

## ORIGINAL ARTICLE

# Opportunities and trends in the study of transcutaneous auricular vagus nerve stimulation: A review and bibliometric analysis

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## ABSTRACT

**Background:** After more than two decades of development, transcutaneous auricular vagus nerve stimulation (taVNS) has surpassed its role as a mere alternative to vagus nerve stimulation and is now applied to various disorders. This study presents a bibliometric analysis to evaluate the global scientific output of taVNS research, aiming to describe its current status and identify potential future trends. **Methods:** We conducted a systematic retrieval of taVNS-related studies published between 2000 and 2022 from the Web of Science database. VOSviewer was used to construct networks based on analyses of country/institution/author co-authorship, journal/reference co-citation, literature citation, and keyword co-occurrence. **Results:** A total of 523 relevant articles and reviews were included. Since 2012, there has been a rapid increase in publications and citations. China emerged as the leading contributor in terms of publication output, whereas Germany received the highest number of citations. Interestingly, research groups from different countries exhibited distinct research ideas and focuses on taVNS, yet collaboration between these groups remained limited. Through a focused examination of key issues in this field, we identified significant opportunities for the advancement of taVNS research. **Conclusion:** This bibliometric analysis emphasizes researchers' interest in and recognition of taVNS as a therapeutic intervention. It also identifies the expansion of clinical applications, the development of more precise stimulation, and the development and commercialization of wearable devices as key opportunities and challenges for taVNS.

**Key words:** transcutaneous auricular vagus nerve stimulation, noninvasive vagal nerve stimulation, bibliometric analysis, auricular branch of the vagus nerve, stimulating peripheral activity to relieve conditions

## INTRODUCTION

Transcutaneous auricular vagus nerve stimulation (taVNS) is a noninvasive method of stimulating the vagus nerve through the skin of the ear. It has gained popularity as a treatment for various conditions, including depression, anxiety, and chronic pain.<sup>[1]</sup>

However, because taVNS is a nascent and rapidly evolving therapeutic method, there is some confusion surrounding it. For instance, there is a lack of consistency in the terminology and stimulation parameters used to describe the stimulation of the auricular branch of the vagus nerve. Furthermore, despite the increasingly broad application of taVNS,

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there are still many unknowns regarding its underlying mechanisms.<sup>[2]</sup> Thus, it is crucial to achieve a comprehensive understanding of the current state of taVNS research and to identify key research tasks, especially in its early, robust stages of development.

Bibliometric analysis is a quantitative method that enables the identification of patterns, trends, and relationships among publications in the scientific literature. It is a valuable tool for exploring the research landscape in a specific field. In this bibliometric analysis, we provide a comprehensive overview of taVNS research published between 2000 and 2022. By examining the existing literature on taVNS, we identify research trends, highlight significant findings, and provide valuable insights for future taVNS research.

## METHODS

### Data sources and search strategy

On January 15, 2023, we systematically searched the Web of Science Core Collection (WoSCC) database, including SCI-EXPANDED, using the following set of terms: (vagus nerve stimulation OR vagal nerve stimulation OR vagal afferent nerve stimulation OR VNS) AND (transcutaneous OR transdermal OR noninvasive OR non-invasive OR tVNS OR t-VNS OR taVNS OR ta-VNS OR auricular OR aVNS OR AVNS) AND (English [Language]). The document type was limited to articles or reviews, and the publication timespan was set to 2000 – 2022. To identify potentially eligible studies, two of the authors (Chen Xin and Shaoyuan Li) independently screened all the titles and abstracts. Any disagreements were resolved through discussion and consensus. The search terms and inclusion criteria were obtained from previously published literature.<sup>[2]</sup> Table 1 presents the search strategy and results.

### Bibliometric analysis and visualization

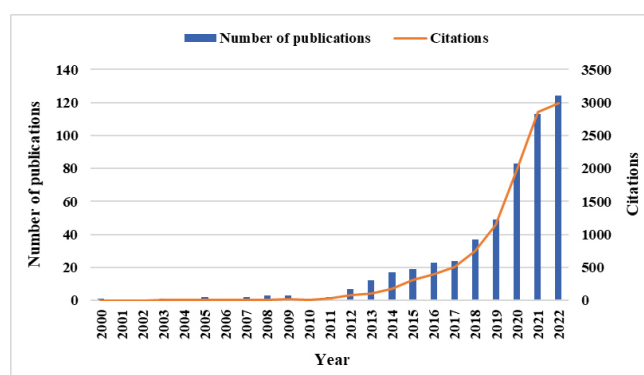
Using VOSviewer (version 1.6.18, Leiden University, the Netherlands), we performed a bibliometric analysis of 523 taVNS-related publications published between 2000 and 2022. We also used VOSviewer to construct networks based on analyses of country/institution/author coauthorship, journal/reference co-citation, literature citation, and keyword co-occurrence. To present the most relevant keywords, we used three kinds of visualization (network, overlay, and density visualization) and focused on the keywords that occurred more than five times. Using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA), we managed the data, created charts and data tables, and calculated the total number of citations per year. We also used Microsoft Excel 2019 to assess the annual publication pattern of countries/regions and institutions as well as

trends over time in the most highly cited publications for different major topics. To determine the impact of the publications included in our study, we collected the journals' impact factors from the 2021 *Journal Citation Reports* (JCR, Clarivate Analytics, Philadelphia, PA, USA).

## RESULTS

### Citation count and publication period

In total, 523 publications were obtained from the WoSCC for the period 2000 – 2022, including 399 articles (76.3%) and 124 reviews (23.7%). Collectively, the publications have been cited 11,368 times to date, with an average of 21.74 citations per article. These publications came from 51 countries/regions; 810 institutions; 2203 authors; and 228 journals. As Figure 1 shows, the annual publication output exhibited a trend of rapid growth beginning in 2012. Moreover, the number of citations these publications received exhibited annual growth after 2012.



**Figure 1.** Trends in the annual number of publications and citations.

A total of 523 taVNS-related articles published between 2000 and 2022 were retrieved from the WoSCC. During this period, global publications in the field exhibited a strong growth trend: Although only one article (0.19%) was published in 2000, 124 were published in 2022. The time curve generated by the logistic regression model indicated that the field has experienced a period of consistent growth in global publication output.

### Distribution of countries/regions and institutions

Figure 2A highlights the respective contributions of the 15 countries with the most publications in the field. The varying sizes of the circles correspond to the number of publications from each country/region. A total of 51 countries and regions contributed publications. Among them, China had the most publications (150), accounting for 28.68% of the articles. The United States followed China closely, with 139 publications (26.58%), and

Table 1: Search strategy.

Set	Result	Search query
#1	8238	Topic Search = (vagus nerve stimulation OR vagal nerve stimulation OR vagal afferent nerve stimulation)
#2	229,132	Topic Search = (transcutaneous OR transdermal OR noninvasive OR non-invasive OR tVNS OR t-VNS OR taVNS OR ta-VNS OR auricular OR aVNS OR AVNS)
#3	1218	#1 AND #2
#4	1202	#3 AND English (language)
#5	906	#4 AND Article or Review (document type)
#6	903	#5 NOT 2023 (year)
#7	523	Screen all the titles and abstracts to identify potentially eligible studies and select studies based on the full text. <sup>[2]</sup>

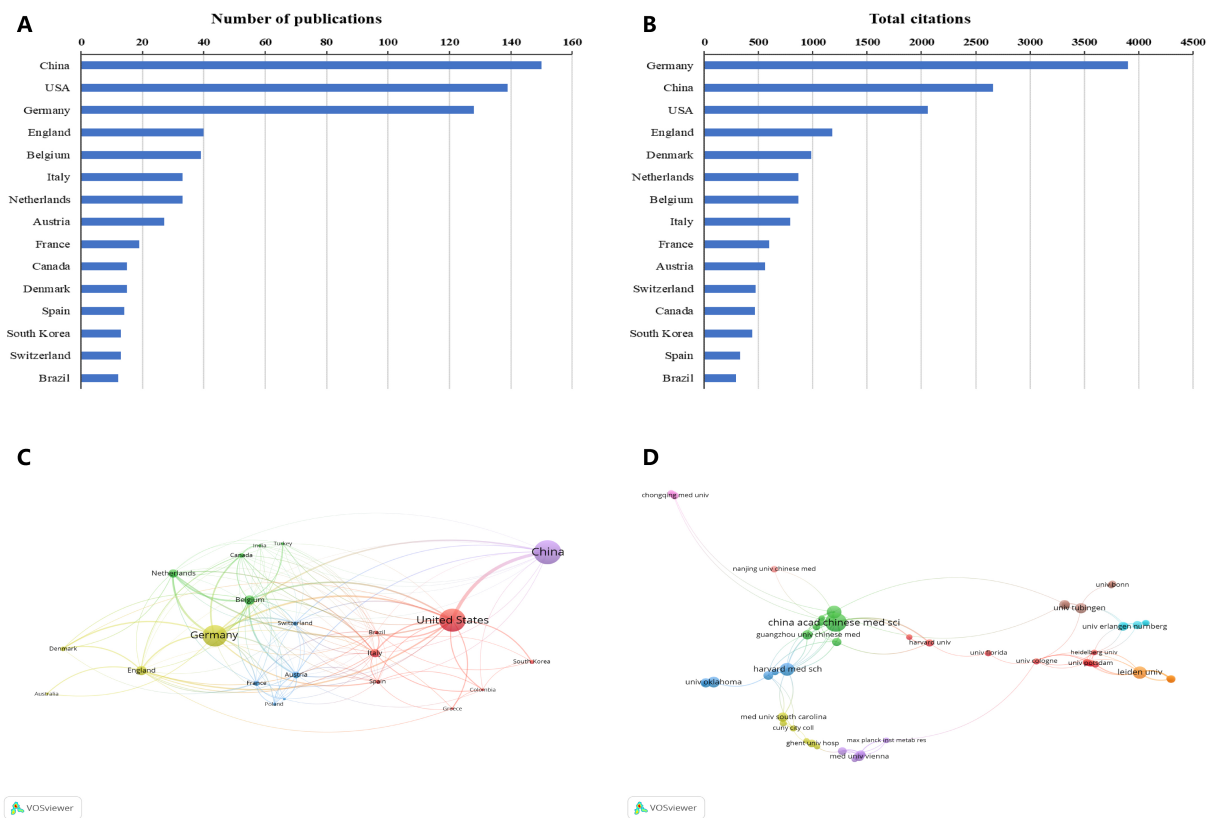


Figure 2. Countries/regions contributing to taVNS research. (A) The 15 countries with the most publications. (B) Total citations of a country/region’s articles in publications from other countries/regions. (C) Network map of countries/regions whose articles were co-cited in more than five publications. (D) Network map of institutions whose articles were co-cited in more than five publications. taVNS, transcutaneous auricular vagus nerve stimulation.

Germany ranked third, with 128 publications (24.47%). Other notable contributors included England (40, 7.65%), Belgium (39, 7.46%), Italy (33, 6.31%), the Netherlands (33, 6.31%), Austria (27, 5.16%), France (19, 3.63%), Canada (15, 2.87%), Denmark (15, 2.87%), Spain (14, 2.68%), South Korea (13, 2.49%), Switzerland (13, 2.49%), and Brazil (12, 2.29%).

Figure 2B provides information about the total citations of a country/region’s articles in publications from other countries/regions. Studies from Germany received the highest number of citations (3905 citations), followed by those from China (2658 citations), the United States

(2058 citations), England (1176 citations), Denmark (987 citations), the Netherlands (869 citations), Belgium (868 citations), Italy (791 citations), France (600 citations), Austria (559 citations), Switzerland (476 citations), Canada (465 citations), South Korea (443 citations), Spain (331 citations), and Brazil (291 citations).

The coauthorship analysis examined 23 countries with more than five publications (Figure 2C). The five countries with the highest total link strength were the United States (total link strength = 123 times), Germany (116), Belgium (78), Italy (63), and China (60).

A total of 765 institutions were identified as contributors to taVNS research. With 51 publications (9.75% of the articles), China Academy of Chinese Medical Sciences led the list, followed by Capital Medical University (24, 4.59%), Harvard Medical School (23, 4.40%), Leiden University (21, 4.02%), and the University of Oklahoma (16, 3.10%).

We analyzed the coauthorship of 56 institutions with more than five publications (Figure 2D). The exclusion of one item that was not connected revealed the collaborations of the other institutions. The five institutions with the highest total link strength were China Academy of Chinese Medical Sciences (total link strength = 59 times), Capital Medical University (33), Leiden University (33), Harvard Medical School (27), and the Medical University of Vienna (22).

### Analysis of journals and research areas

A total of 523 articles were published in 228 journals. Table 2 presents the 10 journals that published the most articles on taVNS. *Brain Stimulation* (32 records, 6.12% of all articles) had the most publications, followed by *Frontiers in Neuroscience* (29, 5.55%), *Autonomic Neuroscience: Basic and Clinical* (22, 4.21%), *Frontiers in Human Neuroscience* (14, 2.68%), and *Scientific Reports* (13, 2.49%).

The co-citation analysis identified 87 journals that were co-cited in more than 50 publications. Table 2 lists the 10 most-cited journals that published taVNS-related articles. *Brain Stimulation* received the largest number of citations (1823 citations), followed by *Epilepsia* (742 citations), *Neurology* (599 citations), *Journal of Neural Transmission* (460 citations), and *Brain Research* (455 citations).

The identified publications were classified under 56 research areas. The best-represented research area was neurosciences neurology, with 303 records, accounting for 57.94% of the articles. This area was followed by psychology (43, 8.22%), research experimental medicine (35, 6.69%), psychiatry (32, 6.12%), and cardiovascular system cardiology (31, 5.93%, Table 3).

The analysis of journals and research areas provided an understanding of the publication landscape of taVNS research, highlighting the prominent journals in the field and the main areas of focus in the research community. This information may be valuable for researchers who wish to explore the existing literature and identify collaboration opportunities in specific research areas.

### Analysis of authors

In terms of the number of publications, Peijing Rong was the most productive author, with 47 articles (8.99% of the articles), followed by Shaoyuan Li (21, 4.02%), Jiliang Fang (21, 4.02%), Bing Zhu (19, 3.63%), and

Kaniasas Eugenijus (16, 3.6%) (Figure 3A). In terms of receiving citations in other authors' taVNS studies, Peijing Rong was ranked first (1168 citations), followed by Bing Zhu (1109 citations), Ellrich Jens (937 citations), Jian Kong (727 citations), and Jiliang Fang (660 citations, Figure 3B).

We analyzed a total of 81 authors that were coauthored in more than five publications (Figure 3C). The exclusion of 41 items that were not connected revealed the collaborations of 40 authors (Figure 3D). The five authors with the highest total link strength were Peijing Rong (total link strength = 201 times), Shaoyuan Li (111), Jiliang Fang (109), Bing Zhu (88), and Liang Li (83).

### Citation and co-citation analyses

The citation analysis showed that 73 articles received more than 50 citations. The exclusion of one disconnected item revealed a collaboration network of 72 articles (Figure 4A). Table 4 presents the 10 articles that received the most citations. The article “Non-Invasive Access to the Vagus Nerve Central Projections *via* Electrical Stimulation of the External Ear: fMRI Evidence in Humans” (Frangos *et al.*, 2015) received 315 citations,<sup>[3]</sup> and “BOLD fMRI Deactivation of Limbic and Temporal Brain Structures and Mood Enhancing Effect by Transcutaneous Vagus Nerve Stimulation” (Kraus *et al.*, 2007) received 236.<sup>[4]</sup> The third most-cited article was “Anti-Inflammatory Properties of the Vagus Nerve: Potential Therapeutic Implications of Vagus Nerve Stimulation” (Bonaz *et al.*, 2016), with 220 citations.<sup>[5]</sup>

We analyzed 30 articles that were co-cited in more than 50 publications (Figure 4B). Table 5 lists the 10 articles that received the most citations. The five articles that received the most citations were by Peuker ET (2002, *Clinical Anatomy*; 213 citations), Frangos E (2015, *Brain Stimulation*; 170 citations), Kraus T (2007, *Journal of Neural Transmission*; 141), Yakunina N (2017, *Neuromodulation*; 124), and Kraus T (2013, *Brain Stimulation*; 116).<sup>[3,4,6–8]</sup>

### Analysis of keywords and topics

We analyzed a total of 68 author keywords that occurred more than five times (Figure 5A). In Figure 5B's mapping of these keywords, the colors indicate the average publication year of the identified keywords. The majority of the keywords were published after 2019 and are indicated with greener or yellower colors. The density visualization in Figure 5C displays the same identified keywords but maps them according to the frequency of their appearance. Among the identified author keywords, the five diseases with the largest number of occurrences were depression (26 times), epilepsy (23), stroke (17), rehabilitation (11), and migraine (11).



Table 2: The 10 most popular and most-cited journals.

Rank	Popular journals	Records (n)	2021 impact factor	2021 JCR partition	Most-cited journals	Citations	2021 impact factor	2021 JCR partition
1	<i>Brain Stimulation</i>	32	9.184	Q1	<i>Brain Stimulation</i>	1,823	9.184	Q1
2	<i>Frontiers in Neuroscience</i>	29	5.152	Q2	<i>Epilepsia</i>	742	6.74	Q1
3	<i>Autonomic Neuroscience: Basic and Clinical</i>	22	2.355	Q4	<i>Neurology</i>	599	12.258	Q1
4	<i>Frontiers in Human Neuroscience</i>	14	3.473	Q3	<i>Journal of Neural Transmission</i>	460	3.85	Q2
5	<i>Scientific Reports</i>	13	4.997	Q2	<i>Brain Sciences</i>	455	3.333	Q3
6	<i>Frontiers in Neurology</i>	11	4.086	Q2	<i>PLOS One</i>	436	3.752	Q2
7	<i>Neuromodulation</i>	11	3.025	Q3	<i>Biological Psychiatry</i>	430	12.81	Q1
8	<i>PLOS One</i>	11	3.752	Q2	<i>Cephalalgia</i>	409	6.075	Q1
9	<i>Frontiers in Physiology</i>	10	4.755	Q1	<i>Frontiers in Neuroscience</i>	359	5.152	Q2
10	<i>Brain Sciences</i>	9	3.333	Q3	<i>Neuromodulation</i>	354	3.025	Q3

JCR, Journal Citation Report.

Table 3: The 10 best-represented research areas.

Rank	Research area	Records (n)	% (of 523)
1	Neurosciences neurology	303	57.93
2	Psychology	43	8.22
3	Research experimental medicine	35	6.69
4	Psychiatry	32	6.12
5	Cardiovascular system cardiology	31	5.93
6	Physiology	28	5.35
7	Science technology	28	5.35
8	Engineering	22	4.21
9	General internal medicine	22	4.21
10	Behavioral sciences	21	4.02

DISCUSSION

General information

Our study provides valuable insights into the general trends and characteristics of taVNS research. This field of research has experienced substantial expansion since its inception in 2000, with a consistent rise in annual publication output and a particularly strong increase in momentum from 2012 onward. This trend indicates the growing interest in and recognition of taVNS as a potential therapeutic intervention. Initially, taVNS was explored primarily as an alternative therapy to vagus nerve stimulation (VNS) for the treatment of epilepsy. However, its application has expanded to include various other conditions, including depression, stroke, rehabilitation period, pain, insomnia, cognitive impairment, cardiovascular disease, glucose-metabolism disorders, tinnitus, and potentially even COVID-19.<sup>[1,9,10]</sup> This diversification of research areas reflects the wide-ranging potential and versatility of taVNS as a therapeutic approach.

In the coauthorship analysis by country, China emerges

as the leading contributor in terms of the number of articles. This finding highlights Chinese institutions’ active involvement and significant output in the field of taVNS research. On the other hand, Germany stands out in terms of the number of citations, which indicates the impact and recognition of German contributions to the field. The analysis also reveals a substantial increase in the number of studies conducted in the United States and England over the past two decades, along with a corresponding increase in the number of citations. This suggests the growing interest and engagement of researchers from these countries in taVNS research and their contributions to the field. Among the institutions, China Academy of Chinese Medical Sciences stands out as the most productive institution, indicating its active involvement and significant output in taVNS research. Moreover, this institution’s high total link strength indicates its strong network of collaboration with other institutions in the field.

Interdisciplinary and international collaboration plays an important role in advancing taVNS research. Currently, there is not a strong partnership between countries; that

**Table 4: Analysis of the 10 most-cited taVNS articles.**

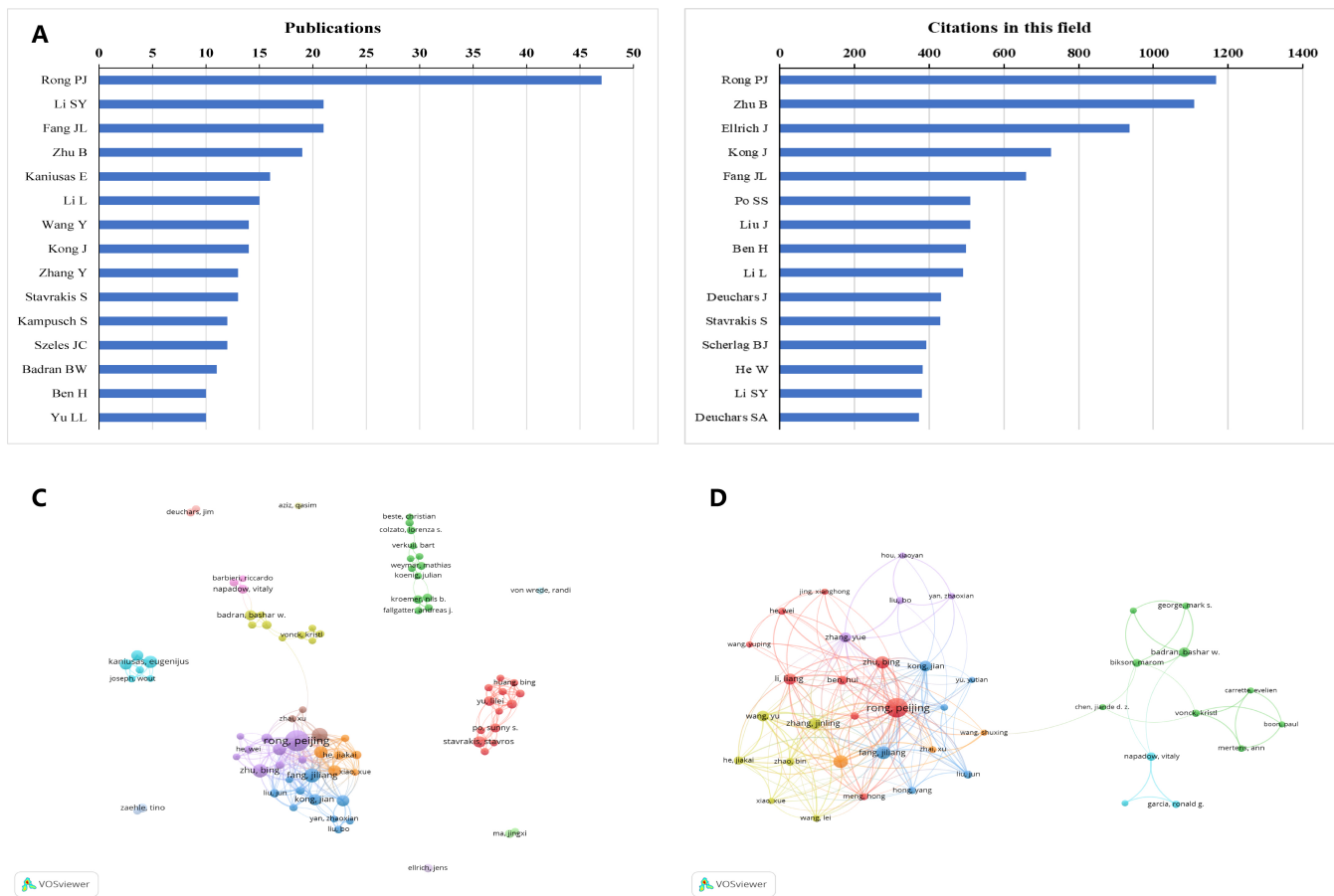
Rank	Title	Authors	Source	Publication year	Citations (n)
1	Non-Invasive Access to the Vagus Nerve Central Projections <i>via</i> Electrical Stimulation of the External Ear: fMRI Evidence in Humans	Frangos <i>et al.</i> , 2015	<i>Brain Stimulation</i>	2015	315
2	BOLD fMRI Deactivation of Limbic And Temporal Brain Structures and Mood Enhancing Effect by Transcutaneous Vagus Nerve Stimulation	Kraus <i>et al.</i> , 2007	<i>Journal of Neural Transmission</i>	2007	236
3	Anti-Inflammatory Properties of the Vagus Nerve: Potential Therapeutic Implications of Vagus Nerve Stimulation	Bonaz <i>et al.</i> , 2016	<i>Journal of Physiology</i>	2016	220
4	Non-Invasive Vagus Nerve Stimulation in Healthy Humans Reduces Sympathetic Nerve Activity	Clancy <i>et al.</i> , 2017	<i>Brain Stimulation</i>	2017	215
5	Optimization of Transcutaneous Vagus Nerve Stimulation Using Functional MRI	Yakunina <i>et al.</i> , 2017	<i>Neuromodulation</i>	2017	176
6	Low-Level Transcutaneous Electrical Vagus Nerve Stimulation Suppresses Atrial Fibrillation	Stavrakis <i>et al.</i> , 2015	<i>Journal of the American College of Cardiology</i>	2015	172
7	CNS BOLD fMRI Effects of Sham-Controlled Transcutaneous Electrical Nerve Stimulation in the Left Outer Auditory Canal – A Pilot Study	Kraus <i>et al.</i> , 2013	<i>Brain Stimulation</i>	2013	169
8	Transcutaneous Vagus Nerve Stimulation Modulates Default Mode Network in Major Depressive Disorder	Fang <i>et al.</i> , 2016	<i>Biological Psychiatry</i>	2016	168
9	A Novel Transcutaneous Vagus Nerve Stimulation Leads to Brainstem and Cerebral Activations Measured by Functional MRI / Funktionelle Magnetresonanztomographie zeigt Aktivierungen des Hirnstamms und weiterer zerebraler Strukturen unter transkutaner Vagusnervstimulation	Dietrich <i>et al.</i> , 2008	<i>Biomedical Engineering / Biomedizinische Technik</i>	2008	160
10	Surgically Implanted and Non-Invasive Vagus Nerve Stimulation: A Review of Efficacy, Safety and Tolerability	Ben-Menachem <i>et al.</i> , 2015	<i>European Journal of Neurology</i>	2015	159

taVNS: transcutaneous auricular vagus nerve stimulation.

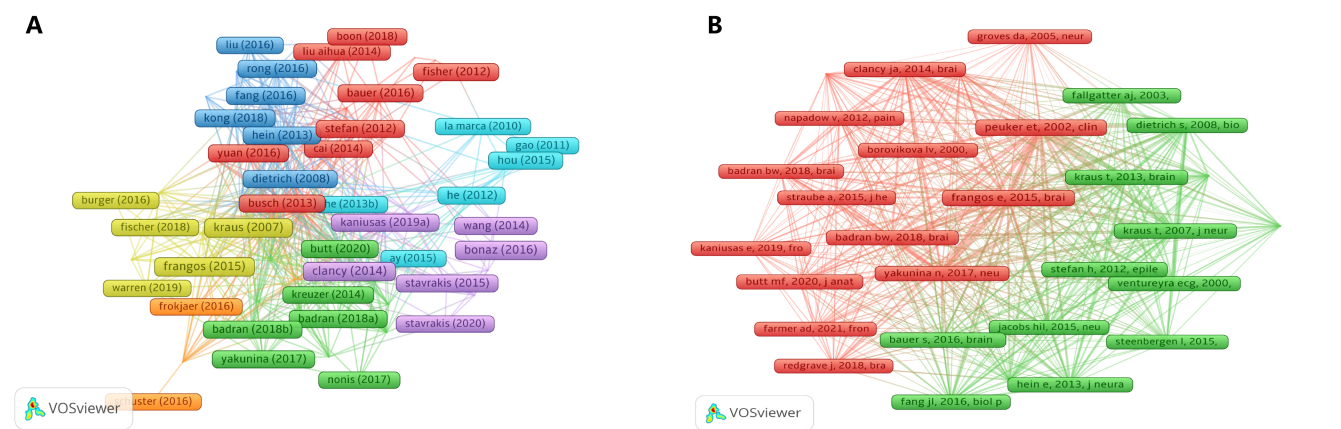
**Table 5: Top ten co-citation analysis of cited reference on taVNS research.**

Rank	Title	Authors	Source	Publication year	Citations (n)
1	The Nerve Supply of the Human Auricle	Peuker <i>et al.</i> , 2012	<i>Clinical Anatomy</i>	2002	213
2	Non-Invasive Access to the Vagus Nerve Central Projections <i>via</i> Electrical Stimulation of the External Ear: fMRI Evidence in Humans	Frangos <i>et al.</i> , 2015	<i>Brain Stimulation</i>	2015	170
3	BOLD fMRI Deactivation of Limbic and Temporal Brain Structures and Mood Enhancing Effect by Transcutaneous Vagus Nerve Stimulation	Kraus <i>et al.</i> , 2007	<i>Journal of Neural Transmission</i>	2007	141
4	Optimization of Transcutaneous Vagus Nerve Stimulation Using Functional MRI	Yakunina <i>et al.</i> , 2017	<i>Neuromodulation</i>	2017	124
5	CNS BOLD fMRI Effects of Sham-Controlled Transcutaneous Electrical Nerve Stimulation in the Left Outer Auditory Canal – A Pilot Study	Kraus <i>et al.</i> , 2013	<i>Brain Stimulation</i>	2013	116
6	Non-Invasive Vagus Nerve Stimulation in Healthy Humans Reduces Sympathetic Nerve Activity	Clancy <i>et al.</i> , 2017	<i>Brain Stimulation</i>	2014	106
7	A Novel Transcutaneous Vagus Nerve Stimulation Leads to Brainstem and Cerebral Activations Measured by Functional MRI / Funktionelle Magnetresonanztomographie zeigt Aktivierungen des Hirnstamms und weiterer zerebraler Strukturen unter transkutaner Vagusnervstimulation	Dietrich <i>et al.</i> , 2008	<i>Biomedical Engineering / Biomedizinische Technik</i>	2008	104
8	Neurophysiologic Effects of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) <i>via</i> Electrical Stimulation of the Tragus: A Concurrent taVNS/fMRI Study and Review	Badran <i>et al.</i> , 2018	<i>Brain Stimulation</i>	2018	90
9	Transcutaneous Vagus Nerve Stimulation Modulates Default Mode Network in Major Depressive Disorder	Fang <i>et al.</i> , 2016	<i>Biological Psychiatry</i>	2016	82
10	Transcutaneous Vagus Nerve Stimulation (t-VNS) in Pharmacoresistant Epilepsies: A Proof of Concept Trial	Stefan <i>et al.</i> , 2016	<i>Epilepsia</i>	2012	82

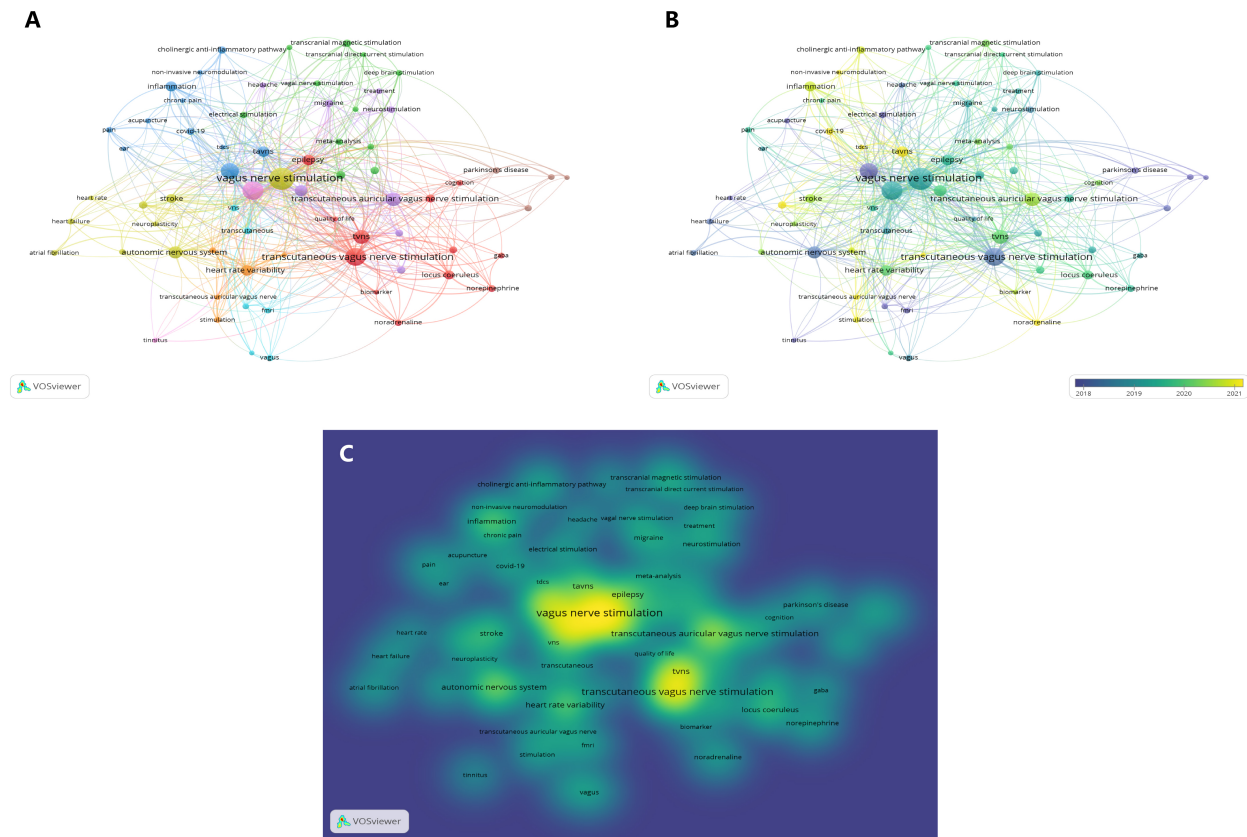
taVNS: transcutaneous auricular vagus nerve stimulation.



**Figure 3.** Authors contributing to taVNS research. (A) The 15 authors with the most publications. (B) Total citations of the 15 most-cited authors. (C) Network map of authors who were co-cited in more than five publications. (D) Network map of authors who were co-cited in more than five publications after excluding 41 unconnected items. taVNS, transcutaneous auricular vagus nerve stimulation.



**Figure 4.** Citation and co-citation analyses. (A) Network map of articles that received more than 50 citations. (B) Network map of articles that were co-cited in more than 50 publications.



**Figure 5.** Co-occurrence analysis of author keywords. (A) Mapping of keywords of articles. (B) Distribution of keywords according to average publication year (blue: earlier; yellow: later). (C) Distribution of keywords according to the mean frequency of appearance. Keywords in yellow occurred with the highest frequency.

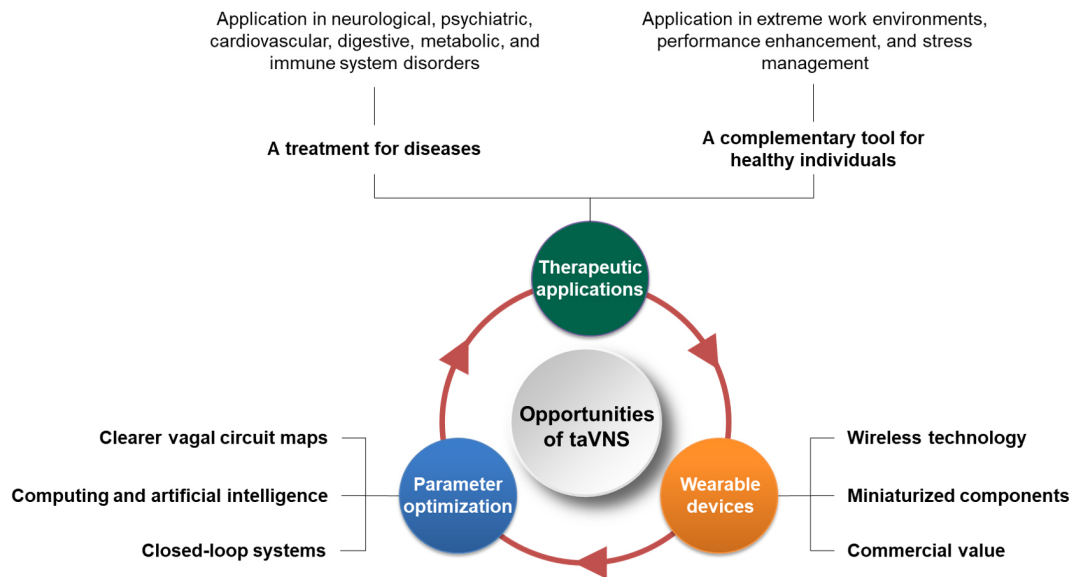
is, research teams from different countries exhibit distinct research ideas and focuses on taVNS. Rong Peijing, from the China Academy of Chinese Medical Sciences, is the most-published and most-cited author. Her clinical trials have demonstrated the efficacy and safety of taVNS in treating multiple conditions, including epilepsy, depression, insomnia, cognitive impairments, and metabolic disorders.<sup>[11–16]</sup> To facilitate the future development of taVNS, she recently proposed strategies to establish a wider range of taVNS criteria, including nomenclature and device criteria.<sup>[1,2]</sup> Kaniusas Eugeniju of the Vienna University of Technology has contributed to the enrichment of taVNS research from an engineering perspective, particularly in the area of computer modeling as a tool for optimizing taVNS.<sup>[17–20]</sup> Vitaly Napardow of Harvard Medical School has developed a taVNS device called respiration-assisted vagus nerve stimulation, which combines deep breathing with taVNS stimulation.<sup>[21]</sup> Nils B. Kroemer is a professor of psychiatry and psychotherapy at the University of Bonn, Germany, whose main contribution to the field is his research on the effects of taVNS on reward processing and motivation.<sup>[22–24]</sup>

Indeed, the diverse expertise of these authors and other researchers has immensely enriched the field of taVNS research, paving the way for further investigation and broader clinical application of taVNS. Our review identifies potential trends of future research and development opportunities that build on these achievements (Figure 6). It is hoped that increased collaboration will be fostered among research teams with common goals and interests in an effort to tackle challenges and explore new frontiers in taVNS research.

## THERAPEUTIC APPLICATIONS OF TAVNS WITH BROAD POTENTIAL

Although taVNS was initially considered an alternative to VNS, its noninvasive and nonsurgical characteristics have expanded its range of application far beyond VNS. The analysis of keywords and topics indicates that the five medical conditions with the most occurrences were depression, epilepsy, stroke, rehabilitation period, and migraine. The extant research has explored the applicability of taVNS to a wide variety of diseases and conditions, including neurological, psychiatric, cardiovascular, digestive, metabolic, and immune-system





**Figure 6.** Graphical abstract of opportunities in taVNS research and development. taVNS, transcutaneous auricular vagus nerve stimulation.

disorders, demonstrating its potential as a versatile therapeutic approach.<sup>[25–29]</sup> In some cases, taVNS has even been shown to be superior to VNS; for example, a meta-analysis showed that patients who received taVNS in the acute/subacute phase of stroke experienced greater effects than patients who received VNS.<sup>[30]</sup> The ease of combining taVNS with other medical procedures also helps to broaden its application. For example, previous studies have explored the combination of taVNS with breathing exercises,<sup>[31,32]</sup> meditation,<sup>[33]</sup> cognitive behavioral therapy,<sup>[24]</sup> and physical rehabilitation,<sup>[34]</sup> each of these combinations may have synergistic effects.

Furthermore, taVNS can be used to enhance cognitive performance,<sup>[35–40]</sup> emotional regulation,<sup>[24,41]</sup> and psychological well-being in healthy individuals,<sup>[42–44]</sup> which may expand its application to areas such as extreme work environments, performance enhancement, and stress management. Thus, the use of taVNS can be extended beyond clinical settings to various fields of endeavor, including sports, education, and workplace productivity. For example, taVNS can be used to enhance cognitive and physical performance in athletes,<sup>[32,45,46]</sup> improve attention and learning in students,<sup>[23,47–51]</sup> and increase productivity and creativity in employees.<sup>[22,52]</sup> Therefore, it can serve not only as a treatment for disease but also as a complementary tool for healthy individuals. It should be noted that further research and validation are necessary to determine the reliability and safety of these effects.

## PARAMETER OPTIMIZATION OF TAVNS FOR ENHANCED PRECISION

Parameter optimization of taVNS is a critical procedure

for determining the most effective and accurate stimulation parameters, including electrode placement and stimulation intensity, frequency, and duration. It is important to recognize that optimal parameter settings may vary depending on individual patients' physiological, clinical, and disease characteristics. The following paragraphs outline some additional considerations and opportunities related to parameter optimization.

**Clearer understanding of mechanisms and vagal-circuit maps:** Ongoing research in Phase 2 of the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program will advance our knowledge of the vagus nerve, including its anatomy and functional characteristics.<sup>[53]</sup> This improved knowledge will provide a valuable resource for optimizing parameters and allow for more precise targeting of specific neural circuits or organ systems. Continued exploration of the vagus nerve's anatomical connectivity and functional aspects, as well as the neural circuits involved in specific diseases or symptoms, will strengthen our understanding of the underlying mechanisms of taVNS.<sup>[54]</sup> Additionally, it is noteworthy that the anti-inflammatory effect of taVNS may account for its wide-ranging applications, suggesting that the effectiveness of taVNS in various chronic diseases is based on a shared mechanism.<sup>[5,55–57]</sup> Mounting evidence indicates that inflammation plays a significant role in chronic illnesses.<sup>[58–63]</sup> Therefore, the potential to achieve targeted modulation of immune cells rather than neural cells through taVNS will open up new possibilities for high-precision stimulation.

**Advances in computing and artificial intelligence:** Advances in computer technology have made it possible to use mathematical models and computer simulations

to optimize parameter settings for taVNS. The purpose of the SPARC portal is to share curated datasets, detailed neuroanatomical maps, and simulations to facilitate experimental computation and visualization.<sup>[64]</sup> Additionally, the program will create an open-source device specification that encompasses hardware, software, firmware, and other necessary technical modules to support the development of neuromodulation tools and stimulation simulations. With these resources, researchers can effectively explore the impact of various parameter combinations on neural circuits and physiological processes using mathematical models and computer simulations.<sup>[17,20]</sup> This advance significantly reduces reliance on animal and human experiments, lowers research costs, and accelerates the process of parameter optimization. It should be emphasized that the ongoing development of artificial intelligence will further accelerate and enhance this progression.<sup>[65]</sup>

**Closed-loop systems and personalized treatment:** Because individual patients may respond differently to taVNS, personalized parameter optimization is crucial. The development of closed-loop taVNS systems that dynamically adjust stimulation parameters based on real-time physiological feedback has the potential to improve precision. These systems can be configured with parameters that correspond to specific health conditions and adjusted in real time according to individual responses, thus meeting the specific needs of each patient and optimizing the effectiveness of neuromodulation.<sup>[66–68]</sup> Personalized treatment represents the pinnacle of precision medicine and is the ultimate goal of high-precision stimulation, the full realization of which requires the integration of the technologies described above with medical-device development.

## WEARABLE TAVNS DEVICES FOR CONVENIENCE AND COMMERCIALIZATION

TaVNS devices play a crucial role in both widespread clinical applications and highly precise stimulation modalities. Although taVNS has a relatively short history of 20 years, the devices incorporating taVNS technology have been continuously updated. As engineering and materials-science technologies have continued to progress, the noninvasive and portable characteristics of taVNS have become increasingly more apparent, giving rise to the trend of wearable devices. A review has provided an overview of the current status of taVNS devices, highlighting the rapid development and improvement of high-tech, intelligent, and compact taVNS devices.<sup>[1]</sup>

Currently, the commercialization of taVNS is showing promising signs; for example, a San Francisco-based

startup has received a significant investment. The funding is directed towards the development of a wireless, earbud-like taVNS device designed to target specific brain regions and address inflammatory diseases like rheumatoid arthritis. The startup had already completed a multicenter, single-arm, 30-patient pilot clinical trial that demonstrated a significant reduction in the severity of rheumatoid-arthritis symptoms.<sup>[69]</sup> The trial's promising results have prompted further investment in ongoing clinical trials.

In summary, the integration of wireless technology and miniaturized components has driven the development of user-friendly and compact taVNS devices, offering convenience and usability to patients who wish to use stimulation therapy in their daily lives. Among other neurostimulation techniques, taVNS stands out due to its unique stimulation site, which makes the taVNS amenable to integration into everyday items like headphones and earbuds. Such seamless integration will allow taVNS to blend into daily routines, thereby mitigating the stigma associated with illness and even creating new fashion trends, which could further enhance the therapy's commercial value.<sup>[69,70]</sup>

## Limitations

To our knowledge, this study is the first bibliometric analysis of taVNS research. Although our literature survey was comprehensive, it may have some limitations. First, we primarily used the WoSCC database for literature retrieval and analysis and did not incorporate other databases, such as PubMed and Scopus, which may have resulted in the omission of some relevant literature. However, it is worth noting that the WoSCC is the most widely used database in scientometrics and that most bibliometric software can recognize and process its format. Second, the results of our keyword analysis may have been influenced by incomplete keyword extraction. Because we presented only keywords that appeared at least five times, we may have overlooked the importance of some relevant keywords. Third, in order to analyze complete annual data, we limited the timeframe of the literature to 2000 – 2022 and thus omitted literature from 2023; this omission may have led to a lack of coverage of the latest research trends and developments. Fourth, the literature on ear stimulation has used various expressions and names for taVNS. We conducted retrieval and analysis based on previous studies, including literature with different names in the field of taVNS as much as possible.

## CONCLUSION

This paper highlights three prominent opportunities in the field of taVNS research: (1) the broad therapeutic potential of taVNS, (2) the optimization of taVNS

parameters to enhance the precision of stimulation, and (3) the development of wearable devices for convenience and commercialization. However, along with these opportunities, certain challenges need to be addressed. This study's findings have the potential to promote consensus building, foster collaboration, and collectively drive the advancement of taVNS technology.

## DECLARATION

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None.

### Author contributions

Xin C: Conceptualization, Writing—Original draft preparation, Writing—Reviewing and Editing. Zhang YZH: Writing—Original draft preparation. Guo J: Conceptualization, Writing—Reviewing and Editing. Wang Y: Conceptualization, Supervision. Wang YF: Conceptualization, Supervision. Zhao YN: Conceptualization, Supervision. Zou NY: Conceptualization, Writing—Reviewing and Editing. Li SY: Supervision, Project administration. Rong PJ: Supervision, Project administration. All authors reviewed and approved the final version of the manuscript.

### Ethics approval

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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.

### Data availability statement

No additional data.

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