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ORIGINAL RESEARCH

Bibliometric Analysis on the Central Regulation of Airway Allergic Hyperreactivity Diseases Based on Bibliometric Analysis: From Lung-Brain Axis to Nasal-Brain Axis

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Aim: This study aimed to systematically analyze the neuro-regulation mechanisms of airway hyperreactivity disease using bibliometrics, focusing on the research status and progress of two key regulatory networks: the "lung-brain axis" and the "nasal-brain axis", to further characterize the "nasal-brain axis".

Methods: A bibliometric analysis of 626 articles published between 1991 and 2024 was conducted to assess the growing interest in the impact of neuro-immune mechanisms and psychological stress on airway diseases, including asthma and allergic rhinitis (AR).

Results: The study findings revealed that interactions between neuro-immune signaling pathways and the central nervous system are crucial for understanding airway hyperreactivity, with the United States leading research contributions. Key themes identified in this study include allergic asthma, neuroinflammation, and the lung-brain axis, revealing bidirectional communication pathways between peripheral and central immune responses.

Conclusion: Based on studies of asthma and the lung-brain axis, we anticipate that AR and the nasal-brain axis likely involve similar neuro-immune mechanisms and peripheral-central response circuits. The nasal-brain axis theory was further supported by its integration with the unified airway hypothesis, solidifying its role as a crucial regulatory mechanism in airway inflammation research.

Keywords: airway hyperreactivity, central regulation, lung-brain axis, nasal-brain axis, neuro-immune, bibliometrics visualization

Introduction

The connection between the central and peripheral immune systems has garnered increasing research interest. Numerous studies have demonstrated a strong connection between central and peripheral immunity. Studies of the brain-spleen axis, lung-brain axis, and the association between atherosclerosis and the brain have revealed bidirectional regulation between the peripheral immune system and central nervous cells from various perspectives.[1–4] The use of chemogenetics, optogenetics, and transgenic mouse models has further elucidated the functional links between central and peripheral inflammation.[5,6] Koren et al demonstrated that, following an inflammatory storm, a "trace" remains in the central nervous system, enabling glutamatergic neurons in the insular cortex to retrieve and directly "encode" specific peripheral inflammatory responses.[7] Moreover, the regulation of airway hyperreactivity in ovalbumin-sensitized asthmatic mice involves several central nuclei, including the nucleus of the solitary tract, parabrachial nucleus, and central amygdala, suggesting that central regulatory mechanisms also play a role in airway hyperreactivity diseases.[8]

Various stimuli, such as allergens, viruses, and bacteria, can induce airway inflammation and bronchospasm, leading to airway hyperreactivity, primarily manifesting as allergic rhinitis (AR) and asthma.[9,10] Recent studies using an asthmatic

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mouse model have identified a complete regulatory circuit for airway hyperreactivity, where antigen stimulation activates DBH+ neurons in the nucleus of the solitary tract (nTS). Simultaneously, nTS activation enhances airway hyperreactivity through norepinephrine release. During AR episodes, the lung's full allergen response circuit leads to the activation of central nuclei. Additionally, functional MRI studies in patients with AR suggest that local histamine stimulation of the nasal mucosa induces changes in the prefrontal cortex, insular cortex, and other brain areas.[11] Patients with AR may experience anxiety, depression, olfactory dysfunction, or cognitive impairment either concurrently or sequentially, indicating that allergens and/or other external stimuli, beyond inducing pathological immune responses, also affect the central nervous system and its associated cortical regions and nuclei.[12,13] Our previous research revealed that circadian rhythm disruption exacerbates AR by reducing tight junction proteins in the respiratory epithelium, which triggers an immune response.[14] Focused ultrasound (FUS) technology was used to monitor real-time changes in the central nervous system of a mouse AR model, revealing a significant enhancement of central cortical and associated nuclear responses in the model group. Additionally, the response curve's waveform and duration were markedly prolonged after the stimulation ended. Based on these findings, our team was among the first to propose the concept of the nasal-brain axis in the *Chinese Journal of Otorhinolaryngology-Head and Neck Surgery*, exploring the bidirectional interaction between peripheral inflammation and the central nervous system through the neuro-immune mechanisms of AR.[15,16]

Bibliometric analysis provides a systematic approach to evaluating research dynamics, highlighting key contributors, and identifying emerging research hotspots. Moreover, bibliometric techniques provide clear visualization of studies related to the central regulation of airway hyperreactivity diseases, uncovering research trends over the past decades. This provides a solid foundation for advancing research on the mechanisms of central regulation in airway hyperreactivity diseases worldwide and unveiling the mysteries of the "nasal-brain axis."

Materials and Methods

Literature Retrieval Strategy

A thematic search was conducted in the Web of Science (WoS) Core Collection database, using SCI-EXPANDED and SSCI as data sources. The WoS database is a widely recognized, comprehensive literature storage and retrieval platform frequently used in literature analysis and measurement research.

To enhance the precision and comprehensiveness of the search results, the final search query was constructed using standardized MeSH terms:

> TS=('airway hyperreactivity disease' OR 'nasal hyperreactivity disease' OR 'allergic rhinitis' OR 'asthma' OR 'airway inflammation' OR 'respiratory inflammation' OR 'airway immune response' OR 'respiratory immune response') AND TS=. ('central nervous system' OR CNS OR 'brain inflammation' OR 'neuroinflammation' OR 'neuroimmune interaction' OR 'neuro-immune interaction' OR 'brain-immune interaction' OR 'central nervous system inflammation' OR 'central nervous system immune response' OR 'psychological stress' OR 'central regulation' OR 'enteric nervous system' OR 'neural circuits' OR 'sickness behavior' OR neuroglia OR 'neuronal populations' OR 'lung-brain axis' OR 'nose-brain axis')

Inclusion and Exclusion Criteria

The inclusion criteria were: (1) studies on the relevant mechanism of neural regulation in airway hyperreactive diseases; (2) studies published in English; and (3) studies completed on or before August 1, 2024; thus, the included articles were published between January 1, 1991, and August 1, 2024.

The exclusion criteria were: (1) studies without data on asthma or AR; and (2) other forms of publications including conference abstracts, editorial materials, letters, announcements, and news.

Bibliometric Analysis

The retrieved literature was exported in txt format and saved with the filename "download_**.txt", where ** is the sequence number of the exported literature. The data were then imported into CiteSpace.6.2.R4 and the bibliometrix package in R for further visualization analysis. The data were visually analyzed by country and region, publishing institution, journal, co-occurrence knowledge graph of high-frequency keywords, keyword clustering, and salience to explore trends and hotspots in airway hyperresponsiveness and central regulation research from 1991 to 2024, and to validate the concept of the nasal-brain axis.

Results

General Data and Annual Output

From 1991 to 2024, 626 articles related to airway hyperreactivity diseases and central nervous regulation were retrieved, encompassing 11 different types of publications. Among them, research articles accounted for approximately 60.5% (Table 1), indicating that most studies in this field were focused on original research. Figure 1 shows that studies on the relationship between airway hyperreactivity diseases and central nervous regulation were relatively scarce before 2002. Subsequently, the global publication volume has fluctuated but has maintained an overall steady growth trend with occasional declines. The highest publication volume occurred in 2014, with 39 articles published, suggesting that 2014 marked a pivotal point in the study of central regulation in airway hyperreactivity diseases. This trend aligns with the growing attention to the role of central nervous regulation in airway hyperreactivity diseases.

Distribution of Countries and Institutions

This study analyzed 626 relevant articles from the database with contributions from 45 countries and regions. Table 2 shows the top 10 countries by publication volume. The United States led with 208 articles (42.975%), followed by China (61 articles, 12.603%), and Germany (46 articles, 9.504%). Figure 2 presents a world map illustrating the geographic distribution of these publications from 1991 to 2024.

The publication output by research institutions in this field reflects their innovation and research competitiveness to some extent. Between 1991 and 2024, 1061 institutions worldwide published articles on airway hyperreactivity diseases and central regulation. The University of Wisconsin–Madison (USA) led with 46 articles (14.024%). This institution's research primarily focuses on immunology, neuroscience, cancer research, public health, cardiovascular research, and biomedical engineering. Among the top 10 institutions, 9 are from the United States. Table 3 provides a detailed list of these top 10 institutions by publication volume, all with significant contributions to research on airway hyperreactivity diseases and central nervous regulation.

Table 1 Quantities of Different Types of Articles

Rank	Document Types	Frequency	Percentage (%)
1	Article	379	60.543
2	Review Article	181	28.913
3	Proceeding Paper	27	4.313
4	Meeting Abstract	14	2.236
5	Editorial Material	8	1.277
6	Book Chapters	5	0.798
7	Early Book Chapters Access	5	0.798
8	Letter	3	0.479
9	Note	2	0.319
10	Reprint	1	0.159
11	Review; Book Chapter	1	0.159

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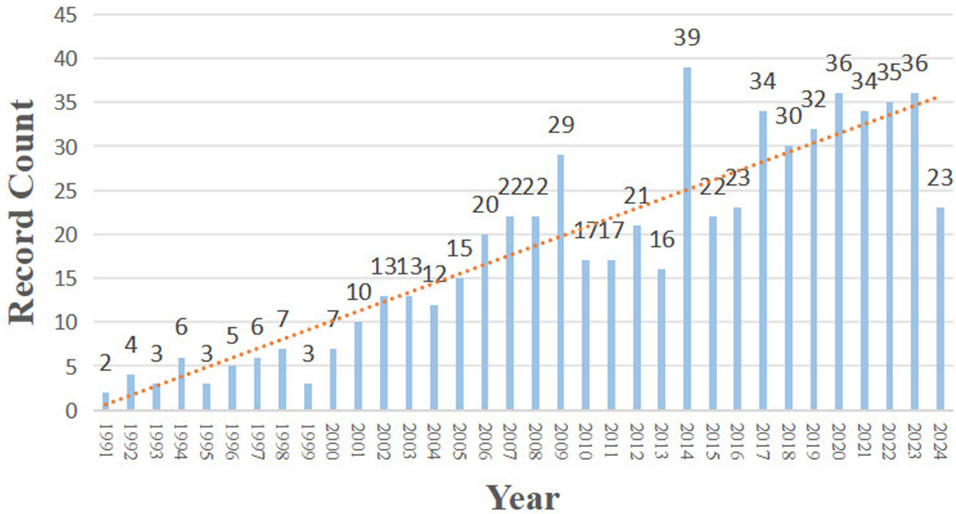

Figure 1 Annual number of published research articles.

Global Distribution of Authors and Analysis of Highly Cited Articles

From 1991 to 2024, 3,026 authors contributed to publications related to airway hyperreactivity diseases and central nervous regulation. Table 4 lists the top 10 authors who contributed the most to this body of research. The H-index is a quantitative measure that indicates a researcher has published H papers that have been cited at least H times, while other papers have fewer than H citations. It is commonly used to assess the quantity and impact of a researcher's academic output, indirectly evaluating their research capabilities. The leading author by publication volume is Melissa Rosenkranz (22 articles, University of Wisconsin–Madison, USA), with an H-index of 49.

This dataset includes five highly cited papers, as identified through the WoS website (Table 5). Among them, the Tesmer La et al seminal paper, Th17 Cells in Human Disease, identified T-helper 17 (Th17) cells, characterized by the production of interleukin-17 (IL-17). Th17 cells play a crucial role in the pathogenesis of various immune-mediated diseases.[17]

Table 2 Top 10 Global Nations Contributing to Research Outcomes

Rank	Country	Frequency	Percentage (%)
1	USA	208	42.975
2	China	61	12.603
3	Germany	46	9.504
4	Canada	40	8.264
5	Japan	39	8.057
6	Sweden	23	4.752
7	Italy	21	4.338
8	Korea	17	3.512
9	UK	15	3.099
10	Brazil	14	2.892

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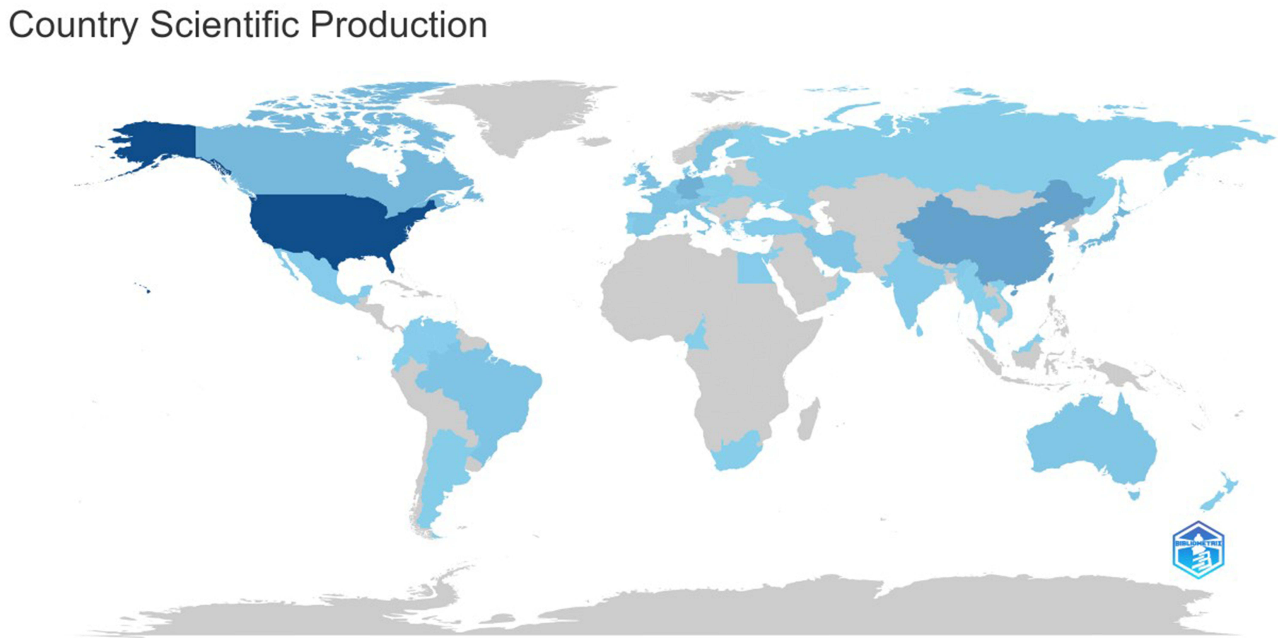

Figure 2 Global distribution density map of publication volume. The color intensity corresponds to the publication density within each geographic region with darker hues indicating higher spatial concentration of scholarly output in specific countries or territories.

Journals and Dual-Overlay Map of Journals

From 1991 to 2024, 359 journals published research on airway hyperreactivity diseases and central nervous regulation. Table 6 lists the top 10 journals by publication volume with seven or more articles published in this field. The Journal of Allergy and Clinical Immunology published the most articles (20 articles, H-index of 292), with a 2024 Impact Factor (IF) of 11.4. Among the top 10 journals by publication volume, The American Journal of Respiratory and Critical Care Medicine has the highest impact factor (2024 IF = 19.3) with 10 articles.

In the journal dual-map overlay, the citing journals are displayed on the left, while the cited journals are shown on the right. The curves connecting the two sides represent citation links, with the z-scores function highlighting stronger and more robust citation pathways. Thicker lines indicate higher scores. Figure 3 illustrates that molecular biology, biology, and immunology (yellow trajectory, z = 7.3427844, f = 5,122) exert a significant influence on medicine, economics, and

Table 3 Number of Publications by Global Research Institutions

Rank	Institutions	Country	Frequency	Percentage (%)
1	University of Wisconsin–Madison	USA	46	14.024
2	University of California System	USA	44	13.415
3	University of Wisconsin System	USA	41	12.500
4	University of Texas System	USA	39	11.890
5	Harvard University	USA	37	11.280
6	University System of Ohio	USA	30	9.146
7	University of California Davis	USA	28	8.537
8	Karolinska Institutet	Sweden	24	7.317
9	University of Texas Southwestern Medical Center Dallas	USA	20	6.098
10	Genentech	USA	19	5.793

Table 4 Top Five Authors with the Most Significant Contributions to the Research Area

Researcher	Frequency	Articles Fractionalized	Organizations	H-index
Rosenkranz, Melissa	22	5.63	University of Wisconsin–Madison	49
Wright, Rosalind J	17	8.36	Icahn School of Medicine at Mount Sinai	68
Chen, Elizabeth	10	2.64	University of Pennsylvania Medicine	2
Kroll, Juliet L	10	1.72	Southern Methodist University	11
Miller, G. E.	9	2.20	Northwestern University	2
Ohno, Isao	9	1.92	Tohoku Medical & Pharmaceutical University	23
Ritz, Thomas	9	1.56	Southern Methodist University	3
Takayanagi, Motoaki	9	1.02	Tohoku Medical & Pharmaceutical University	14
Busse, William W	8	1.08	University of Wisconsin–Madison	88
Brown, E. Sherwood	7	0.86	University of Texas Southwestern Medical Center Dallas	41

Table 5 Highly Cited Papers

Paper	DOI	Total Citations	TC Per Year	Normalized TC
Tesmer LA, 2008, Immunol Rev	10.1111/j.1600–065X.2008.00628.x	861	50.65	9.43
Perry VH, 2007, Nat Rev Immunol	10.1038/nri2015	776	43.11	9.29
Weidinger S, 2018, Nat Rev Dis Primers	10.1038/s41572-018-0001-z	699	99.86	14.54
Desforges M, 2020, Viruses-Basel	10.3390/v12010014	667	133.40	7.30
Proudfoot AEI, 2002, Nat Rev Immunol	10.1038/nri722	600	26.09	3.42

Table 6 Journal Publication Analysis

Publication Titles	Frequency	IF	JCR
Journal of Allergy and Clinical Immunology	20	11.4	Q1
Brain Behavior and Immunity	14	8.8	Q1
Psychosomatic Medicine	14	2.9	Q1
Annals of Allergy Asthma & Immunology	12	5.8	Q2
American Journal of Respiratory and Critical Care Medicine	10	19.3	Q1
Journal of Asthma	9	1.7	Q3
Plos One	9	2.9	Q1
International Archives of Allergy and Immunology	8	2.5	Q3
Allergy	7	12.6	Q1
Frontiers in Pharmacology	7	4.4	Q1

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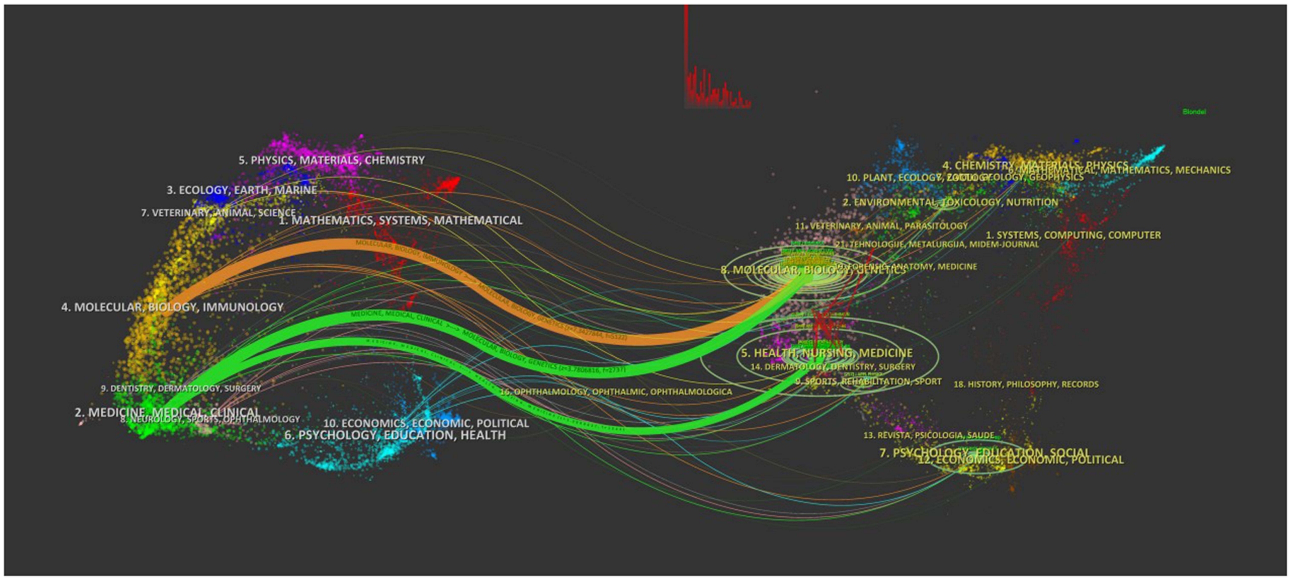

Figure 3 Dual-overlay map of the journals. The length of the ellipses represents the number of authors, and the width indicates the volume of publications.

politics (green trajectory, z = 3.7806816, f = 2,737). A large proportion of the papers are concentrated in molecular biology, biology, and immunology with some influence on medicine, economics, and politics, suggesting interdisciplinary intersections including molecular biology, immunology and medicine in this domain.

Author Collaboration and Institutional Interaction Network Diagram

Using CiteSpace 6.2.R4, we created a visualization map to display the collaboration relationships between authors in the research literature with authors as the nodes (Figure 4A). The network contains 803 nodes and 1,140 links, with a density of 0.0035, suggesting limited but identifiable collaboration between authors. The analysis reveals that Melissa Rosenkranz is the most prolific author, leading the largest research team with multiple relevant papers published in recent years.

Figure 4B shows the collaboration between institutions, highlighting that the institution with the highest centrality is the Icahn School of Medicine at Mount Sinai (centrality = 0.08), followed by Harvard University (0.06) and the Institut National de la Santé et de la Recherche Médicale (0.06). Researchers have established several independent collaboration networks, demonstrating a strong cooperative relationship between these institutions.

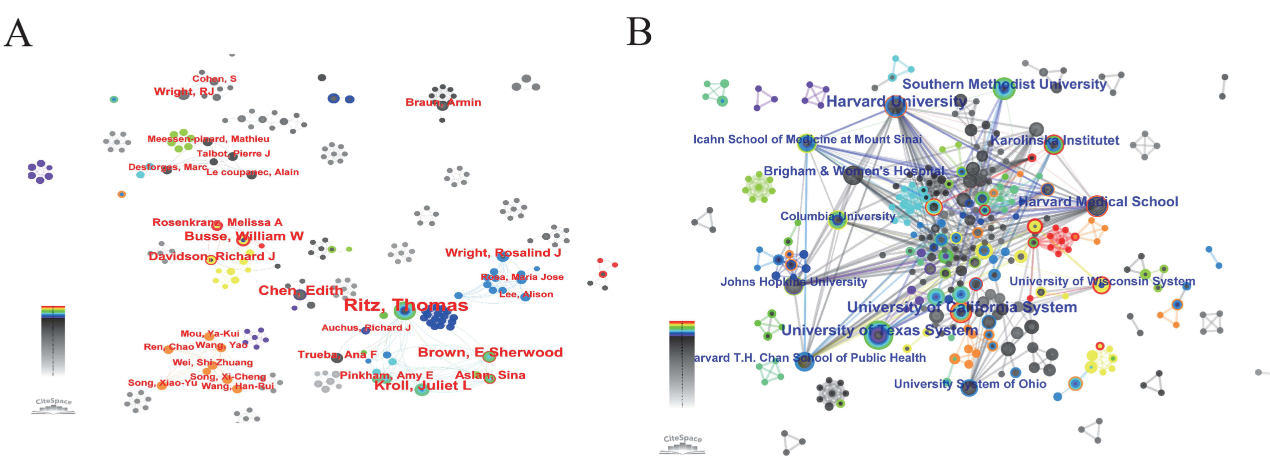

Figure 4 (**A**) Author collaboration network diagram; (**B**) Institutional interaction network diagram.

National or Regional Collaboration Network Diagram

According to the WoS visualization results from previous studies, 45 countries and regions globally have participated in research on airway hyperreactivity diseases and central nervous regulation. Figure 5A shows the collaboration network. Using CiteSpace 6.2.R4 software, the network comprises 55 nodes, 164 links, and a density of 0.1104. The top five countries by centrality are the United States (0.54), China (0.19), Germany (0.18), Italy (0.12), and the United Kingdom (centrality: 0.10).

Figure 5B presents an analysis of international collaboration using the bibliometric online analysis platform. The figure illustrates that collaboration between the United States, China, and Germany is relatively frequent, while Italy and the United Kingdom have less collaboration as compared to the leading countries. The results indicate that US researchers play a dominant role in this field and collaborate most frequently with scholars from other countries.

Figure 5C shows the global contributions to research on airway hyperreactivity diseases and central nervous regulation from 1991 to 2024. The Three-Field Plot is a visualization tool used in bibliometric analysis to display the relationships between three different domains (such as authors, journals, and countries). Typically presented as a Sankey diagram, it depicts the connections between elements across these fields. The Sankey diagram generated in this study (Figure 5D) shows that most contributing institutions are based in the United States, followed by China and Germany. The journal with the most submissions is *The Journal of Allergy and Clinical Immunology*.

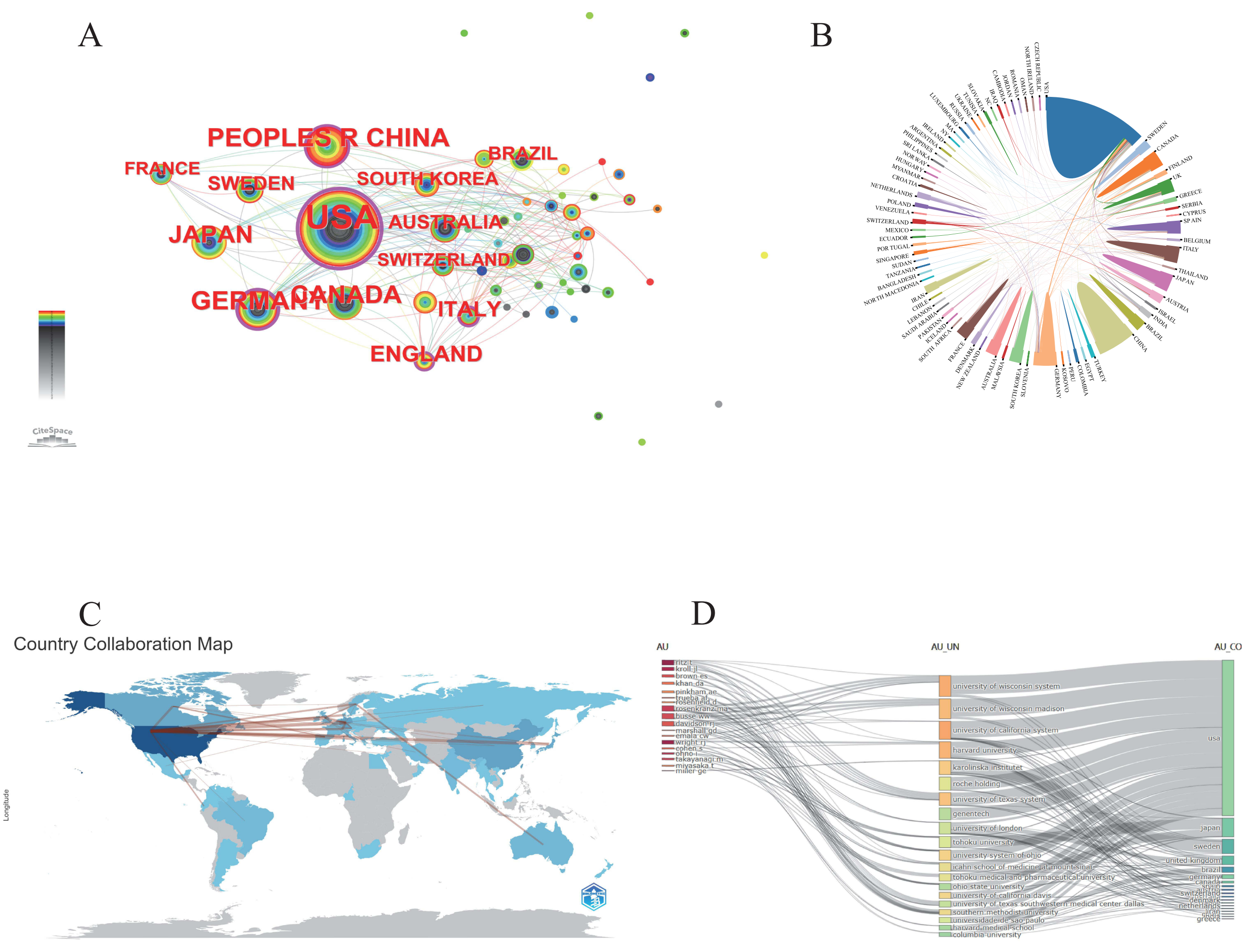

Figure 5 (**A**) National or regional collaboration network map; (**B**) Inter-country collaboration diagram; (**C**) International cooperation world map; (**D**) Sankey diagram.

Keyword Co-Occurrence and Burst

The keyword analysis revealed that the primary focus areas include allergic asthma, depression, T cells, stress, cough, ion channels, inflammatory bowel disease, the lung-brain axis, and the vagus nerve (Figure 6A). The research directions can be categorized into two major themes: psychological stress and neuroimmunology (Figure 6B). The keyword themes were further divided into 11 main categories (Figure 6C).

A timeline diagram is typically used to illustrate the changes in publication volume or research trends in a specific field. Figure 6D the timeline generated from the keyword analysis in this study. Keyword bursts indicate shifts in research hotspots, emerging trends, or technological innovations. Figure 7 shows that 25 keywords with high burst scores were identified, reflecting the evolving focus of research in this area. In the past 5 years, the research hotspots have centered on allergic asthma, the brain, neuroinflammation, oxidative.

Discussion

General Information

The publication trends for airway hyperreactivity diseases largely reflect the historical progression of research in this field. Between the 1940s and 1960s, clinical studies gradually established relationships between asthma, airway hyperreactivity, and related factors such as allergic reactions.[18] Following this period, airway hyperreactivity diseases gained more attention, although related research publications remained sparse and intermittent initially. However, since the 1990s, the volume of research has increased annually, highlighting the growing academic interest in this field. Therefore, the study period was set from 1991 to 2024 to assess continuous growth in the field.

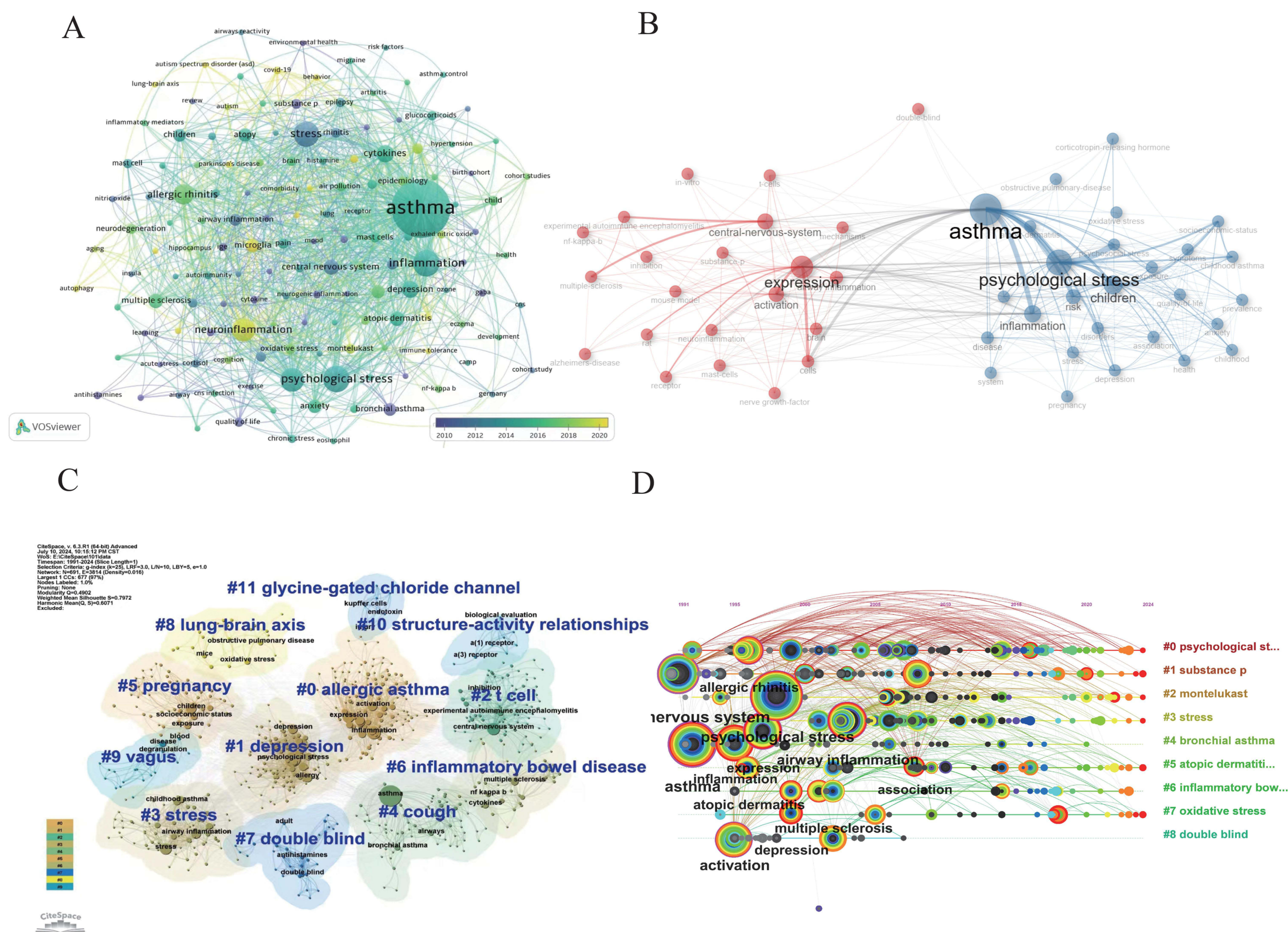

Figure 6 (**A**) Keyword co-occurrence diagram; (**B**) Keyword research direction visualization analysis; (**C**) Keyword cluster analysis; (**D**) Keyword clustering visualization diagram.

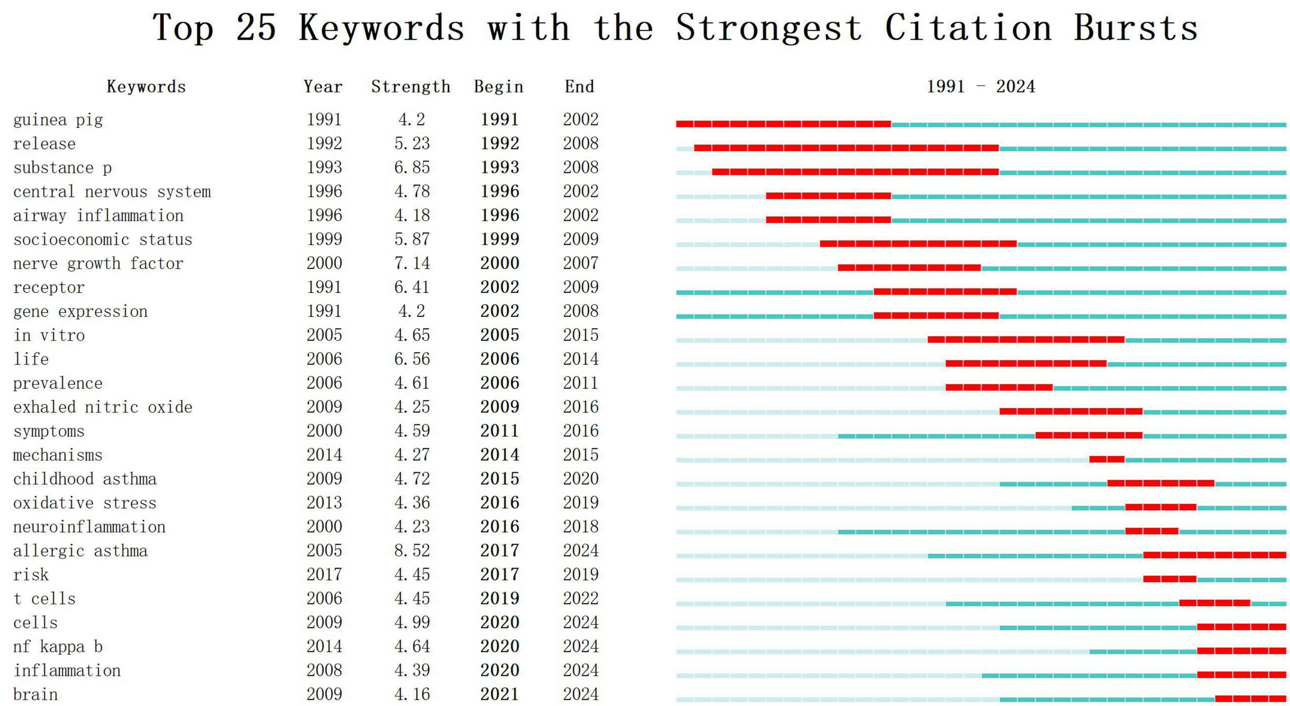

Figure 7 Keyword burst analysis diagram.

This study comprehensively analyzes global research on airway hyperreactivity diseases and central nervous regulation, highlighting key researchers, countries, regions, publishing institutions, journals, and highly cited articles across different periods. Using various visualization methods, this study explores the global distribution of research by analyzing author collaboration, international cooperation, and institutional interactions. Additionally, keyword clustering and burst analysis were employed to identify the latest hotspots and emerging trends related to this field.

Analysis of the Research Strength of Global Researchers, Countries and Regions, Publishing Institutions, and Publishing Journals

In terms of national and regional distribution, the United States currently leads globally in both publication volume and international collaboration in the field of airway hyperreactivity diseases and central nervous regulation, holding a dominant position in scientific cooperation. Following the US, the countries with the highest publication volumes are China, Germany, Canada, and Japan; however, in terms of international research collaboration, the ranking is China, Germany, Japan, and Canada. Despite its second-highest publication volume globally, China shows relatively limited international collaboration.

One notable finding in this bibliometric analysis is that the University of Wisconsin–Madison ranks among the top institutions worldwide in terms of publications related to central nervous regulation in airway hyperreactivity diseases. Among the top 10 institutions by global publication volume, 9 are in the United States with 1 from Sweden and none from China. The University of Wisconsin–Madison leads in publication volume, highlighting its pivotal role in advancing the scientific frontier in this field. This achievement can be attributed to the institution's comprehensive strength in biomedical research, including robust funding, state-of-the-art laboratory facilities, and an environment that attracts world-class scientists and researchers.

Further analysis of publications from the University of Wisconsin–Madison reveals that their research not only covers the mechanisms and drug development for airway hyperreactivity diseases but also extends into clinical applications, exploring new therapies for diseases such as allergic asthma and AR. This research's quality and innovation are evidenced by its high citation rates and widespread academic recognition. Notably, the institution's accomplishments have significantly influenced future research directions and methodologies. For instance, functional magnetic resonance imaging, RNA sequencing, and targeted protein analysis were used to identify the brain neuroinflammation triggered by asthma and its impact on the salience network (cingulate cortex, anterior cingulate cortex, and amygdala). Furthermore, IL17A was identified to be associated with the left anterior insular response, a potential molecular mechanism underlying anxiety, depression, and cognitive decline. The aim was to study the interaction between asthma-related emotions and neuroinflammation.[19,20] Furthermore, Wiesner et al uncovered the role of the TRPV4-calcium pathway in asthma pathogenesis, offering new insights into understanding and potentially preventing asthma.[21] The institution's research on asthma and the lung-brain axis has provided new perspectives on understanding the physiological mechanisms of such diseases and laid the foundation for novel therapeutic approaches and offered valuable evidence supporting the nasal-brain axis theory.

This study identifies the top five researchers by publication volume in this field, all of whom are from the United States. Network analysis of author collaboration revealed that Melissa Rosenkranz from the University of Wisconsin–Madison is the most highly connected and the top-publishing scholar in this field. A closer look at Professor Rosenkranz's contributions shows her significant work on the central nervous regulation of allergic asthma. Her collaboration with experts from other fields, such as immunology and molecular biology, highlights the importance of interdisciplinary work. Her widely cited papers are primarily published in immunology and neuroscience journals.

Among journals, *The Journal of Allergy and Clinical Immunology* leads in publication volume on research related to the central regulation of airway hyperreactivity diseases. As a top-tier journal in the field of immunology, it has consistently published high-quality research papers covering a broad range of topics from molecular mechanisms to clinical practice.

Keyword Analysis

The keyword visualization analysis identified several key areas of focus in the research on central regulation of airway hyperreactivity diseases, including allergic asthma, depression, T cells, stress, cough, ion channels, pregnancy, inflammatory bowel disease, double-blind studies, the lung-brain axis, and the vagus nerve (Figure 6A). The research directions are divided into two major categories, psychological stress and neuroimmunology. This finding reveals that psychological stress and neuroimmunity have become central topics and research hotspots in the study of central regulation of airway hyperreactivity diseases. Wang et al summarized recent advances in research on asthma and brain responses, attempting to elucidate potential lung-brain crosstalk mechanisms and therapeutic approaches for asthma, thereby encouraging further research and offering new hope for the neurological symptoms experienced by patients with asthma.[22] Dill-McFarland et al identified specific inflammatory pathways that link airway inflammation and emotion-related neural functions in asthma, providing new directions for asthma treatment.[20] This study demonstrates the central regulation of asthma and includes research on the central regulation of AR. Several authors have provided evidence supporting the concept of the nasal-brain axis through their studies on the olfactory bulb. Professor Song Xicheng's team, focusing on the nasal-brain crosstalk, explored the role and mechanisms of P2X7 receptors on microglial cells in the olfactory bulb in the context of AR-related olfactory dysfunction and depression. Their findings suggest that olfactory bulb neuroinflammation plays a crucial role in brain responses, particularly in anxiety and depression during AR.[23] Professor Xu Yu's team, investigating "immune-brain communication", discovered that glial cell proliferation and neuronal apoptosis in the olfactory bulb are key mediators of AR-related olfactory dysfunction with the TLR4-NF-κB signaling pathway driving neuroinflammation.[24] Professor Yu Yiqun's team focused on the impact of nasal inflammation on olfactory neuron regeneration and found that different inflammatory states in the nasal cavity (acute vs chronic) suppress olfactory neuron regeneration, highlighting the distinct roles of acute and chronic inflammation in regulating olfactory neuron regeneration and function.[25] Further research has shown that deep nasal infections can allow bacteria to enter the brain via the olfactory and trigeminal nerves, leading to the deposition of amyloid-β protein and increasing the risk of Alzheimer's disease. In Alzheimer's model mice, inflammatory factors in both the nasal cavity and hippocampus were simultaneously elevated.[26] These studies suggest that inflammatory factors in the nasal cavity may spread to the brain through blood or neural pathways, further confirming the nasal-brain axis theory. These studies provide a new hypothesis for the nasal-brain axis theory; however, owing to the indirectness and limitation of the current reports, several animal experiments and clinical trials are needed in the future.

This study's keyword clustering analysis identified 11 primary thematic areas, which, while independent, are interwoven, highlighting the importance of allergic asthma in the central regulation of airway inflammation and its prominence as a research hotspot. As discussed, research on the central regulation of airway hyperreactivity diseases shows that research hotspots on airway inflammation have gradually shifted from the peripheral system to the central nervous system. Research on the interaction between the lung-brain axis and local neuroimmunity has achieved initial success in developing new therapeutic strategies for lung diseases, such as the use of lung injections of MSCs. MSCs have been found to transmit signals via the lung's vagal sensory neurons to the nTS, further activating 5-HT neurons in the DRN, thereby reducing depressive and anxiety-like behaviors.[3] Identifying specific inflammatory pathways that link airway inflammation and emotion-related neural functions in asthma also provides insights into the nasal-brain axis theory.

The keyword burst analysis results indicate growing research interest in brain-related mechanisms, marking a shift in research hotspots on airway inflammation from peripheral to central mechanisms.

This has the potential to identify novel airway-central nervous system circuits and offer new treatment strategies for clinical application.[16,27] Keywords such as "allergic asthma", "brain", and "neuroinflammation" frequently appear in the research, underscoring the increasing prominence of central regulation in allergic asthma as a research hotspot. Studies have confirmed that in allergen-induced airway hyperreactivity mouse models, peripheral airway signals are transmitted via the vagus nerve to DBH+ neurons in the central nucleus of the nTS. Norepinephrine further regulates the nucleus ambiguus, modulating the neural circuitry involved in airway hyperreactivity. Notably, even in the absence of allergen stimulation, activating DBH+ neurons in the nTS enhances airway hyperreactivity.[27] Based on the integrated airway theory,[28,29] research into the neuro-immune mechanisms of the lung-brain axis in asthma provides valuable insights into the nasal-brain axis theory. Functional MRI studies suggest that local histamine stimulation of the nasal mucosa can alter activities in the prefrontal and insular cortices.[11] Patients with AR may experience anxiety, depression, olfactory dysfunction, or cognitive impairment either simultaneously or sequentially, suggesting that allergens and/or other external stimuli not only induce pathological immune responses but also affect the central nervous system, including associated cortical regions and nuclei.[30]

Our team's previous PET-CT studies showed a significant increase in activity in AR rats' prefrontal cortex, amygdala, hippocampus, and olfactory bulb following allergen exposure. These findings were corroborated by c-FOS immunofluorescence staining, indicating increased neural activity in these brain regions during allergic reactions. Furthermore, Pakravan et al suggested that the nasal-brain axis has a bidirectional nature. In animal models of Alzheimer's disease, elevated levels of IFNγ and IL-17 in the hippocampus altered the nasal tissue environment, suggesting an anatomical connection between the brain and nasal tissues with nasal responses involving both regions.[31] The 2024 priority project areas in the Medical Sciences Department of the National Natural Science Foundation of China include "Neuro/Immune Regulation Mechanisms and Interventions in Ear, Nose, Throat, and Head and Neck Diseases (H14)." This underscores the growing importance of AR's neuro-immune (N-I) mechanisms, marking it as a significant national project with extensive societal relevance. Therefore, future research will focus on exploring the nasal-brain axis concept, particularly identifying specific neurons and neurotransmitters in the brain regions associated with AR.

Strength and Limitations

This study utilized CiteSpace software, the bibliometrix package in R, and online analysis platforms to visualize the research hotspots and trend directions in the central regulation of airway hyperreactivity diseases from 1991 to 2024. Bibliometric methods provide a systematic way to map trends, hotspots, and knowledge structures within a field, allowing for the identification of research gaps and emerging topics. This approach is particularly effective for evaluating research in big data contexts, enabling efficient tracking of scientific progress and technological innovations. This study's findings aim to help researchers and institutions gain a deeper understanding of current trends, thereby advancing research on the central regulation of airway hyperreactivity diseases and facilitating the application of scientific findings.

This study has some limitations. First, a single data source, WOS was used in the study, likely resulting in incomplete coverage of relevant literature, failing to include studies from other databases (including Scopus, PubMed, or preprint servers), especially those in emerging fields or specific topics. Second, the research focuses on quantitative analysis, possibly overlooking the quality and depth of the include studies. Recent papers, due to their relatively recent publication dates, may have fewer citations, leading to a potential bias in the quality of included studies. Moreover, bibliometric analysis is essentially quantitative in nature and cannot replace qualitative approaches. It does not delve into specific content, methods, or theoretical contributions of individual studies. Therefore, future research could include qualitative analysis (such as in-depth reviews of highly cited papers or thematic analyses) to gain further comprehensive understanding of the research field. While this study does not delve into foundational research depth, its bibliometric approach offers a more intuitive depiction of focal points and emerging trends in the field. Finally, bibliometric analysis can only offer a "map" of the research domain, revealing hotspots, trends, and gaps in research; however, it cannot replace empirical studies addressing specific research questions. Instead, it provides direction and inspiration for further research.

Conclusion

A bibliometric and visualization analysis of the central regulation of airway hyperreactivity diseases from 1991 to 2024 in the WoS dataset reveals a marked and steadily expanding research focus in this allergy-related field, with significant contributions from American researchers.

Our team was among the first to propose the nasal-brain axis theory in the *Chinese Journal of Otorhinolaryngology-Head and Neck Surgery*, exploring the bidirectional interaction between peripheral inflammation in AR and the central nervous system through neuro-immune mechanisms. Neuro-immune studies on the lung-brain axis in asthma have elucidated complex bidirectional communication pathways, particularly through immune signaling and neuro-immune cell interactions. Immune-inflammatory factors generated during asthma exacerbations reach the brain via humoral and neural pathways, inducing corresponding brain responses through various mechanisms. Airway inflammation in asthma triggers inflammatory pathways, including Th17, which provoke neural responses linked to emotion and cognition, leading to chronic brain health impairment. This framework supports the hypothesis that AR may involve analogous neuro-immune pathways. Lung allergens may directly influence brain function through neural circuits, regulating airway constriction, which may open avenues for targeted control of asthma via neuromodulation. Integrating research on the asthma-lung-brain axis, it is plausible to anticipate that AR and the nasal-brain axis involve similar neuro-immune pathways and peripheral-central feedback loops. The nasal-brain axis theory, as a significant regulatory mechanism in airway inflammation research, warrants in-depth exploration.

Abbreviations

AR, Allergic Rhinitis; CNS, Central Nervous System; DBH+, Dopamine Beta-Hydroxylase-positive; FUS, Focused Ultrasound; H-index, Hirsch index; IF, Impact Factor; IL-17, Interleukin-17; MeSH, Medical Subject Headings; MRI, Magnetic Resonance Imaging; nTS, nucleus of the solitary tract; SCI-EXPANDED, Science Citation Index Expanded; SSCI, Social Sciences Citation Index; Th17, T-helper 17 cells; WoS, Web of Science.

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Disclosure

The authors declare that they have no competing interests.

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