

Visualization Analysis of Research Literature based on Electrical Vagal Nerve Stimulation Therapy with CiteSpace

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Abstract: ***Objective:** Vagus nerve electrical stimulation (Vagus Nerve Stimulation, VNS) therapy is a non-invasive treatment for refractory epilepsy and other neurological diseases, which analyzes the research status and development direction of vagus nerve electrical stimulation therapy in the past 45 years. **Methods:** Using the CiteSpace aims to reveal the research hotspots and development trends in this field. Through bibliometric methods, keywords, authors, research institutions, and time trends, are analyzed to provide reference and inspiration for research in this field. **Results:** 797 articles were included, the annual publications of the field, Fang Jiliang, Li Shaoyang, Wang Yu, Feng Zhen, etc, VNS correlation research in recent 45 years mainly focused on "refractory epilepsy, depression, atrial fibrillation", and the amount of acupuncture showed the rising trend. In this field, 26 co-present keywords and 11 cluster modules were formed through keyword analysis. **Conclusion:** Domestic VNS research is in the development stage, and the research topic focuses on neurological diseases. To strengthen the cooperation between authors and institutions to promote the high-quality development of VNS related research. This study has preliminarily demonstrated the value of VNS for neurological diseases. In the past 45 years, related research perspectives are diverse, and mechanistic research has become a research fever in recent years.*

Keywords: Vagus nerve stimulation, Bibliometry, CiteSpace, Visual analysis, Research hotspot.

1. Introduction

Vagus nerve is the main component of parasympathetic nerve, which participates in the dynamic regulation of body physiological function, containing four kinds of fibers, including somomotor, visceral movement, visceral sensation and somatosensory. As an important part of the parasympathetic nerve, the vagus nerve is distributed to the organs of the heart, lung, esophagus, stomach, intestine, liver, pancreas and kidney. The main function of sympathetic nerve is to mobilize the potential of organs and promote the body to adapt to rapid changes in the environment; while the vagus nerve protects the body, promotes digestion, accumulates energy, and keeps the physiological balance in a quiet state. Its most important function is to transmit the information of internal organs (such as intestine, liver, heart and lung) to the brain. The afferent fibers of the vagus nerve integrate into the brainstem at the level of the solitary tract nucleus and then project to the rest of the central nervous system (parabrachial nucleus, dorsal raphe nucleus, locus coeruleus, hypothalamus, thalamus, amygdala, and hippocampus, etc.) [1]. Vagus nerve stimulation (vagus nerve stimulation, VNS) was first used in the treatment of epilepsy [2]. The initial VNS was surgically fitted with the stimulation device to the neck vagus nerve, called invasive vagus nerve stimulation (invasive VNS, iVNS). There are two non-invasive vagal stimulation (non invasive VNS, nVNS): percutaneous (transcutaneous auricular VNS, taVNS) and percutaneous cervical vagal stimulation (transcutaneous cervical VNS, tcVNS) [3]. In 1951, Dell et al found that stimulating the severed vagus nerve triggered responses in the thalamus. In 1985, it was found that stimulation of the vagus nerve caused changes in electrical activity in the brain and could be used to terminate seizures in the canine model. Although the first human vagal nerve stimulator was put into the body of epileptic patients in Perry et al. in 1988 and achieved good results, two of the patients

had no seizures in 1 year [4-5] But until it was only in 1994 that vagus nerve stimulation was shown to reduce seizure frequency in patients with chronic epilepsy. During the 1997 twenty-year period followed by the FDA treatment for refractory epilepsy with VNS, this method was applied by an increasing number of patients in many countries [6]. Large number of clinical studies [7] found that the frequency of seizures decreased by 47% after implantation of vagus stimulation (VNS), as an effective means to treat refractory epilepsy, has attracted wide attention in recent years. The VNS affects neural activity in the brain by stimulating the vagus nerve, thereby reducing the frequency and intensity of seizures. As research continues, VNS indications also expand, including depression, anxiety disorders, neuropathic pain, insomnia, Alzheimers disease, multiple sclerosis, and eating disorders [8-9] class, VNS can regulate monoamine neurotransmitter, activation and increase related brain area and resting state functional connection, regulate inflammation levels, restore the hippocampus volume, activate the theta rhythm, regulate autonomic nerve function and melatonin levels to effectively promote the clinical symptoms of depression, including low mood, anhedonia, cognitive decline, sleep disorders and somatization symptoms [10]. In order to better understand the current research status and future trends of VNS therapy, the relevant literature was visualized using CiteSpace software. In this study, VNS related literature was collected, and CiteSpace6.2. R4 software was used to conduct bibliometric analysis, to explore the research situation of VNS in recent 45 years, to explore the research hotspot and future research direction of VNS, to provide reference for the research in this field, and to provide ideas for the clinical application of VNS.

2. Research Methods

2.1 Data Collection

The research data were retrieved from Chinese Knowledge Resources General Database (CNKI), Chinese Academic Journal Database (Wanfang Data), Chinese Scientific and Technological Journal Database (VIP), and Chinese Biomedical Literature Database (CBM). The search keywords included "Vagus Nerve Stimulation", "VNS", "Epilepsy", "Neuromodulation", etc. With "China intellectual network (CNKI)" database as the data source retrieval "vagus nerve stimulation" related articles, retrieval time is: January 1, 1979-October 1, 2024 included vagus nerve stimulation related literature, language choice Chinese, CNKI, for example, using boolean logic operator build retrieval type "theme = vagus nerve electric stimulation therapy OR vagus nerve stimulation treatment OR vagus nerve stimulation intervention".

2.2 Literature Screening Criteria

Literature inclusion criteria: (1) With "vagus nerve electrical stimulation therapy" as the research theme, published literature, including clinical research, clinical cases, expert experience, theoretical discussion, basic research and review, etc. (2) literature type for journal literature and dissertation.

Literature exclusion criteria: (1) Non-academic literature (such as draft notice, academic conferences, news reports, letters, etc.) (2) Literature with incomplete information (such as disease, vague treatment description, author or author unit source or unknown source); (3) duplicate literature only retained 1.

A total of 1310 articles were retrieved, and after reading the titles, abstracts and full text of the articles, and then using the EndnoteX9 software, 797 articles were included. The filtered articles were exported in Reworks format and presented as download-*. Name of the txt form.

2.3 Research Tools and Data Processing

CiteSpace Software is a tool for the visual analysis of the scientific literature, Literature ption were imported into CiteSpace6.2.R2 software in reworks-CiteSpace format, The research content is the annual publication information, author (author), organization (institution), key words (keyword) and other information, Set the information mining constraints: the time interval is from January 1979 to October 2024; Unit time slice set to 1; threshold set: select top50, g-index K=25, The rest are the system default parameters, Run the CiteSpace6.2.R4 software to draw the visual map.

3. Finding

3.1 Change and Trend Chart of Literature Publications

During the 45 years from 2001 to 2020, a total of 797 related documents were counted. See Figure Figure 1.11. The annual volume of research articles in this field shows an upward trend, which can be roughly divided into three periods. The first period is a slow growth period, the time span from 1979-1999, the highest annual table volume is 11; the second period is a steady growth period, the time span from 2000 to 2009, the highest annual publication volume is 22; the third period is a rapid growth period from 2010 to 2023, the period of

literature publications appeared a relatively rapid growth, the annual publication peak in 2023, 79, indicating that the clinical research of VNS increasingly attention in academic circles. The author analyzes the reasons for: (1) the continuous improvement of residents living standards, the relative increase of neurological diseases (such as depression, insomnia, migraine, cognitive impairment, etc.), (2) pay more attention to the rapid progress of science and technology, the specific details of disease emergence, development and change; (3) vagal nerve electrical stimulation therapy has become more and more widely used in recent years, to explore the advantages and mechanism of the treatment of the nervous system.

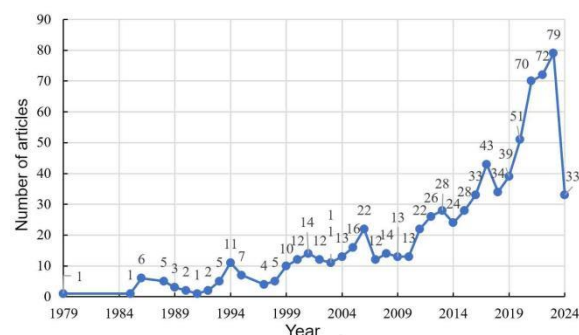


Figure 1: Time distribution of literature publications

3.2 Author Analysis

Using CiteSpace software, 597 nodes and 870 lines were formed. See Figure 2. According to Prices law [15] $N=0.749 N_{max}$ (including N as the core author minimum post, N_{max} for the most of the author), the core author, a total of 20, the field formed 18 main author team, the formation of the field of the first two closely connected team are RongPeicrystal, Fang Jiliang team with Feng Zhen, Dong Xiaoyang team.

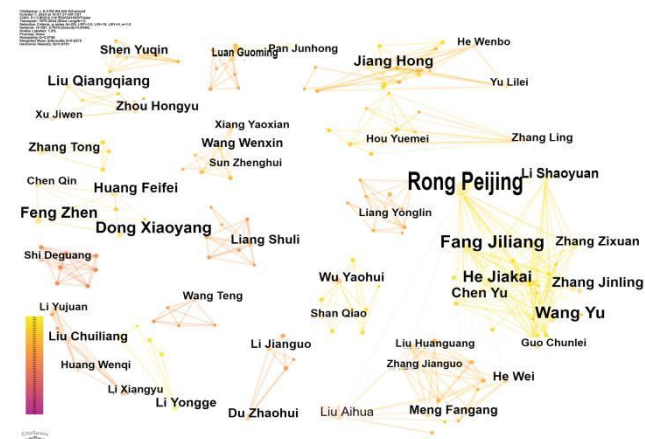


Figure 2: Author co-occurrence map

3.3 Institutional Analysis

After the analysis, it can be seen that the research institutions are mainly medical universities and their affiliated hospitals, among which the top three institutions are Acupuncture Institute of China Academy of Chinese Medicine Sciences, China Academy of Chinese Medicine Sciences and Xinjiang Medical University; the closest cooperation between institutions is the cooperation between Chinese Academy of Chinese Medicine (Institute of Acupuncture and Moxibustion) and its affiliated hospitals. See Figure Figure 3.33. Based on the visual analysis of the CiteSpace software on the

cooperation between institutions and the publication of institutional literature, it is concluded that the related research on vagus nerve stimulation therapy is mainly based on the research of TCM universities and their affiliated hospitals. Compared with western medicine institutions, there is relatively little application of the vagal nerve electrical stimulation therapy in the field of traditional Chinese medicine, whether in basic research or clinical application. In general, the team is close, but there is a lack of communication and cooperation between teams. Research institutions mainly focus on TCM universities and their affiliated hospitals. This cooperative relationship will help improve the quality and efficiency of regional medical services, reduce inter-provincial medical costs, and promote regional resource sharing and collaboration. In the future, we can strengthen academic exchanges and cooperation among various research teams and regions, integrate available resources, and carry out strict randomized controlled experiments with multiple centers and large samples to

promote the development of this field.

3.4 Keyword Visualization Analysis

3.4.1 Co-occurrence analysis

Keywords represent the research direction of the literature and the research hotspots in this field. Keywords were analyzed using CiteSpace software. See Figure 4 for keyword co-occurrence network, including 624 nodes, 2028 connections, and network density of 0.0104. In addition to the subject word "vagus nerve stimulation", the high-frequency keywords are "epilepsy", "electric vagus nerve stimulation", "transcutaneous ear vagus nerve stimulation", "vagus nerve stimulation", "refractory epilepsy" and "depression". Keywords represent more of the core content and research focus of the article. By calculating the occurrence frequency and central value of keywords, it can reflect the research trend of this field to a certain extent [11].



Figure 3: Co-occurrence diagram of the research institutions

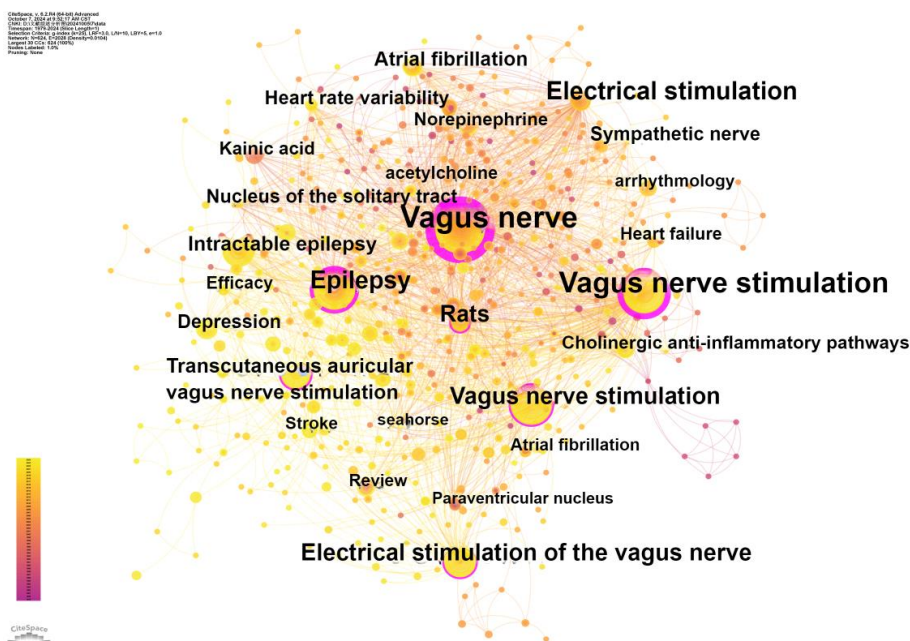


Figure 4: Keyword co-occurrence map

3.4.2 Cluster analysis

Keywords were used according to the LLR algorithm to obtain the keyword clustering map (Figure 5), with a total of 11 clusters. The map effect is judged by the cluster module value (Q) and the average profile value (S), and the Q value is 0.5758, indicating that the network community structure is significant (>0.5), and the silhouette value of 0.8275 indicates that the cluster structure is significant and effective (>0.5)

[12]. Figure "vagus nerve electric stimulation" related cluster overlap is more, prompt vagus nerve electric stimulation research direction is concentrated, cluster are #0 #1 atrial fibrillation, electric stimulation, #2 percutaneous ear vagus nerve electric stimulation, #3 epilepsy, #4 vagus nerve stimulation, #5 vagus nerve electric stimulation, #6 paraventricular nucleus, #7 cholinergic anti-inflammatory pathway, #8 liver depression, #9 atropine, #10 microcirculation, #11 convulsions.

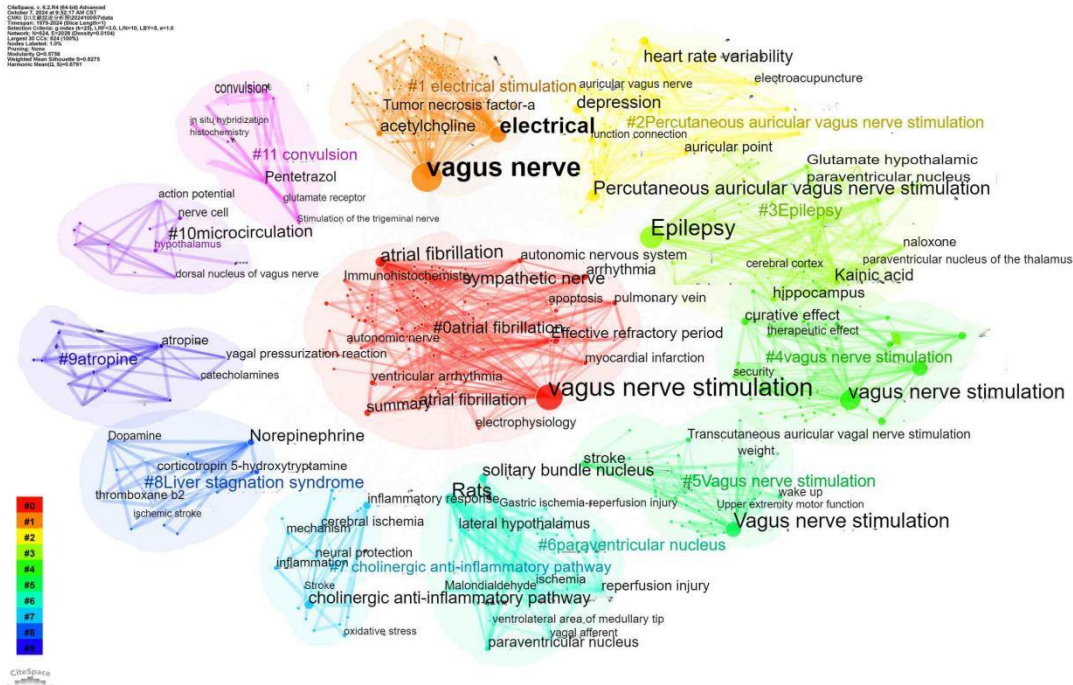


Figure 5: Keyword clustering plot

3.4.3 Present analysis

The emerging keywords can represent the leading edge of the vagus electrical stimulation research in the corresponding time, shown in Figure 6. In years 1986-2011, In this field, electrical stimulation therapy combined with vagus nerve, epilepsy clinical observation and basic research; In year 2006-2014, The research topic is the mechanism and principle of vagus nerve stimulation on atrial fibrillation and heart failure, Expand to the field of cardiovascular disease; In 2013-2021, The research focus focuses on the application of vagus nerve stimulation and the mechanism of refractory epilepsy; In 2019-2024, The research hotspot is the use and adaptation of percutaneous vagal nerve stimulation; And the treatment principle and efficacy of the vagus nerve electrical stimulation on the common nervous system diseases such as: depression, cognitive dysfunction, stroke and other diseases.

4. Summary

As an important part of the human nervous system, the vagus nerve is of great significance to the physiological activities and functions of the human body. With the progress of technology and scientific research means, it will have a more profound understanding of the mechanism, transformation and prognosis of the development of disease and injury, so as to help the better clinical diagnosis and treatment.

Top 17 Keywords with the Strongest Citation Bursts

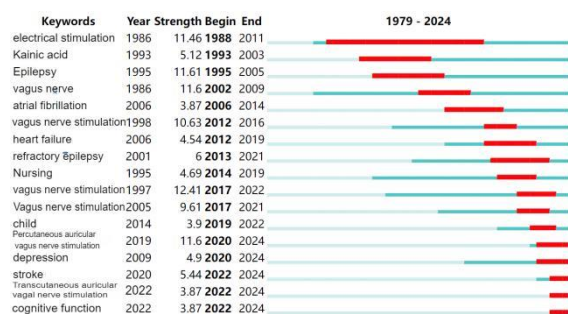


Figure 6: The keywords with the Strongest Citation Bursts

In this study, CiteSpace6.2. R4 software was used to summarize the VNS literature from 1979-2024, summarizing the previous conclusions to help the recent research results. For the time and possible future research hotspots, CiteSpace software should present them through data visualization, and the two complement each other. At the same time, through forming the network co-occurrence map of authors and institutions, CiteSpace software more intuitively shows the cooperation between authors and institutions in a certain field, and provides a clear field pattern for researchers and provides a more intuitive cooperation object. The results showed that the number of research papers published in this field in the visual map of VNS related literature was increasing year by year, indicating that the vagal electrical stimulation has entered the white-hot stage. The author co-occurrence network analysis found that the field has formed a core author group. Rong Peijun, Fang Jiliang, Feng Zhen, Wang Yu, Dong Xiaoyang, He Jiakai, Li Shaoyuan and other authors have a high number of articles. Among them, Rong Peijuns

team is the core team in the field, and its research content is the combination of vagal nerve stimulation, percutaneous nerve stimulation and meridians and acupoints [13], Focusing on VNS treatment-refractory epilepsy, depression, insomnia, and cognitive impairment [14] And other neurological diseases. The remaining authors and their teams are less cooperative. The institutional analysis found that, The main research institution of VNS is the cooperation between China Academy of Chinese Medical Sciences (mainly Institute of Acupuncture and Moxibustion) and its affiliated hospitals, Mainly formed a stable permanent member within the region to cooperate, Form academic barriers at its core, The distribution of research institutions and authors in this field is relatively scattered, And there are few cross-regional studies, Less cooperation with other agencies, Infavorable to the future academic development in the VNS research field, It is suggested that domestic experts and scholars should actively participate in high-level thematic meetings, Promote the close communication between the various teams, The close cooperation between the institutions is pending, There will be a better consensus on the development, outcome and prognosis of such diseases, To jointly promote the development of this field. Keyword analysis found that: (1) high-frequency keywords, in addition to the vagus nerve electrical stimulation, the highest frequency is about epilepsy, refractory epilepsy, percutaneous ear vagus nerve stimulation, vagus nerve stimulation, depression, cognitive function, stroke and other keywords. This indicates that the current research hotspot in this field is the mechanistic analysis of the signaling pathways of VNS in common diseases of the nervous system.(2) Keyword clustering suggests that VNS for cardiovascular diseases such as atrial fibrillation [15], arrhythmia [16], heart failure [17] The action mechanism and efficacy evaluation of VNS in the treatment of epilepsy, refractory epilepsy, depression, cognitive impairment and other diseases were also analyzed.(3) Keywords appear, in recent years, the outbreak point is the percutaneous ear vagus nerve stimulation, depression [18-19], Stroke, etc This is a possible research frontier in the future, and scholars can pay attention to this aspect. In recent years, the content of vagus nerve electrical stimulation therapy is gradually rich, including VNS therapy or combined with other traditional Chinese medicine intervention methods, combined with western medicine drug therapy [20] Is still the future research trend in this field.

5. Future Outlook

Through the relevant literature, we found that in the early stage of the study, mainly basic experiments, vagus nerve stimulation on erythrin [21] The interaction between epilepsy, VNS to treat the disease alone, mostly from the perspective of empirical medicine to give scholars with experience, effective summary, can not explain its treatment mechanism. In recent years, the research on VNS has increased year by year, and the treatment is more specific, targeting different perspectives such as disease period, transformation and damage pathway. However, it cannot express clear therapeutic targets, and the specific links and processes for effective intervention. VNS electrical stimulation therapy is an active and developing research field with broad application prospects and research potential. The application field of VNS will gradually diversify, and may expand to the treatment of more

neuropsychiatric diseases in addition to the existing diseases. As a non-invasive treatment method, VNS has practicality, safety and effectiveness. Compared with drug treatment alone, it has no side effects, improves the penetration rate of clinical non-drug methods to improve sleep, and has obvious social benefits. Non-implantable VNS will become the new direction of research and development to provide safer and more comfortable therapeutic options for patients. In clinical application, the problem of the optimal choice of vagal nerve stimulation and personalized parameter setting are needed to achieve better therapeutic results. VNS can be combined with a variety of acute and chronic cerebral ischemia therapies and conventional rehabilitation therapy for better improvement Nerves after brain injury [22]. And there is research [23] It shows that VNS has a positive regulatory effect on the cholinergic anti-inflammatory pathway, and the interaction between the nervous system and the immune system is crucial for regulating innate immune responses and controlling inflammation. The cholinergic anti-inflammatory pathway is a physiologic neural-immune mechanism that regulates innate immune function and controls inflammation. Compared with the traditional body fluid anti-inflammatory pathway, the cholinergic anti-inflammatory pathway is more direct, more rapid, and more efficient, and can inhibit multiple inflammatory factors simultaneously, with more advantages. Although VNS has achieved good experimental results and feasible theoretical mechanism in animal experiments, the specific mechanism of action needs to be further studied. Vvagnerve stimulation therapy as an emerging treatment in the field of neurorehabilitation [24] Showing great potential and application prospects. Future studies need to focus on its application effect in different diseases and optimize the stimulation parameters [25], Improve the treatment effect, and further explore the mechanism of action, in order to provide patients with more personalized and effective treatment options. With further research and technological advances, VNS is expected to play a greater role in the treatment of neuropsychiatric disorders. The research of vagus nerve electrical stimulation therapy is gradually moving from basic to clinical application, and its efficacy and safety have been more and more recognized. The current research may pay more attention to the optimization of individualized treatment options, the evaluation of long-term efficacy and the exploration of new indications. In the future, it should follow the development trend and conduct more accurate and effective treatment based on the background of big data, artificial intelligence and machine learning, which will have a positive impact on the promotion and development of VNS. In conclusion, the visual analysis of the literature of vagus nerve electroacupuncture therapy with CiteSpace software is of certain clinical significance and help. The disadvantage of this study is that the different software version and parameters may affect the analysis results; meanwhile, there may be omissions when the keywords are combined or excluded. In the future, it can enrich the literature research methods and multi-directional analysis to ensure the comprehensiveness and reliability of the research results.

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