REVIEW
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A comprehensive review of heart rate variability as an indicator in the regulation of the autonomic nervous system by acupuncture: a bibliometric analysis

Yi-Feng Shen[1, 2], Kun Zhu[1, 2], Jun-Long Zhu[1, 2], Xiao-Peng Huang[1], De-Gui Chang[1], Yao-Dong You[1, 2], Dong-Dong Yang[3*]

[1]TCM Regulating Metabolic Diseases Key Laboratory of Sichuan Province, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu 610075, China. [2]Clinical Medicine School, Chengdu University of Traditional Chinese Medicine, Chengdu 610075, China. [3]Department of Neurology, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu 610075, China.

[*]**Corresponding to:** Dong-Dong Yang, Department of Neurology, Hospital of Chengdu University of Traditional Chinese Medicine, No. 37 Shierqiao Road, Jinniu District, Chengdu 610075, China. E-mail: 1241668186@qq.com.

Author contributions

YS and JZ contributed to data collection and verification. XH contributed to the methodology. KZ contributed to data analysis. YS and JZ contributed to writing the original draft. DC and YY contributed to editing, DY contributed to review.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

ANS, autonomic nervous system; HRV, heart rate variability; SNS, sympathetic nervous system; PNS, peripheral nervous system; EA, electroacupuncture; LF, low frequency; HF, high frequency; AF, atrial fibrillation; tVNS, transcutaneous vagus nerve stimulation; VLF, very low frequency; NTS, nucleus of the solitary tract; SDNN, standard deviation of normal to normal intervals; RMSSD, root mean square of successive differences between normal heartbeats; R-Ri, R-R intervals; pNN50, percentage of R-R intervals with duration difference > 50 ms; SDANN, standard deviation of the average NN intervals for each 5 min segment for a 24-hour recording; SD1, the minor axis of the fitted eclipse; SD2, the major axis of the fitted eclipse; taVNS, transcutaneous auricular vagus nerve stimulation; TEA, transcutaneous electrical acustimulation; DMN, default mode network.

Citation

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Abstract

This study sought to conduct a bibliometric analysis of acupuncture studies focusing on heart rate variability (HRV) and to investigate the correlation between various acupoints and their effects on HRV by utilizing association rule mining and network analysis. A total of 536 publications on the topic of acupuncture studies based on HRV. The disease keyword analysis revealed that HRV-related acupuncture studies were mainly related to pain, inflammation, emotional disorders, gastrointestinal function, and hypertension. A separate analysis was conducted on acupuncture prescriptions, and Neiguan (PC6) and Zusanli (ST36) were the most frequently used acupoints. The core acupoints for HRV regulation were identified as PC6, ST36, Shenmen (HT7), Hegu (LI4), Sanyinjiao (SP6), Jianshi (PC5), Taichong (LR3), Quchi (LI11), Guanyuan (CV4), Baihui (GV20), and Taixi (KI3). Additionally, the research encompassed 46 reports on acupuncture animal experiments conducted on HRV, with ST36 being the most frequently utilized acupoint. The research presented in this study offers valuable insights into the global research trend and hotspots in acupuncture-based HRV studies, as well as identifying frequently used combinations of acupoints. The findings may be helpful for further research in this field and provide valuable information about the potential use of acupuncture for improving HRV in both humans and animals.

Keywords: heart rate variability; acupuncture; autonomous nerves system; bibliometric analysis; data mining

Introduction

The autonomic nervous system (ANS) is responsible for regulating various internal bodily functions, such as heart rate, blood pressure, digestion, sweating, and sexual arousal. It consists of three main branches: the sympathetic, parasympathetic, and enteric nervous systems. Typically, these branches have opposing actions. The sympathetic nervous system triggers the "fight or flight" response, while the parasympathetic nervous system promotes the "rest and digest" response. Meanwhile, the enteric nervous system manages the functions of the gastrointestinal tract and operates largely independently [1]. Autonomic disorders can be categorized in several ways, but they generally fall into two types: localized and generalized disorders. Localized disorders affect a specific organ or region of the body, although they may also be part of a larger, generalized disease, such as gustatory sweating in diabetes mellitus. On the other hand, generalized disorders often affect multiple systems, including those responsible for blood pressure control and thermoregulation [2].

Heart rate variability (HRV) is a non-invasive method used to assess the ANS response. HRV is the variation in time between successive heartbeats, which is influenced by the balance between the sympathetic nervous system (SNS) and peripheral nervous system (PNS). A higher HRV indicates a greater influence on the PNS, while a lower HRV indicates a greater influence on the SNS. Thus, HRV can be used as an index of the ANS response to acupuncture. HRV has been also shown to be useful in predicting adverse cardiovascular events [3] and morbidity from common mental and physical disorders [4]. Several metrics can be used to analyze HRV. The most common metrics include time domain, frequency domain, and non-linear dynamics. Time-domain metrics quantify the variability in RR interval measurements, while frequency-domain measurements describe the distribution of power in four frequency bands: ultra-low ($\leq$ 0.003 Hz), very low (0.0033–0.04 Hz), low (0.04–0.15 Hz), and high (0.15–0.4 Hz). The high-frequency spectrum is largely influenced by parasympathetic (vagal) activity, while lower frequency ranges are affected by sympathetic and other factors [4].

Acupuncture is a traditional Chinese medical practice that has gained popularity worldwide for its therapeutic effects. It involves the insertion of thin needles into specific points on the body, known as acupoints, to stimulate the body's natural healing mechanisms. Acupuncture has been used to treat a wide range of health conditions, including those related to the ANS, such as hypertension, heart failure, arrhythmias, migraines, depression, insomnia, dysfunction, indigestion, and constipation. Acupuncture is believed to activate somatic afferents and thereby regulate various autonomic functions. The published literature has focused on the use of acupuncture to regulate cardiovascular disease, gastrointestinal disease, and inflammation [5]. Many acupuncture studies have been conducted to monitor the effect of acupuncture on the ANS using HRV as either a primary or secondary outcome measure. For example, electroacupuncture (EA) treatment at Neiguan (PC6) prevented the abnormally increased ratio of low frequency/high frequency (LF/HF) induced by ACh-$CaCl_2$ administration in atrial fibrillation (AF) rats [6]. Acupuncture has also been found to reduce blood pressure and heart rate in patients with mild hypertension, with LF/HF significantly reduced during acupuncture and HF increased after acupuncture [7]. Several systematic reviews of clinical research on the effect of acupuncture on HRV have been published, including ones by Sanghoon Lee in 2010 [8], Joanne W. Y. Chung in 2014 [9], and Sz Hamvas in 2022 [10].

However, due to the differences in HRV operation methods and index values among studies, the credibility of HRV as an index for acupuncture to affect autonomic nerves is different. Given the significance of acupuncture in regulating the autonomic nervous system and the importance of heart rate variability as a metric, a comprehensive approach is required to fully explore their interrelationship. The purpose of our research is to use literature visualization and data mining methods to analyze the published literature on the effect of acupuncture on HRV, summarize the general situation and research hotspots of the literature, and review the clinical and animal experiments on the effect of acupuncture on HRV to explore the relatively unified HRV measurement method objectively suitable for the evaluation of acupuncture procedures. Bibliometric analysis allows for a systematic overview of existing research, overcoming the limitations of isolated studies. Association rule mining uncovers potential correlations and patterns between acupuncture, heart rate variability, and autonomic nervous system regulation. Network analysis, in turn, visually represents these complex interactions, identifying key nodes and pathways. Collectively, these methods will provide a robust and comprehensive understanding of how acupuncture modulates heart rate variability and its role in the regulation of the autonomic nervous system, thus supporting the clinical application and scientific exploration of acupuncture therapy. This review provides an overview of the current state of research on HRV as an index of the ANS response to acupuncture. It aims to explore the underlying mechanisms and clinical applications of acupuncture in modulating the ANS and improving HRV.

Method

Bibliometric research

A comprehensive literature search was performed in the online databases Web of Science, Scopus, Pubmed, EMBASE, CENTRAL: (*acupuncture* OR acupoint* OR acupressure OR auricular OR acustimulation) AND ((heart rate variab*) OR HRV). The search included papers provided as abstracts from the time the database was created until December 2022. The inclusion criteria were as follows: (1) Human or animal studies of acupuncture using HRV as a primary or secondary indicator. (2) Full text available at the authors' institution. Literature on acupuncture combined with multiple other alternative therapies and clinical study protocols without study outcomes were excluded. The software VOSviewer (v 1.6.18) was used. Disagreements were settled through discussion. We investigated documents and relationships across countries, institutions, and journal, constructed visualization maps with keywords and references. Important keywords generated through literature statistics and visualization, research hotspots, and developed directions were read and summarized in the discussion section.

Association rule mining and network analysis study of acupuncture prescriptions in human

After retrieving relevant literature, we reviewed both abstracts and full texts and identified human studies that reported changes in HRV values and acupoint prescriptions. To identify frequently used acupoint combinations consisting of two or three acupoints, we employed association rule mining. For the association rule mining analysis, we used the Apriori algorithm, which was implemented in IBM SPSS Modeler 14.1. Additionally, we used Heml1.0.3.7 (http://hemi.biocuckoo.org/) to generate a heat map displaying the co-occurrence matrix of acupoints. We utilized Gephi 0.9.2 (https://gephi.org/) for network image visualization, specifically employing the "Fruchterman Reingold" algorithm to establish the central aggregation distribution model, and the "k-core" method to analyze the core acupoints [11].

Result

Bibliometric analysis

There are 536 publications in total, the publication time trend for acupuncture studies based on HRV is shown in Figure 1. from one in 1995 to 44 in 2022, with a faster growth rate of publications in this field from 2007 to 2022 shown in Figure 1A. Analyses of global acupuncture-related HRV research are shown in Table 1 and Table 2. Fifty countries and regions have contributed to publications on this topic. China (177 publications, 2505 citations) provided the most articles, followed by the United States (122 publications, 2410

citations), South Korea (51 publications, 661 citations), Austria (42 publications, 582 citations), and Japan (40 publications, 463 citations). There is a close collaboration between China and the United States, and between China and Austria in the study of HRV in acupuncture, at the same time, the first group of Asia, the United States and Australia, and the second group of Canada, Brazil and Europe formed a regional cooperation group show in Figure 1B. There were 671 institutes engaged in this sector. The most publications were produced by Medizinische Universität Graz (29 publications, 365 citations), followed by Kyung Hee University (25 publications, 523 citations) and China Academy of Chinese Medical Sciences (23 publications, 318 citations). Most of the studies are published in complementary alternative medicine journals, for example *Evidence-Based Complementary and Alternative Medicine* (53 publications, impact factor 2.6) publishes the largest number of publications in this research area. Some of these publications were also published in neuroscience-related publications such as *Autonomic Neuroscience-Basic & Clinical*, *Neurogastroenterology and Motility,* and *Frontiers in Neuroscience*. This indicates that acupuncture research based on HRV is also recognized by journals and scholars in the field of neuroscience. The keywords were analyzed according to their frequency of occurrence. Heart-rate-variability, acupuncture, electroacupuncture, stimulation, ANS, electrical-stimulation pain, mechanisms, and stress were the top 10 keywords in terms of frequency of occurrence. It indicates that electrical stimulation is the main stimulation modality in studies in this field and these studies are mainly related to the ANS. Analysis of disease keywords by frequency of occurrence revealed that HRV-related acupuncture studies were mainly related to pain, inflammation, emotional disorders (stress, anxiety, depression), gastrointestinal function, and hypertension shown in Figure 1C. The top 100 citations in this field are shown in Supplementary Table S1, and the most cited literature is Clancy, JA 2014 [12]. This literature reported that non-invasive vagal stimulation increased HRV in healthy participants and showed a decreased muscle sympathetic nerve activity by microneurographic recordings, which confirms that transcutaneous vagus nerve stimulation (tVNS) can increase HRV and decrease sympathetic outflow. The top 10 citations also focused on evidence showing that acupuncture modulates autonomic nerve activities [13–15], inhibits inflammation [16], improves gastrointestinal motility [17], improves cardiac function [18], and fatigue [19], and treats polycystic ovary syndrome [20, 21].

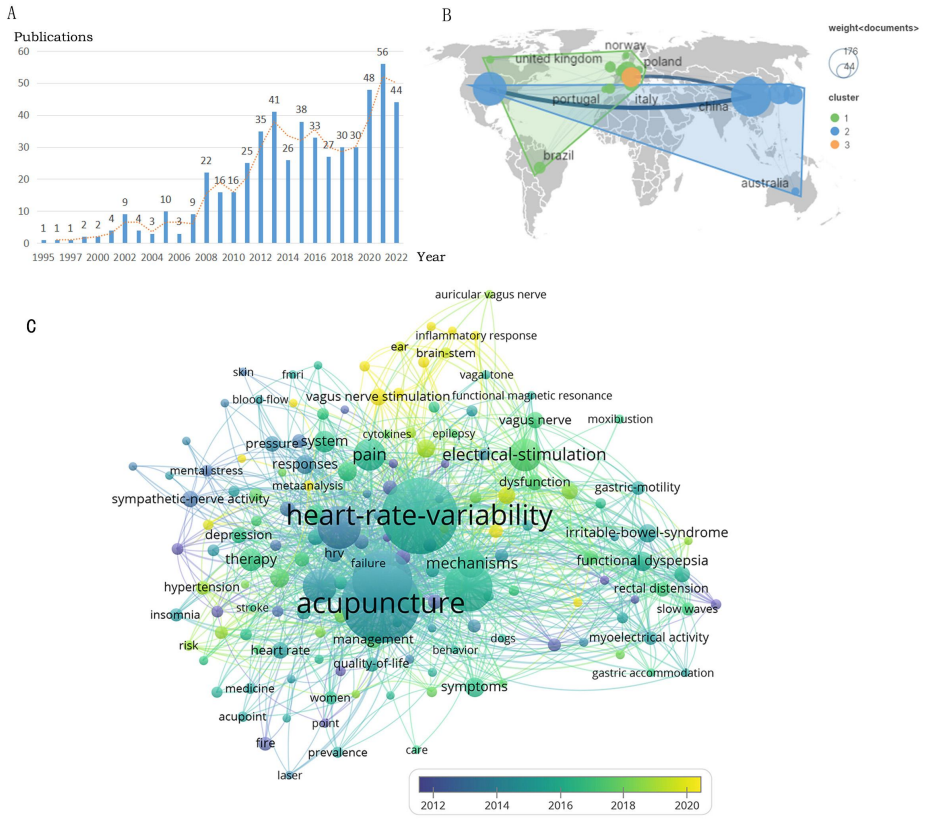

Figure 1 Trend of publications on acupuncture improving HRV. HRV, heart rate variability.

Table 1 Nation, institutions, journal rankings for acupuncture to improve HRV related research

Rank	Top 10 countries in publications			Top 10 institutions in publications			Top 10 journal in publications			
	Country	Documents	Citations	Institutions	Documents	Citations	Journal	Documents	IF (2022)	JCR
1	China	177	2505	Med Univ Graz	29	365	Evidence-Based Complementary and Alternative Medicine	53	2.650	Q3
2	United States	122	2410	Kyung Hee Univ	25	523	Medical Acupuncture	18	N/A	N/A
3	South Korea	51	661	China Acad Chinese Med Sci	23	318	Acupuncture in Medicine	14	1.976	Q3

HRV, heart rate variability; IF, impact factor; JCR, journal citation reports.

Table 1 Nation, institutions, journal rankings for acupuncture to improve HRV related research (*continued*)

Rank	Top 10 countries in publications			Top 10 institutions in publications			Top 10 journal in publications			
	Country	Documents	Citations	Institutions	Documents	Citations	Journal	Documents	IF (2022)	JCR
4	Austria	42	582	Johns Hopkins Univ	17	195	Journal of Acupuncture and Meridian Studies	14	N/A	N/A
5	Japan	40	463	China Med Univ	13	172	American Journal of Chinese Medicine	13	6.005	Q1
6	Germany	37	597	Nanjing Med Univ	12	160	Autonomic Neuroscience-Basic & Clinical	12	2.355	Q4
7	Italy	20	349	Korea Inst Oriental Med	10	136	Neurogastroenterology and Motility	12	3.960	Q2
8	Brazil	15	176	Harvard Med Sch	9	65	Journal of Alternative and Complementary Medicine	11	2.381	Q3
9	United Kingdom	13	638	Johns Hopkins Ctr Neurogastroenterol	9	202	Frontiers in Neuroscience	10	5.152	Q2
10	Spain	11	248	Taipei Vet Gen Hosp	9	144	American Journal of Physiology-Gastrointestinal and Liver Physiology	9	4.871	Q1

HRV, heart rate variability; IF, impact factor; JCR, journal citation reports.

Table 2 Key words rankings for acupuncture to improve HRV related research

Keywords	Occurrences	Disease related keywords	Occurrences
Heart-rate-variability	314	Pain	45
Acupuncture	199	Stress	28
Electroacupuncture	89	Functional dyspepsia	20
Stimulation	73	Anxiety	19
Autonomic nervous system	50	Inflammation	18
Electrical-stimulation	46	Irritable-bowel-syndrome	18
Pain	45	Blood-pressure	14
Mechanisms	36	Depression	14
Stress	28	Hypertension	11
Therapy	26	Insomnia	10

HRV, heart rate variability.

Acupuncture prescriptions analysis

After the abstract and full-text screening, we included 171 studies in human in Supplementary Table S2. Our study included 37 acupoints, which had a total frequency of 414 mentions. The five most frequently used acupoints were PC6, Zusanli (ST36), auricular, Hegu (LI4), and Shenmen (HT7) shown in Figure 2A. We used permutation combination and frequency analysis to generate a co-occurrence matrix of acupoints, which is shown in Figure 2. The most commonly paired acupoints were PC6 and ST36, with a co-occurrence frequency of over 50% shown in Figure 2B. To explore the core acupoints for HRV regulation, we utilized the K-core method. The core acupoints were PC6, ST36, HT7, LI4, Sanyinjiao (SP6), Jianshi (PC5), Taichong (LR3), Quchi (LI11), Guanyuan (CV4), Baihui (GV20) and Taixi (KI3) show in Figure 2C. We summarize the efficacy of the frequently reported acupoints and their corresponding neuroanatomical locations in the Table 3.

Our analysis also included 46 reports of animal experiments on acupuncture and HRV in Supplementary Table S3. Among these reports, ST36 was the most commonly utilized acupoint, with 28 studies reporting its use. PC6 was the second most commonly used acupoint, with 16 mentions, followed by Baihui (DU20), which was reported six times. In contrast, HT7 and LR3 were reported three and four times, respectively. Figure 3 illustrates the marked positions of the most frequently utilized acupoints on rats.

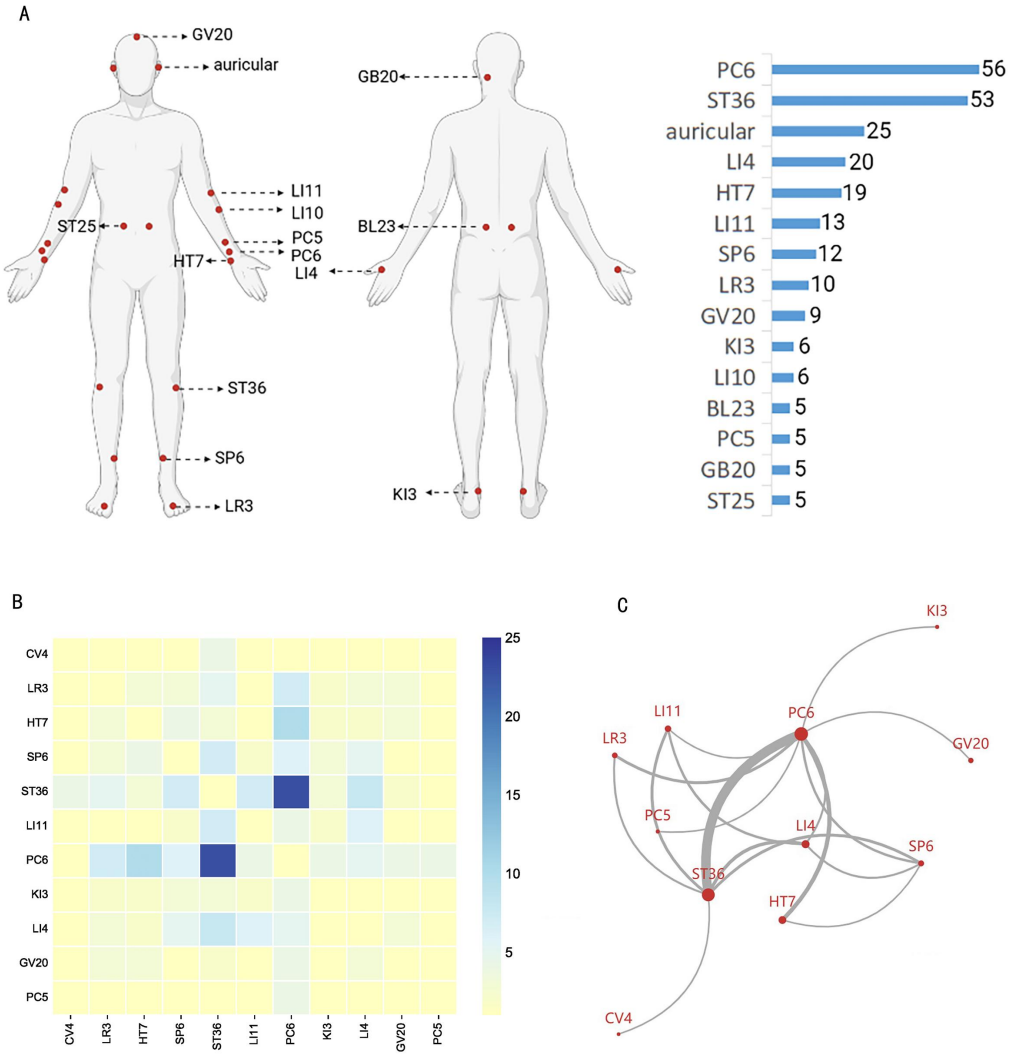

Figure 2 Acupuncture prescriptions analysis on HRV. HRV, heart rate variability.

Table 3 Efficacy and anatomical location of main acupoints on HRV

Acupoints	Acupoints name	Frequency	Therapeutic effect in traditional Chinese medicine	Nerves anatomy at acupoints
PC6	Neiguan	56	Heartache, palpitations, chest pain, stomach pain, vomiting, insomnia, mental illness, depression, dizziness, stroke hemiplegia, asthma, migraine, elbow, and arm pain.	Medial cutaneous nerve of forearm, palmar cutaneous branch of median nerve, volar interosseous nerve of forearm in deep layer
ST36	Zusanli	53	Stomach pain, vomiting, abdominal distension, diarrhea, dysentery, constipation, intestinal abscess, leg pain, mental illness, fatigue.	Cutaneous branch of lateral sural cutaneous nerve and saphenous nerve, deep peroneal nerve in the deep layer
auricular	Erxue	25	Insomnia, motion sickness, tinnitus, myopia, obesity, withdrawal syndrome and various painful diseases.	Ear branch of vagus nerve
LI4	Hegu	20	Headache, eye inflammation, nosebleed, toothache, stroke, sore throat, abdominal pain, constipation, irregular menstruation.	The dorsal palmar nerve of the superficial branch of the radial nerve, and the palmar proper nerve of the median nerve is in the deep layer
HT7	Shenmen	19	Heart disease, upset, palpitations, forgetfulness, insomnia, mental illness, chest pain.	Medial cutaneous nerve of forearm, ulnar nerve
LI11	Quchi	13	Sore throat, toothache, eye infection, rash, upper limb disability, arm pain, abdominal pain, vomiting, high blood pressure, mental illness.	Dorsal cutaneous nerve of forearm, radial nerve in deep layer

HRV, heart rate variability.

Table 3 Efficacy and anatomical location of main acupoints on HRV (*continued*)

Acupoints	Acupoints name	Frequency	Therapeutic effect in traditional Chinese medicine	Nerves anatomy at acupoints
SP6	Sanyinjiao	12	Abdominal distension, diarrhea, irregular menstruation, infertility, nocturnal emission, impotence, enuresis, insomnia, lower limb disability.	Medial cutaneous nerve of the calf, deep posterior with the tibial nerve
LR3	Taichong	10	Headache, dizziness, irregular menstruation, dysuria, enuresis, mental illness, rib pain, abdominal distension, vomiting, sore throat, eye infection, knee pain, foot swelling, lower limb disability.	Dorsal plantar nerve of deep peroneal nerve, medial plantar nerve of tibial nerve deep
GV20	Baihui	9	Headache, dizziness, palpitations, forgetfulness, stroke, mental illness, tinnitus, nasal congestion, rectal prolapse, hemorrhoids, diarrhea.	Greater occipital nerve and frontal nerve branches
KI3	Taixi	6	Headache, dizziness, sore throat, toothache, tinnitus, cough, shortness of breath, chest pain, diabetes, irregular menstruation, insomnia, forgetfulness, nocturnal emission, impotence, frequent urination, low back pain, cold lower limbs, ankle pain.	Medial cutaneous nerve of leg, tibial nerve
LI10	Shousanli	6	Toothache, upper limb disability, abdominal pain, diarrhea.	Dorsal cutaneous nerve of forearm and deep branch of radial nerve
BL23	Shenshu	5	Enuresis, seminal emission, impotence, irregular menstruation, edema, tinnitus, deafness, low back pain.	The lateral branch of the posterior branch of the first lumbar nerve, the deep layer is the first lumbar plexus
PC5	Jianshi	5	Heartache, palpitations, stomach pain, vomiting, irritability, mental illness, elbow pain, arm pain.	The medial cutaneous nerve of the forearm, the lateral cutaneous nerve of the forearm, the palmar cutaneous branch of the median nerve below it, and the deepest layer is the volar interosseous nerve of the forearm
GB20	Fengchi	5	Headache, dizziness, neck pain, eye disease, rhinitis, nosebleed, deafness, stroke, facial paralysis, cold.	Lesser occipital nerve branch
ST25	Tianshu	5	Bloating, abdominal pain, constipation, diarrhea, irregular menstruation.	Tenth intercostal nerve branch

HRV, heart rate variability.

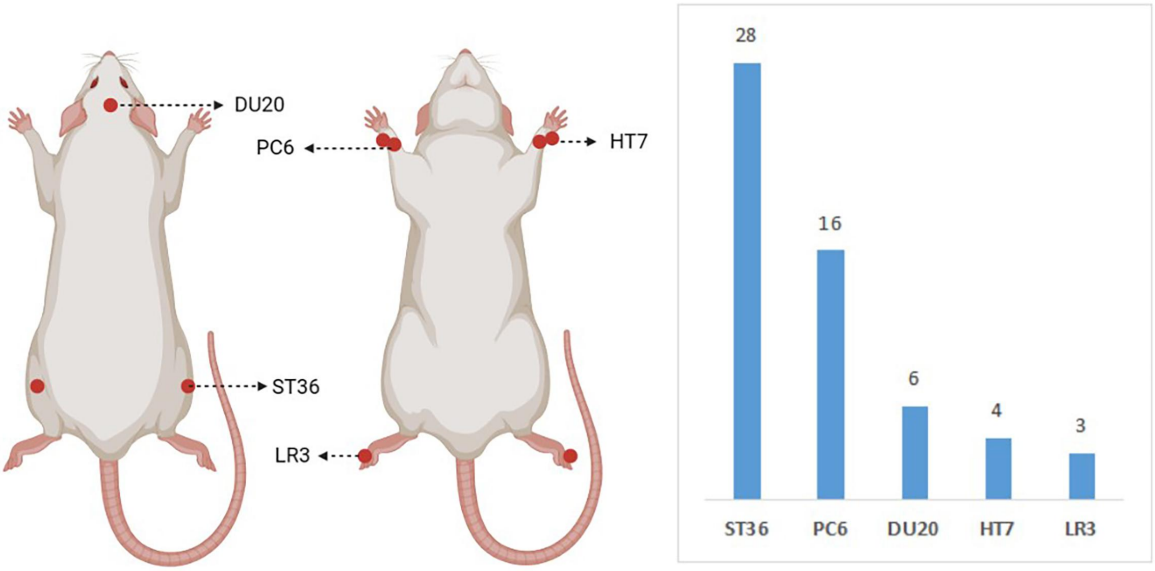

Figure 3 Acupoints count on HRV of animal experiments. HRV, heart rate variability.

HRV changes in human with acupuncture

Reviewing the HRV publications of clinical trials of acupuncture treatment in humans, (1) the immediate effects of acupuncture on HRV of healthy people, (2) the immediate effects of acupuncture on HRV of patients, and (3) the long-term effects of acupuncture on HRV of patients were reported. (1) Experiments have confirmed the immediate effect of acupuncture on HRV changes. The LF/HF value decreased in health volunteers is observed during acupuncture [22]. After treatment, the increase in HF and the decrease in LF/HF have also been reported [23], and with the decrease in blood pressure and heart rate [24], the peripheral pulse range and blood flow rate increase [25, 26]. Even if the needle is pierced into acupoints without rotation and insertion stimulation, the change of HRV can last for 5–10 minutes after removing acupuncture [27, 28]. Some studies have found that the improvement effect of HRV has little correlation with deqi (the sensation felt by patients during acupuncture treatment, indicating effective stimulation of Qi flow within the body) [29]. (2) In patients, this acupuncture can also be seen to improve the immediate effect of HRV. Acupuncture showed a significant immediate effect (30 minutes after receiving acupuncture) in reducing dizziness and vertigo discomfort and visual analogue scale, accompanied by a significant increase in HF [30]. After receiving acupuncture for 30 minutes in patients with septic gastrointestinal dysfunction, acupuncture can regulate the downward trend of vagal tone caused by gastric distension and the upward trend of sympathetic tension caused by gastric distension, the downward trend of HF and the upward trend of LF and very low frequency (VLF) [31]. (3) Acupuncture can have a sustained alteration in patients with HRV changes. Acupuncture may reduce blood pressure in patients with prehypertension and stage I hypertension, and the HF increased at week 4 and week 8 after acupuncture treatment twice a week for 8 consecutive weeks [32]. Patients with mild depression or anxiety disorder had increased HF, and decreased heart rate and LF after receiving 9 sessions of acupuncture [33]. Patients with migraine who received 12 sessions of acupuncture treatment, the clinical responders (with at least 50% reduction of migraine attacks) exhibited a decrease of LF [34].

Studies have shown a correlation between vagal enhancement (reduced LF/HF) during acupuncture treatment and a positive response to acupuncture. Patients who respond to acupuncture tend to show a decrease in LF/HF during acupuncture treatment, while non-responders tend to have no change or an increase in LF/HF [35]. However, the therapeutic effects of acupuncture are not directly related to changes in HRV. Some studies have reported improvements in pain [36] and menopausal symptom scores [37], these symptom score improvements were accompanied by no HRV changes or little association. The systematic review from Sanghoon Lee in 2010 [8] concluded that there was no clear evidence indicating any specific effect of acupuncture on HRV. Another systematic review by Joanne W. Y. Chung in 2014 [9] analyzed studies of healthy populations, patients, and combined effect sizes of both groups. The review found that acupuncture reduced LF and LF/HF ratios in non-healthy subjects, but had no effect on the HF component of HRV. A third systematic review by Sz Hamvas in 2022 [10] differentiated the effect sizes of crossover and parallel studies, and found that real acupuncture was more effective than placebo acupuncture at increasing parasympathetic tone. These reviews demonstrate the need to consider various factors in the interpretation of research findings, such as the type of population studied and the experimental design used.

HRV changes in animals with acupuncture

The autonomic nervous system plays a vital role in regulating the cardiovascular system, which includes the heart, blood vessels, and blood pressure. Acupuncture has been shown to have a beneficial effect on the autonomic nervous system, particularly in regulating the balance between sympathetic and parasympathetic nervous system activity. Animal studies have shown that acupuncture can modulate the activity of the sympathetic nervous system, reduce sympathetic nerve activity, and enhance parasympathetic nervous system activity. This may be responsible for the beneficial effects of acupuncture on a variety of cardiovascular conditions, including hypertension, myocardial ischemia, atrial fibrillation, and cerebrocardiac syndrome. Acupuncture at LR3 has been shown to reduce sympathetic activity (reduction in LF/total power and LF/HF) and improve baroreflex sensitivity in renovascular hypertensive rats, possibly by upregulating the nucleus of the solitary tract (NTS) alpha-2 adrenergic receptor expression and functional activities [38]. Acupuncture has been shown to improve heart rate variability indices, standard deviation of normal to normal intervals (SDNN) increased and LF/HF decreased, and regulate β-adrenergic receptor expression [39]. This may contribute to the beneficial effects of acupuncture on hypertension and other cardiovascular conditions. In myocardial ischemia, acupuncture intervention has been shown to improve cardiac parasympathetic tension and balance sympathetic/parasympathetic nerve activities (HF increased, LF/HF decreased), thereby reducing ischemic myocardial injury [40]. Similarly, in atrial fibrillation, acupuncture at PC6 has been shown to reverse the increased sympathetic and decreased vagal nerve activity (HF increased, LF and LF/HF deceased) [41]. Acupuncture has also been shown to be effective in reducing cardiac excitability induced by left stellate ganglion stimulation, which is associated with a correction of cardiac sympathovagal balance (LF and LF/HF deceased) [42]. In addition, acupuncture has been shown to be a neuroprotective therapy for cognitive dysfunction induced by acute myocardial ischemia-reperfusion by balancing the autonomic nervous system. Acupuncture has also been shown to improve cerebrocardiac syndrome by reducing cerebral glutamate and aspartic acid levels and suppressing the excitability of sympathetic nerves (LF/HF deceased) [43].

The digestive system and the autonomic nervous system have a complex and bidirectional relationship, with the autonomic nervous system playing a crucial role in regulating gastrointestinal function and maintaining homeostasis. Research has shown that stress is an independent factor that can cause and exacerbate gastrointestinal symptoms, including visceral pain. In a rodent model of functional dyspepsia, acute restraint stress induces gastric dysrhythmia, which can be improved by EA at ST36 through central and autonomic pathways, including the NTS and vagal efferent pathway [44]. Moreover, EA has been found to ameliorate gastric hypersensitivity in iodoacetamide-treated rats, and this effect may be attributed to improved sympathovagal balance (HF increased, LF and LF/HF deceased) and a decrease in stress hormones [45, 46]. In dogs, EA has been shown to accelerate gastric emptying of liquids and potentially treat gastroparesis by improving gastric slow wave rhythmicity and antral contractile activity, likely involving the vagal pathway (HF increased, LF/HF deceased) [47]. Additionally, EA at ST36 has been found to restore rectal distension impairment in both colonic contraction and transit by enhancing vagal activity (HF increased, LF deceased) and mediated via the cholinergic pathway in dogs [48]. EA at ST36 and PC6 can suppress colorectal distension-induced increase of mean arterial pressure, heart rate, and LF/HF, indicating the beneficial effects of EA in relieving visceral pain and mediating the autonomic nervous system [49]. EA at ST-36 has demonstrated great therapeutic potential in treating opioid-induced constipation by improving the transit of every organ along the gut via autonomic mechanisms (HF increased, LF and LF/HF deceased) in both normal rats and rats with Loperamide-induced constipation [50]. Chemotherapy-associated dyspepsia syndrome is a severe side effect of cancer treatment, but EA has been shown to ameliorate dyspepsia symptoms and improve gastric dysmotility induced by Cisplatin through vagal (HF increased, LF/HF deceased) and gastrointestinal hormonal mechanisms [51]. In diabetic rats, EA at ST36 has been found to improve gastric dysrhythmia, delayed gastric emptying and intestinal transit, and impaired accommodation, mainly mediated via the vagal pathway (HF increased, LF/HF deceased) [52]. EA at ST36 and PC6 has been shown to have a prokinetic effect on small intestinal

transit and gastric emptying, regulatory effects on small intestinal slow waves, and an analgesic effect on postoperative pain, possibly mediated via autonomic mechanisms (HF increased, LF/HF deceased) [53].

Acupuncture has been demonstrated to modulate the sympathovagal balance and reduce stress-induced physiological and behavioral responses in various animal models. In horses [54] and dogs [55] exposed to startle or sounds of thunder, acupuncture resulted in a shift towards parasympathetic modulation and decreased the prompt increase in LF/HF ratio and cortisol levels or cardiac interval spectrum, respectively. However, this acupuncture treatment modality did not observe acute HRV changes in healthy horses without startle [56]. In addition to reducing sympathetic tone and decreasing heart rate in polycystic ovary syndrome rats [57], EA has been shown to have anti-inflammatory effects in obese rats by enhancing vagal activity (LF/HF deceased) and promoting the expression of 7nAChRs and Ach in the mesenteric white adipose tissues. This suggests that EA may be a promising treatment option for individuals with polycystic ovary syndrome or obesity-related inflammation or obesity [58, 59]. Acupuncture also showed potential in alleviating clinical signs of tracheal collapse in dogs, reducing malondialdehyde levels and improving sympathovagal balance (root mean square of successive differences between normal heartbeats (RMSSD), percentage of R-R intervals (R-Ri) with duration difference $>$ 50 ms (pNN50), and HF increased, LF/HF deceased) [60].

Discussion

General trends in publications

The current study aimed to investigate the global research trends, publication patterns, and key topics related to acupuncture research based on HRV. The results showed a notable growth in publications on this topic, with a faster growth rate observed between 2007 and 2022. The analysis of global research revealed that China and the United States were the leading contributors to HRV-related acupuncture research. Moreover, close collaboration was observed between China and the United States and between China and Austria in this field. The study also revealed that complementary and alternative medicine journals were the primary publishers of these studies, but a few publications were also published in neuroscience-related journals. The analysis of keyword frequency indicated that electrical stimulation was the primary stimulation modality used in these studies, and the main topics were related to pain, inflammation, emotional disorders, gastrointestinal function, and hypertension. The top 10 citations in this field were also identified, with the most cited literature reporting on the efficacy of non-invasive vagal stimulation in increasing HRV and decreasing sympathetic outflow. Overall, the study provides valuable insights into the current research trends and knowledge gaps related to acupuncture research based on HRV, which may guide future research in this area.

Autonomous nerve function and HRV indicator

Several methods have been developed to quantify autonomic nerve dysfunction. These methods primarily assess the autonomous nerve function of cardiovascular and sweat. HRV can be measured during rest, while sympathetic nerve skin reactions can be recorded [61]. Other techniques include measuring plasma norepinephrine concentration, discharge rate on the muscle sympathetic nerve fiber, the sensitivity of α and β adrenaline in the heart and blood vessels, and the conduction speed of the vagus nerve fiber change [62]. In addition to the previously mentioned methods for quantitatively assessing autonomic nerve dysfunction in animals, several other techniques are also available. One such method is baroreflex sensitivity, which measures the sensitivity of baroreceptors located in blood vessels that detect changes in blood pressure. The respiratory sinus arrhythmia is another useful indicator of autonomic function, which measures the variation in heart rate that occurs during breathing. Plasma catecholamines, including epinephrine and norepinephrine, can also be used to assess sympathetic activity, while gastric motility can be measured to provide insight into autonomic function in the gastrointestinal tract. Finally, the pupillary light reflex, which measures changes in pupil size in response to light stimulation, can also be used to evaluate autonomic function in animals [63–65].

HRV periods can be divided into three categories: long-term ($\geq$ 24 hours), short-term (5 min), and ultra-short-term ($<$ 5 min) [66, 67]. HRV can be analyzed using a variety of time-domain, frequency-domain, and non-linear parameters that are derived from the electrocardiogram generated RR interval signal. In the time domain, statistical indices such as R-Ri translate fluctuations in the duration of the cardiac cycle into means. The statistical indices in the time domain include SDNN, standard deviation of the average NN intervals for each 5 min segment for a 24-hour recording (SDANN), RMSSD, and pNN50. While SDNN and SDANN indicate both sympathetic and parasympathetic activities, they cannot distinguish between changes in HRV that are due to increased sympathetic tone or withdrawal of vagal tone. In contrast, RMSSD and pNN50 indices are representative of parasympathetic activity. The sympathetic index is another measure of sympathetic nervous system activity, which is derived from the RR interval histogram. Non-linear methods such as the Poincare plot can also be used to measure autonomic activity. The minor axis of the fitted eclipse (SD1) represents the PNS, while the major axis (SD2) is influenced by both the SNS and PNS activity, and their ratio (SD2/SD1) represents the autonomic balance. One can obtain frequency-domain parameters from spectral analysis of the RR interval signal. These parameters include VLF, LF, and HF bands. The VLF band is influenced by thermal and hormonal controls, along with vasomotor activity, and is not associated with the autonomic nervous system. The HF band, on the other hand, represents parasympathetic activity. The LF band is influenced by both sympathetic and parasympathetic activity, and the LF/HF ratio is used as an indicator of autonomic balance [68, 69].

The literature reviewed focused primarily on studying the immediate effects of acupuncture on heart rate variability in humans, some studies employed electrocardiogram to monitor changes in short-term HRV, while others used Holter with long-term HRV to report the long-term effects. The animal studies mostly used short-term (5 min) measurements of heart rate variability before and after acupuncture treatment while under anesthesia. Other studies involved implanting sensors subcutaneously in awake animals to assess changes in heart rate variability. Non-invasive experiments in animals such as horses or dogs trained the animals to undergo heart rate variability assessment using electrocardiography while conscious. Most studies used the numerical changes of LF, HF and LF/HF to measure the functional changes of ANS.

Analysis of acupoint prescriptions for regulating HRV

The present study aimed to identify the most frequently used acupoints for HRV regulation through data mining and review of existing literature. In the acupoint prescription statistics, the top 5 acupoints found to be the most frequent are PC6, ST36, auricular point, LI4 and HT7. We found that most of the points with variable effects on HRV were in the head and extremities. While the selection of acupoints is founded on the principles of traditional Chinese medicine, the spatial arrangement of such acupoint treatment sites bears certain similarities to those of peripheral nerve stimulation and transcutaneous electrical nerve stimulation. The anatomic locations of the PC5 and PC6 acupoints fall within the median nerve innervation area. Extensive literature has established the efficacy of median nerve stimulation in regulating ANS dysfunction, including conditions such as hypoxia, post-operative recovery following heart valve replacement, ischemia, and cardiac contractility [70]. ST36 acupoint is located in the deep peroneal nerve area. Research has shown that the neural regulation of the deep peroneal nerve can stimulate renal nerve activity and arterial inhibition in spontaneously hypertensive rats. Despite this, peroneal nerve stimulation is predominantly used for lower limb function recovery in clinical practice and is rarely used to treat other medical conditions [71]. Posterior tibial nerve stimulation is similar to SP6, KI3 points, reported improvements in

constipation and urination [72, 73]. Transcutaneous auricular vagus nerve stimulation (taVNS), which stimulates the auricular branch of the vagus nerve following a well-defined neuroanatomical pathway, holds the potential for therapeutic efficacy by eliciting changes in HRV resulting from transient alterations in parasympathetic-vagal cardiac activity. This approach bears some resemblance to the treatment of auricular points in Chinese medicine, although in traditional Chinese medicine theory, the auricle is partitioned into distinct regions that are believed to be associated with the treatment of specific diseases [74].

Other types of acupoints stimulation

In Chinese medicine and acupuncture, early texts mention tactile stimulation of the auditory meatus. Auricular acupuncture, which mimics tVNS, is reported to be effective in treating insomnia and relieving acute and chronic pain, as confirmed by numerous systematic reviews. The similarities between auricular acupuncture and neuromodulation therapies such as tVNS suggest that they may share common mechanisms of action [75]. In recent studies, auricular stimulation at acupuncture points 2.5 Hz resulted in significant improvements in patients with HRV, increased parasympathetic vagal tone (HF) by 56% and reduced sympathetic stress [76]. Another study demonstrated that taVNS can increase the activity of the vagus nerve and regulate the balance of the autonomic nerve function in reducing gastric sensitivity in rats with functional dyspepsia, both taVNS and acupuncture at the ST36 acupoint have similar effects in regulating vagus nerve function [77]. Auricular acupressure has also been reported to improve HRV in patients with hypertension [78], irritable bowel syndrome [79], and insomnia [80]. While traditional acupuncture involves the insertion of needles into the skin and muscles, research has shown that the acupoint-modulating effect on the ANS is also present in needle-free transcutaneous electrical stimulation [81] and laser acupuncture [82, 83]. Transcutaneous electrical acustimulation (TEA) can reduce sympathetic excitation and improve the sympatho-vagal balance in different clinical conditions. TEA at PC5 and PC6 can improve the autonomous nerve balance of the heart transplant, and SDNN increases during TEA and recovery [84]. TEA at PC6 and ST36 can improve gastrointestinal function and visceral hypersensitivity in patients, increase HF and improve LF/HF ratio [85, 86]. Studies compared the needle puncture and electricity stimulation in TEA found that there was no difference in the improvement of HRV indicators between the two methods, both puncture and electrical current can cause changes in HRV, found that needleless TEA at ST36 is as effective as EA in ameliorating intestinal hypomotility rat caused by rectal distention [87, 88].

Acupoint specificity

The effect of acupuncture on the ANS HRV varies depending on the specific acupoints used. For instance, the Zhongchong (PC9) and Zhongzhu (TE3) have been found to increase LF or LF/HF (e.g., sympathetic activity), while Guanchong (TE1) and PC5 increase HF (e.g., parasympathetic activity) in HRV [89]. The modulating effect of acupuncture on HRV, however, is not only dependent on the stimulation point, but also on the functional status of the subjects. The study has employed healthy volunteers to receive acupuncture intervention in both fatigue and non-fatigue states, and found that acupuncture in a state of fatigue can increase HF, reduce LF, and decrease LF/HF, but these changes are not as evident in a non-fatigue state [90]. Different stimulation intensities can cause different results. In healthy volunteers, it was found that ST36-37, 2 Hz EA can activate the parasympathetic system (increase HF), and 15 Hz EA activates the sympathetic system (increase LF) [91]. Another study also found that low-frequency 2 Hz EA can increase HF more than high-frequency 100 Hz EA [92]. The effect of EA at ST36 on gastric motility in healthy rats is associated with its stimulation of vagal activity. Conversely, the inhibitory effect of EA at Tianshu (ST25) on gastric motility is linked to its stimulation of sympathetic nerve activity [93]. After EA in healthy rabbits at the wrist (Shenmen, HT7), elbow (Shaohai, HT3) or axils (Jiquan, HT1) sections of heart meridian, the LF/HF of power spectrum was decreased, with the decrease being most significant at the wrist section and least significant at the axils section [94].

The mechanism of acupuncture on HRV

Some studies have detected the brain functional magnetic resonance imaging and HRV at the same time, speculating that acupuncture changes the HRV's brain functional region change mechanism. Acupuncture was found to enhance connectivity in the hippocampal formation of the default mode network (DMN), with a negative correlation observed between acupuncture-induced increases in sympathetic-related HRV metric and DMN connectivity, and a positive correlation observed between acupuncture-induced increases in parasympathetic-related HRV metric and DMN connectivity [95]. A study was conducted to investigate the neuronal correlates of sensations and autonomic reactions during acupuncture by combining brainstem-sensitive functional magnetic resonance imaging with heart rate recording and time-resolved rating of the needling sensation. The results indicated that on the cortical level, the needling sensation activated typical pain-related areas, including the ventromedial and dorsolateral prefrontal cortex and perigenual anterior cingulate cortex, which were further involved in mediating the heart rate response. Furthermore, the study found that the needling sensation activated the nuclei of the descending pain control system in the brainstem, and identified a network of hypothalamus, periaqueductal gray, rostral ventromedial medulla, and ventrolateral medulla as the source of the heart rate changes [96]. Acupuncture can modulate the itching response induced by histamine in healthy volunteers. In experiments, it was observed that HF involved in parasympathetic activation was increased, and LF and LF/HF were decreased. This mechanism is related to the putamen and the posterior part of the midcingulate cortex [97]. Animal studies have shown that EA treatment can activate neurons in the nucleus ambiguus and enhance cardiac parasympathetic tone, balancing cardiac sympathetic/parasympathetic nerve activities to improve ischemic myocardial injury in myocardial infarction rats [40]. In rats with AF, EA at PC6 was found to have the potential to reverse the increased sympathetic and decreased vagal nerve activity by regulating the expression of c-Fos in various brain regions. The downregulation of c-Fos expression in the paraventricular nucleus, rostral ventrolateral medulla, and dorsal motor nucleus of the vagus, along with the upregulation of c-Fos expression in the nucleus ambiguus, may contribute to the modulation of autonomic nervous system activity by EA at PC6 in AF rats [41]. In renovascular hypertensive rats, EA at LR3 was found to enhance baroreflex sensitivity and decrease sympathetic activity, potentially through the upregulation of NTS alpha-2 adrenergic receptor expression and activity that had been decreased [38]. The modulation of the ANS during stress responses has been linked to the frontal lobe. Acupuncture has been shown to decrease the LF/HF ratio and increase HF power. These changes in ANS activity are accompanied by alterations in cerebral blood oxygenation, as evidenced by changes in oxyhemoglobin levels in the bilateral prefrontal cortex [98]. Acupuncture has also been shown decreasing β1-AR expression and improving β2-AR expression following renal sympathetic activation through enhanced renin release to improve HRV indices, such as SDNN and LF/HF [39]. During acupuncture, supraspinal reflection appeared to be the primary factor in altering ANS function, while electroencephalogram activity indicating cortical relaxation and vigilance played a secondary role [99]. When laser acupuncture was applied below the level of injury among patients with complete spinal cord injury, there was no observed physiological effect on heart rate variability, whereas healthy individuals showed the opposite pattern. This comparison between pre- and post-treatment data suggests that the effect of laser acupuncture on heart rate variability is dependent on the presence or absence of a spinal cord injury [100]. Furthermore, acupuncture can mediate HRV even after pharmaceutical blocking (injection of atropine and β-blocker) of autonomic function in animals, indicating that its effects on HRV are not solely reliant on the autonomic nervous system, but also involve the central nervous system [101].

Limitation

The study is limited by the search terms used to identify relevant literature. The search terms may have inadvertently excluded some relevant publications, leading to bias in the analysis. Future studies could use systematic review methods to identify relevant literature, reducing the risk of bias in literature selection. The study did not assess the quality of the included studies, which could affect the reliability of the findings. Future studies should include an assessment of the quality of the included studies to ensure the reliability of the findings. The study only focused on acupuncture prescriptions for improving HRV in humans. The findings may not be generalizable to other acupuncture treatments or health conditions. Future studies could include clinical data, such as randomized controlled trials, to verify the effectiveness and safety of the acupuncture prescriptions identified. Future studies could also compare the efficacy of the acupuncture prescriptions identified to other acupuncture treatments for improving HRV or other health conditions.

Conclusion

In summary, the study underscores a growing body of evidence supporting the beneficial role of acupuncture in improving HRV. With a significant increase in related publications since 2007, particularly from China and the United States, acupuncture is emerging as a potential therapeutic intervention for a range of conditions. The most commonly used acupoints, including PC6, ST36, and their pairing, indicate a specific focus on modulating ANS activities.

The diverse applications of acupuncture in pain management, inflammation reduction, emotional disorders, gastrointestinal function enhancement, and hypertension treatment highlight its comprehensive therapeutic potential. The top-cited literature in this field further corroborates acupuncture's ability to modulate ANS activities, suppress inflammation, and enhance various physiological functions.

While these findings are promising, they also underscore the need for further research to fully elucidate the mechanisms underlying acupuncture's effects and establish its definitive efficacy. Future studies should aim to address methodological inconsistencies, explore long-term effects, and investigate interactions with other treatment modalities. With continued efforts, acupuncture may emerge as a viable and effective treatment option for a wide array of ANS-related disorders.

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