussion beyond the simple proposition that IBD is associated with CNS involvement and instead directs attention to the biological routes through which this influence may occur.

Phenotypic Stratification: Beyond Monolithic CNS Involvement

Bibliometric evidence also suggests that the field has evolved toward a more stratified CNS phenotype framework. Rather than a variety of clinical symptoms, previous studies treated CNS manifestations as a monolithic complication of

IBD.[2] In contrast, the co-citation timeline (Figure 4B) in our analysis shows that depression, functional magnetic resonance imaging, and Parkinson's disease are clustered together as a persistently active group. Figure 6A shows that topics such as depression, pain, stress, and diagnosis are situated within the region of high connectivity. This pattern indicates that the scope of IBD-related CNS manifestations has broadened to include anxiety, depression, pain-processing abnormalities, stress-related symptoms, white matter changes, and possible long-term neurodegenerative.[56,57] More importantly, recent systematic reviews and meta-analyses have shown that IBD may be associated with increased risks of Parkinson's disease, dementia, and related neurodegenerative outcomes, although effect sizes and causality remain uncertain.[58–61] Therefore, neurodegeneration should be viewed as an important and growing clinical frontier rather than as a definitively established consequence of IBD. The current research focus is shifting from whether CNS involvement exists in IBD to what kinds of CNS phenotypes are present in different patient subgroups. The recent prominence of themes such as chronic pain and magnetic resonance imaging suggests that future studies should establish a stratified CNS phenotype spectrum according to disease subtype, disease activity, age, medication exposure, and symptom dimensions. Longitudinal neuroimaging and neuropsychological assessment will be particularly important for determining which patients progress from functional abnormalities to structural alterations.

Translational Shifts: From Descriptive Correlations to Targeted Interventions

The phenotypic expansion described above provides the basis for a further translational shift. Primary research topics have moved from earlier concepts such as autoimmunity and tight junctions toward more recent subjects including the gut-brain axis, nutrition, infliximab, and epidemiology (Figure 7). This pattern suggests that the literature is no longer concerned only with explaining the plausibility of gut–brain interactions but is increasingly focused on how these insights may be applied in clinical settings.[29,33,34,37,62]

At the same time, the prominence of the natalizumab-related cluster (Figure 4) and the early appearance of progressive multifocal leukoencephalopathy (Figure 6) indicate that early translational concerns were largely centered on neurological safety. More recently, the scope has broadened to include biologic-response stratification, nutritional and microbiota-targeted interventions, MRI-based monitoring, and population-level risk prediction.[63,64] Combining the continuously emerging references in Figure 5 over the past few years, as well as the multi-disciplinary intersection shown in the double-layered graph in Figure 3,these trends suggest that future research should move from descriptive association toward clinically useful prediction, dynamic monitoring, and mechanism-informed intervention. However, whether dietary regulation, microbiota-directed therapy, or treatment optimization can modify CNS manifestations in IBD still requires stronger longitudinal and interventional evidence.

Limitations

There are some limitations inherent in this study. First, all data were sourced exclusively from the WoSCC, despite its extensive coverage and standardized citation metrics, which may not comprehensively encompass all academic disciplines or journals. This limitation could potentially result in the overrepresentation or underrepresentation of specific research areas. Second, non-English literature was not included in the database or analysis, possibly resulting in linguistic source bias. Furthermore, the IBD–CNS literature remains fragmented across partially connected areas, including psychiatric symptom research, neurological comorbidity research, and microbiota–gut–brain axis–oriented mechanistic studies. This fragmentation may hinder cross-field synthesis and cause bibliometric analyses to reflect parallel research streams rather than a fully integrated knowledge base. In addition, citation-based prominence should be interpreted cautiously, as citation counts may be influenced not only by scientific contribution but also by factors such as author reputation, journal impact, and self-citation. Accordingly, highly cited publications should be viewed primarily as indicators of visibility and influence within the field, rather than direct proxies for evidentiary strength. Finally, publication and citation patterns may be shaped by funding availability and publication bias.

Conclusions

This bibliometric analysis provides a macro-level overview of the IBD–CNS research landscape and reveals how the field has evolved over time. The findings indicate sustained growth in publication output, increasing interdisciplinary

interaction, and a conceptual shift from inflammation-centered and symptom-oriented research toward microbiota-centered gut–brain mechanisms, phenotypic stratification, and translationally oriented investigation. Among the emerging hotspots identified in our analysis, gut microbiota and gut–brain axis-related mechanisms appear to be the most prominent, whereas neurodegenerative disorders represent an important and expanding clinical frontier within the broader IBD–CNS spectrum. Future progress in this field will require stronger international and interdisciplinary collaboration, especially through multicenter longitudinal cohorts, harmonized protocols, and integrated multimodal phenotyping, in order to bridge fragmented research streams and clarify which CNS manifestations in IBD are most clinically relevant, mechanistically informative, and potentially modifiable.

Data Sharing Statement

The data in this study is not of a confidential nature and is accessible in the public domain.

Ethical Approval

Ethical informed consent was not required because no clinical trials or patient consent were involved.

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Author Contributions

Chen Liu, conceptualization, methodology, supervision, writing – review and editing. Jingwen Li, methodology, investigation, data curation, formal analysis, visualization, writing – original draft preparation. Ru Wen – Methodology, investigation, data curation, validation, writing – review and editing. Yan Zhao, methodology, validation, writing – review and editing. All authors read and approved the content of the manuscript, have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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