Mapping trends and hotspot regarding gastrointestinal microbiome and neuroscience: A bibliometric analysis of global research (2002–2022)

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Background: Scholars have long understood that gastrointestinal microorganisms are intimately related to human disorders. The literature on research involving the gut microbiome and neuroscience is emerging. This study explored the connections between gut microbiota and neuroscience methodically and intuitively using bibliometrics and visualization. This study’s objectives were to summarize the knowledge structure and identify emerging trends and potential hotspots in this field.

Materials and methods: On October 18, 2022, a literature search was conducted utilizing the Web of Science Core Collection (WoSCC) database for studies on gut microbiota and neuroscience studies from 2002 to 2022 (August 20, 2022). VOSviewer and CiteSpace V software was used to conduct the bibliometrics and visualization analysis.

Results: From 2002 to 2022 (August 20, 2022), 2,275 publications in the WoSCC database satisfied the criteria. The annual volume of publications has rapidly emerged in recent years (2016–2022). The most productive nation (n = 732, 32.18%) and the hub of inter-country cooperation (links: 38) were the United States. University College Cork had the most research papers published in this area, followed by McMaster University and Harvard Medical School. Cryan JF, Dinan TG, and Clarke G were key researchers with considerable academic influence. The journals with the most publications are “Neurogastroenterology and Motility” and “Brain Behavior and Immunity.” The most cited article and co-cited reference was Cryan JF’s 2012 article on the impact of gut microbiota on the brain and behavior. The current research hotspot includes gastrointestinal microbiome, inflammation, gut-brain axis, Parkinson’s disease (PD), and Alzheimer’s disease (AD). The research focus would be on the “gastrointestinal microbiome, inflammation: a link between obesity, insulin resistance, and cognition” and “the role of two important theories of the gut-brain axis and microbial-gut-brain axis in diseases.”
detection analysis showed that schizophrenia, pathology, and psychiatric disorder may continue to be the research frontiers.

**Conclusion:** Research on "gastrointestinal microbiome, inflammation: a link between obesity, insulin resistance, and cognition" and "the role of two important theories of the gut-brain axis and microbial-gut-brain axis in diseases" will continue to be the hotspot. Schizophrenia and psychiatric disorder will be the key research diseases in the field of gut microbiota and neuroscience, and pathology is the key research content, which is worthy of scholars' attention.

**KEYWORDS**
gastrointestinal microbiome, neuroscience, bibliometric, visualization analysis, WoSCC, research trends, hotspots

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**Introduction**

Gut microbiota represents a complex and dynamic microbial community in the gastrointestinal tract (Quercia et al., 2014). Since the dawn of humanity, these microbes have developed niche ecosystems tailored to particular habitats and adapted to the physiological requirements of their hosts (Lloyd-Price et al., 2016). The term "neuroscience" refers to studies in non-clinical fields like neurobiology and neurochemistry as well as clinical specialties like neurology, neurosurgery, neuropsychiatry, and psychology (Adolphs, 2015). The brain and gastrointestinal tract communicate in both directions through the hypothalamus-pituitary-adrenal (HPA) and microbiota-gut-brain (MGB) axes (Cenit et al., 2017; Wiley et al., 2017). We now understand that certain neurological and neuropsychiatric conditions, including Alzheimer's disease (AD), Parkinson's disease (PD), depression and anxiety, and autism spectrum disorder (ASD), may be significantly influenced by the gastrointestinal microbiome. This influence is also bidirectional, as shown by the comorbidities of certain neural pathologies and intestinal dysbiosis (such as irritable bowel syndrome (IBS), insulin-resistance, inflammatory bowel disease, or alterations in the ratio of bacterial species of the microbiota itself detected in patients with depression) (Wu, 2012). Physiologically, microbiota affects amygdala maturation in mammals, and baseline neuronal activity in the amygdala is altered in germ-free animals, leading to neurodevelopmental disorders (Stilling et al., 2015). Among the factors associated with the field of neuroscience pathology, the gut microbiota can affect a broad range of host neuroscience disorders by interacting with the host through immune, metabolic, neural, and endocrine pathways (Afzal et al., 2020). In recent decades, the relationships between the gastrointestinal microbiome and neuroscience in animals and humans have been widely studied. For instance, many probiotic strains known as "psychobiotics," such as Bifidobacteria, Lactobacillus helveticus had a positive impact on cognition (Savignac et al., 2015; Ni et al., 2019), Saccharomyces boulardii (Tao et al., 2021) and Lactobacillus rhamnosus (Chivero et al., 2021), as well as multi-species probiotics, have been shown to improve neurological diseases by regulating intestinal flora (Ma T. et al., 2021; Rajanala et al., 2021). Multiple studies have presented evidence that nervous system disease leads to microbiome changes or microbiota changes lead to neuroinflammation that can trigger neurological diseases and indicate a causal relationship between them (Yang et al., 2020; Farooq et al., 2022). Many human studies have also shown that gut microbiota is closely related to the development of neurological diseases. Such as specific bacterial taxa commonly associated with mental disorders, including lower levels of bacterial genera that produce short-chain fatty acids (e.g., butyrate), higher levels of lactic acid-producing bacteria, and higher levels of bacteria associated with glutamate and GABA metabolism (Anonymous, 2022). Additionally, some clinical trials have been conducted to explore the feasibility of probiotics for the treatment of neurological diseases. Such as probiotics can improve cognitive function in patients with Alzheimer's disease and major depression (Agahi et al., 2018; Rudzki et al., 2019).

The bibliometric analysis is one method for measuring the development of an area of study (Flay, 1986; Milat et al., 2011), and it may be applied to explore, analyze, and summarize the formation of knowledge's structure in the spatiotemporal dimensions. This approach, which has been used in a variety of domestic and international fields, offers a diverse perspective that traditional literature reviews and systematic reviews cannot (Chen et al., 2014; Cesarano et al., 2021; Ma S. et al., 2021; Pan et al., 2021; Pasin and Pasin, 2021; Shi et al., 2021; Wu et al., 2021a; Fu et al., 2022). Bibliometric analysis has been widely used in the field of microbial science, such as microbiome and COVID-19 (Xavier-Santos et al., 2022), gut microbiota and
host immune response (Ni et al., 2022), gut microbiota and atherosclerosis (Wang Y. et al., 2022), microbiome-gut-brain axis (Wang H. et al., 2022), gut microbiota and heart failure (Mu et al., 2022), gut microbiome and cancer (Zyoud et al., 2022), the intestinal microbiome and inflammatory bowel disease (Xu et al., 2022), gut microbiota and Parkinson’s disease (Cabanillas-Lazo et al., 2022), and gut microbiota and depression (Zhu et al., 2022).

The link between gut microbiota and neuroscience has not yet been subjected to a bibliometric study. However, the volume of research on gut microbiota and neuroscience has exploded, making it challenging to uncover specific data and make more accurate predictions. Therefore, bibliometrics and visualization were employed in this study to intuitively and methodically disclose the connections between gut microbiota and neuroscience, the objectives were to summarize the knowledge structure and identify emerging trends and potential hotspots in this field.

Materials and methods

Data collection

This study utilized the Web of Science Core Collection (WoSCC) database as its data source. The WoSCC database, one of the most comprehensive, systematic, and authoritative databases, has been extensively used by a substantial number of academics for scientometric analysis and visualization of scientific literature (Chen et al., 2020; Devos and Menard, 2020; Wu et al., 2021b; Zhang et al., 2021).

“Gastrointestinal microbiomes” was searched in the Medical subject headings (MeSH) of PubMed to obtain Gastrointestinal microbiome-related terms. Then these terms were used to do searches on WoSCC, the search strategy was as follows: “Topic: ((gastrointestinal microbiomes) OR (microbiome, gastrointestinal) OR (gut microbiome) OR (gut microbiomes) OR (microbiome, gut) OR (gut microbiota) OR (gut microorganisms) OR (microbiota, gut) OR (gastrointestinal flora) OR (flora, gastrointestinal) OR (gut flora) OR (flora, gut) OR (gastrointestinal microbiota) OR (gastrointestinal microorganisms) OR (microbiota, gastrointestinal) OR (gastrointestinal microbial community) OR (gastrointestinal microorganisms) OR (microbial community, gastrointestinal) OR (gastrointestinal microflora) OR (microflora, gastrointestinal) OR (gastric microbiome) OR (microbiome, gastric) OR (gastric microorganisms) OR (intestinal microbiome) OR (intestinal microorganisms) OR (microbiome, intestinal) OR (intestinal microflora) OR (intestinal microorganisms) OR (intestinal microorganisms) OR (intestinal flora) OR (flora, intestinal) OR (enteric bacteria) OR (bacteria, enteric) ) AND Language: (English) AND Document Type: (Article OR Review) AND Web of Science Categories: (Neurosciences) AND Publication Date: (2002-01-01 to 2022-08-20)” (Searchable link)1. “Full Record and Cited References” of the catalogue are exported in “Plain Text” format and were named “download .txt.” The search was completed on 18 October 2022, a total of 2,275 articles were chosen and then used to perform a bibliometric analysis.

Data analysis and visualization

Excel 2016 was used to import and analyze data related to the number of articles published each year on the gastrointestinal microbiome and neuroscience. Use “thesaurus_terms.txt” in VOSviewer 1.6.17 to create thesaurus files, such as merged “ischemic-stroke” and “ischemic stroke,” “gut microbiome” and “gastrointestinal microorganisms,” “gut-brain-axis” and “gut-brain axis,” “Chinese acad sci” and “univ Chinese acad sci” in term analysis. We utilized VOSviewer 1.6.17 to locate the top prolific journals, institutions, countries/regions, citations of documents, co-cited references, terms, and related knowledge maps.

CiteSpace V (Version 6.1 R2)2 was used to detect a citation-burst analysis of WoS-generated keywords. Parameters of CiteSpace were set as follows: time slicing (2002–2022), years per slice (1 year), term source (keywords), node type (keywords), selection criteria (top 50), burstness (γ 1.0).

Results

Annual growth trend

There were 2,275 articles on the gastrointestinal microbiome and neuroscience in the WOSCC from 2002 to 2022 (August 20, 2022), including 1,433 original research articles and 842 reviews. The annual publication is exhibited in Figure 1. The growth of the publications showed three stages. The first stage was from 2002 to 2009, the second stage was from 2010 to 2015, and the third stage was from 2016 to 2022. The overall trend of articles and reviews was consistent with annual publications, but the number of articles was higher than that of reviews.

Top active countries/Regions

A total of 2,618 institutions from 83 countries/regions contributed to 2,275 publications. The United States produced the most publications (732, 32.18%), then China (500, 21.98%), Canada (177, 7.78%), Ireland (137, 6.02%), and England (132, 5.80%) (Table 1). Figure 2A shows that the number of

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1 https://www.webofscience.com/wos/woscc/summary/156f3a2d-3623-4356-9a8a-55d8db4f6efc/relevance/1
2 https://sourceforge.net/
publications in a country is positively correlated with its gross domestic product (GDP). Figure 2B is a cooperation network of countries/regions to study the gastrointestinal microbiome and neuroscience. This map showed 41 countries/regions with a minimum of 10 publications. The most cooperation with other countries/regions is the United States (links: 38), followed by England (links: 35), Australia (links: 32), Germany (links: 31), and Canada (links: 31).

Top active institutions

The top 10 institutions were from the USA (4/10), Australia (2/10), China (2/10), Ireland (1/10), and Canada (1/10) (Table 2). University College Cork (105, 4.62%) published the most papers, followed by McMaster University (50, 2.20%), Harvard Medical School (35, 1.54%), Nanjing Medical University (31, 1.36%), and the University of Melbourne (31, 1.36%) (Table 2). A collaboration network of institutions to research the gastrointestinal microbiome and neuroscience is shown in Figure 3. This map shows 87 institutions with a minimum of 10 publications. The Harvard Medical School has the most collaborations with other institutions (links: 31), followed by University College Cork (links: 30), Deakin University (links: 25), Massachusetts General Hospital (links: 21), and McMaster University (links: 21).

Authors and co-cited authors

A total of 11,617 authors were involved in gastrointestinal microbiome research in the field of neuroscience. Cryan JF published the most papers (n = 100), followed by Dinan TG (n = 79), Clarke G (n = 38), Stanton C (n = 23), and O’Mahony SM (n = 19) (Table 3). The authors (n = 52) who published at least eight papers (T ≥ 8) belong to the core authors in this field and they were included to build the network map of core authors (Figure 4). The same color represented the same cluster.

Co-cited authors are authors who have been co-cited together in a range of publications (42). Among 75,329 co-cited authors, 119 were co-cited over 100. Cryan JF (n = 860) ranked first, followed by Dinan TG (n = 632), Bercik P (n = 563), Desbonnet L (n = 562), Mayer EA (n = 459). The remaining five top authors were co-cited from 408 to 437 (Table 3). The distribution of countries shows that the authors with high co-citation frequencies are mainly from Ireland and the United States. The authors (n = 119) with co-citations of at least
FIGURE 2
Contributions of different countries/regions to research on gastrointestinal microbiome and neuroscience. (A) Number of publications, sum of citations (Actual Value $\times$ 0.01), and GDP (Actual Value $\times$ 10 per trillion dollar) in the top 10 active countries/regions. (B) Cooperation network of countries/regions to study the gastrointestinal microbiome and neuroscience. Map of countries/regions cooperation showed 41 countries/regions with a minimum of 10 publications.

100 ($T \geq 100$) were used to make the density map (Figure 5), this type of knowledge map could present the high-frequency co-cited authors clearly.

**Top active journals**

To discover the most active journal research in gastrointestinal microbiome and neuroscience, we conducted citation journal analyses using VOSviewer. The results showed that 2,275 papers were published in 214 academic journals. Neurogastroenterology and Motility published the most papers (158, 6.95%), followed by Brain Behavior and Immunity (147, 6.46%), Frontiers in Neuroscience (127, 5.58%), Frontiers in Aging Neuroscience (72, 3.16%), and Journal of Alzheimer's Disease (67, 2.95%) (Table 4). Among the top 10 journals, five had an Impact Factor (IF) of more than five, and three were in the Q1 JCR division (Table 4).

**Top cited publications and co-cited references**

Tables 5, 6 display the top 10 gastrointestinal microbiome-related cited articles and co-cited references in the discipline of neuroscience. The most often cited article on research in
TABLE 2 The top 10 institutions research the gastrointestinal microbiome and neuroscience.

| Rank | Institutions                          | Countries | Counts | %   | Citations | Avg. citations |
|------|--------------------------------------|-----------|--------|-----|-----------|----------------|
| 1    | University College Cork               | Ireland   | 105    | 4.62% | 8093      | 77.08          |
| 2    | McMaster University                   | Canada    | 50     | 2.20% | 5165      | 103.30         |
| 3    | Harvard Medical School                | USA       | 35     | 1.54% | 1447      | 41.34          |
| 4    | Nanjing Medical University            | China     | 31     | 1.36% | 165       | 5.32           |
| 5    | The University of Melbourne           | Australia | 31     | 1.36% | 969       | 31.26          |
| 6    | The Ohio State University             | USA       | 30     | 1.32% | 1655      | 55.17          |
| 7    | Zhejiang University                  | China     | 30     | 1.32% | 1848      | 61.60          |
| 8    | University of California, San Francisco | USA     | 29     | 1.27% | 1009      | 34.79          |
| 9    | Deakin University                    | Australia | 28     | 1.23% | 728       | 26.00          |
| 10   | University of Illinois               | USA       | 28     | 1.23% | 969       | 34.61          |

gastrointestinal microbiome and neuroscience was Cryan JF’s 2012 article on the impact of gut microbiota on the brain and behavior (Table 5). Four of the documents appeared on both lists, which were, respectively completed by the team of Cryan JF, Erny D, Sudo N, and Clarke G (Sudo et al., 2004; Cryan and Dinan, 2012; Clarke et al., 2013; Erny et al., 2015). The statistics imply that the articles on research in gastrointestinal microbiome and neuroscience by Cryan JF, Erny D, Sudo N, and Clarke G have been a significant contributor to the growth of the subject.

Analysis of keywords

A map of keyword co-occurrence reflects research hotspots. Co-occurrence and cluster analysis keywords were presented using VOSviewer (c). A total of 7,900 terms were extracted from keywords of all the 2,275 publications. High-frequency
TABLE 3 Top 10 productive and most co-cited authors on gastrointestinal microbiome and neuroscience research.

| Rank | Author       | Counts | %   | Centrality | Institution       | Country   | Co-cited authors       | Citations | TLS   | Country    |
|------|--------------|--------|-----|------------|-------------------|-----------|------------------------|-----------|-------|------------|
| 1    | Cryan JF     | 100    | 4.41%| 0.06       | University College Cork | Ireland  | Cryan JF               | 860       | 15,583 | Ireland    |
| 2    | Dinan TG     | 79     | 3.47%| 0.06       | University College Cork | Ireland  | Dinan TG               | 632       | 14,926 | Ireland    |
| 3    | Clarke G     | 38     | 1.67%| 0.13       | University College Cork | Ireland  | Bercik P               | 563       | 13,970 | Canada      |
| 4    | Stanton C    | 23     | 1.01%| 0.01       | University College Cork | Ireland  | Desbonnet L           | 562       | 15,163 | Ireland    |
| 5    | O'Mahony SM  | 19     | 0.84%| 0.01       | University College Cork | Ireland  | Mayer EA              | 459       | 10,349 | USA         |
| 6    | Bienenstock J| 16     | 0.70%| 0.07       | McMaster University     | Canada    | O'Mahony SM           | 437       | 11,349 | Ireland    |
| 7    | Hashimoto K  | 15     | 0.66%| 0.01       | Chiba University        | Japan     | Bravo JA              | 428       | 9,476  | Ireland    |
| 8    | Burnet PWJ   | 14     | 0.62%| 0.00       | University of Oxford    | England   | Sampson TR            | 421       | 6,871  | USA         |
| 9    | Maes M       | 14     | 0.62%| 0.02       | Chulalongkorn University | Thailand | Maes M                | 416       | 6,872  | Thailand    |
| 10   | Neufeld KAM  | 13     | 0.57%| 0.01       | McMaster University     | Ireland   | Clarke G              | 408       | 10,881 | Ireland    |

FIGURE 4
The co-occurrence map of authors on gastrointestinal microbiome and neuroscience research (T ≥ 8).

keywords (more than 40 times) were the subject of a clustering study. As shown in Figure 6, there were 91 nodes and 3,396 links in the network map, the size of each node indicates the occurrence of the keyword. As we can see from Table 7, the gastrointestinal microbiome was the highest frequency term with 1,850 co-occurrences, followed by inflammation, gut-brain axis, Parkinson's disease, and Alzheimer's disease. Five clusters were shown in different colors, and nodes with common attributes were classified into a color-coded cluster, represented by red, green, blue, yellow, and purple.

In Figure 7, VOSviewer could mark keywords included in the overlay visualization map with different colors based on their average appearance year. The color blue stood for the keywords that appeared on the time course far earlier than those in yellow and red. As can be seen from Figure 7, large numbers of research hotspots related to gastrointestinal microbiomes and neuroscience have emerged in recent years, which indicates that the field is evolving at a tremendously fast pace.

Analysis of bursts
Top 35 keywords with the strongest citation bursts
Burstiness of Keywords CiteSpace was employed to carry out burst keyword detection (Figure 8). Keyword burstiness
FIGURE 5
The density map of co-cited authors on gastrointestinal microbiome and neuroscience research (≥100).

TABLE 4 The top 10 journals publishing articles in the gastrointestinal microbiome and neuroscience.

| Rank | Journal                                | Counts | %     | IF (2021) | JCR   | Country |
|------|----------------------------------------|--------|-------|-----------|-------|---------|
| 1    | Neurogastroenterology and Motility      | 158    | 6.95% | 3.96      | Q2    | UK      |
| 2    | Brain Behavior and Immunity             | 147    | 6.46% | 19.23     | Q1    | USA     |
| 3    | Frontiers in Neuroscience               | 127    | 5.58% | 5.15      | Q2    | Switzerland |
| 4    | Frontiers in Aging Neuroscience         | 72     | 3.16% | 5.70      | Q1    | Switzerland |
| 5    | Journal of Alzheimer’s Disease         | 67     | 2.95% | 4.16      | Q2    | Netherlands |
| 6    | Frontiers in Neurology                 | 63     | 2.77% | 4.09      | Q2    | Switzerland |
| 7    | Prog Neuro-Psychoph                    | 48     | 2.11% | 5.20      | Q2    | UK      |
| 8    | Behavioural Brain Research             | 47     | 2.07% | 3.35      | Q2    | Netherlands |
| 9    | Neuroscience and Biobehavioral Reviews | 43     | 1.89% | 9.05      | Q1    | UK      |
| 10   | Nutritional Neuroscience               | 43     | 1.89% | 4.06      | Q2    | UK      |

can represent new academic trends, foretell future avenues for frontier study, and highlight prospective hotspots in a discipline. The burst detection is represented as a red segment on the blue timeline, which denotes the start year, end year, and duration of the burst. The timeline is shown as a blue line. We were especially interested in terms that have research relevance among the top 35 keywords with the highest burst intensity. These terms represented the research trends in the fields of gut microbiome and neuroscience (Figure 8). The duration of “bacterial translocation” outbreaks is the longest (2003–2018). Irritable bowel syndrome had the highest burst intensity from 2002 to 2022 (32.54), followed by gastrointestinal microbiome (20.72) and anxiety-like behavior (17.41). The top 35 keyword outbreak cycles with the most number of occurrences covered the entire period from 2002 to 2022. Notably, the burst of schizophrenia, pathology, and psychiatric disorder is still ongoing.

Discussion

This bibliometric article analyzes publications research in gastrointestinal microbiome and neuroscience using visual analysis software. 2,275 publications from the WoSCC database in total were analyzed. The first stage (2002–2009) was the flat period of the development of this field, with less than
TABLE 5 Top 10 highly cited publications on research in gastrointestinal microbiome and neuroscience.

| Rank | First author | Source (IF) | Publication year | Cited by | Document type |
|------|--------------|-------------|------------------|----------|---------------|
| 1    | Cryan JF (Cryan and Dinan, 2012) | Nature Reviews Neuroscience (38.755) | 2012 | 2,184 | Review |
| 2    | Erny D (Erny et al., 2015) | Nature Neuroscience (28.771) | 2015 | 1,427 | Article |
| 3    | Sudo N (Sudo et al., 2004) | Journal of Physiology-London (6.229) | 2004 | 1,405 | Article |
| 4    | Foster JA (Foster and Neufeld, 2013) | Trends in Neurosciences (16.979) | 2013 | 1,170 | Review |
| 5    | Jiang HY (Jiang et al., 2015) | Brain Behavior and Immunity (19.227) | 2015 | 984 | Article |
| 6    | Clarke G (Clarke et al., 2013) | Molecular Psychiatry (13.437) | 2013 | 967 | Article |
| 7    | O'Mahony SM (O'Mahony et al., 2015) | Behavioural Brain Research (3.352) | 2015 | 853 | Review |
| 8    | Zheng P (Zheng et al., 2016) | Molecular Psychiatry (13.437) | 2016 | 849 | Article |
| 9    | Neufeld KM (Neufeld et al., 2011) | Neurogastroenterology and Motility (3.960) | 2011 | 809 | Article |
| 10   | Fung TC (Fung et al., 2017) | Nature Neuroscience (28.771) | 2017 | 776 | Review |

TABLE 6 Top 10 highly co-cited references on research in gastrointestinal microbiome and neuroscience.

| Rank | First author | Source (IF) | Publication year | Citations | Document type |
|------|--------------|-------------|------------------|-----------|---------------|
| 1    | Cryan JF (Cryan and Dinan, 2012) | Nature Reviews Neuroscience (38.755) | 2012 | 396 | Review |
| 2    | Bravo JA (Bravo et al., 2011) | P Natl Acad Sci USA (12.778) | 2011 | 377 | Article |
| 3    | Heijtz RD (Diaz et al., 2011) | P Natl Acad Sci USA (12.778) | 2011 | 341 | Article |
| 4    | Sudo N (Sudo et al., 2004) | Journal of Physiology-London (6.229) | 2004 | 319 | Article |
| 5    | Erny D (Erny et al., 2015) | Nature Neuroscience (28.771) | 2015 | 299 | Article |
| 6    | Sampson TR (Sampson et al., 2016) | Cell (66.849) | 2016 | 286 | Article |
| 7    | Clarke G (Clarke et al., 2013) | Molecular Psychiatry (13.437) | 2013 | 244 | Article |
| 8    | Hsiao EY (Hsiao et al., 2013) | Cell (66.849) | 2013 | 243 | Article |
| 9    | Schepers F (Schepers et al., 2015a) | Movement Disorders (9.698) | 2015 | 243 | Article |
| 10   | Bercik P (Bercik et al., 2011) | Gastroenterology (33.883) | 2011 | 234 | Article |

10 papers published annually. The second stage (2010–2015) was a slow growth period, the number of related publications showed an overall increasing annual trend, the number of published articles increased by dozens per year, and the annual number of published papers was less than 100. The third stage (2016–2022) was the rapid development stage, and the annual number of published papers was more than 100, accounting for more than 91% of the total number of included studies. The volume of literature will continue to grow in the future, and the research in this field will still attract the attention of scholars in the next few years.

Knowledge structure of global Countries/Regions

The United States was the leading contributor in this field with 732 publications, followed by China, Canada, Ireland, and England, which accounted for more than 73% of the total number of articles included in the study. GDP is an important factor in the number of publications of a country. The output of publications in the United States and China is far ahead, which is closely related to the top ranking of GDP (Figure 2A). One could presume that significant financial investments, such as the Human Microbiome Project (HMP) started by the NIH in 2007 and a remarkable research project on the gut microbiota-brain axis in 2013, affected research output on gut microbiota and neuroscience (Turnbaugh et al., 2007; Proctor, 2011; Human Microbiome Project Consortium, 2012, Robles-Alonso and Guarner, 2014). In addition, numerous experts in microbiology and neuroscience from Ireland, China, the United States, and other countries have studied the characteristics of the gastrointestinal microbiota in health and neuroscience disease states, the connection between pathological function and neuroscience disease, and other topics. These professionals, who serve as a foundation for the creation and publication of papers in this area, include Cryan JF, Dinan TG, Clarke G, Stanton C, O’Mahony SM, Bastiaanssen TFS, Yang C, Xie P, Bailey MT, Green SJ, Keshavarzian A, and Forsyth CB (Cryan et al., 2013; Dinan et al., 2014; Mayer et al., 2014; Stilling et al., 2015; Tarr et al., 2015; Dodiya et al., 2020; Joers et al., 2020; Li et al., 2020; van de Wouw et al., 2020; Frausto et al., 2021; Zheng et al., 2021; Connell et al., 2022; Teng et al., 2022). It is worth noting that the citations of articles published in the United States rank first, followed by Ireland and China. To some extent, the number of citations is related to the quality of the literature, but also to paying service, the time of publication of the paper, and the research hotspots or trend changes. In
addition, it can be seen from the cooperation Network of countries/regions (Figure 2B) that compared with high-output countries such as the United States, England, and Australia, China has less cooperation with other countries in this field. To improve China’s influence in this field, it is necessary to improve the quality of literature and strengthen the exchange and cooperation with other high-output countries in this field.

Institutions

A total of 2,618 institutions around the world have been studying the gastrointestinal microbiome in neuroscience. We can see from Table 2, University College Cork was the most productive and influential institution located in Ireland, and the top 10 institutions active in research of gastrointestinal microbiome and neuroscience came from the top 10 nations or regions. The top 10 institutions in this sector helped the United States, Australia, China, Ireland, and Canada overtake other countries as the most active ones in this field. Notably, as seen in Figure 3, whereas some of these institutions have worked closely together, some have not. Therefore, it is strongly advised that nations and institutions with similar research topics broaden and deepen their cooperation and work together to advance the development and prosperity of this field.

Authors

Our results demonstrated that Cryan JF was the most productive author and the highest number of co-cited authors, who reviews the field of gut microbiota and neuroscience and discusses many theories (O’Mahony et al., 2009; Cryan and Dinan, 2012; Dinan and Cryan, 2012; Clarke et al., 2013; Mayer et al., 2014). The team represented by Cryan JF is active in this field and has more research results on the relationship between gastrointestinal microbiota and neuroscience, which plays an important guiding role. We also noticed that the top three frequently productive authors (Cryan JF, Dinan TG, and Clarke G) are all from the University College Cork (Table 3) and had a high centrality, suggesting that the University College Cork is an important institution in the research field. The co-occurrence map of authors (Figure 4) manifested there were active collaborations among authors in the same cluster, such as Cryan JF, Dinan TG, and O’Mahony.
TABLE 7  The top 40 keywords related to research in gastrointestinal microbiome and neuroscience.

| Rank | Keyword                          | Counts | Rank | Keyword                        | Counts |
|------|----------------------------------|--------|------|--------------------------------|--------|
| 1    | Gastrointestinal microbiome      | 1,850  | 21   | Obesity                        | 114    |
| 2    | Inflammation                     | 432    | 22   | multiple sclerosis             | 109    |
| 3    | Gut-brain axis                   | 369    | 23   | Cognitive function             | 108    |
| 4    | Parkinson’s disease              | 278    | 24   | Double-blind                   | 104    |
| 5    | Alzheimer’s disease              | 267    | 25   | Major depression               | 104    |
| 6    | Depression                       | 265    | 26   | Microbiota-gut-brain axis      | 99     |
| 7    | Probiotics                       | 245    | 27   | Alpha-synuclein                | 98     |
| 8    | Mice                             | 230    | 28   | Sfas                           | 97     |
| 9    | Irritable-bowel-syndrome         | 226    | 29   | Metabolism                     | 95     |
| 10   | Chain fatty-acids                | 220    | 30   | Diet                           | 94     |
| 11   | Stress                           | 219    | 31   | Blood-brain-barrier            | 91     |
| 12   | Neuroinflammation                | 217    | 32   | Cognitive impairment           | 91     |
| 13   | Anxiety                          | 198    | 33   | Butyrate                       | 90     |
| 14   | Oxidative stress                 | 166    | 34   | Autism                         | 84     |
| 15   | Mouse model                      | 154    | 35   | Enteric nervous system         | 80     |
| 16   | Central-nervous-system           | 143    | 36   | Ischemic stroke                | 77     |
| 17   | Dysbiosis                        | 131    | 37   | Mechanisms                     | 77     |
| 18   | Microglia                        | 130    | 38   | Risk-factors signaling pathway | 77     |
| 19   | Autism spectrum disorder         | 128    | 39   | Animal-models                  | 76     |
| 20   | Anxiety-like behavior            | 116    | 40   | Cytokines                      | 76     |

FIGURE 7  The overlay visualization map of keywords in title/abstract fields of publications related to gastrointestinal microbiome and neuroscience. Different colors were applied for each keyword based on their average appearance time in the overlay visualization map. Blue color represented the keywords that appeared relatively earlier than those in yellow and red upon time course.

SM, Clarke G, and Maes M, etc. Close cooperation was also observed among clusters, such as Dinan TG and Clarke G, Dinan TG and Neufeld KAM, Clarke G and Neufeld KAM, etc. However, some active authors on gastrointestinal microbiomes and neuroscience still lack collaboration with other scholars, such as the authors Hsiao EY, Bailey MT, and
Han Y, etc., who have not yet formed a stable collaborative team.

**Journals**

Most relevant studies were published in the journals (Q1/Q2 journals) with world-class influence, such as Brain Behavior and Immunity, Frontiers in Aging Neuroscience, and Neuroscience and Biobehavioral Reviews (Table 4). These results suggested that the link between gastrointestinal microbiota and neuroscience has attracted the attention of numerous scholars, and its research difficulties and value have also been recognized by scholars. All the top 10 journals are in the discipline of neuroscience and are established in the UK, Switzerland, Netherlands, and USA. When researchers produce and read studies on gastrointestinal microbiota and neuroscience, the top 10 journals may be given preference.

**Publications and references**

The publications and references analysis has revealed the important references in the field of gastrointestinal microbiota and neuroscience in the past 20 years. The cited publications and co-cited references listed in Tables 5, 6 would provide an important reference for the study in this field. The findings revealed that multi-seed subjects closely related to research hotspots were highlighted in the top 10 highly cited publications and co-cited references. Four articles appear together in both...
lists (Tables 5, 6). The article with the most citations was on the impact of the gut microbiota on the brain and behavior by Cryan and Dinan (2012), which was published in Nature Reviews Neuroscience in 2012 and has a total of 2,184 citations. This research examines how the gut microbiota interacts with the central nervous system (CNS) via neural, endocrine, and immunological pathways, possibly affecting brain activity and behavior and influencing the regulation of anxiety, mood, cognition, and pain. The second article was published by Erny et al. (2015) from Nature Neuroscience in 2015. This study showed that the diverse microbiota partly restores microglia impairment while the host bacteria play a critical role in regulating microglia maturation and function. Research by Sudo et al. (2004) from the Journal of Physiology-London is the third most cited article. According to this study, the postnatal development of the hypothalamic-pituitary-adrenal (HPA) stress response in mice can be influenced by commensal bacteria. The fourth article came from Molecular Psychiatry and was produced by Clarke et al. (2013). This study showed that the absence of normal gut microbiota might seriously disturb 5-hydroxytryptamine neurotransmission in the central nervous system (CNS). The top 10 frequently cited publications and co-cited references may be given priority when researchers read and refer to articles on the gastrointestinal microbiome and neuroscience.

Research focus and trends of global

According to the co-occurring keyword analysis, we identified some of the most important hotspots in this field over the past two decades, including the gastrointestinal microbiome, inflammation, gut-brain axis, Parkinson's disease, and Alzheimer's disease. The most widely studied diseases in this field are Parkinson's disease and Alzheimer's disease. Reichmann (2011) speculates that bacteria may be responsible for the development of PD, it may spread out from the enteric nervous system of the gut via the vagal nerve up to the brain. Since 2015, “Parkinson’s disease” has become the new top hotspot in this field. Gut microbiome composition is significantly associated with Parkinson’s disease (Schepersjans et al., 2015b). Kumari et al. (2020) studied the salivary metabolic profiling of saliva were studied in patients with PD (n = 76) and healthy controls (HC, n = 37) were analyzed and differentiated PD from HC. It is found that patients with PD might be characterized by metabolic imbalances like gut microflora system, energy metabolites, and neurotransmitters (Kumari et al., 2020). The ratio of Firmicutes to Bacteroidetes increased and bacterial diversity decreased in the gut of PD mice treated with rotenone (Yang et al., 2018). The abundance of Prevotella in PD patients is decreased, which affects the gastrointestinal dysfunction of PD patients (Metsalma et al., 2017). AD is the most common neurodegenerative disease. Priming of the innate immune system by the microbiota may enhance the inflammatory response to cerebral amyloids (such as amyloid-beta and alpha-synuclein), leading to neuro-system-related diseases such as Parkinson’s disease and Alzheimer’s disease (Friedland, 2015). Probiotic supplementation (Lactobacillus acidophilus, Lactobacillus bifidobacterium, and Lactobacillus fermentans) improves cognitive function and metabolic status in patients with Alzheimer’s disease (Akbari et al., 2016). Moreover, fecal microbiota transplant (FMT) technology, an ancient administration route traced back to fourth-century China (Zhang et al., 2012), is receiving increasing attention. Accumulating studies suggest that FMT has potential therapeutic effects on neuropsychiatric areas-related disorders, owing to the increase in microbiota diversity (Kang et al., 2021; Wang et al., 2021).

Cluster analysis is a statistical method for dividing the subjects of a particular field into several groups, which can reflect the research focus in the field (van Eck and Waltman, 2010; Xu et al., 2022). Our clustering analysis of keywords identified five focus areas of the research in gastrointestinal microbiome and neuroscience utilizing VOSviewer. Cluster 1 (red nodes) was the larger cluster with 29 co-occurrence terms: gastrointestinal microbiome, Parkinson's disease, chain fatty acids, multiple sclerosis, short-chain fatty acids, alpha-synuclein, metabolism, ischemic stroke, mechanisms, enteric nervous system, nervous system, brain axis, metabolites, fecal microbiota transplantation, metabolomics, vagus nerve, etc. The topic of Cluster 1 is the mechanism of the gastrointestinal microbiome in Parkinson’s disease, multiple sclerosis, and ischemic stroke. Cluster 2 (green nodes) is primarily concerned with the effect of probiotics (e.g., lactobacillus, bifidobacteria) on depression, anxiety, major depression, schizophrenia, etc., and the “gut-brain axis” and “microbiota-gut-brain axis” are two important theories that are involved. This cluster includes 27 terms, such as gut-brain axis, depression, probiotics, anxiety, anxiety-like behavior, major depression, cognitive function, double-blind, microbiota-gut-brain axis, lactobacillus, schizophrenia, neurotrophic factor, bifidobacteria, psychological stress, etc. Cluster 3 (blue nodes) focuses on the mechanism of neurodegenerative diseases, such as Alzheimer’s disease and dementia, which contains 13 terms: Alzheimer’s disease, neuroinflammation, oxidative stress, mouse model, central-nervous-system, microglia, blood-brain-barrier, cognitive impairment, dementia, neurodegenerative disease, amyloid-beta, etc. Cluster 4 (yellow nodes) is mainly related to “gastrointestinal microbiome, inflammation: a link between obesity, insulin resistance, and cognition” with 12 terms: inflammation, obesity, high-fat diet, intestinal permeability, lipopolysaccharide, TNF-alpha, bacterial translocation, insulin-resistance, glucagon-like peptide-1, etc. The topic of Cluster 5 (purple nodes), which includes the keywords mice, autism spectrum disorder, autism, animal models, immune system, sex differences, and more, is “the function of the gut...
microbiome in autism spectrum disorder and autism.” Despite the increasing recognition of these hotspots, as these research directions develop, further innovations and breakthroughs may be hindered. Therefore, in the coming years, it will be important to focus more on the frontier research topics that the burst keyword analysis has shown.

The “burst keywords” can be categorized into three phases based on when they started and ended. Studies in this field initially concentrated on controlled trials involving bacterial translocation and irritable bowel syndrome from 2003 to 2007 (O’Mahony et al., 2009; Dinan and Cryan, 2012; Kennedy et al., 2012; Park et al., 2013; Garate et al., 2014; Brzozowski et al., 2016; Pigrau et al., 2016; Azpiroz et al., 2017; Morris et al., 2017; Sundman et al., 2017; Lin et al., 2018; Roomruangwong et al., 2018, 2019). The second stage, which lasted from 2008 to 2014, concentrated on animal trials involving anxiety, the central nervous system, diet-induced obesity, experimental autoimmune encephalomyelitis, and the brain-gut axis (Ochoa-Reparaz et al., 2011; Foster and Neufeld, 2013; Winek et al., 2016; Scott et al., 2017; Vaughn et al., 2017). The research flora focused on lactobacillus helveticus and probiotic bifidobacterium, while the modeling method concentrated on the high-fat diet (McKernan et al., 2010; Ohland et al., 2013; Ait-Belgnaoui et al., 2014; Kang et al., 2014; Mayer et al., 2014; Liang et al., 2015; Magnusson et al., 2015; Guillemot-Legris et al., 2016; Baker et al., 2017; Li et al., 2018; Schachter et al., 2018; Hassan et al., 2019; Beraldi et al., 2020). After 2015, the main diseases studied were functional gastrointestinal disorders, stress response, ulcerative colitis, prenatal stress, schizophrenia, and mental disorders (Daulatzai, 2015; Schmidt et al., 2015; Davis et al., 2016; Evrensel and Ceylan, 2016; Gur et al., 2017, 2019; Abautret-Daly et al., 2018; Jasarevic et al., 2018; Ju et al., 2020; Bioque et al., 2021; Luo et al., 2021; Yanguas-Casas et al., 2021; Urbonaite et al., 2022). Brain-derived neurotrophic factors and Toll-like receptors were the key research factors (Zeraati et al., 2019; Haghighat et al., 2021). Pathological experiments were the primary study methodology, while probiotic therapy was the primary research topic (Akkari et al., 2016; Kozyrev et al., 2020; Banermeran et al., 2022; Pochakom et al., 2022). Notably, including “schizophrenia” (burst strength 4.35), “pathology” (burst strength 3.81), and “psychiatric disorder” (burst strength 3.26), which are the current research frontiers in this field and are currently within the burst period.

**Conclusion**

In this study, 2,275 original studies from 2002 to 2022 (August 20, 2022) related to the research in gastrointestinal microbiome and neuroscience were downloaded from the WoSCC database and analyzed using VOSviewer to generate knowledge maps. The number of articles on the research in gastrointestinal microbiome and neuroscience has increased rapidly in recent years. The United States and China have made the most notable contributions to the research in gastrointestinal microbiomes and neuroscience. Research on “gastrointestinal microbiome, inflammation: the link between obesity, insulin-resistance and cognition” and “the role of two important theories of the gut-brain axis and microbial-gut-brain axis in diseases in neuroscience” will continue to be the hotspot. Further studies on the mechanisms linking gastrointestinal microbiome and neuroscience will promote neuroscience disease therapy.

**Data availability statement**

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

**Author contributions**

DL and YD conceived the study and performed critical revision of the manuscript. JY designed the study, performed statistical analyses, and drafted the manuscript. YC, YL, LP, and ZL performed the article retrieval, data interpretation, and provided supervision. All authors read and approved the final manuscript for publication.

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**Conflict of interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
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