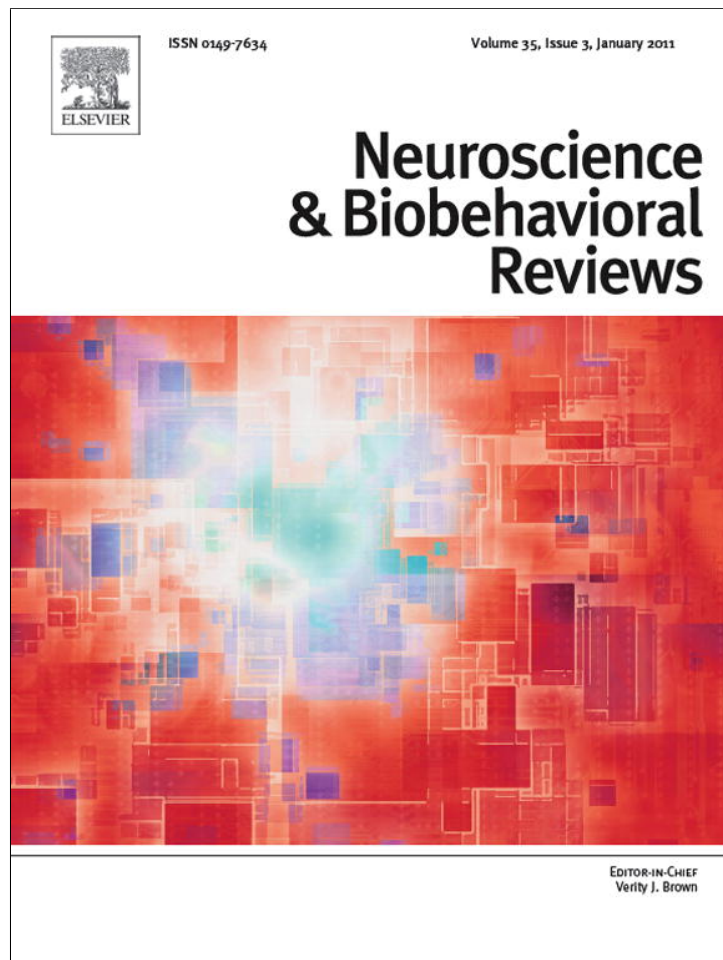


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Review

Global trends and performances of acupuncture research

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ABSTRACT

This study was designed to evaluate the global scientific output of acupuncture research in the Science Citation Index-Expanded and to assess the tendencies and research performances of leading countries/territories and institutes. Articles referring to acupuncture were assessed by distribution of document types, languages, journals, subject categories, source countries, and source institutes. Results showed that 15 languages were represented in articles from 65 countries/territories. *Journal of Alternative and Complementary Medicine* published the most articles, followed by *American Journal of Chinese Medicine* and *Acupuncture & Electro-Therapeutics Research* which were listed in category of integrative & complementary medicine. In the study period of 1991–2009, USA was the top producing country, followed by China (mainland) with a sharply growth trend. In 2009, publication of China (mainland) ranked top one in the world. In addition, an acupuncture research trend was found in two phases in terms of the increase of number of SCI-expanded journals' articles. Among the acupuncture research, pain control has been the most prevalent direction of study, and brain imaging is attracting the most recent attention.

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1. Introduction

Acupuncture originated in China over three thousand years ago and was widely accepted in Chinese society. In 1979, the World Health Organization (WHO) conducted a symposium in Beijing, China to identify the conditions that might benefit from the therapy (World Health Organization, 2002). The international participants drew up a list of 43 suitable diseases. However, that was not based on formal clinical trials. In 2002, the WHO published a book entitled “Acupuncture: Review and Analysis of Reports on Controlled Clinical Trials”, in which 29 conditions were identified for which acupuncture has been proved, through controlled trials, to be an effective treatment. Among the 29 conditions, 12 were related with pain. Today, the analgesic effect of acupuncture is well established, although controversy still exists whether acupuncture can be regarded as a stand-alone technique for the treatment of various kinds of disease (Dajczman et al., 1991; Ulett et al., 1998). After four decades of intense basic research and clinical practice, it is time to have a global look at the history and current situation of acupuncture research.

Bibliometrics is a type of research method used in library and information sciences. It utilizes quantitative analysis and statistics to describe patterns of publications within a given topic, field, institute, or country. This paper was aimed to study all of the literatures related with acupuncture that published in journals listed in Science Citation Index-Expanded (SCI-Expanded). Bibliometric method has already been applied to traditional medical related topics such as rehabilitation (Tesio et al., 1995), AIDS (Macias-Chapula, 2000), cancer molecular epidemiology (Ugolini et al., 2007), tuberculosis (Ramos et al., 2008), Parkinson's disease (Li et al., 2008), and Alzheimer's disease (Sorensen, 2009). In addition, topics related to complementary and alternative medicine were also reported (Danell and Danell, 2009), such as acupuncture (Zhang, 1995), qigong (Zhang et al., 1997), homeopathy (Chiu and Ho, 2005), and Chinese medicine (Leung et al., 2006). The SCI-Expanded, from the Institute for Scientific Information (ISI) Web of Science databases, is the most frequently used source database for a broad review of scientific accomplishment in all fields.

In this study, a bibliometric method was used for the analysis of languages, subject categories, journals, article countries/territories, and article institutes to describe the performances and research trends in acupuncture. In addition, discussion on some interesting issues emerging on the path of acupuncture research was also presented.

2. Method

The data were from the online version of SCI-Expanded, Web of Science. According to Journal Citation Reports (JCR), it indexed 7,347 major journals with citation references across 174 scientific disciplines in 2009. “Electroacupuncture”, “electro-acupuncture”, “acupoint*”, “acupunctur*”, and “percutaneous electrical nerve stimulation” were used as keywords to search titles, abstracts, and keywords from 1991 to 2009. The word “acupoint*” might stand for “acupoint” and “acupoints”; and “acupunctur*” might stand for “acupuncture”; “acupunctures”; “acupuncturelike”; “acupunctural”; “acupunctured”; “acupuncturist”; and “acupuncturists”. Articles originating from England; Scotland; Northern Ireland; and Wales were reclassified as from the United Kingdom (UK). Articles from Hong Kong were not included in China (mainland). Besides, the reported impact factor (IF) of each journal was obtained from the JCR in 2009. Contributions of different institutes and countries/territories were estimated by the affiliation of at least one author to the articles. Collaboration type was determined by the addresses of the authors; where the term “single-country article”

was assigned if the researchers' addresses were from the same country. The term “internationally collaborative article” was designated to those articles that were coauthored by researchers from multiple countries/territories. The term “single institute article” was assigned if the researchers' addresses were from the same institute. The term “inter-institutionally collaborative article” was assigned if authors were from different institutes.

According to a limitation of the SCI-Expanded database, abstract information was available since 1991. The topic search can trace the related information in titles, abstracts, and keywords at one time. Thus publications before 1991 would not be considered in this study, which is a major limitation of the present article, since many of them were the pioneer works in this field. All the articles during the past 19 years (1991–2009) were assessed by the following aspects: document types and languages of articles; distribution of journals and subject categories; publication outputs of article countries/territories and institutes with five indicators such as total, independent, collaborative, first author, and corresponding author articles. Furthermore the highly cited papers in SCI-Expanded database were also discussed.

3. Results

3.1. Document type and language of publication

There were 6,004 publications with 13 document types indexed in the SCI-Expanded, which include 3,975 articles. The article, as the most popular document type, comprises 66% of the total production and was followed distantly by reviews (508; 8.5%), letters (458; 7.6%), meeting abstracts (457; 7.6%), editorial materials (286; 4.8%), proceedings papers (213; 3.5%), and the remainder having less significance were news items (38), corrections (32), notes (24), reprints (6), book reviews (4), biographical-items (2), and addition correction (1). Journal articles represented the majority of document types, therefore only the 3,975 articles were analyzed in further study.

There were 15 languages in use. English, as the most popular language, comprises 93% of the total articles and was followed by German (168; 4.2%). Some other languages that were less used were Russian (50) and French (22). Still some other languages generally less appeared were Portuguese (10), Chinese (8), Spanish (8), Japanese (3), Hungarian (2), Korean (2), Turkish (2), Polish (2), and one for Czech, Slovene, and Ukrainian, respectively.

3.2. Publication patterns

The total amounts of SCI-Expanded journals' publications including searching words “electroacupuncture”, “electro-acupuncture”, “acupoint*”, “acupunctur*”, and “percutaneous electrical nerve stimulation” in titles only from 1900 were counted and displayed in Fig. 1. As a whole, the development of acupuncture literature can be divided into two phases in terms of the increase in the number of SCI-Expanded journal papers. The first phase is between 1973 and 1997, in which number of articles fluctuated to form a plateau, averaged 85 per year. The number of articles showed a dramatic increase of 40% in 1998. The extrapolation from Fig. 1 suggests that the development in this field will continue in the fast growing tract after 2009. According to a limitation of the SCI-Expanded database, searching keywords in titles, keywords, and abstracts can only obtain for publications since 1991. A development trend is also found for all documents and articles, searched by titles, keywords, and abstracts (Fig. 1). There is an increase in all documents from 2 in 1921 to 703 in 2009 and an increase of articles from 1 in 1921 to 451 in 2009.

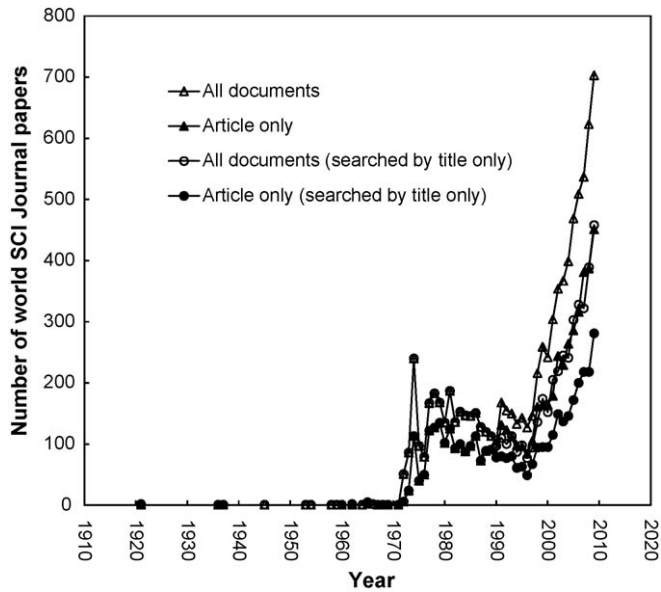


Fig. 1. Number of SCI-Expanded journals' papers referring to "electroacupuncture", "electro-acupuncture", "acupoint*", "acupunctur*", and "percutaneous electrical nerve stimulation" since 1900.

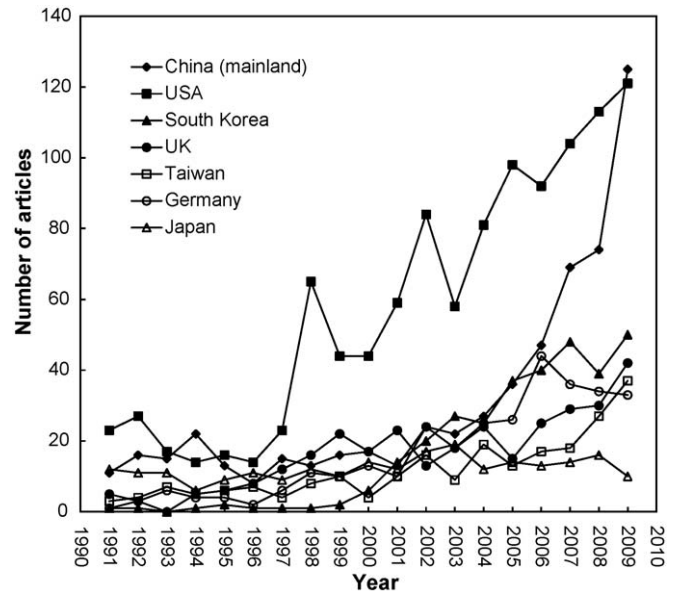


Fig. 2. Comparison of the publication growth trends of top seven countries.

3.3. Subject categories and journals

Based on the classification of subject categories in JCR in 2009, the article output data of acupuncture research was distributed in 117 SCI subject categories. Top four main subject categories were integrative & complementary medicine (976; 25%), neurosciences (750; 19%), general & internal medicine (555; 14%), and clinical neurology (504; 13%).

In total, 3,975 articles were published in 927 journals including specialty journals and journals of other disciplines. Out of the 927 journals, 487 (53%) journals contained only 1 article and 151 (16%) contained two. One-third of all articles were published in 14 core journals (Table 1). *Journal of Alternative and Complementary Medicine* published the most acupuncture articles (258), followed by *American Journal of Chinese Medicine* (222), *Acupuncture & Electro-Therapeutics Research* (176), *American Journal of Acupuncture* (141), and *Neuroscience Letters* (111). However, *American Journal of Acupuncture* was not listed in JCR since 1996. The *CA-A Cancer Journal for Clinicians*, which ranked not only the top one journal in the ISI category of oncology but also in all 7,347 journals listed in JCR in 2009, with the IF as 87.925, was the leading journal on acupuncture research.

3.4. Countries/territories' research performances

The contribution of different countries/territories is estimated by the location of the affiliation of at least one author of the published articles. There were 110 (1.8%) articles without author address information in the ISI. For this reason, not all of the articles were included in this analysis. Total number of articles, independent, and collaborative articles have been applied to be indicators to evaluate countries/territories research performance (Chiu and Ho, 2007). In recent years, five indicators including the total, independent, collaborative, first author, and corresponding author articles, were also used for countries/territories research performance (Malarvizhi et al., 2010). Table 2 shows the top 11 countries/territories which published at least 100 articles ranked by the number of total articles with the five indicators. Among the 3,865 articles with author address information, international collaborations accounted for 14% of the articles compared to 86% from

single countries/territories. Single-country articles were published by 59 different countries/territories, most of which originated from the USA (819; 25%) followed by China (mainland) (428), the UK (232), South Korea (222), and Germany (222). The USA had the most-frequent partners accounting for 51% of the internationally collaborative articles, followed by China (mainland) with 28%. Moreover, the USA also had high first author articles (24%) and corresponding author articles (25%) followed by China (mainland) with 13%. Canada (42%) had a relative high percentage of internationally collaborative articles (%C), while Taiwan (14%), Sweden (16%), and Japan (17%) were ranged as the lower ones. The time series analysis among top seven countries/territories with more than 200 articles was displayed in Fig. 2. An obvious sharp rise could be found in the number of articles related to acupuncture research of the USA and China (mainland) in last 6 years. In Asian region, China (mainland), South Korea, Taiwan, and Japan ranked among the top seven. However, Japan did not increase in number of articles in the study period.

3.5. Institutes' research performances

The contribution of different institutes was estimated by the institute of the affiliation of at least one author of the published articles. Of the 3,865 articles with author addresses, 1,821 (47%) were single institute articles and 2,044 (53%) were inter-institutionally collaborative articles. The top 10 institutes were ranked by the total number of articles, including the number and percentage of single institute articles and inter-institutionally collaborative articles, as well as first author articles and corresponding author articles (Table 3). However, a bias appeared because some institutes changed their status, for example, from a college to a university; and two universities were merged to be one. Only data for these institutes appeared in Table 3 were grouped together under the new name. For instance, in 2000, Fudan University and Shanghai Medical University were merged to be Fudan University, and Peking University and Beijing Medical University were also merged to be Peking University. Whereas China Medical College changed its name to China Medical University, articles published under both institutional names were grouped together under the new university's name. Among the top 10 institutes, 3 of them were derived from the USA, followed by South Korea and China (mainland) with two

Table 1
The 14 most productive journals with the number of articles, IFs, SCI categories of journals, and the position of the journal in its category.

Journal	TP (%)	IF	SCI subject category	Position
Journal of Alternative and Complementary Medicine	258 (6.5)	1.685	Integrative & Complementary Medicine	5/17
American Journal of Chinese Medicine	222 (5.6)	1.422	Integrative & Complementary Medicine	7/17
Acupuncture & Electro-Therapeutics Research	176 (4.4)	0.250	General & Internal Medicine	57/132
			Integrative & Complementary Medicine	15/17
American Journal of Acupuncture	141 (3.5)	N/A	Neurosciences	221/230
			Clinical Neurology	–
Neuroscience Letters	111 (2.8)	1.925	Neurosciences	165/230
Complementary Therapies in Medicine	95 (2.4)	1.950	Integrative & Complementary Medicine	4/17
Pain	63 (1.6)	5.371	Anesthesiology	1/25
			Clinical Neurology	16/167
			Neurosciences	34/230
Brain Research	52 (1.3)	2.463	Neurosciences	132/230
Anesthesia and Analgesia	47 (1.2)	3.083	Anesthesiology	6/25
Clinical Journal of Pain	37 (0.93)	3.005	Anesthesiology	7/25
			Clinical Neurology	47/167
Alternative Therapies in Health and Medicine	35 (0.88)	2.250 ^a	Integrative & Complementary Medicine	–
Brain Research Bulletin	31 (0.78)	2.184	Neurosciences	149/230
Neural Regeneration Research	30 (0.75)	N/A	Cell Biology	–
Neurological Research	27 (0.68)	1.277	Neurosciences	–
			Clinical Neurology	118/167
			Neurosciences	191/230

TP: number of article; IF: impact factor; N/A: not available.

^a Impact factor in 2008 JCR.

Table 2
Eleven most productive countries/territories between 1991 and 2009.

Country/territory	TP	TPR (%)	SPR (%)	CPR (%)	FAR (%)	RPR (%)	%C
USA	1,097	1 (28)	1 (25)	1 (51)	1 (24)	1 (25)	25
China (mainland)	583	2 (15)	2 (13)	2 (28)	2 (13)	2 (13)	27
South Korea	316	3 (8.2)	4 (6.7)	3 (17)	3 (7.5)	3 (7.7)	30
UK	313	4 (8.1)	3 (7.0)	5 (15)	5 (6.9)	5 (7.1)	26
Germany	310	5 (8.0)	4 (6.7)	4 (16)	4 (7.3)	4 (7.3)	28
Japan	232	6 (6.0)	6 (5.8)	7 (7.3)	7 (5.3)	7 (5.1)	17
Taiwan	224	7 (5.8)	6 (5.8)	9 (5.9)	6 (5.6)	6 (5.6)	14
Sweden	170	8 (4.4)	8 (4.3)	12 (4.9)	8 (4.1)	8 (3.9)	16
Canada	124	9 (3.2)	10 (2.2)	6 (9.5)	9 (2.3)	9 (2.6)	42
Australia	103	10 (2.7)	9 (2.3)	13 (4.8)	10 (2.3)	10 (2.3)	25
Austria	100	11 (2.6)	11 (2.1)	10 (5.7)	11 (2.2)	11 (2.1)	31

TP: the number of total articles; TPR (%), SPR (%), CPR (%), FAR (%), RPR (%): the rank and percentage of total articles, the rank and percentage of single-country articles, internationally collaborative articles, first author articles, corresponding author articles in total articles; %C: country collaboration ratio, the percentage of collaborative articles in total articles for each country.

institutes, and one institute for each of the UK, Taiwan, and Sweden (Fig. 3).

Concerning the trends of top four institutes with more than 80 articles, Peking University and Fudan University started to publish acupuncture-related articles since 1970s and remained a mild increase across the four decades. Harvard University began to publish acupuncture-related articles in 1993 and 1997, and increased quickly since then. Most dramatic change occurred in South Korea where the Kyun Hee University started to step into this field in the

late-1990s, beginning to march in the 21st century and became the most published institution in 10 years.

3.6. The most frequently cited article

The most frequently cited article in the field of acupuncture was “unconventional medicine in the United States—prevalence, costs, and patterns of use” published by Harvard University, where all unconventional medicine, including massage, chiroprac-

Table 3
Top 10 most productive institutes of articles during 1991–2009.

Institute	R (TP)	R (SP)	R (CP)	R (FA)	R (RP)	%C
Kyung Hee University, South Korea	1 (149)	3 (37)	1 (112)	2 (108)	2 (103)	75
Fudan University, China (mainland) ^a	2 (132)	1 (91)	7 (41)	1 (115)	1 (107)	31
Harvard University, USA	3 (98)	12 (13)	2 (85)	5 (42)	6 (38)	87
Peking University, China (mainland) ^a	4 (88)	2 (41)	4 (47)	3 (73)	3 (55)	53
University of Exeter, UK	5 (66)	4 (28)	9 (38)	4 (46)	4 (44)	58
China Medical University, Taiwan ^a	6 (64)	18 (10)	3 (54)	8 (35)	10 (27)	84
Seoul National University, South Korea	7 (60)	9 (18)	6 (42)	6 (41)	5 (41)	70
Karolinska Institutet, Sweden	8 (59)	12 (13)	5 (46)	10 (26)	8 (29)	78
University Maryland, USA	9 (54)	10 (15)	8 (39)	7 (37)	7 (32)	72
University of California, Los Angeles, USA	10 (46)	8 (19)	15 (27)	9 (31)	8 (29)	59

TP: the number of total articles; SP, CP, FA, RP: the number of single institute articles, inter-institutionally collaborative articles, first author articles, corresponding author articles; R: rank; %C: the percentage of collaborative articles in total articles for each institute.

^a Fudan University includes Shanghai Medical University; Peking University includes Beijing Medical University; China Medical University includes China Medical College.

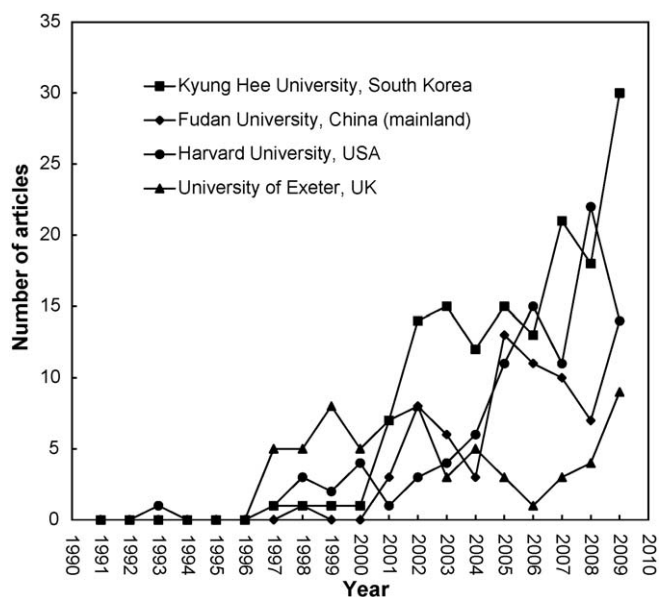


Fig. 3. Comparison of the publication growth trends of top four institutes.

tic, acupuncture, were analyzed (Eisenberg et al., 1993). It has been cited 2,095 times since its publication to 2009. The 3 most cited papers related to acupuncture mechanism, written by Pomeranz and Chiu (1976), Mayer et al. (1977) and Sjolund et al. (1977) were all about the evidence that the analgesic effect of acupuncture is mediated by opioid substances via opioid receptors. In addition, the most frequently cited review paper in early years was “neurochemical basis of acupuncture analgesia” in the *Annual Review of Pharmacology and Toxicology* in 1982 prepared by Han and Terenius (1982). It has been cited 270 times since its publication to 2009. The paper prepared by Ramsay et al. (1998) on “acupuncture” published in *JAMA-Journal of the American Medical Association* in 1998 constituted a mile stone of acupuncture history in the western world where the efficacy of acupuncture was formally endorsed by National Institute of Health of the United States. It summarized the consensus that reached in the NIH sponsored “Consensus Development Conference on Acupuncture” which was held on November 3–5, 1997 in Bethesda, MD. The great impact of this paper was shown in the fact that after its publication, the insurance company started to pay the costs of acupuncture treatment for certain diseases, such as pain and nausea/vomiting. In later years, the most frequently cited review was “postoperative nausea and vomiting: its etiology, treatment, and prevention” published in *Anesthesiology* (Watcha and White, 1992). It has been cited 706 times since its publication to 2009.

3.7. The general trends of acupuncture research

Analysis of the 3,975 articles related with acupuncture from 1991 to 2009 showed that 1,647 (41%) were dealt with pain and analgesia. Among the pain-related articles, 366 (22%) were dealt with opioid mechanisms. Furthermore, analysis of the most cited 100 articles concerning acupuncture showed a similar trend. Acupuncture treatment for pain conditions and the opioid mechanisms for acupuncture-induced analgesia were among the most prevalent topics.

One of the recent trends is the use of brain imaging technique to trace the brain matrix mediating acupuncture effect. This is one of the most successful non-invasive approaches to explore the sites and the characteristics of the functional changes occurred in human brain in response to acupuncture intervention.

In 1995, the first attempt of using fMRI to evaluate brain response to acupuncture was presented (Yoshida et al., 1995). Since then to 2009, 133 related papers, including 99 articles were published in SCI-Expanded journals. Thirty-two articles were published in journals with impact factor > 5.

Another hot topic is the discussion on how important is the role played by placebo (psychological) effect as compared to the physiological effect induced by acupuncture. In order to assess the placebo effect related to acupuncture, a placebo needle (touching but not piercing the skin) was designed by Streitberger and Kleinhenz (1998), and being widely used in clinical trials.

4. Discussion

4.1. Two waves of development of acupuncture-related literature

From the historical point of view, the first surge shown in Fig. 1 may be related with the clinical practice of “acupuncture anesthesia” in China when acupuncture was used as a technique to induce analgesic effect in place of anesthetics during surgical procedures. That was started in the late-1950s (Wu, 2007). This non-conventional practice raised the interest of not only medical professionals over the world, but also basic researchers who would like to explore the possible mechanisms. The Chinese government started to invest research funding to support the studies in this field. Added on the story was the report written by James Reston in New York Times, introducing his personal experience of using acupuncture to stop his post-appendectomy pain in 1971 (Reston, 1971), followed by the visit of US president Nixon to China in 1972 (American Acupuncture, 2009).

The marked increase in acupuncture-related publication in 1998 might be encouraged by the very successful “NIH Consensus Development Conference on Acupuncture” held in 1997 in Bethesda, MD. Consensus was reached at the conclusion of the meeting that (a) acupuncture can be used for the treatment of dental pain and meliorating nausea vomiting and (b) studies on the mechanisms of action revealed that acupuncture can increase the production and release of opioid peptides in the central nervous system, resulting in a pain killing effect. Another related event was that a National Center for Complementary and Alternative Medicine (NCCAM) was inaugurated under the NIH, USA in 1998. Fundings from NCCAM, in conjunction with those from the National Institute of Drug Abuse (NIDA), greatly supported the research on acupuncture, hence the production of research papers in the new millennium.

4.2. The designing of the control group

As stated before we have put much emphasis on papers in the category of “articles” which comprises about two-third of all types of publications. In the earlier years of 1970s almost all clinical articles on acupuncture were open trials, since acupuncture treatment required close interaction between the acupuncturist and the patient in order to obtain the maximal sensation of deqi (a complex feeling under the needle) for best therapeutic effect. In this case the placebo effect is hardly avoidable. Starting from the late seventieth, clinical trials were requested to set a control group to blind the patient (single blind) at least, if not the acupuncturist (double blind). The randomized controlled clinical trial (RCT) started to emerge at 1992, being 12 articles in 2000, and increased by 9 fold to reach 113 articles in 2009. It has now become a mainstream category in SCI publications in the current century. However, one must confess that much difficulty has been encountered in designing an ideal control group for acupuncture trials. Needless to say, it is almost impossible to blind the acupuncturist who performs the maneuver. For choosing the site and method of needle insertion,

one could either use a true acupuncture (piercing the skin with the needle to a certain depth) at a wrong point, or a sham acupuncture (touching the skin) at a true point. However, controversies exist upon the definition of the “wrong” point. For example, how far a needle should be placed apart from the “real” acupoint in order to be considered as “inert”? Since the acupoints are supposed to locate along the meridian (“Jin”, also translated as “channel”) and the meridian is supposed to possess multiple branches (“Luo”), it is hard to find a place on the body surface without the influence of “Jin” and “Luo”. It is for these reasons that there is so far no “golden standard” for a classical control setting. In order to do meta-analysis of the RCTs (a total of 904 papers during the period of 1991–2009), many review papers appeared, the number of which (253) reaches 28% of the total RCTs.

It is generally agreed that one of the aims of performing a RCT is to minimize the interference of placebo effect against a true “therapeutic” effect. However, certain kind of placebo or nocebo effect is practically unavoidable. The key is to leave the doctor and the patient unaware of the real difference between the verum and the control settings. In this case, electrical stimulation has the priority compared to manual stimulation, since the detailed parameters of the electrical stimulation can be precisely identified and modulated. For example, Wang et al. (2000) reported that spinal trauma-induced muscle spasm can be ameliorated by acupoint electrical stimulation only with high frequency of 100 Hz, but not low frequency of 2 Hz. In fact, even the clinicians performing the treatment did not know which frequency will be effective for relieving muscle spasm. In this case, if 100 Hz, but not 2 Hz, is finally approved to be effective, then the 2 Hz can be regarded as a best control, with exactly the same degree of conditioning and expectation.

One can also design a control group using the very low intensity stimulation (“minimal stimulation”) as the control. Lambert et al. (2009) reported that acupoint electrical stimulation was effective for relieving tobacco urges in dependent smokers by an intensity of 10 mA, but not by intermittent (1 min on and 2 min off) 5 mA. In the later case, the intensity is low, but can still be felt, and the duration of stimulation is cut by 66.7%, therefore the stimulation is not strong enough to induce a therapeutic effect.

4.3. The brain imaging studies

The most cited paper in brain imaging for acupuncture mechanisms was the one published by Cho et al., 1998, entitled “new findings using functional MRI for the study of acupuncture mechanisms”. The authors claimed that stimulation of the vision-related acupoint (VA1), located in the lateral aspect of the foot, induced activation of occipital lobes, whereas stimulation of the eye with light results in similar activation in the occipital lobes, suggesting that eye-related meridian had a connection with the vision-related brain structures. Unfortunately, this well cited article was withdrawn by the authors in 2006 (Cho et al., 2006). Wu et al. (1999) were among the first to show that acupuncture at acupoints LI4 and ST36 of the healthy persons resulted in activation of the hypothalamus and nucleus accumbens and deactivation of the rostral part of the anterior cingulate cortex, amygdala and hippocampus, while control stimulations did not result in such activations and deactivations. After 10 years of study, Hui and her group reported that manual acupuncture at 3 representative points (LV3, LV2, ST44) and one sham point at hand produced similar changes in the hemodynamic response (BOLD signal changes). Acupuncture was reported to produce extensive deactivation of the limbic–paralimbic–neocortical system, and activation of the sensorimotor cortices (Fang et al., 2009; Hui et al., 2000). In a detailed study at SP6 point, Napadow et al. (2009) found that compared to sham (touching) stimulation, the real

acupuncture produced stronger but more variant and more longer lasting BOLD changes, leading to increased cognitive/evaluative (posterior dmPFC) and emotional/interoceptive (anterior dmPFC) cortical regions. Napadow et al. (2005) also found that overall, electroacupuncture (particularly at low frequency) produced more widespread fMRI signal increase than what manual acupuncture did, and all acupuncture stimulations produced more widespread responses than what tactile control stimulation did. If acupuncture produced frank pain, there will be simultaneous activation and deactivation of the brain activities and there is no lineal relationship between the intensity of the pain and brain activations and deactivations (Kong et al., 2010). It seemed important to note that the duration of manual acupuncture needling would affect changes in fMRI in the human brain, such that the effect produced by 180 s of needling was significantly stronger than that of 30 s (Li et al., 2006a,b). Collectively, neuroimaging data strongly suggest that acupuncture modulates many distributed cortical and subcortical (i.e., brainstem, limbic, cerebellum) brain areas. These brain areas, supporting endogenous antinociceptive mechanism and part of the pain neuromatrix (Fields and Basbaum, 1999; Casey, 1999; Hofbauer et al., 2001), may contribute to the therapeutic effect of acupuncture by shifting autonomic nervous system (ANS) balance, and altering the affective and cognitive dimensions of pain processing (Peets and Pomeranz, 1978; Clementjones et al., 1980).

Summarizing all the papers of fMRI studies on acupuncture, one can hardly see any major breakthrough on the understanding of acupuncture mechanisms. One may therefore ask, is there anything wrong with the basic principles of using fMRI for the study of acupuncture mechanisms. One of the concerns is the reliability or the reproducibility of the brain imaging result (Bennett and Miller, 2010). The standard method to quantify the reliability is the intraclass correlation (ICC) of the voxelwise clusters of two tasks. The average ICC in two runs of working memory tasks within 1 h was only about 0.33. Kong et al. (2007) compared the ICC value between BOLD signal changes induced by finger tapping and EA stimulation in a test–retest experimental design. They found that fMRI signal changes evolved by EA stimulation were significantly more variable than those from the control finger tapping task.

Even more important is the timing of event related data acquisition. Unlike the visual and hearing sensations that bear a clear on and off characteristics, the complex feeling produced by acupuncture, described as “deqi”, is difficult to characterize (MacPherson and Asghar, 2006). It comes with different time latencies (Ho et al., 2009) and lasts for a different length of time. The later may serve as the cause of “carryover” effect (Ho et al., 2008) or “time-varied characteristics” of acupuncture (Liu et al., 2010). In fact, the physiological or therapeutic effects induced by one session of acupuncture (20–30 min) may last for hours or even days. Therefore, the commonly used block design of on and off for 1 min each, which is ideal for visual or motor tasks, is hardly applicable for acupuncture research. Due to the delayed effect of acupuncture, its temporal characteristic may violate the assumptions of the block-designed model-based analysis estimates (Bai et al., 2009a). Therefore, the model-based analysis becomes impractical when the precise timing and duration of acupuncture cannot be specified a priori. For this purpose, the data-driven analysis, free of any hypothesis about the temporal profile of acupuncture-related changes, can be regarded as a more optimal choice instead (Bai et al., 2009b,c).

Napadow et al. (2009) also stressed the time variant fMRI activity induced by electroacupuncture. In contrast to Tian’s group who observed changes after the 30 min period of stimulation, Napadow et al. (2009) observed the changes of fMRI signals within the period of 30 min. They found linearly decreasing fMRI activation in sensorimotor brain areas which they attributed to habituation. Verum acupuncture also produced time variant fMRI response in limbic regions, which is not habituation, but rather, an early activation

and later deactivation by the end of the 30 min scan run. These changes were not observed in sham point stimulation, suggesting an impact on its therapeutic effect.

Most of the work shown above was performed in normal persons, without any description of the physiological effects induced by acupuncture itself. This is against the tradition of using acupuncture as a therapeutic technique. To fulfill this requirement, two approaches can be considered. One is to observe the physiological effects produced by acupuncture in normal persons, and the other is to observe the therapeutic effect in patients.

Zhang et al. (2003) in Han's group tried to correlate the BOLD signal changes in brain areas activated or deactivated by transcutaneous electrical acupoint stimulation (TEAS) of the LI4 point with the magnitude of analgesic effect. They characterized 8 brain regions showing positive correlation of the BOLD signal activation with the analgesic effect and 2 brain regions showing negative correlations (deactivation). They also showed that the brain areas involved in 2 Hz TEAS were partially overlapped with that induced by 100 Hz. In either frequency, the averaged fMRI activation of bilateral secondary somatosensory area and the insula, the contralateral anterior cingulate cortex and thalamus were positively correlated with the TEAS-induced analgesic effect across the subjects. Negative correlation was observed in bilateral hippocampi in 2 Hz, and bilateral amygdala in 100 Hz. These brain regions may have been involved in the modulation of pain perception.

Harris et al. (2009) used positron emission tomography (PET) scan to compare the effects of traditional Chinese acupuncture (TA) versus sham acupuncture (SA) treatment on the *in vivo* μ opioid receptor (MOR) binding availability in chronic pain patients diagnosed with fibromyalgia (FM). One session of acupuncture evoked short-term increases in MOR binding potential in multiple pain and sensory processing regions including the cingulate cortex, insula, caudate, thalamus, and amygdala. Multiple sessions of acupuncture therapy (8 treatments in 4 weeks) evoked long-term increases in MOR binding potential in some of the same structures including the cingulate, caudate, and amygdala, associated with greater reductions in clinical pain. These short- and long-term effects were absent in the sham group where small reductions were observed. This was an important contribution to show the involvement of opioid receptors in identified brain areas to mediate the analgesic effect of acupuncture.

One of the most exciting fMRI studies is the study on the interaction and dissociation of expectation of pain relief and acupuncture effect. It is well known that expectation is mixed with the genuine effect of acupuncture. It is very difficult to distinguish the two factors. Kong et al. (2009) reported that conditioning positive expectation can amplify acupuncture analgesia as detected by subjective pain sensory rating changes and objective fMRI signal changes in response to calibrated noxious stimuli. They also found that sham acupuncture and verum acupuncture may produce similar degree of analgesic effect, yet the verum acupuncture induced more prominent activation of certain brain areas than that induced by sham stimulation. Brain substrates involved in this process include bilateral rACC/MPFC, left DOPFC and DLPFC. This is the first brain imaging study to elucidate the brain mechanisms underlying the ability of positive expectation to influence the therapeutic effects of verum acupuncture treatment.

4.4. Assessing acupuncture effect in normal or diseased subject

While most basic physiological researches on acupuncture are performed in naïve animals or normal volunteers, one must consider whether information obtained in normal subjects can represent the therapeutic effect in patients. Studies showed that compared with normal persons, patients who suffered from chronic pain (White et al., 2007) or strokes (Li et al., 2006a,b) seem to be

more sensitive to acupuncture treatment. This is also true in animal models of chronic pain. Huang et al. (2008) showed that in CFA-induced monoarthritic rats, 100 Hz EA produced more marked antinociceptive effect (assessed by tail flick latency) and a faster development of the tolerance, due probably to the warming up of the dynorphinergic systems by the inflammatory process (Neil et al., 1986). Therefore it may be advisable that more studies on acupuncture should be performed in patients or animal models of pathological conditions whenever possible.

4.5. Limitations

Lastly it should be mentioned that in order to make a thorough review on papers related with acupuncture from bibliometric point of view, we recruited only papers published in SCI-Expanded journals. In order to ensure a high quality bibliometric analysis, one has to pay a price that a considerable amount of papers published in non-SCI journals, especially those pioneer works published before 1991, are missing. The contrast is especially dramatic when one sees the fact that compared to the vast amount of acupuncture literature in Chinese, only 8 papers were represented in the present bibliometric study. To correct this pitfall, another study aiming to systemically review the non-SCI papers may be warranted.

5. Conclusions

Thirteen document types were used in acupuncture publications. English was the most predominant language used by the scientists for communication. 3,975 articles were published in 927 different journals which were listed in 117 SCI subject categories during 1991–2009. Fifty percent of articles were inter-institutionally collaborative articles. Fourteen percent of articles were internationally collaborative articles. The most productive institutes were Kyung Hee University at South Korea and Fudan University at China (mainland) in the recent 19 years. Starting from the 1970s the publication on acupuncture grew slowly and entered into a high speed tract in late-1990s, especially in the first decade of the 21st century. These changes bear a historical background. With the development of the modern technology and the ever increasing demand for a more efficient and cost effective health care system, we may expect a new surge for the research on acupuncture in the near future.

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