Ying Xia *Editor*

Translational Acupuncture Research

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Preface

Acupuncture has been broadly used in many clinical settings worldwide. Although the precise mechanism underlying the therapy is not well understood yet, it is generally accepted that acupuncture, by either manual or electrical stimulation, can trigger nerve signals in the acupoints that get transmitted from the peripheral to the central nervous system and elicit a therapeutic effect through neural and humoral regulation. In recent years, our serial books (Xia Y. et al.: Acupuncture Therapy for Neurological Diseases—A Neurobiological View. Springer-Tsinghua Press, 2010; Xia Y. et al.: Current Research in Acupuncture. Springer, 2012; Xia Y.: Neural Functions of the Delta-opioid Receptor. Springer 2015) have presented comprehensive information on acupuncture mechanisms and provided future perspectives in acupuncture research.

This new book features a translational view of acupuncture research. Written by many scientists and clinicians from China, USA, Canada, and other countries, this monograph discusses translational research on acupuncture. Besides general topics on acupuncture practice (e.g., different styles and techniques of acupuncture), topics include some refractory diseases such as chronic fatigue syndrome, Parkinson's disease, cardiovascular dysfunction, chronic pain, post-concussion syndrome, post-traumatic stress disorder, and cancer-related symptoms. The factors influencing acupuncture research are comprehensively addressed in the final chapter. This unique book provides a translational perspective on modern acupuncture for not only acupuncturists, but also neuroscientists, neurologists, and other clinicians. For medical students and undergraduate and graduate students majoring in biology, this book is an advanced course for learning the progress in alternative and complementary medicine.

I hope that this book will help promote acupuncture research in both basic and clinical sides and further improve our understanding of acupuncture mechanisms and increase acupuncture efficacy.

I am very grateful to all authors for their significant contributions and considerable efforts that made this book happen. I would also like to thank Ms. Simina Calin of Springer for her support and help for making this book to actuality from my proposal.

Shanghai, China Ying Xia

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About the Editor

Ying Xia is a Fudan Distinguished Professor at Fudan University, the Executive Director of Shanghai Key Laboratory of Acupuncture Mechanism and Acupoint Function, and Director of Molecular Neurology Laboratory at Shanghai Research Center for Acupuncture and Meridians, Shanghai, China. He obtained his medical training at Soochow Medical College, China. After being a clinical physician for almost 4 years, he pursued his graduate study and obtained a Master Degree of Medicine and a Doctoral Degree of Medical Science (Ph.D.) in Neurobiology and Integrative Medicine at Shanghai Medical University (now Shanghai Medical College of Fudan University), China. He was then appointed as a lecturer of Integrative Medicine and Neurobiology there. Dr. Xia joined Yale University School of Medicine in 1988 for his postdoctoral training and initiated his laboratory at Yale in 1994. During his 22-year academic career at Yale University School of Medicine, he was appointed as a faculty member in 1993 and promoted to Associate Professor in 2002. From May 2010 to August 2016, he worked at the University of Texas Medical School at Houston (now the University of Texas McGovern Medical School) and the University of Texas Graduate School of Biomedical Sciences at Houston as a Full Professor, Chairman of Research and Promotion Committee, and Vice-chairman for Research in the Department of Neurosurgery. He was recruited by Fudan University in September 2016.

Dr. Xia's early research focused on cardiovascular regulation, interactive modulation of endogenous opioids and other neurotransmitters, and the mechanism of

acupuncture. His laboratory currently investigates neural functions of the delta-opioid receptor, neuroprotection against ischemic/hypoxic injury, Parkinson's disease and other neurodegenerative disorders, and acupuncture effects on neurological diseases (e.g., stroke, epilepsy, and hypoxic encephalopathy).

His research has been consecutively supported by NIH, American Heart Association, March of Dimes Foundation, Cerebral Palsy Foundation, The Vivian L. Smith Neurologic Foundation, Memorial Hermann Foundation, Science and Technology Commission of Shanghai Municipality, and the National Natural Science Foundation of China since 1994.

He has been invited to deliver speeches by many academic institutions (e.g., NIH and Harvard University) and international conferences. He has been serving as a manuscript-reviewer for many international journals and as a grant reviewer for NIH, US National Science Foundation, other American foundations (e.g., American Heart Association; US Civilian Research and Development Foundation), European foundations (e.g., Scotland Medical Research of UK; Wellbeing of Women of UK; National Science Center of Poland), Hong Kong University Grants Committees, and National Natural Science Foundation of China.

Introduction

Written by many scientists and clinicians from China, USA, Canada and other countries, this monograph discusses translational research on acupuncture. Besides general topics on acupuncture practice (e.g., different styles and techniques of acupuncture), topics include some refractory diseases such as chronic fatigue syndrome, Parkinson's disease, cardiovascular dysfunction, chronic pain, post-concussion syndrome and post-traumatic stress disorder and cancer-related symptoms. The factors influencing acupuncture research are comprehensively addressed in the final chapter. This unique book provides a translational perspective on modern acupuncture for not only acupuncturists, but also neuroscientists, neurologists, and other clinicians. For medical students and undergraduate and graduate students majoring in biology, this book is an advanced course for learning the progress in alternative and complementary Medicine.

Acupuncture: A Therapeutic Modality, But not a Placebo

Martin Wang

Abstract It is still a hot argument if acupuncture only has a placebo effect because both positive and negative reports have been published in the past. After reviewing literature from both China and Western countries, we found strong evidence supporting acupuncture as a therapeutic modality, but not as a placebo. A placebo effect requires a person with clear mind to react to the placebo hint, and believe in the hinted result. However, acupuncture works in some clinical conditions in which patients are in a condition without, or with very weak, consciousness such as coma, shock, persistent vegetable state, general anesthesia, delayed wake-up after surgical operation, and so on. Moreover, the healing effect of acupuncture varies significantly among different acupuncture techniques. Acupuncture can also work in infants and animals. Acupuncture and control acupuncture have different influences on physical and chemical conditions of the body. All these observations suggest that acupuncture has a unique and specific healing effect, independent of the placebo effect. In this chapter, we discuss possible reasons leading to the problematic bias that acupuncture is only a placebo. The most important reason is the failure to use appropriate acupuncture groups and correct treatment plans (e.g., low treatment frequency and fewer number of total treatment sessions). The low healing effect seen in acupuncture groups is therefore easily affected by the variations in the healing effect from the control acupuncture group, thus making inconsistent results in clinical acupuncture studies. We recommend that acupuncturists should follow the Chinese style of acupuncture to increase the success rate in acupuncture studies.

Keywords Acupoints · Acupuncture efficacy · Acupuncture techniques · Physical therapy · Placebo

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1 Introduction

Acupuncture has been studied for more than 50 years and both positive and negative results are still being published again and again (Fleckenstein et al. 2016; Schiller et al. 2016; Feng et al. 2016). Most published studies support that acupuncture has a unique healing effect, while there are also a lot of data that do not support this claim, since the acupuncture healing effect seen is not significantly different from that in a control acupuncture group. Due to this, some researchers believed that acupuncture is simply a placebo (Colquhoun and Novella 2013; Miller et al. 2009; O'Connell et al. 2009; Moffet 2009).

A placebo effect means that a person believes and expects a hinted result which exists only in their mind. As acupuncturists, we know that acupuncture has been used to treat some clinical conditions, in which the patients were without, or with very weak, consciousness, such as coma, shock, persistent vegetative state, general anesthesia, delayed wake-up after surgical operation and so on. Theoretically, if acupuncture is only a placebo, it should have no healing effect under those conditions. In this article, we review research data for acupuncture treatment in those conditions. We also check studies on acupuncture treatment for infants and animals, as well as comparison studies between different ways of acupuncture treatment.

2 Acupuncture Treatment for Clinical Conditions in Which the Patients Were Without Consciousness

2.1 Treatment of Coma with Acupuncture

There should be no argument that a placebo effect only happens when a person is conscious and with a clear mind able to analyze stimulations from outside of the body. Now let us see if and how acupuncture can be used to treat some special clinic conditions in which the person is unconscious, such as coma, shock, persistent vegetative state, anesthesia, etc.

For the treatment of coma patients with brain trauma and stroke, we collected about 40 articles (Xu et al. 2014; Zhang and Song 1994; Fu et al. 2009; He and Li 2012; He et al. 2004; Lu 2013, 2015; Liu et al. 2006, 2010; Liu and Liu 2010; 2014; Wu 2005; Tang et al. 2002; Sun et al. 2009a; Song et al. 2007; Feng et al. 2008; Zhang et al. 2013a; Zhang 2014a, 2015a; Peng et al. 2010; Xu and Wang 2006; Cao et al. 2011; Li et al. 2003; Li 2014; Mei et al. 2008; Tang et al. 2004; Tu et al. 2010; Bi 2004; Wang and Cheng 2014; Wang and Wang 2005; Xiang et al. 2012; Hou 2012; Ge 2014; Cheng et al. 2013a; Cheng 2011; Ma et al. 2006; Gao et al. 2012; Lu and Li 2014; Feng 2005; Bi et al. 2014; Jiang et al. 2009; Wang et al. 2015; Wei et al. 2007). For such coma patients, acupuncture, together with conventional rehabilitation therapies, can speed up the wake-up rate from 51 $\pm$ 17% to 79 $\pm$ 12% (Fig. 1), or increase the degree of consciousness (the GCS index increased from 3.02 $\pm$ 1.2 to

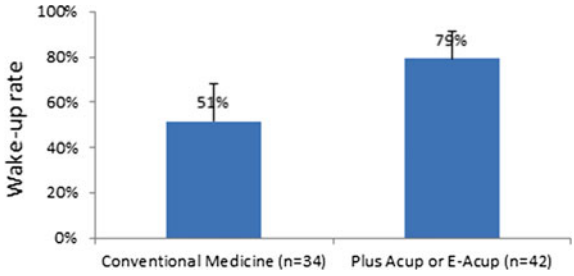

Fig. 1 Wake-up rate with or without acupuncture treatment in coma patients with brain trauma. n = published articles

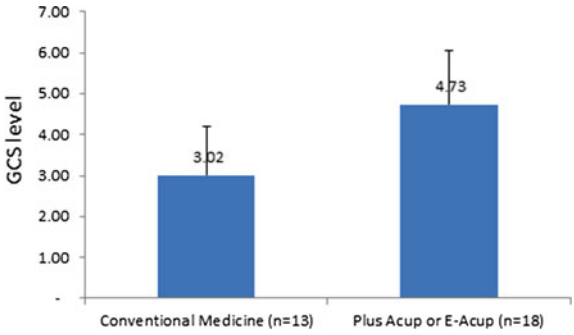

Fig. 2 Consciousness level increase in coma patients after treatment with or without acupuncture or eletroacupuncture. n = published articles

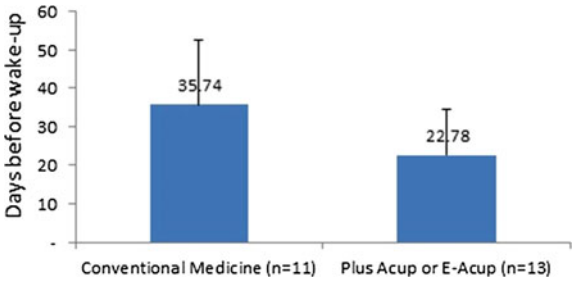

Fig. 3 Number of days before wake-up after treatment with or without acupuncture. n = published articles

4.73 ± 1.3) (Fig. 2). Or, it can be said that acupuncture treatment can shorten the time needed to wake-up from 35.74 ± 16.7 days down to 22.78 ± 11.7 days (Fig. 3).

Acupuncture alone can also reach such healing effect (Zhang and Song 1994; Mei et al. 2008; Ge 2014). The combination of Western conventional treatment with acupuncture treatment can no doubt increase the cure rate and to reduce the sequela rate (data not shown).

It should be pointed out that, when acupuncture is used for the treatment of such severe conditions, it is performed at least once a day. It would not be possible to achieve such healing effect if it was performed only once a week as in current Western style acupuncture, e.g. acupuncture once or twice per week (see below).

2.2 Treatment of Shock with Acupuncture

Doctors at the Second Affiliated Hospital of Hunan Medical College (1973) (Wei 1982) reported on their way of treatment of shock for 160 cases. Besides ordinary conventional emergency supporting treatment, all cases were given acupuncture treatment first. If blood pressure did not increase within 30 min, then the addition of pressor agent was given. With this method, blood pressure in 122 cases clearly increased. The apparent effective rate was 76.3% and total effective rate is 87.5%. This means that the blood pressure in only 23.7% of patients did not respond to the acupuncture treatment. This suggests that acupuncture treatment can increase blood pressure in shock patients. These doctors found that for half of patients, their blood pressure can start to increase within 30 min, some after 60 min. There had been 9 patients for whom the use of the pressor agent did not work satisfactorily, but after the addition of acupuncture, blood pressure increased in 8 cases (systolic pressure up to 90 mmHg). This suggests that for those cases where the blood pressure increase is not stable, acupuncture can work to help the pressor agent. For some patients, if the manipulation of the needles (by twisting) stopped for a longer time, the blood pressure would tend to reduce. After stronger manipulation, the blood pressure would increase again, suggesting that manipulation of needle can influence the healing effect.

Cai (1961) treated 27 patients with shock due to toxic dysentery. Within 10–30 min of acupuncture, the blood pressure started to increase. Only 2 cases needed medicine to increase blood pressure.

Yu (1997) reported that doctors in the department of gynecology and obstetrics in the Jiangyin Hospital of Traditional Chinese Medicine treated 52 cases of shock patients after induced abortion. The patients showed, during or after the operation, pale face, cold hands and feet, palpitation, pressure in the chest, nausea or vomiting, even reduction in blood pressure, coma, etc. Body condition became worse very quickly and changed very fast. The blood pressure of the 52 cases all increased after stimulation of Sanyinjiao (SP6) point for several seconds. The patients then turned conscious to recovery. No one case needed intravenous infusion or other conventional emergency treatment.

Song (1996) treated 40 cases of shock patients due to allergic reaction to penicillin by using acupuncture and epinephrine. For all of the patients, after injection of epinephrine and acupuncture on Neiguan (PC6) point for 5 min, the face turned pink, sweat stopped, consciousness returned, blood pressure increased, and pulse increased. The healing effect showed within an average of 10 min (as fast as 5 min). Except for one case who needed additional intravenous infusion and steroid medicine, the other 39 cases recovered within 5–15 min. There were no deaths. It can be commented that in this clinical report, there was no control group to tell how much the death rate might have been without the use of acupuncture during the emergency treatment. However, according to our own previous work experience in an emergency department in China, acupuncture has been a very effective emergency treatment for those patients who are already in a coma, seen when their lives were saved within 5–15 min.

Liu (1999) and his colleagues treated hemorrhagic shock in 33 cases with acupuncture (no pressor agent). After a half hour, systolic pressure increased from an average of 62.6 mmHg to an average of 98.3 mmHg. With the same condition, similar shock patients in 31 cases were treated without acupuncture (with pressor agent). Their systolic pressure increased from an average of 67.7 mmHg to an average of only 77.9 mmHg.

Zhao (2008) and his colleagues treated various kinds of shock in 40 cases. After acupuncture for 30 h (no pressor agent), systolic pressure increased from an average of 70.9 mmHg to an average of 95.6 mmHg. With the same conditions, another 40 cases were given a pressor agent (no acupuncture), and their systolic pressure increased from an average of 68.9 mmHg to only an average of 85.5 mmHg. For diastolic pressure in the acupuncture group, within half an hour of treatment, it increased from an average of 42.3 mmHg to an average of 58.7 mmHg. In the pressor agent group, it increased from an average of 43.2 mmHg to only 55.24 mmHg.

Fu et al. (2008) treated various shock patients in 138 cases. Within less than 30 min of acupuncture (no pressor agent), systolic pressure increased from an average of 83.1 mmHg to an average of 101.1 mmHg. Under the same conditions, with pressor agent use on another 138 shock patients, systolic pressure increased from 83.3 to 89.2 mmHg. In the acupuncture group and within less than 30 min of acupuncture (no pressor agent), the diastolic pressor increased from an average of 49.5 mmHg to an average of 59.3 mmHg. The diastolic pressure in the pressor agent group increased from an average of 48.8 to 50.4 mmHg.

Ji (1999) treated allergic shock in 50 cases. With conventional emergency treatment, the total effectiveness rate is 76%, while it was 90%, when the conventional method was combined with acupuncture.

The successfulness of acupuncture treatment is of course also related to the intensity of the shock. The effectiveness with low to mild level of shock is higher than with severe shock. It is also related to the type of shock. Generally speaking, the effectiveness with allergic shock and infective shock is higher, but with cardiac shock and hypovolemic shock, lower.

Wu and Huo (2000) reported on their treatment of cardiac shock, hypovolemic shock, infectious shock and allergic shock with conventional medicine plus acupuncture. The total effectiveness for these different types of shock was 80%, 82.6%, 100% and 100%, respectively.

Zhang (1989) reported that, treated with acupuncture alone (no pressor agent) for cardiac shock, the total effective rates for hypovolemic shock, infectious shock, allergic shock, nervous shock and traumatic shock are 90%, 95%, 93.3%, 95%, 93.3% and 96%, respectively.

It should be noticed that acupuncture cannot only work together with a pressor agent to increase the emergency treatment of the shock (Song 1996; Zhao et al. 2008; Ji 1999; Wu and Huo 2000), but can also solve the emergency condition by itself alone (Wei 1982; Cai 1961; Yu 1997; Song 1996; Liu et al. 1999; Zhao et al. 2008).

Clinical studies suggest that (Zhao et al. 2008), in the treatment of shock with acupuncture, the blood pressure increase occurs mostly within 30 min, while when performed with a pressor agent, mostly after 3 h. With acupuncture treatment, the

blood pressure increased earlier and higher. This often happened in the earlier stages of shock. This is very important to improving the functions of important organs, such as the heart, brain, and kidney, so as to prevent irreversible damage to these organs.

To treat shock, every minute is very important to a patient's life. There is no time to allow us to have a control group or a non-treatment group for comparison. It should be acceptable to compare an acupuncture-alone group with the acupuncture plus pressor agent group, e.g. to compare conventional treatment with or without acupuncture. Studies here all tried a half hour of acupuncture first. If the blood pressure did not increase, it was added right away with a pressor agent. The results showed that the combination with acupuncture worked much better than without acupuncture. Indeed, control acupuncture and no-treatment groups have been used in animal shock models. There are many such animal studies, but these are not used as data sources for our articles here.

Patients with low-level shock appear to have anxiety, cloudy consciousness and slow reaction. With middle to severe-level shock, patients lose consciousness. That acupuncture can increase blood pressure when the patients has very low level consciousness suggests that a placebo effect is not the only mechanism by which acupuncture works, and that acupuncture works not only for subjective disorders, such as pain, but also objective disorders, such as blood pressure.

2.3 Treatment of Persistent Vegetative State by Acupuncture

Along with the development of medical diagnosis technique and emergency treatment, the death rate of emergency patients has been dramatically reduced. At the same time it has also induced a new social and medical problem: there are more patients with persistent vegetative state. There are higher death rates and cripple rates in such groups of patients. The persistent vegetative state is hard to treat, causes a heavy burden to a patient's family and society, even if after lots of effort with medical services. It has become a very serious social concern inside and outside of China (Xia et al. 2006).

Estraneo et al. (2010) observed 50 cases of persistent vegetative state. Under the treatment of conventional medicine, only 10% of patients regressed into shallow consciousness, and another 14% returned to consciousness, but all happened after one year of treatment. Before the publication of his paper, it was commonly believed that it is almost impossible to get recovery of consciousness for persistent vegetative state due to brain trauma lasting more than one year (The Multi-Society Task Force on the Persistent Vegetative State 1994; Higashi et al. 1981; Levin et al. 1991). For a long time, due to no effective way of treatment (Machado et al. 2012), the attitude of medical society has been negative and passive for persistent vegetative state. In the US, doctors can stop any treatment and nurse service to allow the patient to euthanasia, according to a patient's will before becoming sick and with the agreement of a patient's family (Yang et al. 1998).

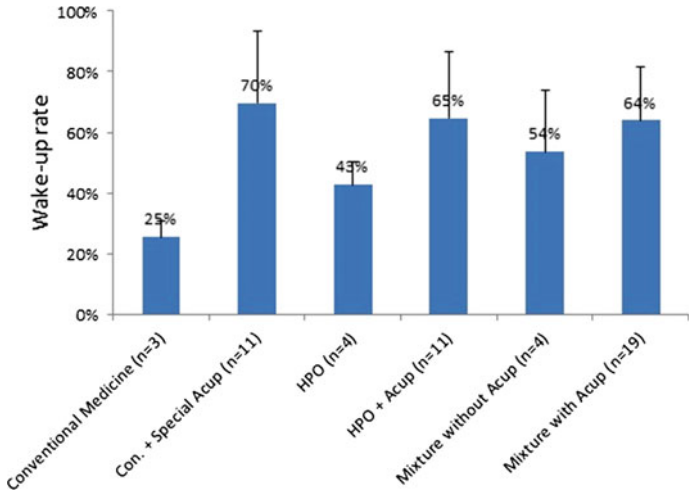

Fig. 4 Wake-up rate of persistent plaintive conditions treated with or without acupuncture (data from China). n = number of experiments. Acupuncture in the "Mixture with Acup" and "Mixture without Acup" groups are ordinary acupuncture. Con: conventional supportive therapies. HPO: high pressure oxygen. Mixture: high pressure oxygen, rehabilitation therapy (exercise), tuina, massage, physiotherapy, sound-light simulation therapy

However, there is quite a different picture for the treatment of persistent vegetative state in China. A lot of studies and clinical reports suggest that acupuncture can work to speed the wake-up of patients with persistent vegetative state (Xia et al. 2006; Yang et al. 1998, 2002; Wang and Wu 2006; Zhang et al. 1996, 2009, 2015; Chu et al. 2003; Wu et al. 1998, 2002, 2003; Guo 1999; Cui et al. 2005; Cheng et al. 2008; Tang and Xia 2002; Zheng 2005; Zeng et al. 2014; Li et al. 2006, 2008a; Huang et al. 2004; Cao and Xiong 2003; Lu et al. 2012; Zeng 2001; Zhu et al. 2005; Liu et al. 2007; Zhang and Luo 2014; Qian 2015; Wang et al. 2000, 2005; Hong et al. 2000; Qian and Ao 2002; Wang and Nie 1998; Ye and Wang 1997; Yin and Shi 2009; Zhang and Li 2013; Sun et al. 2007; Li et al. 2001a).

We can make a summary of these data in Fig. 4.

Data in Fig. 4 suggest that, if treated with traditional conventional medicine, the wake-up rate for persistent vegetative state is 25%. For conventional medicine plus high-pressure oxygen, the wake-up rate can increase to 43%. When conventional medicine is combined with high-pressure oxygen, rehabilitation, and sound-light stimulation, it increases furthermore to 54%. With high-pressure oxygen plus acupuncture, the wake-up rate is 67%. When high-pressure oxygen plus ordinary acupuncture, is combined with rehabilitation, plus sound-light stimulation, the wake-up rate remained the same (64%). For conventional medicine plus special acupuncture, the wake-up rate reaches 70%, suggesting that the special acupuncture technique works much better than the ordinary acupuncture technique, and is also better than a combination of complex and expensive therapies. Even with ordinary acupuncture,

the combination with high-pressure oxygen works better than combination with other rehabilitation remedies.

The effectiveness of acupuncture treatment for persistent vegetative state is related to the length, the severity and the cause of the disorder, the length of treatment course of acupuncture, the age of the patient, etc. (Xia et al. 2006; Estraneo et al. 2010; Yang et al. 1998; Lu et al. 2015). The longer the disorder before acupuncture treatment, the more difficult the treatment is. Persistent vegetative state due to brain trauma is easier to treat than that due to cerebrovascular accident. Persistent vegetative state due to cerebral infarction is the most difficult to treat. Acupuncture does not work if the length of treatment is not long enough.

There are data (Estraneo et al. 2010; Bender et al. 2015) suggesting that 37–43% of patients with persistent vegetative state may still have slight or shallow consciousness and be able to respond to the doctor's orders. However, such shallow consciousness is not complete consciousness. It is similar to the consciousness in early stages of shock, in which the ability of patient to remember things or to analyze outside stimulation is doubtful. We can image our own consciousness and ability to respond to a hint when we have not slept for two nights. Yes, we have consciousness, but our response to outside stimulation would be very slow and our mind would be cloudy to hints. Therefore, it would be very difficult to link the increased wake-up rate of those patients after treatment with acupuncture to a hint or to a placebo effect.

Here we paid attention to the wake-up rate, not to the recovery of body function or life ability after waking up. We emphasize that acupuncture can work when a patient is, almost is, unconscious. Some papers report not the wake-up rate, but a PVS scale. Some report a grade mark, such as the rate of basically cured, dramatically cured, improved, or no change, or such as improved, effective, no effective. For the former grade report, we chose their "basically cure + dramatically improved" as an indication of waking up. In the later grade paper, we only chose their "improved" as the wake-up rate.

Therefore, in the calculation of wake-up rate, we have tried to exclude those patients who only come into a shallow consciousness state after treatment.

2.4 Acupuncture Used Before or During Anesthesia

Liang et al. (2007) reported the use of transcutaneous electrical stimulation (HANS machine, 30 min before anesthesia until the end of operation, stimulating acupuncture points) for 30 cases of breast cancer undergoing radical mastectomy (HANS group). The patients were given intravenous induction plus general anesthesia. Another 30 similar cases were only given intravenous induction plus general anesthesia but no acupuncture (control group). It was found that, 12 h after operation, the pain level (VAS scale) in the HANS group was dramatically lower than control group (2.14 ± 0.85 vs. 3.38 ± 0.91). The HANS group showed a much lower rate of nausea/vomiting than the control group (19% vs. 34%).

Xie and He (2008) treated 30 cases of patients for radical resection of colon cancer. The patients were given general anesthesia plus scalp acupuncture (Acupuncture group). Another 30 similar patients were given general anesthesia only (no acupuncture; control group). Acupuncture started 20 min before anesthesia and lasted until the end of the operation. They found that the involvement of scalp acupuncture reduced the pain during skin incision (isoflurane MAC is 0.75 and 0.88, respectively), showed some level of pain inhibition and anesthesia (the isoflurane MAC during operation is 0.95 and 1.29, respectively). It means that the use of acupuncture reduced the use of anesthesia drugs by 26%.

Ouyang et al. (2009) allocated 100 patients who were having Laparoscopic gastrointestinal surgery, randomly and blindly, into two anesthesia groups: general anesthesia plus acupuncture (acupuncture group, 50 cases) and general anesthesia only (control group, 50 cases). The acupuncture (on Neiguan (PC6) point both sides) was started before induction and lasted until the end of operation. After operation, the needle was removed. The acupuncture points were covered with an opaque tape. It was found that the incidence rate of nausea for 6 h after the operation was 12 and 28% in the acupuncture group and the control group, respectively. The postoperative pain level was no different between the two groups. (Acupuncture point Neiguan (PC6) is not normally used for pain.)

Chi et al. (2014) randomly allocated 160 patients who were to have a heart valve replacement operation, into general anesthesia plus electro-acupuncture (acupuncture group, 80 cases) and general anesthesia only (control group, 80 cases). Electro-acupuncture (on Zhongfu (LU1), Chize (LU5) and Ximen (PC4) points) was started 20–30 min before induction, and lasted until the end of the operation. The anesthesia in the acupuncture group did not use trachea cannula, only a small amount of anesthesia. The result was that the acupuncture group and the control group had similar levels of anesthesia, but the acupuncture group showed a smaller amount of anesthesia drug, fewer cases who needed a blood infusion, an earlier time leaving the bed, a shorter time staying in observation room, less days in hospital, less expense for medical costs, fewer cases with lung infection, an earlier time to start to eat, fewer days using antibiotics, all of which were significant different.

Wu et al. (2013) randomly allocated 40 cases of craniotomy into two groups: 20 cases were given general anesthesia (control group) and 20 cases were given general anesthesia plus electro-acupuncture (Acupuncture group). The acupuncture started 20 min before anesthesia and lasted until the end of the operation. For the control group, an electrical patch was adhered to the acupuncture points, but no electrode was connected. They found that, compared with the control group, the acupuncture group showed a shorter time to waking up (15 min vs. 20 min) after operation, and needed less anesthesia (an average of 2000 mg vs. 2500 mg). Note that the control group is a control group.

Xin et al. (2012) and his colleague randomly allocated 60 patients undergoing subtotal thyroidectomy surgery into two groups of anesthesia: general anesthesia group (control group, 30 cases) and general anesthesia plus transcutaneous acupoint electrical stimulation (TAES) (Acupuncture group, 30 cases). TAES started 20 min before induction of anesthesia and lasted until the end of the operation. They found

that the use of TEAS could significantly stabilize the blood circulation (heart rate, blood pressure), reduce the time of the extubation (6.43 ± 1.08 vs. 10.83 ± 2.64 min), shorten the time in the observation room (12.31 ± 1.79 vs. 17.83 ± 2.87 min), reduce the usage of anesthesia drugs (46.7 ± 6.3 mg vs. 67.5 ± 5.6 mg), and reduce the cost of medicine used (211.78 ± 34.5 vs. 291.53 ± 22.81 Chinese yuan).

Zhang et al. (2014a) randomly and blindly allocated 60 patients undergoing Gynecologic laparoscopic surgery into two groups: electro-acupuncture plus general anesthesia (acupuncture group, 30 cases) and general anesthesia alone group (control group, 30 cases). Electro-acupuncture started 30 min before induction and lasted until the end of the operation. They observed the effect of electro-acupuncture on the gastric function of these patients, by observing the changes of gastric mucosal partial pressure of CO_2 ($PgCO_2$), arterial partial pressure of CO_2 ($PaCO_2$), and the partial pressure difference [$P(g\text{-}a)CO_2$] during surgery. They found that after intervention, there were significant differences in comparing $PgCO_2$ and [$P(g\text{-}a)CO_2$] ($P < 0.01$, $P < 0.05$). The intra-group differences in comparing all indexes were statistically significant between both groups ($P < 0.01$). They commented that electro-acupuncture adopted in laparoscopic surgery with general anesthesia can guarantee the supply of blood oxygen to gastric mucosa, thus protecting the gastric function. Please note that the control group is also a control group.

An et al. (2011) and his colleagues randomly and double blindly allocated 80 patients undergoing supratentorial tumor resection into two anesthesia groups: general anesthesia group (control group, 40 cases) and general anesthesia plus electro-acupuncture (acupuncture group, 40 cases). The electro-acupuncture was started from the beginning of the induction until the end of the operation. In the control group, they only attached electric lines to the acupuncture points (on skin) but there was no connection to electricity. Compared with the control group, the acupuncture group showed less consumption of anesthesia drugs, less time needed to restore automatic breath, less time to extubation and to open eyes, less time to restore automatic movement and automatic direction, and a shorter time in the operation room. After the operation, incidences of irritation, nausea and vomiting, all were fewer in the acupuncture group. For example, the time needed to open eyes in acupuncture group and in the control group was 18.5 ± 8.5 min and 28.5 ± 13.4, respectively.

An et al. (2013) randomly allocated 120 patients undergoing supratentorial tumor resection into three anesthesia groups: electro-acupuncture plus general anesthesia (acupuncture group, 40 cases), TENS plus general anesthesia (TENS group, 40 cases), and a general anesthesia only group (control group, 40 cases). Acupuncture and TENS started before induction and lasted until the end of the operation. In the control group, there were electrical wires attached to the acupuncture points, but no electricity was connected. They found that, during the recovery period, the time needed for automatic breathing, extubation time, time to open eyes, time to have automatic movement, time to regain directional ability, and time to leave operation room were all shorter in the acupuncture group and the TENS group, compared to that in the control group. The postoperative pain level (VAS scale) in the acupuncture group (3.33 ± 1.09) and the TENS (3.40 ± 1.30) group was lower than that in the control group (6.43 ± 1.52).

Yu et al. (2009) randomly allocated 60 patients undergoing modified radical mastectomy into two groups of anesthesia: TENS plus general anesthesia (TENS group, 30 cases) and general anesthesia (control group, 30 cases). TENS started before induction and lasted until the end of operation. They found that the heart rate, blood pressure, blood concentration of catecholamine, and cortisol after extubation are all increased at the end of operation in each group. The increment in the TENS group was significantly less than that in the control group. The Airway adverse reaction was also much lower in the TENS group than that in the control group.

Gong et al. (2013) randomly allocated 80 patients undergoing elder abdominal operation into two groups: general anesthesia plus acupuncture (acupuncture group, 40 cases) and general anesthesia only (control group, 40 cases). The electro-acupuncture started 20 min before induction and lasted until the end of the operation. They found that the usage of anesthesia drugs, the time to open eyes, the time to finish order, the time to restore normal direction, and the restless rate, were all lower in the acupuncture group than those in control group. For example, the time to wake up in the acupuncture group was 7.18 ± 2.73 but in the control group was 12.81 ± 4.42 min. They concluded that combined acupuncture with assisted general anesthesia could stabilize the hemodynamics and reduce the stress to the surgery in elderly patients undergoing abdominal surgery, thus being suitable and favorable for these patients.

Lin et al. (2013) randomly allocated 75 elderly patients undergoing colorectal cancer resection surgery into two groups: general anesthesia plus acupuncture (acupuncture group, 38 cases) and general anesthesia only (control group, 37 cases). The electro-acupuncture started 20 min before induction and lasted until the end of the operation. They found that the time needed to wake-up was shorter in the acupuncture group than that in the control group (20.35 ± 6.05 min vs. 28.24 ± 7.68 min). The rate of disorder of recognition was also lower in the acupuncture group than in the control group (23.7% vs. 35.1%).

Yang et al. (2012) randomly allocated 90 patients undergoing gynecologic laparoscopic surgery into three groups: general anesthesia plus HANS (acupuncture group I, on Zusanli (ST36) and Sanyinjiao (SP6) points, 30 cases), general anesthesia plus HANS (acupuncture group II, on Hegu (LI4) and Taichong (LV3) points, 30 cases) and general anesthesia only (control group, 30 cases). The TENS acupuncture started 30 min before induction and lasted until the end of the operation. They found that Sevoflurane concentration during operation as much lower in the two acupuncture groups (acupuncture group I was much lower than that in acupuncture group II). The blood pressure and heart rate were more stable in the acupuncture group. The time before opening eyes and removing the tube were shorter. The anxiety scale, pain level, nausea scale, and incidence to hold the lower jaw were all lower in the two acupuncture groups than those in the control group. The time before passing gas was also shorter in the two acupuncture groups than that in the control.

Zhou et al. (2002) randomly allocated 66 cases undergoing video assisted thoracoscopy into two groups: acupuncture plus pain-killer anesthesia group (acupuncture-drug group, 33 cases) and general anesthesia group (control group). The acupuncture started 30 min before induction and lasted until the end of the operation. They found that the consumption of the pain killers was much less in the acupuncture-drug group

than that in the control group (0.039 ± 7.419 ml/kg vs. 0.068 ± 0.023 ml/kg). The blood pressure and heart rate were similar in both groups. The good anesthesia rate of the acupuncture-drug group was 78.8%.

Gu et al. (2004) randomly allocated 22 patients undergoing tumorectomy into two groups: general anesthesia plus acupuncture (acupuncture group, 11 cases) and general anesthesia only (control group, 11 cases). The acupuncture started 20 min before induction and lasted until the end of the operation. They found that the inhibition effect of the surgical operation was less in the acupuncture group than in the control group. The blood circulation was more stable during the operation in the acupuncture group than in the control group.

Gu et al. (2010) randomly allocated 90 patients undergoing cholecystectomy into three groups: general anesthesia plus traditional electro-acupuncture (acupuncture group, 30 cases), general anesthesia plus control acupuncture (control group, non-acupuncture points, also with electric stimulation, 30 cases), and general anesthesia only (control group, 30 cases). The acupuncture started 15–30 min before induction and lasted until the end of the operation. The acupuncture needles in the control group were inserted into non-acupuncture points and also connected with electrical stimulation. They found that the consumption of anesthesia drug in the acupuncture group was much less than in the control group and in the control group. For example, the consumption of Propofolum in the acupuncture group, the control and the control groups were 451.33 ± 136.30 mg, 524.57 ± 180.66 mg, and 600.47 ± 153.84 mg, respectively. The time before opening eyes, before extubation, and before recovery of direction ability were all shorter in the acupuncture group than those in the control group and in the control group. The use of painkillers after the operation was also much less in the former than that in the latter two groups. The postoperative pain level was less in the former than that in the latter two groups. Acupuncture at acupoints can enhance the anesthetic effect of compound general anesthesia and prolong the analgesia period. Acupuncture at non-points has certain effect, but their effectiveness is less than that of acupoints. Thus, the acupoint has specificity and accurate acupoint selection is the key factor affecting analgesia effect.

Ding et al. (2013) randomly allocated 90 patients undergoing cholecystectomy into three groups: general anesthesia plus traditional electro-acupuncture (acupuncture group, 30 cases), general anesthesia plus control acupuncture (control group, non-acupuncture points, also with electric stimulation, 30 cases), and general anesthesia only (control group, 30 cases). The acupuncture started 15–30 min before induction and lasted until the end of the operation. They found that acupuncture can stabilize blood circulation, reduce CO_2 pneumoperitoneum, reduce postoperative stress reaction, and enhance postoperative pain-reducing effect, compared with the control and control groups. The time before opening the eyes, time before extubation, and time before recovery of direction ability, all are significantly shorter than in the control group and in the control group. The acupuncture groups recovered better than the control group.

Wang et al. (2012a) randomly allocated 80 patients undergoing pneumonectomy into four groups: control group (control acupuncture plus general anesthesia, 20 cases), acupuncture (2 Hz) plus anesthesia (2 Hz Acupuncture group, 20 cases),

acupuncture (100 Hz) plus anesthesia (100 Hz acupuncture group, 20 cases), and 2/100 Hz acupuncture plus anesthesia (2/100 Hz acupuncture group, 20 cases). The acupuncture started 30 min before induction and lasted until the end of the operation. In the control group, an electrical patch was attached to the acupuncture point spots, but no electricity was connected. They found that the consumption of fentanyl during surgery was less in the 2 and 100 Hz acupuncture groups than in the control and 2/100 Hz acupuncture groups. In all groups, the average arterial pressure increased after intubation, compared to that before induction, but the increase range in all acupuncture groups as less than that in the control group. For similar comparison, the heart rate increased significantly in the control group, but not so in all the acupuncture groups. After the surgery, the index for auto-immune function reduced, but not so in all the acupuncture groups. They concluded that, with the use of acupuncture during surgery, with less usage of anesthesia drugs, the body circulation and immune function can be more stable, so as to reduce body stress reaction and to protect organ function. The electrical frequency of 2 and 2/100 Hz were better than the 100 Hz.

Tang et al. (2001) randomly allocated 45 patients undergoing radical operation of carcinoma of the esophagus into three groups: electro-acupuncture group plus general anesthesia (acupuncture group, 15 cases), electrical patch plus anesthesia (patch on acupuncture points, connected with electrical stimulation) (patch group, 15 cases), and general anesthesia only (control group, 15 cases). The acupuncture and the patch stimulation started 10–30 min before induction and lasted until the end of the operation. They observed the anesthesia effect in the three groups. The number of patient reached anesthesia level I in acupuncture group, patch group and control group were 11 (73.3%), 10 (66.7%), and 4 (26.7%), respectively. The efficiency of the electro-acupuncture plus general anesthesia and electrical patch stimulation plus general anesthesia worked better than general anesthesia alone. The authors commented that acupuncture point stimulation can adjust body function status to increase pain threshold. Using acupuncture alone, there is the possibility that the suppression of pain is not complete, muscle is not completely relaxed, and the contraction reaction is strong, so that its application in the surgical area is limited somehow. On the other hand, anesthesia drug tends to inhibit functions of cardiovascular and respiratory systems. The inhibition effect is related to the dose used. Inhibition is risky to patients with cardiovascular diseases, if it is over used. When the acupuncture point stimulation technique (needle or electrical patch stimulation) is used together with general anesthesia, the patients' heart rate and blood pressure are stable. The patients lose consciousness without painful faces and do not realize the surgical course. The usage of the anesthesia drug is reduced. The safety of the combined anesthesia is increased; the anesthesia effect is steady or improved; the cost of the anesthesia is also reduced.

Fu et al. (2002) randomly allocated 40 patients, after general anesthesia, into two groups: TENS group (20 cases) and control group (no TENS stimulation, 20 cases). The electrical stimulation on acupuncture points started 10 min before skin incision, and lasted for 30 min. They found that the heart rate and average arterial pressure were increased in both groups 10 min after skin incision, but the increment range in the TENS group was much less than that in the control group. For example, for

average arterial pressure 10 min after skin incision, it was increased by 25 and 35% in the TENS group and in the control group, respectively. Meanwhile, the heart rate increased by 15.9 and 27.6%, in the two groups, respectively. This result suggests that stimulation of acupuncture points by electrical stimulation could stabilize and buffer the body's stress reaction due to skin incision. Because the fact that the electrical stimulation started after anesthesia when the patients lost consciousness, the stabilization effect of acupuncture point stimulation cannot be understood as a placebo effect.

Guo et al. (2002) reported on electrical stimulation of acupuncture points one hour after general anesthesia on five patients undergoing excision of intracranial tumor. The electro-acupuncture could increase systolic blood pressure by 22.40 ± 3.19 mmHg, diastolic blood pressure by 12.00 ± 1.41 mmHg, mean arterial pressure by 15.99 ± 1.65 mmHg, and heart rate by 24.00 ± 6.66 bpm. They commented that, after anesthesia, stimulation of acupuncture can still improve cardiovascular function.

Yin et al. (2005) randomly allocated 69 patients undergoing rectal cancer surgery into three groups: acupuncture before anesthesia (pre-acupuncture group, 23 cases), acupuncture after anesthesia (post-acupuncture group, 23 cases) and anesthesia alone (control group). They found that the efficiency of anesthesia was better in the pre-acupuncture group than that in the post-acupuncture group, and much better than in the control group. Although it cannot be excluded that this is due to the longer stimulation of acupuncture points in the pre-acupuncture group than in the post-acupuncture group, it indicates that stimulation of acupuncture points after induction of anesthesia could also enhance anesthesia level, and reduce the consumption of anesthesia drugs.

Wang (1959) have reported on the acupuncture treatment of surgical accidents, such as stoppage of breath (2 cases), diaphragmatic spasm (11 cases), tachyarrhythmia (2 cases), hypotension (2 cases) and shock (3 cases). Though the earlier reports did not designate a control group, control group, or blind group, they suggested that, under anesthesia, acupuncture can still exercise healing effects. Such implications have been well documented in later studies.

Based on the reports above, it can be said that the combination of general anesthesia with acupuncture (ordinary acupuncture, electro-acupuncture or TENS), could stabilize blood circulation, immune system, and reduce the consumption of anesthesia drugs, while enhancing the anesthesia effect. It might be due to the reduction of the consumption of anesthesia drugs, which makes possible shorter time before opening eyes, time in the observation rooms, time before extubation, time to recover direction ability, lower level of postoperative pain, and lower incidence of postoperative nausea and vomiting (Wang et al. 2011; Ding and Gu 2008; Shen et al. 2011).

Ouyang et al. (2009) study showed that the reduction of postoperative nausea/vomiting rate is much more in the acupuncture group than that in the control group, suggesting that acupuncture has its own specific healing effect.

Data from Wu et al. (2013), An et al. (2011), (2013), Gu et al. (2004), (2010), Ding et al. (2013), Wang et al. (2012a) all showed that the benefit of acupuncture is much higher in the acupuncture group than in the control group (no matter the

control is inserted or non-inserted needles), also suggesting that acupuncture indeed has a unique healing effect in such unconscious patients.

Then, the question is, is the reduction in the consumption of anesthesia drugs (and other benefits of acupuncture) due to the acupuncture stimulation in the period before anesthesia, or to that during anesthesia, or both? Data from Fu et al. (2002), Guo et al. (2002) and Yin et al. (2005) indicates that even if patients were under anesthesia condition (unconscious), acupuncture can still work to stabilize blood circulation and to buffer stress reaction of the body to surgical operations. Acupuncture during the period before anesthesia surely would also work for this effect (Yu et al. 2010a; Peng et al. 2005; Zhu et al. 2011; Li et al. 2001b; Shen and Cheng 2012; Zheng et al. 2014; Lin et al. 2002), and the only thing we do not know is how long such effect could extend into the period during anesthesia (during operation) and after operation. A review article also supports the positive function of acupuncture during the anesthesia (Asmussen et al. 2016).

2.5 Acupuncture Started After General Anesthesia

Alizadeh et al. (2014) randomly allocated 227 patients undergoing general anesthesia into two groups: acupuncture on Neiguan (PC6) points (112 patients) and acupuncture on Neiguan (PC6) and Hegu (LI4) points (115 patients). The acupuncture started after the induction of general anesthesia and lasted until the end of the operation. They found that both groups had reduced incidences of postoperative nausea/vomiting.

Arnberger et al. (2007) randomly allocated 220 patients undergoing general anesthesia into two groups: electro-acupuncture group (110 cases) and control group (electrical stimulation on non-point spots, 10 cases). Stimulation started after general anesthesia and continued until the end of the operation. They found that incidences of postoperative nausea in the acupuncture group and the control group were 33% and 51%, respectively, and that of vomiting was 16% and 25%, respectively.

There was a report by Liodden et al. (2015) that acupuncture started after the induction of anesthesia showed no more effect than with a control group. However, as pointed out by Alraek and Birch (2016), the acupuncture stimulation dose in this study was not at all sufficient to create a healing effect in the acupuncture group. When applied after anesthesia, the acupuncture stimulation should be kept during the whole course of the operation.

All of these data clearly suggest that, when acupuncture is started after general anesthesia, in which the patient is unconscious, the acupuncture still works to reduce post-operative incidences of nausea/vomiting, suggesting that acupuncture has its own specific healing effect, not a placebo effect. The reduced incidences of nausea/vomiting are not due to the awareness of patients before anesthesia of which group they were allocated to.

Streitberger et al. (2004) used acupuncture before and after general anesthesia to patients undergoing abdomen and breast surgical operations. They stimulate Neiguan (PC6) point for 20 min before or after induction of general anesthesia. They found that

the post-operative incidence of nausea/vomiting in the acupuncture group was 38.9 and 48.1%, while those in the placebo group were 47.3 and 54.9%, suggesting that acupuncture did not induce significant healing effect. However, most of the acupuncture studies on this topic using acupuncture either started before general anesthesia or after induction of general anesthesia, and lasted until the end of the surgical operation, and the incidences of post-operative nausea/vomiting reported were between 17.7 and 21%. Therefore, the Streitberger et al. (2004) experiment does not mean that acupuncture does not work, but that the 20-min acupuncture is not sufficient to bring out a healing or preventive effect for post-operative nausea/vomiting.

2.6 Delayed Wake-Up After General Anesthesia

If, 90 min following the use of general anesthesia medicine for 90 min, the patient still does not wake-up, this can be regarded as delayed wake-up. This is a common complication after general anesthesia and one of the reasons that it is risky to a patient's life.

Zhai (2011) randomly allocated 30 patients in the delayed wake-up status into two groups: conventional medicine plus acupuncture treatment (acupuncture group, 15 cases) and conventional medicine only (control group, 15 cases). The acupuncture is a kind of modified acupuncture technique. The needles were kept for 30 min, manipulated by hands once every 10 min. The acupuncture was repeated once every 2 h until consciousness returned. In the acupuncture group, the mean wake-up time was 150 min (30–380 min), while that in the control group was an average of 300 min (90–1080 min). The difference was significant.

Zhang et al. (2014b) randomly allocated 50 patients in the delayed wake-up status into two groups: conventional medicine plus acupuncture treatment (acupuncture group, 30 cases) and conventional medicine only (control group, 20 cases). The acupuncture is similar as that noted above: the needles were kept for 30 min, manipulated by hands once every 10 min. The acupuncture was repeated once every 2 h until consciousness returned. The average wake-up time in the acupuncture group was 90 min (30–380 min) and in the control group, 300 min (90–1080 min).

Delayed wake-up is commonly seen in elderly patients. The reasons are varied. Older patients have declined body function, slower metabolic rate, and are sensitive to anesthesia so that anesthesia may remain in the body and cause delayed wake-up.

Wang et al. (2014) randomly allocated 80 elderly patients (after general anesthesia and surgical operation) into two groups: conventional medicine plus acupuncture (acupuncture group, 40 cases, acupuncture started after operation) and conventional medicine only (control group, 40 cases). They found that the average time before wake-up was 15.3 ± 1.9 min in the acupuncture group, while it was 18.7 ± 2.4 min in the control group. The difference was significant.

2.7 Anesthesia in Shock Patients

Acupuncture used in anesthesia may not only have pain-reducing effect, but also a clear anti-shock effect. When the blood pressure of patients is very low or there is no blood pressure, it would be very dangerous to give anesthetic drugs, since the anesthesia medicine tends to inhibit the nervous system, and the medicine has side effects too, both of which could make the shock condition worse, bringing risk to the surgical operation and causing complications after surgery.

Wu et al. (1980) treated 99 shock patients who needed a surgical operation. The systolic pressure for all was below 90 mmHg. The reasons for shock included hypovolemic shock, toxic shock, traumatic shock, and so on. They treated the patients with conventional medical methods, such as infusion, oxygen, infusion of blood, antibiotics, correction of electrolyte disturbances, and so on. They also used body acupuncture, ear acupuncture, nose acupuncture, or mouth lip acupuncture on the patients. After induction with acupuncture for 15–25 min, it was observed that there was an increase in blood pressure. During the induction period, blood pressure increased between 10–20, 21–30, 31–40 mmHg and more than 41 mmHg in 41, 22, 7, and 14 cases, respectively. In 3 cases, the blood pressure went down, and in 12 cases, there was no change. Among the 99 cases, only 11 cases changed to epidural anesthesia due to incomplete anesthesia with acupuncture. 15 cases needed the addition of 0.5% procaine (local anesthesia medicine). The authors pointed out that acupuncture may not only have a pain inhibition effect, but also a relatively apparent anti-shock effect. After acupuncture, 84.85% of patients had blood pressure increased, while at the same time, similar of patients with continuous epidural anesthesia, none had a blood pressure increase. In 81% of patients blood pressure decreased, and 72% of the patients had blood pressure go down to zero. During acupuncture, blood pressure, pulse and breath were relatively stable (less variable). The recovery after surgery was faster. No side effects happened. Inhibition to respiratory and cardiovascular systems by the anesthesia was prevented.

Doctors in the Department of Anesthesia of the Forth Hospital of Harbin City (1973) reported on their treatment of 30 shock patients who needed anesthesia. The reasons for the shock were toxic shock and hypovolemic shock. Acupuncture was mostly body acupuncture. 12 cases were also with auricular acupuncture. Upon skin incision, 21 cases were given a little amount of local anesthesia medicine. During surgical operations, there were no accidents with respiratory inhibition as easily seen in medical anesthesia. For anesthesia efficiency level, 2 cases reached excellent level, 10 cases reached good level, 13 reached acceptable level, and 5 cases failed and changed to medical anesthesia. The blood pressure-increasing effect by acupuncture was gradual with less variation. After increasing, it was easy to keep consistent, unlike the blood pressure increased by pressor agents in which blood pressure could easily fluctuate. Except for 1 case whose blood pressure did not increase, in all other 29 cases, the blood pressure increased and stayed at some level as well. The acupuncture could work in coordination with pressor agents. Under acupuncture, the use of pressor agents was much less than when pressor agent alone was used: the

pulse was stronger; the difference between systolic and diastolic pressure was larger, and breath was stronger. All of these are helpful to solving the shock condition. In hypovolemic shock, the use of acupuncture reduced the volume of blood infusion needed. It reduced the blood infusion average by about 400 ml. Shock patients often have failure of functions in the liver and kidney. Under such condition, the use of medical anesthesia tends to make the condition worse, especially after the operation, and cause severe consequences. Upon acupuncture usage, no case had worsened liver-kidney function due to anesthesia, since the internal environment was disturbed less with acupuncture anesthesia.

Doctors in the Department of Anesthesia of the Affiliated Hospital of Anhui Medical College (1973) reported the treatment of 50 cases of shock with severe patients undergoing surgery. The shock included hypovolemic shock, toxic shock, and traumatic shock. In the 50 cases, they used auricular acupuncture (27 cases), auricular acupuncture plus body acupuncture (7 cases), nose acupuncture (6 cases), nose acupuncture plus auricular acupuncture (4 cases), auricular acupuncture plus ear-root point injection (1 case), auricular acupuncture plus body acupuncture plus ear-root point injection (1 case), and nose acupuncture plus intradermal acupuncture (4 case). After acupuncture for about 10–15 min, the blood pressure would start to increase. Together with intravenous infusion of liquid and blood, correction of acid toxic and pressor agent, the blood pressure returned to normal gradually. In all the 50 cases, blood pressure increased 10–20 mmHg, 21–30 mmHg, 31–40 mmHg, and more than 41 mmHg in 21, 16, 7, and 5 cases, respectively. Only one case had no change in blood pressure. The whole course of the operation was stable. For the acupuncture anesthesia level, 43 cases were satisfied and 7 cases had incomplete anesthesia and had to change the method of anesthesia. Among the 43 success cases, 8 cases used local anesthesia in the skin incision spot with 0.5% procaine.

It was commented (Alraek and Birch 2016) that the adrenal gland point on the ear has a stronger blood pressure-increasing effect. Nose acupuncture works better for surgical operations in the lower abdomen for muscle loss. Nose acupuncture plus intradermal acupuncture works well for reducing pain during skin incision. Using acupuncture in hypovolemic shock, the volume of blood necessary for infusion can be reduced but the blood pressure goes up gradually. It was commonly found that, with medical anesthesia, the increased blood pressure may reduce again, so that the use of pressor agents is very common. But it would be dangerous to use large amount of pressor agents. With acupuncture for anesthesia, it is rare that blood pressure would go down again. The author (Fleckenstein et al. 2016) reported that they treated 50 cases of shock in severe patients and, except for only one case, all patients had blood pressure increased after acupuncture induction. Only 12 out of the 50 cases used a little amount of pressor agents, which was much less than with ordinary medical anesthesia. Therefore, acupuncture used in shock patients also prevented the side effect of pressure agents (especially as noradrenalin), such as skin necrosis and reduced volume of urine. With intratracheal anesthesia, the chance of complications increased, but with acupuncture anesthesia, it was never seen such complication as respiratory inhibition as seen with former.

Doctors in the Department of Anesthesia of the Affiliated Hospital (1973) reported on their treatment of 45 shock patients undergoing anesthesia. Among the 45 cases, light shock, middle shock and severe shock were 8, 26, and 12 cases, respectively. Most patients did not receive any medicine before acupuncture. Several patients got the painkiller Sauteralgyl, or sedative Phenergan, or atropine or Dong Lang scopolamine. Among the 45 cases, 33 cases combined with local anesthesia (73.3%) and 27 cases with Sauteralgyl (60%). 12 cases did not use any of these medicine (26.7%). The anesthesia efficiency as very good at 71.1%, not good at 28.9%. Blood pressure increased in 82.2% of patients, did not change in 6.7%, and reduced in 11.1% of patients, at the end of the surgical operation.

Doctors in the Department of Anesthesia of the 5th Hospital of Guangzhou City (1975) reported on their treatment of 55 shock patients who needed a surgical operation. The operations included cesarean, subtotal gastrectomy, ectopic pregnancy, ovariohysterectomy, cholecystectomy, intestinal resection and anastomosis, splenectomy, debridement, and suture fixation. Before operations, only the sedative luminal was used. During operations, they used only acupuncture for anesthesia (did not use anesthesia). The anesthesia efficiency was at a very good level for 67.3% of patients and more than 100 mg of Sauteralgyl was needed in another 25.4% of patients. Acupuncture anesthesia failed in 7.3% of patients. Post-operative blood pressure increased more than 100 mmHg in 87.2% of patients, increased 80–90 mmHg in 10.9% of patients, and failed to increase in 1.8% of patients. Only 2 cases needed pressor agents.

Yang (1987) reported on their treatment of 60 shock patients undergoing anesthesia and surgical operation. Among the 60 cases, 28 had hypovolemic shock and 32 infectious shock. 14 cases used 50 mg Sauteralgyl and 0.5 mg atropine. 16 cased used 50 mg Sauteralgyl only 7 cased used 0.5 mg atropine only. They did not use any other painkiller or sedative. 56 cases used auricular acupuncture, and 4 cases used body acupuncture. The anesthesia efficiency reached level I, II, III, and IV in 21, 22, 12, and 5 cases, respectively. The authors stated that for abdominal surgery, auricular acupuncture worked better.

Doctors in the Department of Anesthesia of Shanggao People's Hospital of Jiangxi Province (1977) reported on their treatment of 37 shock patients who needed a surgical operation. They used acupuncture on 37 patients (acupuncture group), and medical anesthesia (medical anesthesia group) in 15 cases (including general anesthesia, lumbar anesthesia, epidural anesthesia, and local anesthesia). In the acupuncture group, most of the patients did not use sedatives, a few patients used a painkiller, 25–50 mg Sauteralgyl, and used local anesthesia during operation. The type of shock present was mostly hypovolemic shock and toxic shock. Of the 37 patients, blood pressure increased after acupuncture in 70.3%; there was no change in 24.3%; there was reduced blood pressure in 2.7%; and it fluctuated in 2.7%. In the medical group, the blood pressure increased in 13.3% of cases; as not changed in 26.7%; reduced in 40% and fluctuated in 20% of patients. Anesthesia efficiency reaching level I, II, and III in the acupuncture group was 29.7%, 56.8%, and 13.5%, respectively.

The Acupuncture-anesthesia cooperation group in Yulin, Guangxi Province (1975) reported on acupuncture anesthesia given to 88 shock patients who needed

a surgical operation. The shock present was hypovolemic and toxic shock. The surgery was stomach, intestine, gall bladder, and uterine surgery. During acupuncture and operation, blood pressure increased less than 10 mmHg in 39 cases; increased 11–20 mmHg in 10 cases; increased 21–30 mmHg in 7 cases and there was no change in 32 cases.

Hu and Luo (1978) reported on acupuncture anesthesia given to 60 shock patients who needed a surgical operation. Among the patients, 26 had hypovolemic shock; 28 ad toxic shock; and 6 had traumatic shock. 30 min before the operation, patients were given 0.5 mg atropine and 0.1 g luminal sodium intramuscular injection. Acupuncture anesthesia was given: nose acupuncture plus auricular acupuncture in 49 cases; nose acupuncture plus auricular acupuncture plus body acupuncture in 8 cases. Before operation, Sauteralgyl was injected intramuscularly. It was not used if the condition was not severe. The anesthesia efficiency reached level I, II, III, and IV, in 10, 19, 29, and 2 cases, respectively. After acupuncture started, intravenous infusion of liquid and blood, oxygen inhalation, and other procedures were performed too. After 15–20 min of acupuncture, blood pressure started to increase. At the end of operation, 91.6% of patients had blood pressure increased gradually with larger differences between the systolic and diastolic pressure. The heart beat sound grew stronger gradually and microcirculation started to improve gradually too. In the 32 patients with hypovolemic and traumatic shock, the systolic pressure increased an average of 24 mmHg, in which 12 patients increased by 30 mmHg. In the 26 with hypovolemic shock, the hemochrome was an average of 7.6 g, with an average loss of blood of 1500–1800 ml, while the blood infusion needed was only 230 ml, which was less than 1/6 of the lost blood volume.

Doctors in the Group of Acupuncture Anesthesia, Yuling District, Guangxi Province (1977) reported on acupuncture used for 61 shock patients who needed a surgical operation. The reasons of the shock were hypovolemic (14 cases), toxic (19 cases), traumatic (2 cases), and severe diseases (26 cases). The acupuncture used included body acupuncture in 27 cases, body acupuncture plus auricular acupuncture in 15 cases, body acupuncture plus mouth lip acupuncture in 4 cases, body acupuncture plus nose acupuncture in 5 cases, auricular acupuncture in 2 cases, mouth lip acupuncture in 5 cases, and there was no record in 3 cases. The anesthesia efficiency was excellent in 55.7% of cases, acceptable in 37.7%, and failed in 6.5%.

Doctors in the department of anesthesia in the Affiliated Hospital of Shandong Medical College (1973) summarized the use of acupuncture on shock patients, saying that (1) acupuncture could clearly increase blood pressure. The most safe anesthesia in shock patients is local anesthesia but it was found that when the operation area is too large, the use of local anesthesia cannot produce complete anesthesia and satisfactory relaxation of muscles. During the operation, blood pressure could be reduced due to the operation stimulation and the pain reaction, and the pulse could become faster, so as to make the shock worse, even causing accidental death. Intravertebral anesthesia inhibited the use of intraspinal anesthesia in shock patients. Epidural anesthesia is also not a good choice for shock patients. Because the shock patients had poor tolerance to the medicine used in epidural anesthesia, personal variation was very large and it was very easy to cause relative over-dose of anesthesia due to improper anesthesia,

causing blood pressure to be reduced and accidental death. Ether inhalation is hard to keep stable and even shallow anesthesia and the breath tract is hard to keep smoothly open. It is also not a good choice for a shock patient and it should not be used. The most ideal anesthesia might be the combination of ether and muscle relaxer. This can not only induce satisfactory muscle relaxation and keep open the breathing tract, but also reduce the use of ether and use an evenly shallow anesthesia for longer; block the operation stimulation to the brain, provide satisfactory muscle relaxation and keep the breathing tract open. However, this way of anesthesia requires expert skill from the anesthesia operator and the equipment is complex. The advantage of acupuncture used in the shock patients is that (1) it does not use medicine, so there is no possibility to inhibit respiratory or blood circulation system, so not interfere the body function, (2) acupuncture per se has no side effects, but has benefits to the body (such as stabilizing the body's internal environment), (3) for acute patients, especially for acute traumatic upper digestive tract bleeding, and acute intestine obstruction, there is no way to inhibit food intake to empty stomach, and because the patients are awake during acupuncture, it prevents vomiting or mis-inhalation by accident, (4) for acupuncture used with shock patients, the anesthesia efficiency is satisfied, and it is simple to operate. The most important thing with acupuncture anesthesia is that it is safe and ensures no worry about possible overdose of medicine or blockage of the breathing tract, etc. Therefore, it is easily handled by ordinary anesthesia operators, and it is a better choice for shock patients undergoing a surgical operation.

From above reports, it can be seen that acupuncture alone can be used with shock patients to reduce the amount of usage of painkillers and sedative medicines, reduce the volume of blood infusion, to reach satisfactory anesthesia levels and to improve shock conditions at the same time.

Because a shock patient is in a severely diseased condition, their consciousness is cloudy, or even lost, and they have difficulty reacting to outside language or actions hinting at a placebo effect.

Someone may have questioned that for the acupuncture anesthesia, there is still the use of painkillers and sedative medicine. The above data shows that for most patients and in most reports, painkillers and sedatives are not used. Even when they are used, the amounts are lower than normal.

2.8 Dementia Treatment by Acupuncture

Dementia can be separated into senile dementia and vascular dementia. Vascular dementia is one of the most common kinds of dementia in China, which is caused by a disorder in brain blood circulation. The word dementia describes a set of symptoms that can include memory loss and difficulties with thinking, problem solving or language. In vascular dementia, these symptoms occur when the brain is damaged because of problems with the supply of blood to the brain. It has become a serious problem to human mental health, and has caused a severe burden to family life and society. It is a hard problem for medical society to solve. It was reported that among

patients over 65 years of age, about one third (25–41%) would develop into vascular dementia within three months after an acute cerebral accident (Paul et al. 2003). An epidemiologic study in the US showed that among survivors over 60 years of age of acute cerebral accident, about 26.3% developed vascular dementia (Ye et al. 2011).

Currently, there is no effective therapy for the treatment of any kind of dementia (Yu et al. 2005; Leng 2010). Because dementia patients have slow mental reactions, poor analysis skills, and poor memory, it would be hard to believe that such patients could react to a hint, as normal people, and develop a placebo effect during treatment. So, let us have a look at how acupuncture can work for dementia.

We also collected data from China (Cui et al. 2015; Ding 2014; He 2001; Wang et al. 2009, 2013, 2015; Dou 1999; Cai and Wang 2009; Liu and Wang 2011; Fu 2004; Ye et al. 2011; Zhang et al. 2006, 2008a, b, 2010, 2013b, 2015a, b; Li and Jiao 2014; Li et al. 2008b, 2009, 2011, 2012, 2013, 2014; Mao 2015; Fu 2015; Qi et al. 2007; Liu et al. 1997, 2003, 2005; Wu 2010; Zhou and Zhou 2012; Sun et al. 2009b, 2012; Zhuang et al. 1999; Ji et al. 2007, 2012; Lai et al. 2000; Yu et al. 2002, 2007; Zhou and Yang 2008; Peng et al. 2004; Wang 2003, 2005, 2007, 2012; Li and Yan 2010; Mu et al. 2001; Ji and Wang 2006; Zheng et al. 1999; Jin and Jin 2004; Jin et al. 2002; Cheng et al. 2013b; Qi 1999, 2004; Zhao 2009; Zhang 2002, 2014b, 2015b; Yang 2007; Zhu and Zhu 2008; Yang et al. 1996; Bian et al. 2009; Lu et al. 2013; Zhou et al. 2011a, 2013; Wu et al. 2008, 2010; Lu and Lin 2006; Meng et al. 2009; Su 2012; Hao et al. 2012; Cheng and Wang 2006; Gao 2004; Ouyang and Ouyang 2012; Duan 2009; Jin and Zhang 2013; Sun and Xue 2008; Fu et al. 2014; Yu and Han 2007; Feng et al. 2013; Shi 2014a; Shi et al. 2009; An et al. 2014; Wang and Du 2013; Wang and Li 2014; Guan et al. 2009; Xue et al. 2013; Zhao and Xu 2013; Xing et al. 2007; Huang et al. 2011). As usual, the effective rate from China was either reported as a grade improvement (the rate of cure, much improved, improved, or no effect), or on the MMSE scale (or HDS scale). For grade reports, we combined the "cure rate" and "much improved rate" together and got Fig. 5. For the latter, we got Fig. 6.

Figure 5 shows that, treated with conventional medicine, the Cure-much-improved rate is 33.4 ± 19%. With treatment with acupuncture, it was 44.7 ± 20%. With Chinese herbal therapy, it was 40.0 ± 24%. With combination of conventional medicine and acupuncture, it was increased to 61.8% ± 19%. With combination of acupuncture and Chinese herbal therapy, it was similarly increased to 57.2 ± 20%

Data showed via MMSE change (Fig. 6) also showed similar results. The effective rate of the acupuncture group (20.6 ± 11%) was higher than conventional medicine alone (14.3 ± 8%). With the combination of conventional medicine with acupuncture, the MMSE result increased by 23.8 ± 8%. With the combination of acupuncture with Chinese herbal therapy, MMSE can be increased by 27.1 ± 10%. (Some paper only reported grade effectiveness change, some showed only MMSE change, and therefore, the basic data for each figure might not be the same.)

Apparently, acupuncture has a specific healing effect. Combination of acupuncture with either conventional medicine or Chinese herbal therapy can further increase the healing effect.

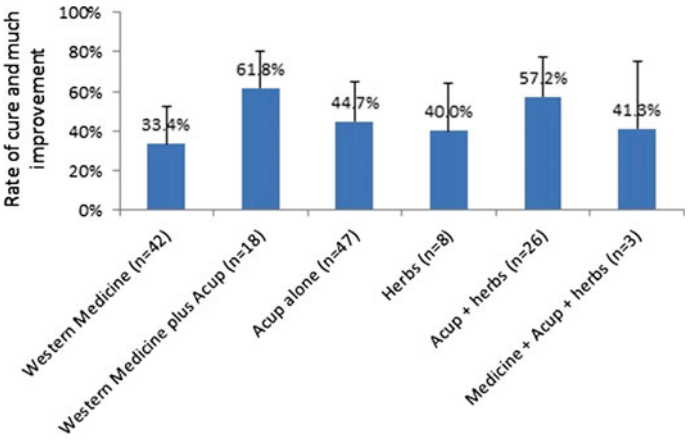

Fig. 5 Healing effect on vascular dementia by different therapies. n = experiment groups

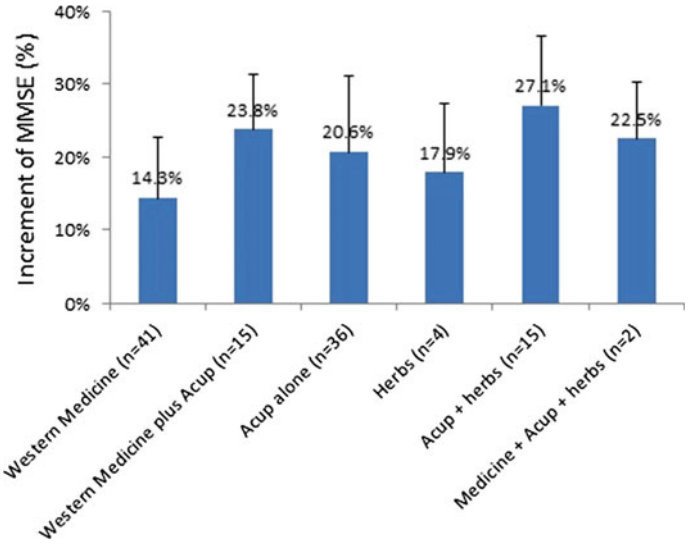

Fig. 6 Increase in MMSE points in vascular dementia after treatment with various therapies. n = experiment groups

Brief summary:

(1) Placebo effect requires a person with a clear mind. Data here shows that acupuncture works in a condition when a person is without or with a very week level of consciousness, such as coma, shock, persistent vegetative state, general anesthesia (before, during, of after operation). This is direct evidence that acupuncture has its own specific healing effect.

(2) Data in the acupuncture treatment of dementia are listed as indirect evidence, since in the dementia, some patients could still have clear mind though they could have a poorer ability to remember.

3 Different Healing Effect with Different Acupuncture Techniques

If acupuncture is only a placebo, then under the same experiment conditions, acupuncture on different acupuncture points, or manipulation of the needle in different ways, or using different frequency of electrical stimulation, should yield a statistically similar or the same results. Indeed, there are some studies by acupuncturists in Western countries on this topic, which show that this is so. However, when we reviewed these studies, we found that they performed acupuncture in a very low treatment frequency, while similar studies by acupuncturists in China were performed with higher treatment frequency, and found quite different results, suggesting that acupuncture points have relative specificity, and that acupuncture is not a placebo effect.

3.1 Different Acupuncture Points

Yu and Qin (2014) randomly and single-blindly allocated 50 patients with cardiac premature beat into two acupuncture groups: electro-acupuncture on Neiguan (PC6) points (Neiguan group, 30 cases) and on Xuanzhong (GB39) points (Xuanzhong group, 20 cases). They found that the total effective rate in the Neiguan (PC6) group was 50%, while that in the Xuanzhong (GB39) group was 5%. They did acupuncture once a day for 10 days.

Xu et al. (2014) randomly allocated 82 coma patients with severe traumatic craniocerebral injuries into two groups: acupuncture on Suliao (GV25)-focused point (Suliao group, 42 cases) and on Shuigou (GV26)-focused point (Shuigou group, 40 cases). Using the same method of acupuncture, the cure-improvement rate in the Suliao (GV25) group was 45.2%, while that in the Shigou (GV26) point was 22.5%. The acupuncture was performed once a day, five-day a week, in a two-week as a course.

Yiu et al. (2006) randomly allocated 24 dysphonia patients into two electro-acupuncture treatment groups: acupuncture on Renying (ST9), Lieque (LU7) and Zhaohai (KI6) points (12 cases) and on Kunlun (BL60) and Houxi (SI3) points (control, 12 cases). The acupuncture was performed for 10 sessions over 20 days. After treatment, the voice frequency range in the former increased by 28.8%, while there was almost no change in the control group.

Yu et al. (2010b) randomly allocated 66 cases of primary dysmenorrhea in women into two acupuncture treatment groups: acupuncture on Sanyinjiao (SP6) (33 cases) and on Xuanzhong (GB39) points (33 cases). The acupuncture was performed during menstruation for 5 min. They found that, the reduction in the pain level and the increase in the arterial blood flow in the Sanyinjiao (SP6) group was much more dramatic than that in the Xuanzhong (GB39) group.

Cen et al. (2007) randomly allocated 138 patients with unstable urine bladder function into two acupuncture treatment groups: acupuncture on Huiyang (BL35) points (93 cases) and on Huantiao (GB30) point (45 cases). After three rounds of acupuncture, various symptoms in the Huiyang (BL35) group were significantly improved, while only urine retention feeling and urgent feeling were improved in the Huantiao (GB30) group. Both groups could reduce their I-PSS scale and improve quality of life but the Huiyang group worked better than the Huantiao (GB3) group. After 5 rounds of acupuncture, the healing effect was even better than that for acupuncture performed 3 times in the Huiyang (BL35) group. They commented that acupuncture on Huiyang (BL35) points could adjust the function of urine bladder and the effect can be accumulated with more times of acupuncture treatment.

Lai and Huang (2006) randomly allocated 50 VD patients into five electro-acupuncture groups: conventional acupuncture group (Convention group); conventional acupuncture plus Baihui (GV20) points (Baihui group); plus Shuigou (GV26) point (Shuigou group); plus Shenmen (HT7) points (Shenmen group), or plus Baihui GV20), Shuigou (GV26) and Shenmen (HT7) points (combined group). Each group had 10 patients. The acupuncture was performed once a day for 5 days, then had a break for 2 days. They repeated this for 6 courses. They found that, after treatment, the SECF sore in the combined group was dramatically increased. In the Baihui group, the sense of direction, short-term memory, long term memory, animal name memory, calculation, classification and category separation, etc. improved dramatically. In the Suigou (GV26) group, the sense of direction, money spending, calculation, classification, and grouping were much improved. In the Shenmen (HT7) group, the range of figure, name of animals, classification and grouping were much improved. They summarized that the acupuncture points Baihui (GV20), Shuigou (GV26), and Shenmen (HT7) could improve recognition in VD patients. There was relative specificity of their healing effects. The combination of the three points worked better than using them individually.

Yu et al. (2001) randomly allocated 64 patients with duodenal ulcers into 4 acupuncture treatment groups: point Zusanli (ST36) plus ranitidine (Zusanli group, 16 cases), point Shangjuxu (ST37) plus ranitidine (Shangjuxu group, 16 cases), point Xiajuxu (ST39) ranitidine (Xiajuxu group 17 cases), and ranitidine alone group (15 cases). They found that the three acupuncture groups worked better than the ranitidine alone group in the improvement of pain-cessation time, clear rate of Helicobacter pylori and some other symptoms. Again the Zusanli (ST36) group worked better than the Shangjuxu (ST37) group and Xiajuxu (ST39) group. But the Shangjuxu (ST37) group and the Xiajuxu (ST39) group worked similarly. They commented that acupuncture worked in the treatment of duodenal ulcers using the Zusanli (ST36),

Shangjuxu (ST37) and Xiajuxu (ST39) points, but there was relative specificity in the extent of healing effect among the three points.

Wang et al. (2012b) randomly allocated 116 functional indigestion patients into three acupuncture treatment groups: acupuncture on Zuyangming stomach meridian points (point group, 36 cases), on other points on the same meridian not normally used for the treatment of indigestion (non-points group, 39 cases), and on spots that do not belong to any acupuncture points or meridians (non-meridian-non-points group, 41 cases, shallow insertion). Acupuncture was performed once a day for five days, with a break of 2 days before next healing course with 4 courses in total. After treatment, the improvement in FDI score and SF-36 score in the point group was much better than that in the other two groups. The improvement of these two parameters in non-points was also better than that in the non-point-non-meridian points. Apparently there are relative specificity among acupuncture points and between the acupuncture points and control points.

Lan et al. (2010) randomly allocated 60 patients who suffered from functional indigestion, into two acupuncture treatment groups: acupuncture on specific acupuncture points that are normally used for the treatment of indigestion (acupuncture group, 30 cases) and acupuncture on non-points. The acupuncture was performed once a day for 5 times, and continued for 4 courses. They found that, after the treatment, the improvement of symptoms of upper stomach bloating feeling, early fullness, upper stomach pain and upper stomach burning sensation, were 85.72%, 78.26%, 94.11%, 60% in the acupuncture group, and 19.23%, 20%, 6.25%, 7.69%, in the non-point groups, respectively. Though the non-point stimulation also showed some improvement compared with before-acupuncture, the improvement in the acupuncture group as always much better than the non-point group.

Ma et al. (2015) randomly allocated 230 patients with functional indigestion into two acupuncture groups: acupuncture on far-away points (far-away group, 116 cases) and acupuncture on local points (local group, 114 cases). The acupuncture was performed once a day for 5 days, for a total of 4 weeks. After treatment, the healing effects in the far-away group were much better than the local group.

He et al. (2006) randomly allocated 278 peripheral facial palsy patients into two acupuncture groups: acupuncture on far-away points (far-away group, 145 cases) and acupuncture on local points (local group, 133 cases). The acupuncture was performed once a day for 6 days per week, for a total of 3 weeks. After treatment, the healing effects in the far-away group were much better than the local group. The cure-much-improvement rate in the far-away group was 88.3%, while that in the local group was 64.7%.

We noticed that acupuncturists in Western countries also did some comparison studies to test if there is difference in the healing effect between different acupuncture points, or between acupuncture points and non-points. For example, Allen et al. (2006) randomly allocated 105 severe depression patients into 3 acupuncture treatment groups: acupuncture on traditional acupuncture points that are normally used for the treatment of depression (acupuncture group, 53 cases), and acupuncture on non-specific points that are normally not used for the treatment of depression (non-specific group, 52 cases), and that on non-points that do not belong to any acupunc-

ture point/meridian (non-points group, 52 cases). The acupuncture was performed twice a week for 4 weeks, then once a week for another 4 weeks (typical Western style acupuncture). After treatment, the improvement rates in the three groups were 43.5%, 47.8% and 21.7%, respectively. They said that there was no specificity among acupuncture points. As we will discuss (see below) the failure to find relative specificity among acupuncture points could well be due to the low treatment frequency in this study.

3.2 Between Acupuncture Points and Non-points

Some other studies show that with acupuncture on traditional acupuncture points versus on non-points, the healing effects were similar (Scharf et al. 2006; Macklin et al. 2006; Sui et al. 2012).

Berman et al. (2004) allocated 336 patients suffering from osteoporosis of knee joint into two acupuncture groups: acupuncture on points that are normally used for the treatment of osteoporosis of knee joint (acupuncture group, 173 cases), and that on non-points (non-point group, 163 cases). The acupuncture was performed twice a week for 8 weeks, then once a week for two weeks, then again once every two weeks for 4 weeks (total 23 sessions). WOMAC functional score improved in the acupuncture group much more than that in the non-point group, but not on the WOMAC pain scale.

Melchart et al. (2005) randomly allocated 195 tension headache patients into two acupuncture treatment groups: traditional acupuncture group (132 cases), and non-acupuncture point group (63 cases). The acupuncture was performed twice a week for 4 weeks, then once a week for 4 weeks. After 8 weeks, the headache score reduced in the acupuncture group by 47.2%, while that in the non-acupuncture points was 44.3%. There was no significant difference between the two groups.

Assefi et al. (2005) randomly allocated 99 patients with fibromyalgia into four acupuncture treatment groups: traditional acupuncture group (25 cases), non-point acupuncture group (24 cases), acupuncture-needle-not-inserted group (25 cases) and non-specific acupuncture group (e.g. the acupuncture points normally not used for the treatment of fibromyalgia, 25 cases). The acupuncture was performed twice a week for 12 weeks. They found that the pain reduction rate in the acupuncture group, the non-specific group, non-points group and non-inserted group, were 21.4%, 20.3%, 41.1% and 33.8%, respectively. There was no significant difference between the groups. (Date are deduced from figure in the article.)

Witt et al. (2005) randomly allocated 224 patients who suffered from osteoarthritis of the knee into two acupuncture treatment groups: acupuncture group (150 cases) and non-acupuncture point group (74 cases). The acupuncture was performed twice a week for 4 weeks, then once a week for 4 weeks. After the treatment, the pain was reduced by 62.4% and 51.5% in the acupuncture group and in the non-point group, respectively, without significant difference.

Macklin et al. (2006) treated primary hypertension by acupuncture and said that the healing effect was similar in the acupuncture group and the non-point group. We noticed that the acupuncture performed in this study was twice a week. But for the treatment of hypertension in China, it is usually once a day (Zheng et al. 2012; Yang 2011; Wang and Yang 1989; Wang et al. 2007; Han 2015), or even twice a day for 28 days (Shen and Shi 2010).

Cabrini et al. (2006) randomly allocated 32 patients undergoing branchofiberoscope into two acupuncture groups, both performed 20 min before the surface anesthesia: acupuncture on traditional points (acupuncture group, 16 cases), and that on non-points (non-point group, 16 cases). In both groups, the needles were kept until the end of the exam. The results showed that, after acupuncture for 20 min, the anxiety level was reduced by 42.7% in the acupuncture group, but did not change in the non-point group.

The studies above are mostly done with acupuncture once a week or twice a week, rarely three times a week. The difference between the acupuncture group and the non-point group are usually insignificant. When the acupuncture was performed with higher frequency of treatment, the difference between the two groups tended to be significant. Such data are mostly from China.

Wan et al. (2014) randomly allocated 28 patients with primary migraine (hyperactivity of liver-Yang type in TCM) into two acupuncture treatment groups: acupuncture group (14 cases), and other-points group (points that are normally not used for the treatment of migraine, 14 cases). The acupuncture was performed once a day for 10 days. The number of points used in both groups was the same (4 points). After treatment, the pain level was reduced in the acupuncture group and in the other-point group 50.0% and 26.2%, respectively.

Zhang et al. (2013c) randomly allocated 59 migraine patients into two acupuncture treatment groups using the same numbers of acupuncture points: acupuncture group (30 cases) and non-acupuncture point group (29 cases). The acupuncture was performed once a day for 5 days. They had a two-day break between healing courses, with 4 courses in total. They found that the pain was reduced by 42 and 10.4%, in the acupuncture group and in the non-point group, respectively.

Zhang et al. (2007) randomly allocated 255 constipation patients into two electro-acupuncture treatment groups: acupuncture group (126 cases) and non-point group (129 cases). The acupuncture was performed once a day for 28 days. The results showed that electro-acupuncture treatment can dramatically improve symptoms, speed up the content passing speed inside the intestines, and reduce the usage of Constipation Relief Suppositories Glycerol and evacuant. The total effectiveness rate in the acupuncture group was 94.4% and that in the non-point group was 61.3%.

Fan et al. (2005) randomly allocated 53 depression patients into two acupuncture plus auricular acupressure treatment groups: acupuncture group (28 cases) and non-point group (25 cases). Acupuncture was performed twice per week for 3 months. After treatment, the cure rate and the much-improve rate in the acupuncture group was 28.6% and 28.6%, respectively, while those in the non-point groups were 8.0% and 20.0%, respectively.

Cho et al. (2005) randomly allocated 40 patients with later stage of uremia with itchiness into two acupuncture treatment groups: acupuncture group (20 cases) and non-point groups (20 cases). Acupuncture was performed three times a week for one month. They reported that the itch level was reduced by 54.7 and 2.6% in the acupuncture group and in the non-point group, respectively.

The results of some studies that also compare the healing effect of an acupuncture group and a non-point group (Dechartres et al. 2013) were cited as not supporting the relative specificity between acupuncture points. But actually they were not proper studies for this purpose. For example, in the study by Vickers et al. (2005), they used non-inserted needle, not the inserted needles into the skin. (The original text is:placebo needles consist of a blunted needle that moves up inside its handle instead of into the skin.)

Also, in the study by Scharf et al. (2006) they used both traditional acupuncture points and non-points together with physiotherapy. It is hard to evaluate the actual amount of healing effect in a mixed treatment program. Again, both acupuncture and manual therapy of the physiotherapy are very dependent on personal skill. The overall healing effect could be even more variable. In the Western style physiotherapy, the practitioners usually ask clients to do physical exercise, while in Chinese acupuncture, we ask patients stop physical activity whenever the pain is very severe. Too much physical activity would make the pain worse, rather than better. The ways of the treatment and the requirement of patients are quite different between these two therapies.

3.3 Between Different Acupuncture Techniques

There are many studies in China comparing the healing effect of acupuncture between ordinary techniques and various modified techniques.

Mei et al. (2008) randomly allocated 56 patients who suffered from coma due to severe cerebral trauma into two acupuncture treatment groups: one is with comprehensive combined treatment (including scalp acupuncture, auricular acupuncture and body acupuncture, 36 cases) and another with body acupuncture alone (20 cases). The acupuncture was performed once a day. Each course was 10 days with a 3-day break between courses. They found that the effective rate in the two groups was 69.4% and 40%, respectively.

Cui et al. (2005) randomly allocated 100 persistent vegetable states patients into two acupuncture treatment groups: ordinary acupuncture (50 cases), and special acupuncture technique (50 cases). The acupuncture was performed twice a day for 24 sessions. They found that the wake-up rate in the two groups were 62 and 86%, significantly different.

Sui et al. (2012) randomly and blindly allocated 293 patients of high blood pressure into different treatment groups for one-time acupuncture. They found that, though the control group (in this group the patients do not feel Deqi sensation) showed some

deduction of blood pressure, the blood pressure deduction was much more in the Deqi acupuncture treatment groups.

In the above studies, in the comparison between a special acupuncture technique and conventional acupuncture technique, the common characteristic is that needles are real and inserted treatment. This means that, the group that was used as a control (the ordinary acupuncture group), can also be regarded as a control group (though it is not a perfect control, because it has its own healing effect too). The similarity between the two groups is that both are performed with the same treatment frequency and same level of emotional influence to the patients. However, readers might still question that the number of acupuncture points used, the amount of stimulation to the points, all are different between the two groups, so that the placebo effect might be stronger in the group in which more acupuncture points were used, and stronger simulation was given.

For this question, we can also show some other studies, in which the kind of acupuncture points, the number of the points, and treatment frequency between the groups, were exactly the same. The differences between the groups are the direction of needles after they are inserted into the point. These still show that the acupuncture with special technique works better than conventional acupuncture.

Sun et al. (2015) randomly allocated 200 patients with cervicalspondylotic radiculopathy into two acupuncture treatment groups: conventional treatment (100 cases) and special acupuncture technique (100 cases). The acupuncture was performed once a day. There were 10 session in each course and 2 total courses. They found that the pain level reduced by 79% and 45.4%, respectively, in the special group and in the conventional group.

Shang et al. (2018) randomly allocated 64 patients with shoulder periarthritis into two acupuncture treatment groups: special acupuncture technique (32 cases) and conventional technique (32 cases). The acupuncture points used were the same, and the acupuncture was done once a day for 6 days, with a one day break before the next course, for a total of 2 courses. They found that the cure rates were 53.1% and 31.2%, in the special acupuncture group and the conventional group, respectively.

Shi (2014b) randomly allocated 150 stomach pain patients into three acupuncture groups: special acupuncture technique I (special group I, 50 cases), special acupuncture technique II (special group II, 50 cases), and conventional acupuncture (conventional group, 50 cases). They used the same acupuncture points, but used different ways of manipulating the needles. The acupuncture was performed once a day for one week. They reported that the effective rate was 96%, 94%, and 60%, in the special I, special II, and conventional group, respectively.

Li et al. (2015) randomly allocated 160 patients who suffered from prolapse of lumbar intervertebral disc into two acupuncture treatment groups: special acupuncture technique (Wen-tong technique, 80 cases) and conventional acupuncture (80 cases). The acupuncture points used were the same. The acupuncture was performed once a day, with 15 days in a course. They reported the excellent healing rate was 97.8% and 78.8% in the special acupuncture group and the conventional group, respectively.

Cheng et al. (2007) randomly allocated 165 sciatica patients into two acupuncture treatment groups: special acupuncture technique (special group, 82 cases) and conventional electro-acupuncture technique (83 cases). Both groups used the same acupuncture points. The acupuncture was performed once every other day. There were ten session per healing course. They reported that the cure-much-improved rates in the special group and the conventional group were 88.7% and 57.5%, respectively.

Brief summary:

Another way to test if an acupuncture treatment has a placebo effect is to compare the healing effect between different acupuncture points, between acupuncture points and non-points, and between different acupuncture techniques under the same experimental conditions. Again, such a comparison must be compared using higher treatment frequency. With low treatment frequency, such a comparison might or might not be significantly different. With higher treatment frequency, it tends to be statistically significant. This is additional evidence that acupuncture is not a placebo.

4 More Examples that Acupuncture is not a Placebo

We can cite more evidence that acupuncture is not a placebo, such as acupuncture used in children and in animals.

4.1 Acupuncture in children

Acupuncture can not only be used to treat diseases in adult, but also those in infants (Schwartz et al. 1999; Duncan et al. 2004; Lee et al. 1998; Yentis and Bissonnette 1992) and children (Gold 2009). It can be used for the treatment of various diseases including various pains (Kemper et al. 2000; Zeltzer et al. 2002), migraine (Pintov et al. 1997), infant catatonia (Duncan et al. 2004), bedwetting (Bower et al. 2005; Radmayr et al. 2001), constipation (Broide et al. 2001), allergic rhinitis (Ng et al. 2004), saliva incontinence (Wong et al. 2001), spastic paralysis (Lee et al. 1998), laryngismus (Yentis and Bissonnette 1992), postoperative vomiting (Wang and Kain 2002; Kabalak et al. 2005; NIH Consensus Conference 1998; Dune and Shiao 2006), nausea/vomiting after chemotherapy (Reindl et al. 2006) and so on.

Ecevit et al. (2011) reported that, by only doing acupuncture on Yintang (EX) point, it can reduce the pain level in premature babies with pain in the heels after taking blood samples for analysis. The crying time can reduce from an average of 138.1 down to 72.8 s. At the same time, the heart rate can be reduced from 152.2 times per min down to 138.3 times per min. The pain index can be reduced from 6.1 down to 4.2, suggesting that the tolerance of the premature baby to pain increased.

Liodden et al. (2011) did acupuncture on 77 children undergoing tonsillectomy and adenoidectomy. The acupuncture started after induction of general anesthesia on

Neiguan (PC6) points. The needles were taken out before wake-up of the children and a plastic needle was put on the same points for 24 h (covered). Another group was a control group. It was found that the incidence of post-operative nausea/vomiting in the acupuncture group was 46.8% but that in the control group was 66.2%. It is interesting that incidences in children ages 1–3 (26.7%) was less (59.6%) than that in older children (4–11 years of old). Generally speaking, we should expect that the older children of 4–11 years should be more affected by the placebo effect of treatment, but the results here show the opposite. A possible explanation is that the acupuncture stimulation in the younger children group is relatively more than that in the older children (Kabalak et al. 2005).

A survey in North America for 43 children's hospitals showed that about one third of the hospitals supply acupuncture treatment (Lin et al. 1999). Most of other studies said that the number of children who are suggested for acupuncture treatment is also large. Generally speaking, the parents of the children also accepted this therapy and were satisfied the healing effect (Zeltzer et al. 2002). This is quite different from most of people though since, generally speaking, children may fear the needles (Lee et al. 2013) and the parents may not want to increase pain and fear in the children (Zeltzer et al. 2002; Tsao et al. 2005).

The age of the children who accepted acupuncture treatment can be as little as one month (Ecevit et al. 2011). For children so young, how can we expect that the baby can accept a placebo effect?

Weimer et al. (2013) conducted a review from which we know several other things about the placebo effect in children and adolescents. We learned that the placebo responder rate is generally higher than that in adults, that the mechanisms behind the placebo effect in children might be different from that in adults, and that the clinic study design in children might need to be different from that in adults too. However, it seems that it is very rare that the studies included paid attention to comparing children younger than one year old with those aged more than that, for example, 6 years or 12 years of old. We suspect that the placebo responder rate and placebo effect in these groups might be different.

Someone may believe that the placebo effect can also happen in children younger than 2 years of old (Paul et al. 2004, 2014). However, this is not accepted by others; the latter suggested that the placebo effect in such young children might be due to the parent placebo effect, as proxy-placebo effect, which causes the bias report in the younger children (Taylor and Opel 2014; Kossowsky and Kaptchuk 2015; Hutton et al. 1991).

4.2 Acupuncture on Animals

If we are still not convinced by data of acupuncture on children, and still suspect that the acupuncture effect is a placebo, let us see the animal studies on acupuncture. Acupuncture not only works in human beings, but also on animals. A lot of clinical studies support this.

Gakiya et al. (2011) randomly allocated 30 dogs undergoing mastectomy into three groups: electro-acupuncture group, control group, and no-acupuncture control group. Each group had 10 dogs. After the treatment, the number of dogs that needed painkillers in the electro-acupuncture group, the control group, and the non-treatment group were 2, 6, and 6, respectively. They summarized that acupuncture could reduce the post-operative consumption of morphine and promote satisfactory analgesia in dogs undergoing mastectomy.

Cho and Kim (2008) did acupuncture for a dog suffering from cervical sympathetic paralysis syndrome, once a day for two days. After two days, all the symptoms disappeared. This data suggests that acupuncture everyday worked better.

Ceccherelli (1996) randomly allocated rats into three groups: acupuncture group (14 cases), morphine group (10 cases), and non-treatment control (20 cases). They found that acupuncture can significantly reduce the experimental swelling in the feet of the rats. Data from Zhang et al. (2005) reported similar findings.

Carneiro (2005), Carneiro et al. (2010) randomly allocated rats into acupuncture group, non-point acupuncture group, activity-limited group, and no-treatment group. All rats were sensitized with heat-solidified hen egg-white implants. Using clinical acupuncture points, electro-acupuncture treatment began 2 days after antigen priming and was repeated on alternate days for 2 weeks. They found that electro-acupuncture efficiently diminishes the bronchial immune-mediated inflammation induced in rats and that this effect is dependent on the choice of specific acupoints.

Luna et al. (2015) conducted a study on dogs undergoing ovariohysterectomy. They found that acupuncture or pharmacopuncture were as equally effective as morphine or carprofen to control postoperative pain in females undergoing ovariohysterectomy.

Cassu et al. (2008) compared the analgesic effect of uni- and bi-lateral electroacupuncture in response to thermal and mechanical nociceptive stimuli and investigated the cardiorespiratory, endocrine, and behavioral changes in dogs submitted to electroacupuncture. They found that bilateral electro-acupuncture produced a shorter latency period, a greater intensity, and longer duration of analgesia than unilateral stimulation, without stimulating a stress response. The effect of electro-acupuncture for pain reduction was confirmed by their later studies again (Cassu et al. 2012). Although Gakiya et al. (2011) did not find a difference between the acupuncture group and the non-point group for the pain level reduction, but they did find that the painkiller used in the acupuncture was less than non-acupuncture group.

Groppetti et al. (2011) found that plasma β-endorphin levels in dogs receiving electro-acupuncture increased significantly against baseline values 1–3 h after surgery. Moreover, the end-tidal isoflurane concentration needed for second ovary traction was significantly lower in acupuncture-treated dogs than in control animals. All animals having electro-acupuncture experienced prolonged analgesia, over 24 h at least, while four out of six dogs treated with butorphanol needed post-surgical ketorolac and tramadol supplementation to their pain relief.

Koh et al. (2014) studied the effects of maropitant, acepromazine, and electroacupuncture on vomiting associated with administration of morphine to dogs. They found that maropitant treatment was associated with a lower incidence of vomit-

ing and retching, compared with control treatments, and acepromazine and electroacupuncture appeared to prevent an increase in severity of nausea following morphine administration in dogs.

Jaeger et al. (2006) reported in their study that seventy-eight dogs with pain due to hip dysplasia were studied in a controlled, double-blind clinical trial to evaluate gold bead implantation as a pain-relieving treatment. The dogs were randomly assigned to two groups, 36 in the gold implantation group and 42 in the placebo group. Both groups were treated equally regarding anesthesia, hair clipping, and penetration of the skin with the same type of needle. The gold implantation group had small pieces of 24 carat gold inserted through needles at five different acupuncture points and the placebo group had the skin penetrated at five non-acupuncture points so as to avoid any possible effect of stimulating the acupuncture points. A certified veterinary acupuncturist marked the points, and two surgeons performed the implantations according to a randomization code made in advance. After 14 days, three months and six months, the owners assessed the overall effect of the treatments by answering a questionnaire, and the same veterinarian examined each dog and evaluated its degree of lameness by examining videotaped footage of it walking and trotting. The treatment was blind for both the owners and the veterinarian. There were significantly greater improvements in mobility and greater reductions in the signs of pain in the dogs treated with gold implantation than in the placebo group. The veterinarian and the owner assessments corresponded well.

Laim et al. (2009) studied the effects of adjunct electro-acupuncture on severity of post-operative pain in dogs undergoing hemilaminectomy because of acute thoracolumbar intervertebral disk disease. Dogs were alternately assigned to treatment (conventional analgesics and adjunct EAP) and control (conventional analgesics alone) groups. Analgesic treatment was adjusted as necessary by the attending clinician, who was not aware of group assignment. They found that the total dose of fentanyl administered during the first 12 h after surgery was significantly lower in the treatment group than in the control group, though dosages of analgesics administered from 12 through 72 h after surgery did not differ between groups. Pain score was significantly lower in the treatment group than in the control group 36 h after surgery, though it did not differ significantly between groups at any other time.

Some people have explained the healing effect of acupuncture in animal as conditioning. Due to repeated conditioning, animals could also have psychological and physiological responses, so as to have improvement in their symptoms. For example, to bring a dog to a veterinary station, the dog may shake its body. This might be because the dog had been brought to the station before and suffered from pain stimulation, such as an injection. If bringing the dog to a quiet and peace environment, the dog could show lower levels of symptoms. This might be easy to understand.

For this, Ramey D (https://www.sciencebasedmedicine.org/is-there-a-placebo-effect-for-animals/) explained that conditioning theory proposes that bodily changes result following exposure to a stimulus that previously produced that change. This is perhaps the most intuitively acceptable explanation for any placebo effects in animals. Indeed, animal studies support such a model for placebo effects, starting with the first descriptions on salivating dogs by Pavlov. Both human and animal studies

support the idea that conditioning forms some basis for placebo responses. Since conditioning requires learning, it would be expected that repeated visits to a practitioner (of any particular persuasion) might increase the strength of the association between a learned stimuli and response in animals, good or bad. There are numerous examples of dogs shaking in fear when being taken into a veterinary clinic; on the other hand, a dog that enjoyed being handled in a soothing environment might appear to receive some relief from a chronic condition; as it learned to associate its visits with the comforting handling, and conditioning effects could occur. This could certainly serve as reasonable explanations for purported placebo effects in animals. Nevertheless, the hypothesis that a healing or therapeutic effect can be dependably provoked as a result of conditioning cannot be supported at this time by any evidence.

Expectancy theory proposes that bodily changes may occur to the extent that the person receiving the therapy expects them to. There is considerable overlap between expectancy and conditioning, because learning is one of the major ways that expectancies are formed. To the extent that therapies are expected to provide relief from disease, or at least provide the client and/or veterinarian with a feeling of control over the disease process, they may alleviate adverse mental states (in the humans). Certainly, in humans, therapies that help restore patient control may evoke therapeutic effects, at least short-term, but studies that investigate the expectancy model in animals have so far not been performed. Still, if animals were able to form an association between treatment-related signals (the attention and handling received, the way that the owner behaves towards the animal when it is receiving treatment) and the relief of its distress, expectancies of treatment effects might develop (on the part of both animal and owner).

There is a good body of research that demonstrates that human contact has measurable effects on animals. For example, petting by humans reduces heart rates in dogs and horses and causes major vascular changes in dogs. Gentle handling increases productivity in dairy heifers and increases reproductive efficiency in sows. Thus, it is plausible that human-animal contact might play an important role in the observed responses to therapeutic interventions. To take an "alternative" example, it has been shown that a single acupuncture treatment is as effective as petting a horse, when it comes to relief of signs of chronic airway disease; that is, there's no demonstrable effect of acupuncture beyond simple handling. (9) On the other hand, handling may also be stressful to animals, so responses to handling may not necessarily be beneficial. Still, there's no question that human contact can invoke responses from animals and animals may behave quite differently when they are not being observed; those shouldn't be confused with placebo-effects, however.

It was reported that, after taking a sedative, a dog was left in a room but its owner left the room, then let a stranger come in the room. The dog showed quietness, rather than anxiety or stress as if it was not given a sedative before. On the third time, the dog was given a vitamin, not a sedative; again the coming in of a stranger in the room did not create the same level of anxiety and stress reaction of the dog. This experiment suggested that, once a therapy worked, the following similar therapy or a control therapy could produce the same healing effect. Here, it should be noticed that, a precondition for such "replacing phenomenon" to happen is that the previous

therapy worked. In the experiments above, the animals had acupuncture only once before surgery. There was no previous healing effect for the dog to remember. It is the same for human beings (Suchman and Ader 1992).

Goebel et al. (2008) conducted a study. Patients with allergic rhinitis underwent a conditioning protocol, receiving desloratadine, an H_1 receptor antagonist, paired with a novel drink, for five consecutive days. After the washout period, patients who were re-exposed to the novel drink plus a placebo showed improved symptom scores, decreased wheal size on the skin prick test, and diminished basophil activation (Suchman and Ader 1992; Goebel et al. 2008; Vits et al. 2013). Numerous other pharmacological conditioning trials have shown that these placebo responses mimic active drug effects and that prior exposure to an effective treatment is an important part of the conditioned placebo response (Goebel et al. 2008; Vits et al. 2011; Meissner et al. 2011).

However, no matter for the expectancy, conditioning, or such replacement effect, the animal needs a previous experience to the stimulation. For acupuncture treatment, the acupuncture was only one time treatment, before the surgery, and it worked to reduce the incidence of post-operative nausea/vomiting. The animal did not receive repeated acupuncture. The expectancy, the conditioning, or the replacement effect should not be established.

Another explanation is that the animal might get more care after being sick, that they would become quiet and calm, and so the symptoms would be reduced. They explain this possibility as a broad concept of a placebo. However, this theory has no experimentation to support it, neither is it able to answer how much care could reduce a symptom. In addition, such care to reducing a symptom should not be confused with what is discussed here as the placebo effect.

Based on the current data, it is most likely that the disease-treatment reaction in an animal is similar to that in an infant or children. They are not easily affected by a placebo effect (hint effect). They may be more affected by a calm effect. That means that the reduction of a symptom in an animal or in a child might become less after they get care and conciliation from the owner or parents. They may have reduced heart rate and reduced blood pressure. However, the pain level may not really be reduced by such conciliation. Such calming of an animal or child might be regarded as evidence of a reduction of pain. But we, as adults, know that, under conciliation, the emotion may become calm, but the pain level may not really be reduced.

Therefore, the results of acupuncture studies on animals or on children support less as a placebo effect but some kind of conciliation effect. If, under the conciliation, the animal still is not willing to move, or a child is still crying, it should be regarded as the pain level (symptoms) not being improved yet. If, after acupuncture, the animal has more motion, or if a child stop crying, it should be regarded that the symptom has been improved. Animals and children belong to a not-cheating group. We do not really need to insist that the improvement of symptoms after acupuncture is an exaggeration of the improvement by owner or parents as proxy-placebo.

Brief summary:

Small children or animals are less apt to a placebo effect. That only one or two times of acupuncture treatment could reduce their symptoms suggests that the healing effect of acupuncture cannot be simply explained by a placebo effect or a conditioning effect. The only explanation is that acupuncture indeed has its own specific healing effect.

5 Effect of Placebo Effect on Subjective or Objective Index of Healing Effect

5.1 Effect on Continuous Parameter and Binary Parameter

Hróbjartsson and Gøtzsche (2001, 2010), Hrobjartsson (2002) has paid attention to the relationship in the healing effects between the control group and the non-treatment group for some years. The authors separate the healing effect into a continuous index and a threshold index. The example of the continuous index is the commonly used VAS score and the threshold index is usually measured by an incidence rate, such as smoking rate, pregnancy rate, alcohol rate, nausea rate, survival rate, death rate and so on, in which the patient can only answer yes or no.

They collected the articles that involve as much as 46 kinds of clinical conditions, such as depression, insomnia, pain, nausea, phobia, smoking, vitiligo, hypertension, obesity, jet lag, secondary erectile dysfunction, dry eye, patient involvement in adolescent diabetic care, difficulty of colonoscopy, alcohol abuse, Alzheimer's disease, anemia, anxiety, asthma, attention-deficit hyperactivity disorder, bacterial infections, benign prostatic hyperplasia, carpal tunnel syndrome, common cold, compulsive nail biting, enuresis, epilepsy, fecal soiling, herpes simplex infection, hypercholesterolemia, hyperglycemia, ileus, infertility, insufficient cervical dilatation, labor, marital discord, menopause, mental handicap, orgasmic difficulties, Parkinson's disease, poor oral hygiene, Raynaud's disease, schizophrenia, sea sickness, stress related to dental treatment and undiagnosed ailments.

The author found that, among the 44 articles using threshold index, there is no clear relationship between the control group and the non-treatment group, e.g. the healing effect of the control group is not statistically significant more or less than that of the non-treatment group. In the articles using continuous index (158 articles), the effect of the control becomes smaller along with the increase of the sample size. Analysis showed that there are large variations among the articles that tested the pain level changes (even among the articles that belong to well-designed articles) from very significant to almost significant and can be omitted. Even in the significant reports, the control group could only reduce the pain level for 6 mm (0–100 mm scale). There was a mild level of, and consistent influence on, the nausea rate. For phobia and asthma, the influence was largely variable and very inconsistent among articles (Hróbjartsson and Gøtzsche 2006).

Hróbjartsson A reports suggest: (1) the influence of the control group is largely variable among different diseases and for the same disease among different studies; (2) it is very hard to tell if the control group has more a subjective index or an objective index of the healing effect. The placebo effect in a control group might affect pain, but not dry eye syndrome, difficulty of colonoscopy, prostate enlargement, carpal tunnel syndrome, herpes simplex infection, menopause syndrome, Raynaud's disease, etc. For many emotional or psychometric syndromes, the control treatment seems to have no effect or the effect is small and inconsistent: depression, phobia, insomnia, smoking, alcohol abuse, patient involvement in adolescent diabetic care, jet lag, secondary erectile dysfunction, compulsive nail biting, fecal soiling, marital discord, orgasmic difficulties, poor oral hygiene, sea sickness, and stress related to dental treatment, etc.

Wood et al. (2008) also found that there was little evidence of bias associated with lack of blinding in trials assessing all-cause mortality or other objectively assessed outcomes.

Manheimer (2011) believed that for the outcomes of pregnancy and birth, which are probably the most objective of all outcomes with the possible exception of mortality, there is a low risk of bias due to lack of blinding and that the use of a control group as control in acupuncture facilitated studies in IVF is unnecessary, since most kinds of control acupuncture methods are not inert and work as an ideal control. Acupuncture indeed can improve the success rate of IVF, as verified by many studies.

Kaptchuk et al. (2006) compared control acupuncture and control pills. They also found that the placebo effect was confined to self-reported, subjective outcomes (e.g., pain) and that there was no placebo effect (i.e., no improvement from baseline) for either the placebo acupuncture or placebo pill on the completely objective outcome that they measured (i.e., grip strength). Their findings suggest that an enhanced placebo effect of acupuncture, or indeed any placebo effect of acupuncture, is confined to subjective outcomes. Indeed, Kapchuk and colleagues concluded "that the differential placebo effect was confined to self-reported measures (and not to grip strength) suggests an effect that may be confined to subjective outcomes."

It has been well accepted that when comparing acupuncture with a non-treatment group, the acupuncture treatment indeed works to improve the clinical conditions, for most of the conditions above, even if it is with Western style acupuncture. Only after the involvement of a control group, which per se is very largely variable in its healing effect, makes it variable in the comparison between the acupuncture group and the control group. Therefore, we would ask: how can we use an unstable index (control group) to differentiate another index (acupuncture and other therapies).

For the above conditions using a threshold index to tell healing effects, acupuncture treatments in China, generally speaking, work effectively (comparing to non-treatment group and/or Western medicine treatment), no matter if it is a subjective or an objective index. We have listed a lot of data in this article. It should be pointed out that the acupuncture again is performed mostly at a high rate of frequency.

In the articles from China, the healing effect is most often expressed as a grade index, as cure rate, much improved rate, improved rate, or no effect rate and so on. Here, the cure rate can be regarded as a threshold index as well, since it tells if the

disease has been cured or not. The commonly used continuous index in the Western clinic studies cannot tell how many patients have been really cured without needing to come back.

5.2 *Effect on Physical Parameters and Biochemical Parameters*

Meissner et al. (2007) reported that the placebo effect affected physical parameters more (such as blood pressure, swelling after surgical operation, etc.), and less for biochemical parameters (such as blood sugar, blood RBC content, or blood cholesterol level, etc.), in peripheral diseases. They found that, in total, 50% of trials (8 of 16 trials) measuring physical parameters showed significant placebo effects, compared with 6% of trials (1 of 18 trials) measuring biochemical parameters.

Wei (2016) treated type II diabetes with acupuncture. Acupuncture was performed once every other day for 12 sessions per course, with 3 courses in total. After the treatment, blood sugar level was reduced by more than 30 in 22.9% of patients, and reduced by more than 10% in 41.6% of patients. With the combination of acupuncture and moxibustion was used, the reduction in the blood sugar was more apparent: the blood sugar level reduced by more than 30% and 10%, in 66.6% and 29.2% of patients, respectively.

Li et al. (2016a) treated hypercholesterolemia patients with acupuncture. The acupuncture was once a day, 10 sessions per course, with 2 courses in total. After treatment, blood total cholesterol level reduced from 6.59 to 4.81; LDL went down from 4.68 to 3.55; HDL increased from 1.08 to 1.22 mg/dl.

Wang et al. (2016) treated patients with blood leucopenia with acupuncture (39 patients). The treatment was once a day, 6 sessions per week for two weeks. The reasons for the disease were chemotherapy or radiation therapy (12 patients), hypersplenia (4 patients), side effects from drugs (4 patients), aplastic anemia (2 patients), or no clear reasons given (17 patients). The white blood cells before the treatment were $<3.5 \times 10^9$/L. After the treatment, the BWC was $\geq 4.0 \times 10^9$/L in 19 patients. WBC increased on the top of original level for 1.0×10^9/L in 17 cases.

Sunay et al. (2011) allocated 53 menopause syndrome patients into two acupuncture treatment groups: an acupuncture group (27 cases) and a control acupuncture group (26 cases). The acupuncture was performed twice a day for 10 days. After the treatment, the Menopause Rating Scale (MRS) reduced by 60% and 4.0% in the acupuncture group and the control group, respectively. The FSH and LH hormone reduced while Oestradiol dramatically increased in the acupuncture group, but almost not at all in the control group. That acupuncture could change the blood concentrations of these hormones was confirmed by other studies (Zhou et al. 2011b; Xia et al. 2008; Jin et al. 2007; Shen et al. 2005). These studies suggest that it might be due to the change of the hormone secretion function of the hypophysis-hypothalamus-

ovary axis, which changes the balance of female hormones, so as to be benefit for the correction of menopause syndrome.

Data here suggests that, if the statement by Meissner et al. (2007) is indeed correct, that control acupuncture does not affect biochemical parameters of the body, then acupuncture can.

The data showing that the acupuncture treatment can correct the blood biochemical marks are very popular in Chinese literature. But please note again that the acupuncture was performed with a high frequency schedule and usually with more than 20 sessions.

5.3 Cure or Not

Spiro (1997) suggested that placebo effects have the power to ameliorate illness but not to cure or control disease. Considerable scientific evidence supports this hypothesis.

Miller et al. (2009) stated that the best evidence for placebo effects derives from two situations. First, laboratory experiments have demonstrated short-term symptomatic relief, especially for pain. Second, patients with chronic conditions marked by pain or distress have obtained significant and lasting symptomatic relief following control acupuncture, as compared with no-treatment and usual care control groups. There is little reliable evidence that the placebo effect can cure or control disease by modifying pathophysiology. Several meta-analyses of observed placebo response rates in cardiovascular conditions (including hypertension) have shown changes in both symptoms and pathophysiology, but these trials have not controlled for natural history. For oncological diseases, a systematic review of randomized trials found that placebo treatment is associated with improvement in subjective complaints like pain and appetite (Chvetzoff and Tannock 2003). Slight rates of tumor response in placebo-treated patients were attributable to changes normally associated with "spontaneous remission". This cursory examination of observed placebo responses in randomized trials without solid and consistent evidence of objective improvement in disease outcomes could easily be extended.

Miller et al. (2009) suggests that placebo effects that derive from other psychological mechanisms may inherently lack the potential to produce therapeutic benefit beyond symptomatic relief.

Acupuncture cannot only control the symptoms, but also cure disease. The simplest example is the wake-up of patients with coma, persistent vegetative status, delayed wake-up after general anesthesia, and the restoration of blood pressure in shock patients. It can also cure many other diseases, such as Bell syndrome, herpes zoster, etc.

Wang (2008) treated patients with post-stroke shoulder-hands syndrome with ordinary acupuncture (63 cases) and special acupuncture technique (77 cases). The acupuncture was performed once a day with 30 days per course. After the treatment, the cure rate in the ordinary acupuncture and the special acupuncture group was

34.9% and 44.1%, respectively. The index for the cure was the disappearance of pain and swelling, no restriction in joint movement, and no wastage for small muscle in hands.

Lin (2007) treated post-stroke shoulder-hand syndrome with acupuncture (40 cases) and joint-injection (40 cases). Acupuncture was performed once a day, with 30 days per course. Joint-injection was twice a week. After treatment, the cure rate for acupuncture and the joint-injection group was 45% and 25%, respectively. The index for cure is the same as in the above report.

There are more clinical reports for the principle cure of such post-stroke shoulder-hand syndrome (Shen et al. 2009; Du 2013; Yan et al. 2015).

Wu and Wei (2011) treated Bell syndrome with acupuncture plus moxibustion (67 cases) and Western medicine (67 cases). Acupuncture was performed once a day for 20 days. After treatment, the cure rate in the acupuncture group and the medicine group was 56.7% and 17.9%, respectively.

Liu (2016) treated facial nerve paralysis in children, with acupuncture (51 cases) and Western medicine (51 cases). Acupuncture was performed once a day, with 5 days per course, with 2 day breaks between the courses, and 6 courses in total. After the treatment, the cure rate in the acupuncture group and the medicine group were 62.7% and 35.2%, respectively.

Wang and Wang (2016) treated acute facial nerve paralysis 128 cases. Acupuncture was performed once every other day, 12 days per course, for one to two courses. The cure rate for the patients in acute state, stable state and recovery state, were 88.2%, 62.6% and 51.8%, respectively.

Wang and Wang (1996) also treated facial nerve paralysis. The acupuncture was performed once a day, or once every other day, with 10 days per course. The average cure rate was 74%.

It was found that the cure rate of specific facial nerve paralysis is closely related to the start time of the acupuncture treatment. The cure rate for starting within 5 days of the onset of the disease is much higher than starting after 7 days (Zhong and Huang 2011).

There are more trials reporting that acupuncture can cure or speed up the cure of facial nerve paralysis (Yang 2013; Yang and Hu 1978; Qin et al. 2009).

Li et al. (2016b) treated herpes zoster in 80 cases. Acupuncture was performed once a day, with 6 sessions per course. After 3 courses, the cure rate (skin rash disappears, no clinical sign disappears, no sequel of pain) was 40–57.5%.

Also, there are more reports suggesting that acupuncture can cure herpes zoster (Zhu et al. 2016; Liu 2015; Liu et al. 2013).

The above examples indicate that acupuncture can not only improve the symptoms but also cure diseases. This is additional difference between acupuncture and control acupuncture.

5.4 Brain Imaging Study

For the different influences of the control and verum acupuncture on the brain Enck et al. (2010), had a good summary: (For references, please check the original article.)

Acupuncture but not control acupuncture was found to induce both cerebellar as well as limbic cortex activation indicating both motor as well as affective component modulation of the pain matrix. Acupuncture resp. electroacupuncture at non-acupuncture points and tactile stimulation alone served as controls in early fMRI studies. Verum acupuncture in contrast to non-penetrating placebo needles activated cortical centers involved in affective pain modulation also in more recent studies. It was, however, noted that cortical activation following acupuncture shows substantial within as well as between-subject variations across different sessions.
Differences between true and control acupuncture were also found for the same regions by Napadow et al. (2009a); these authors also noted greater activation of sensorimotor areas (S1, S2, insula) by their control procedure (superficial manipulation at acupuncture points) than by true acupuncture. In another study of the same group, Napadow et al. (2009b) noted variances in time of central activation between verum and control acupuncture that they attributed to stronger peripheral actions of true acupuncture.
In a recent ^{11}C-carfentanil PET study with fibromyalgia patients, acupuncture therapy but not control acupuncture (at non-acupuncture points) elicited significant activation of muopioid receptor binding capacity in typical areas of the "pain matrix", the cingulate, the caudate, the thalamus and the amygdala both short-term (after one session) as well as long-term (after 4 weeks) while with control acupuncture, small deactivations of this matrix was noted, an effect that has been seen also with placebo analgesia.

Chae et al. (2009) compared an acupuncture group with a control acupuncture group. Verum acupuncture stimulation elicited significant activation in both motor function-related brain areas, including the caudate, claustrum, and cerebellum, and limbic-related structures, such as the medial frontal gyrus, the cingulate gyrus, and the fusiform gyrus.

Harris et al. (2009): Traditional Chinese acupuncture and placebo (control) acupuncture are differentiated by their effects on μ-opioid receptors (MORs). Acupuncture therapy evoked short-term increases in MOR binding potential, in multiple pain and sensory processing regions including the cingulate (dorsal and subgenual), insula, caudate, thalamus, and amygdala. Acupuncture therapy also evoked long-term increases in MOR binding potential in some of the same structures including the cingulate (dorsal and perigenual), caudate, and amygdala. These short- and long-term effects were absent in the control group where small reductions were observed, an effect more consistent with previous placebo PET studies. Long-term increases in MOR BP following TA were also associated with greater reductions in clinical pain.

Kong et al. (2009) investigated acupuncture and control acupuncture (Streitberger needle) with and without expectancy manipulation in healthy subjects in a cross-over

design and found that both acupuncture and control acupuncture—when coupled with high expectation—produce analgesia of similar magnitude, but the verum acupuncture elicits higher deactivation of the pain matrix than did control acupuncture and expectancy analgesia alone. This also underlines different central mechanisms of analgesia between expectancy and acupuncture.

Chu et al. (2012) reported that rectal distension induced significant activation of the anterior cingulated cortex, prefrontal cortex, thalamus, temporal regions and cerebellum at baseline. During and immediately after electro-acupuncture, increased cerebral activation from baseline was observed in the anterior cingulated cortex, bilateral prefrontal cortex, thalamus, temporal regions, and right insula in both groups. However, true electro-acupuncture led to significantly higher activation at right insula, as well as pulvinar and medial nucleus of the thalamus when compared to control acupuncture.

Napadow et al. (2014) reported that acupuncture reduced itch and itch-evoked activation in the insula, putamen, and premotor and prefrontal cortical areas. Neither itch sensation nor itch-evoked brain response was altered following antihistamine or placebo acupuncture. Greater itch reduction following acupuncture was associated with greater reduction in putamen response, a region implicated in motivation and habitual behavior underlying the urge to scratch, specifically implicating this region in acupuncture‘s antipruritic effects.

There are more data showing that the brain imaging in acupuncture is different from that in control acupuncture treatment (Chae et al. 2009a, b; Liu et al. 2012; Kong et al. 2010; Zyloney et al. 2010).

5.5 Peripheral (Autonomic) Effects of Acupuncture Versus Control Acupuncture

Schneider et al. (2006) and (2007) tested the effect of acupuncture and control acupuncture in the treatment IBS. They found significant differences between verum acupuncture and controls (control acupuncture) in autonomic (diurnal profile of saliva cortisol) and phasic autonomic responses (heart rate variability following a cardiac challenge).

The author stated: “While with acupuncture, both measures were significantly correlated, this was not the case with control acupuncture indicating a sustained and consistent parasympathetic activation after acupuncture treatment while the response in the control groups resembles more the effects of a placebo response. The placebo and verum effects not only with acupuncture treatment often look similar with clinical efficacy endpoints (e.g. in depression treatment when the Hamilton Anxiety Depression Scale is used, see Leuchter et al. 2002), and require the inclusion of moderators of efficacy for better distinction of true treatment and placebo effects.”

Table 1 Healing effect of acupuncture treatment in Western countries or in China

Disorder/disease	Index	Western countries	China
Non-specific low back pain and neck pain	Pain intensity	37.2 ± 21% (n = 30)	50.8 ± 25.4% (n = 5)
Migraine/tension headache	Pain intensity	28.0 ± 17.9% (n = 18)	42.7 ± 19.2% (n = 8)
Post-operative nausea/vomit	Incidence	35.6 ± 17.0% (n = 17)	17.7 ± 8.0% (n = 4)

n = published articles. Mean ± SD. Data do not include electro-acupuncture

6 Why People Say That Acupuncture has a Placebo Effect

Now, if we are confident to believe that acupuncture is not a placebo effect, why do researchers developed the idea that "Acupuncture is a theatrical placebo"? (http://www.dcscience.net/2013/05/30/acupuncture-is-a-theatrical-placebo-the-end-of-a-myth/) Without being able to answer this question and finding out the possible reasons that cause the failure of some acupuncture trials, it seems incomplete to convince everyone.

After thoroughly compare the trials done in Western countries and in China (Wang 2016), we found that possible reasons might be the following.

6.1 Narrow Deference Between the Acupuncture and the Control Group

In the studies from Western countries, the healing effects of acupuncture groups are in a low level (Table 1) (Wang 2016). Therefore, once the effects in the control groups are higher, it would be easy to lose statistical significance between the two groups. We found that when the healing effect in the control group exceeds 31, 75% or trials fell into negative reports (Wang 2016).

Then the question is why the healing effect in the acupuncture group is lower in the studies reported in the Western countries, compared with that reported in China?

According to the data we could collect, we believe that the reasons might be the following:

(1) Low treatment frequency.

Most of the trials applied acupuncture once or twice a week in Western countries, while it is performed five to six sessions per week in China. 77.4% of trials in China (n = 195) did acupuncture five to six sessions per week, (or 93.8% of trials did it more than 3 sessions per week), while in Western trials (n = 90), 52.2% of them did acupuncture twice a week and another 31.1% of trials did it once a week.

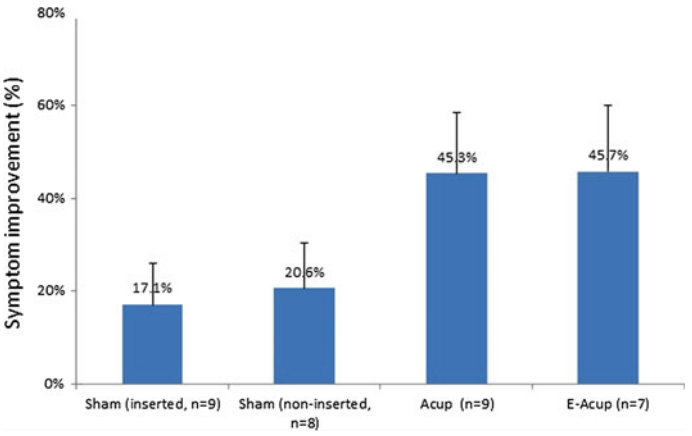

Fig. 7 Acupuncture treatment at middle-high treatment frequency. n = experiment groups. E-Acup: electro-acupuncture. Control inserted: acupuncture needles penetrated into the skin. Control non-inserted: acupuncture needles did not penetrate into the skin. (Diseases treated by acupuncture groups in this figure are migraine (3 articles), cancer-related fatigue (1), menopause syndrome (1), obesity (1), refractory uremic (1), periarthritis of shoulder (1), depression in menopause (1); that by electro-acupuncture groups is chronic low back pain (1), residual insomnia (1), primary insomnia (1), depression (1), functional dyspepsia (2), and migraine (1). It is hard to compare the healing effect of acupuncture group with that of electro-acupuncture group, since that of the acupuncture group is largely depending on personal skill and other factors, such as the diseases treated.)

(2) Less total number of treatments.

83.9% of trials in China (n = 112) had acupuncture more than 11 sessions (50% of trials were 11–20 sessions; 24.1% were 21–30 sessions; and 9.8% of trials were more than 31 sessions). In the Western trials (n = 97), 70.6% did acupuncture for 1–10 sessions only; and 22.0% of trials did it for 11–20 sessions.

Apparently, in terms of treatment frequency and total number of sessions, Western trails had much less stimulation during acupuncture than in Chinese trials.

According to the current data, with higher treatment frequency and higher total number of treatment sessions, the healing effect of acupuncture groups tends to be higher and that of a control group remains low, so that it is easy to yield a positive report (Fig. 7). (It is very rare that acupuncture trials in the Western countries did acupuncture more than 3 times per week for more than 10 sessions. On the other hand, acupuncture trials in China basically did not involve a control group. Therefore it is hard to get sufficient trials with high treatment frequency and high total number of treatment sessions, as well as with a control group.)

It is interested to see that, with high treatment frequency and high total number of treatment sessions, the healing effect in the control groups, inserted or non-inserted, are pretty much the same, suggesting that the failure of acupuncture trials is not due to the types of control group used.

That the increased treatment frequency is related to the higher healing effect is more clearly indicated with the treatment by TENS or Laser acupuncture (Fig. 8),

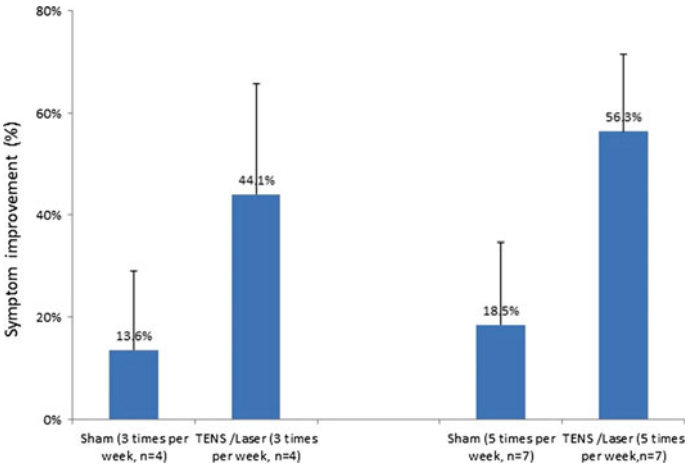

Fig. 8 Treatment by TENS or Laser at three sessions per week or five sessions per week. n = experiment groups (The diseases treated in this figure, the 3-session group is chronic knee pain (3), Tinnitus (1); in the 5-sessions group, chronic knee pain (3), urinary urgent incontinence (1), carpal tunnel syndrome (1), low back pain (1), and functional constipation (1))

after the acupuncture stimulation dose can be standardized for each session with the TENS or Laser (compared with manual acupuncture technique in Fig. 7). It can be noticed in Fig. 8 that all the control groups are non-inserted control groups and that their healing effect remains at a low level despite the increase in treatment frequency.

Therefore, we recommend that acupuncture should be performed at a high treatment frequency for most kinds of disease. For some special diseases, performing acupuncture even once a day is not sufficient. We have to use special acupuncture techniques, pay attention to proper time, etc. to get a higher healing effect. The examples of such diseases are cancer, migraine, post-stroke coma, persistent vegetative state, etc.

(3) Single or double blind design of the study

Such design blocked the communication between the acupuncturist and the patient. This makes it impossible for the acupuncturist to know the feeling of the patients in responding to the needle manipulation, so it is hard for the acupuncturist to induce along-meridian feelings to reach the highest healing effect. The acupuncturist would also feel challenged to get a response from the patients so as to be able a change the treatment schedule or the way of the acupuncture to match the individual need for the treatment.

For this reason, we say that this is a researcher-modified acupuncture. It is not a "real" or a "clinical" acupuncture. It is an "imaged" acupuncture for the acupuncture researchers in the Western countries.

(4) The personal skill of acupuncturist is not guaranteed

It is common sense that the personal skill among acupuncturists (as well as among physiotherapist, chiropractic, massage practitioners) is variable. Indeed it can also be verified from reported trials that there is a large variation in healing effect produced by different acupuncturists (White et al. 2012; Hawk et al. 2005; Forbes et al. 2005).

For a therapy that depends mostly on the personal skill, if the person is not good enough in personal skill, the result of a study cannot be expected to be good. However, in Western countries, some physiotherapists, chiropractic practitioners, or physicians, can also get a license for acupuncture after taking part in acupuncture training for some time. For example, a physician can get an acupuncture certificate after 140 h training and would even be allowed to participate in an acupuncture study (Melchart et al. 2005; Witt et al. 2005; Linde et al. 2005; Brinkhaus et al. 2006; Diener et al. 2006; Endres et al. 2007; Haake et al. 2007; Witt et al. 2006). Sometimes, even newly graduated students can participate in the research (Joos et al. 2006; McKee et al. 2013). We noticed that in more than 40% of acupuncture trials, acupuncture was performed by non-acupuncturists (Wang 2016).

If the personal skills among several acupuncture operators are so different, how can we trust the study involving 67 physiotherapists (Foster et al. 2007), 122 physician (Endres et al. 2007), or 320–340 physicians (Scharf et al. 2006; Haake et al. 2007)?

6.2 No Significant Difference Between Various Study Groups and Control Groups

Generally speaking, there aren't many trials that make comparisons in Western countries. But once there is such comparison study, its influence is very big on the research society.

Among them, one is the study by Yuan et al. (2009), who compared two treatment frequencies: twice a week for five weeks and once a day for five day per week for two weeks. The author did not find a difference between the two groups. However, they used moxibustion and cupping together with the acupuncture. It was a comprehensive treatment, not an acupuncture-alone comparison. It can only mean that, with the combination of other therapies as in real clinical situation with moxibustion or cupping, the acupuncture treatment can be done twice per week. Also in this study, the healing effect in the 5-session group was better than in the 2-session group in the treatment of severe cases. Moreover, the healing effect in the 2-session group saw no more improvement in the following weeks, but the treatment in the 5-session group may have had further improvement if the treatment was continued for more weeks. This means it's possible that after five weeks, the healing effect in the 5-session group might be better than in the 2-session group.

There is only a limited number of such comparison studies in Western countries, and they were mostly performed at a low treatment frequency, so that it is easy to get negative reports showing that there was no difference between the groups. This

easily leads people to create a wrong impression that acupuncture does not depend on proper choice of acupuncture points, not on the Deqi feeling, not on treatment frequency either.

There are lots of comparison studies in China however (see above) and they are mostly performed at high treatment frequency. Their results clearly show differences between the compared groups. This is one of the major reasons why acupuncturists in China do not believe that there is no relative specificity between acupuncture points/meridians, and that the non-point could work evenly to, or even better than, a typical acupuncture point.

6.3 Improper Way to Calculate Specific Healing Effect in Acupuncture

Generally, it is believed that the total healing effect of an acupuncture group is the sum of the acupuncture specific effect and the placebo effect (deduced from control group). Therefore, if we know the amount of healing effect from a control group, we can get the amount of the specific acupuncture effect by deducting the control effect from the total effect in the acupuncture group. This consumption omits a common phenomenon: when two or more therapies are used at the same time, the total effect is usually not the sum of the healing effect of each therapy when they are used alone, no matter the placebo effect has been deducted from the total effect or from each of the therapy or not (Wang 2016). Therefore, in the acupuncture group, we cannot tell exactly how much is control and how much is the contribution of the acupuncture specific effect, even if we know the amount of the healing effect in the control group. Current ways of estimation of acupuncture specific effect in the acupuncture group underestimate it.

6.4 Improper Select of Acupuncture Points

Some researchers heard that acupuncture point Neiguan (PC6) can be used to treat nausea or vomiting; they then use this point to treat nausea/vomiting for any reasons, such as postoperative nausea, post-chemotherapy/radiation therapy nausea, and so on. They also observed the healing effect of only one such acupuncture point, rather than using other complementary points according to different reasons for the symptom. If the acupuncture they tried using this way does not work, they comment that acupuncture does not work (Vickers 1996).

Chang et al. (2005) used electro-acupuncture on the Zusanli (ST36) points of healthy volunteers, to see if the acupuncture could adjust the heart rate after a person was given atropine. The result was that there was no effect. Actually, in Traditional Chinese Medicine theory, the acupuncture meridian that may affect heart function the

most is the Xin Jueyin meridian, especially the Neiguan (PC6) points. The Zusanli (ST36) point used in this study belongs to Stomach meridian. We normally do not use this point to affect the heart rate or heart function. Therefore, the result of such a study should not be regarded as evidence that acupuncture does not work.

Cho et al. (2005) treated refractory skin itch due to late stage uremia with acupuncture. Although it was shown that the healing effect of the acupuncture group was higher than the control group, this study might be hard to reproduce with other researchers. This is because the patients were in the late stage of the disease. The basic reason for the skin itch remained unchanged during and after acupuncture treatment. Also, the acupuncture was three times per week for one month. This is not a high-reproductive study design for acupuncture treatment. The positive result in this study is very much by chance.

6.5 Study on Non-dominated Disease for Acupuncture

Acupuncture is only one of the therapies, not the main therapy in Chinese medicine used in China. It can be used for the treatment for some kinds of diseases, but as with any type of therapy, it cannot be used for all kinds of diseases. This is the same for Western medicine. For example, Western medicine cannot solve AIDS. We cannot therefore deduce that Western medicine does not work. For acupuncturists in Western countries, it is not proper to study diseases that are not on the list of recommended diseases for acupuncture treatment (by acupuncturists in China). Otherwise, the failure of the trial is due to acupuncture not working for the disease tested (in the authors' hands), but not that acupuncture in general does not work.

For some diseases it might not be proper to use acupuncture for the treatment, at least for the movement, such as fibromyalgia (Harris et al. 2005). Patients with fibromyalgia are very sensitive to skin touching or pressure. They cannot tolerate even slight touch on this tender skin, let alone the needle insertion and the Deqi feeling. For this reason, that some studies that showed negative results (Harris et al. 2005) should not be regarded as acupuncture not working for other diseases (Yang et al. 2014). (In clinic, many people suffered from painful muscle and pain is very broad in size. It might be diagnosed as fibromyalgia but patient can well tolerate the needle stimulation. Many times, according to us, it is not fibromyalgia.)

6.6 Confusion in the Healing Effect of Various Other Therapies as that of Acupuncture

Indeed, all of these therapies belong to Traditional Chinese Medicine and used are broadly used in acupuncture clinics. But each therapy has its own proper way of use and with favorite diseases. To include their healing effects with that of acupuncture

is not proper. Acupuncture may work better than them, or not, depending on many things.

In many review articles on acupuncture these various therapies are involved into the review as acupuncture. For example they are included in the review by Colquhoun and Novella (2013), Furlan et al. (2010) and by Linde et al. (2009a, b).

Liu et al. (2015) had a review about acupuncture. They chose 33 articles from 867 total articles. Among these, 17 articles are negative and 23 articles are positive. From the 33 articles, we could remove the studies using electro-acupuncture, auricular press, auricular acupuncture, or finger press (Foster et al. 2007), acupuncture injection or cupping (Kim et al. 2011), acupuncture being not the main therapy (Lin et al. 1999; Zhang et al. 2012; Scheewe et al. 2011), only paying attention to the treatment cost changes (Whitehurst et al. 2011), observing the residence days and cost of acute disease (Painovich and Herman 2012), only observing long term healing effect (Haake et al. 2007), and wrong summary for the study results (such as to comment a negative result as a positive result) (Smith et al. 2011). Then, the negative articles become 7, and positive articles 14.

Azad and John (2013) listed 25 so-called negative articles about acupuncture. Among them, there are 8 articles that used intradermal needling, acupuncture point press, auricular press, or magnetic therapy. The diseases treated by acupuncture are in four categories: fatigue and hot flashes due to cancer or due to chemotherapy, or post-operative pain (8 articles); nausea/vomiting after chemotherapy (5 articles), xerostomia after chemotherapy or radiation therapy (3 articles); and leucocytopenia after chemotherapy (1 article).

In the first category, the acupuncture was mostly done once or twice a week. Only one study was three times a week. Among these, there are 5 clearly positive articles (Hervik and Mjåland 2009; Molassiotis et al. 2007; Bokmand and Flyger 2013; Wong et al. 2006; Crew et al. 2010), and 2 negative articles (both are acupuncture once or twice a week) (Deng et al. 2007; Balk et al. 2009), while in one article, some parameters were positive and others were negative (Liljegren et al. 2012). In the 8 articles, the healing effect in the control group averaged $12 \pm 16\%$, but that in the acupuncture group (including 2 electro-acupuncture groups) was $35 \pm 19\%$, higher than in the control group.

In the Azad and John (2013) review, in the articles about nausea/vomiting after chemotherapy or radiation therapy, 2 articles are positive (Gan et al. 2004; Shen et al. 2000), and 3 are negative (Streitberger et al. 2003; Enblom et al. 2011; Enblom et al. 2012) (the basic data and summary in the last two articles are exactly the same). In the articles about xerostomia after chemotherapy or radiation therapy, 2 articles are positive (Meng et al. 2012; Blom et al. 1996); another article is partly positive and partly negative (Cho et al. 2008).

The one article (Lu et al. 2009) about leucocytopenia after chemotherapy is positive: acupuncture can increase blood number of white blood cells.

Therefore, in the 25 articles cited in the Azad and John (2013) review, only 4 articles can be used as negative against acupuncture. For the diseases studied by these 4 articles (the side effects of chemotherapy and/or radiation therapy), however, there are also a lot of positive studies against their negative results.

Apparently, in the current review articles, there are many non-acupuncture studies. This is a common phenomenon of the review articles in Western countries. They regard such largely variable therapies all as acupuncture.

6.7 Superstitious Belief on Large Scale Experiments

Theoretically, in a clinical study, the larger the sample size, the more believable the results are (Dechartres et al. 2013). This can be verified in Western drug studies, but may not be so in studies on acupuncture (Yang et al. 2009).

In acupuncture studies, even if the selection of acupuncture points, the number of the points, and the treatment frequency are all the same, the personal skill among the acupuncturists could still be variable. Such operator's variation is not easy to control. Therefore, in large scale acupuncture studies, when the study involve large number of acupuncturists and a large number of clinics or hospitals, the results of the study would tend to narrow the difference in the healing effects between the acupuncture group and the control group, so as to produce a negative summary. While in the acupuncture study, as in other medical studies, the data from a large-scale study is highly praised.

6.8 Co-exit of Opposite Ways in Acupuncture Treatment

In acupuncture treatment, there are some quite different or opposing ways of handling the needle or choosing acupuncture points. It seems that both work and this phenomenon is very difficult to understand. Even for us, we cannot explain all of the opposing ways but both work. For example, we focus on the deep insertion of needles, but there are also some other styles of acupuncture in which the needle is inserted shallowly, such as in Wrist-ankle acupuncture, floating acupuncture, or some Japanese shallow needle acupuncture. We use body acupuncture, in which we may choose acupuncture points in any part of the body, but we may also only use local acupuncture technique, in which the acupuncture points are chosen from a very small part of the body, such as from one ear, one eye, the nose, the tongue, one hand, or one foot. The acupuncture point chosen can be only one point, such as the Neiguan (PC6) point that is used in the treatment of nausea/vomiting, or we may need to choose many acupuncture points for the treatment. We may need only a single acupuncture treatment or we may need multiple treatments. We said that the acupuncture needle should be inserted into a so-called acupuncture point, but it may also work if the needle is inserted into a non-point. The acupuncture points might be chosen from the sick side of the body, or from non-sick side of the body, or from upper part of the body, or from lower part of the body, or from local points, or from distance points. It is said it should be considered to choose the first acupuncture point according to the time of the day (Zi Wu Liu Zhu), but we apparently do not need to do so.

All of these discrepancies certainly bring people to question if acupuncture is a placebo effect, because this is the simplest and easiest way to explain all of these discrepancies.

6.9 Not Care or Omit Large Amount of Positive Results

Almost all of the diseases studied in Western countries with acupuncture have some negative studies, but also a large amount of positive studies too. If we include those articles published in China, the number of positive studies is much larger.

When in a study, negative and positive data showed up again and again, it suggests that there is some factor(s) that we have not realized and that it affects the reproducibility of the study. If one study cannot reproduce the data of another one, especially in the study of acupuncture, it might be due to the difference in the study design, the steps of the study, or personal skills. If the reviewer is really a qualified scientific researcher, he or she must be very careful and patient in making a conclusion, not just push 3000 articles off of the desk and leave for coffee.

After we collect more data, especially from China, we can easily find the difference in the way of acupuncture done between Western countries and China. In China, high frequency of acupuncture treatment may be associated with high healing effect, while a relatively low treatment frequency is associated with unstable results (positive or negative). It is necessary for acupuncturists in Western countries to test the acupuncture effect with higher treatment frequency. Whenever we test the efficiency of a therapy and fail to find the effectiveness, we may suspect that therapy really does not work, but it may also to be due to our inability to make it work. This is true for those of therapies that need personal skill.

Brief summary:

There are many reasons that make some researchers in acupuncture studies in Western countries believe that acupuncture is a placebo effect. The most important reason is that the difference in the healing effect between acupuncture group and the control group is not significantly different, which, to us, is due to failure in the acupuncture group mostly, which again is mostly due to the low treatment frequency and fewer total treatment sessions done by acupuncturists in Western countries.

7 Conclusions and Perspectives

The easiest way to test if acupuncture treatment is a placebo effect is to test its healing effect in some clinical conditions, in which the patient is unconscious or has a very limited level of consciousness, such as in coma, shock, persistent vegetative state, under general anesthesia, during delayed wake-up period after surgical operation, etc. Unfortunately it is very rare that acupuncturists in Western countries study

acupuncture in those conditions, but fortunately there are quite a lot of trials from China on them. Data from China strongly supports the healing effect of acupuncture in speeding wake-up or increasing blood pressure, in these serious conditions. In these conditions, the involvement of a control group is meaningless. Not having a control group does not reduce the credibility of these trials at all.

Acupuncture on children older than 2 years means they might be able respond to hints, so as to have a placebo effect in acupuncture treatment, but acupuncture in infants or in animals can hardly be explained by a placebo effect. The theory of conditioning cannot explain the healing effect of acupuncture, since conditioning needs repeated stimulation and the responder needs to remember the stimulation. But the acupuncture can work with only one treatment, such as in the treatment of post-operative nausea. The conditioning cannot be developed after only one stimulation. The replacement theory cannot explain the healing effect of acupuncture either, since it needs the first treatment to work. If the first treatment of acupuncture does not work, the replacing effect cannot happen.

Additionally, there are many differences between the acupuncture group and the control acupuncture group, in terms of their effect on body conditions. Control acupuncture seems not to influence objective parameters for disease, but acupuncture does. For subjective parameters, control acupuncture affects the pain, but not others, such as anxiety, but acupuncture does. Control acupuncture seems have no effect on binary parameters, such birth rate, incidence of smoking, or incidences of post-operative nausea, but acupuncture does. The influence of acupuncture and control acupuncture on neural chemical secretion or signal transduction is different. In addition, the brain image shown for control acupuncture treatment and for verum acupuncture is quite different too. All suggest that, even if there could be an accompanying placebo effect during an acupuncture treatment, the mechanism by which the control acupuncture procedure and acupuncture influence the body is different.

For acupuncture studies with most ordinary diseases or disorders, there are both positive and negative reports about acupuncture. This is the major reason for the idea that acupuncture might be a placebo effect. After comparing the acupuncture trials in China, we found that the acupuncturists in China used higher treatment frequency and a higher total number of treatment sessions for the acupuncture treatment, whereas the healing effect of acupuncture by those researchers are also much higher than those reported by acupuncturists in Western countries. Current data reveals that, under the Chinese style of acupuncture, the healing effect of acupuncture group tends to be high and that of control acupuncture group remains low. This suggests that one of the most important reasons for the failure of acupuncture trials in Western countries is their improper method of acupuncture. With the current low treatment frequency of acupuncture (once or twice per week) and the low total number of treatment sessions (about 10 sessions) used in Western style of acupuncture, the healing effect of the acupuncture group is low, and it is very easy to be overshadowed by that of control acupuncture group, and cause inconsistent results.

Theatrically, if acupuncture is placebo effect, it should have no difference for acupuncture treatment using different acupuncture points or using different techniques, if the treatment is on the same schedule and so on. Indeed it was found by

some acupuncturists in Western countries that there was no significant difference between these comparisons. However, lots of studies from China with Chinese style acupuncture found significant differences between the comparisons.

Acupuncture comes from China. If we are to test its healing effect, it is better to follow the way of the Chinese, rather than to follow a modified form and discredit its effectiveness with the original acupuncture form.

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Acupuncture Styles in Current Practice

Martin Wang

Abstract There are many different styles of acupuncture in current practice. Some follow the traditional acupuncture meridian system, some do not. Each style has its advantages and disadvantages in clinical application. As an acupuncturist, it is better to know the difference among the various acupuncture styles, so as to choose the proper style of acupuncture for the treatment. For acupuncture researchers, it is necessary to know that the textbook style of acupuncture, which is currently under extensive study for its clinic efficacy, is only one of several acupuncture styles, though it is used more than other styles in clinics. For research into the efficacy of a given acupuncture style, it is necessary to follow the exact procedure that is requested for that style of acupuncture, from the diagnosis to the treatment. For research on the acupuncture mechanism, it should be kept in mind that any hypothesis for the mechanism needs to explain the whole acupuncture style, not only parts of it.

Keywords Acupuncture · Technique · Style · Meridian · Holographic theory

Introduction

There are many styles of acupuncture in ancient and current practice. The acupuncture manipulation described in older acupuncture textbooks is usually limited to several common styles of acupuncture. However, there are many styles of acupuncture in practice, especially in China. It would be helpful for both acupuncturists and acupuncture researchers in Western countries to know this important fact in order to gain better acupuncture efficacy and research products.

In this chapter, I summarized a variety of acupuncture manipulation methods in practice for acupuncturists' reference and for researchers who have little or no clinical experience and who have limited theoretical knowledge of acupuncture. Hopefully, the contents of this chapter help achieve better clinical and research outcomes.

I will mainly focus on the needle-based acupuncture styles. I will not focus on some modified acupuncture or acupuncture-like therapies such as point injection, fire acupuncture, electro-acupuncture, bundle needle, dermal needle, bleeding needle, small knife-needle technique and so on. I also exclude information on other

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techniques that are commonly used in Traditional Chinese Medicine (TCM) and acupuncture clinics, e.g., various moxibustion, cupping, Hans machine, TENS, acupressure, tapping, TDP, or bleeding therapy. Because of space limitation, I will only make a brief introduction to each style of acupuncture here and it is impossible to explain the concepts (such as Five-element theory, Five-shu theory, Time-circle theory, Nine-palace theory, Eight-diagram theory, the relationship between the meridians in the body, and so on) and terminology used in each acupuncture style.

For those who are interested in any of the specific styles of acupuncture, I recommend reading the relevant books or journal articles in detail, or obtaining special training. The names of acupuncture points used in this book are indicated with Chinese Pinyin, not the letter-number as used in an acupuncture textbook, since many acupuncture points cannot be easily indicated by this letter-number system.

In the below contents, I regards all of the founders of the acupuncture styles as "Doctor" (Dr.) although many of them may not have graduated from any medical school with a medical degree.

1 Classification of Acupuncture Styles

1.1 Meridian-Based Whole Body Acupuncture Group

According to the principle of acupuncture points, the acupuncture style can be separated into whole body acupuncture groups and local acupuncture groups.

1.1.1 Textbook Acupuncture Style (教材针灸法)

This is the acupuncture style that students in acupuncture schools in Western countries or China learn from their textbook (Liang 2005; Sun 1997). We do not use "traditional Chinese acupuncture" to name this style of acupuncture because there are many other types of acupuncture that should also belong to the "traditional" acupuncture group, but they are not introduced in the textbook.

Many of the contents that have been introduced in the textbook, such as Time-circle acupuncture theory and Five-shu acupuncture, are not suggested in the treatment plan for the treatment of a disease (see below) in the textbook. Most of the acupuncturists who graduate from acupuncture schools are neither using such Time-circle acupuncture technique nor the Five-element theory in the Five-shu style.

Therefore we define the acupuncture style that uses mostly the textbook-suggested treatment plan, as textbook acupuncture.[1] In the textbook acupuncture, the acupuncture points are selected mostly from traditional meridians (Qiu and Zhang 1985).

In the textbook acupuncture style, acupuncturist uses either meridian diagnosis or TCM organ diagnosis (to tell if a disease is in the Yin and Yang aspect, if it is on the body's surface or inside the body, if it belongs to Cold or Hotness, or if it has sufficient or insufficient status) to guide the selection of the acupuncture points.

For example, for the treatment of lower back pain, when using the meridian diagnosis, if the disease is in the Urine bladder meridian, acupuncture points are mostly chosen from the Urine bladder meridian as basic points: Shen Shu, Weizhong. With further organ diagnosis from TCM, if the lower back pain is due to Cold-Wetness, we use the Yaoyangguan point. If it is due to denegation we use Geshu and Ciliao. If it is due to Kidney deficiency, we use Mingmen, Zhishi and Taixi. To enhance the healing effect, it is also recommended to use some special points such as Jijia, and the A Shi point (painful spot).

For the treatment of headaches or migraines, the choice of acupuncture points depends on the location of the headache (the meridian diagnosis), or TCM organ diagnosis, or a combination of both.

For a headache on the top of the head, use point Baihui, Tongtian, Xingjian; on the front of the head, use point Shangxing, Touwei, Hegu; on the side of the head, use point Shuaigu, Taiyang, Xiaxi; on the rear of head, use Houding, Tianzhu, Kunlun. If the headache is diagnosed from TCM point of view as Liver-Yang overwhelming, use point Fengchi, Baihui, Xuanlu, Xiaxi and Xingjian; if it is Qi and Blood deficiency, use Baihui, Qihai, Ganshu, Pishu, Shenshu, Hegu, and Zusanli; if it is Blood stagnation, use Shangxing, Touwei, Shuaigu, Taiyang, Houding. To enhance healing, the A Shi point can be used too.

For the treatment of asthma, it belongs to the disorder in the Lung system, so the Hand Lung meridian is chosen. Again, if it is diagnosed according to TCM as Phlegm-heat, other acupuncture points are also used too: point Feishu (on the Du meridian), Dingchuan (Extra point), Tiantu (Ren meridian), Chize (Lung meridian), Fenglong (Foot Yangming meridian) (Deng et al. 2012).

For the same kind of diagnosis as Phlegm-heat type of asthma, the suggested acupuncture points may different from textbook to textbook. For example, also for the treatment of Phlegm-heart type of asthma introduced by another acupuncture textbook (Steve and Giovanni 2008), the points suggested are Chize (Lung meridian), Zhongfu (Lung meridian), Quchi (Large intestine meridian), Fenglong (Stomach meridian), Dazhui (Du meridian).

In fact, there are several types of asthma with the TCM diagnosis, including Wind-cold, Phlegm-heat, Lung-deficiency, and Kidney-deficiency. Therefore, for a group

[1] This is not to look down the acupuncture system introduced in the text book, but anyway, it is only a part of the whole "traditional Chinese acupuncture". This is similar to the Chinese herbal therapy: in the text book of Chinese herbology, the Shang Han Lun is also introduced, but in the suggested treatment plan for almost all the diseases, the way of herbal therapy in the Shang Han Lun is not recommended, so that we still separate the herbal therapy of the Shang Han Lun from the textbook herbology.

of patients with asthma, their diagnosis from the TCM point of view could be very different, so that the acupuncture treatment should also be different in terms of the choice of acupuncture points and how to manipulate the needles, etc. To use the same way of acupuncture for the treatment of all the patients with the same Western medicine-diagnosed diseases (such as knee arthritis or sciatic pain), is the way of Western style of acupuncture, and is not typical TCM acupuncture.

Depending on whether the disease belongs to overwhelming (e.g. excessive) or weak (deficiency) of Qi in the meridian(s), the needles have to be manipulated as nourishing or depleting in technique.

The acupuncture points used can also be on points that do not belong to any meridian. These are called extra-ordinary points. In recent years, more and more such extra-ordinary points have been found (Chen et al. 1985; He 2012) and the total number of extra points might be more than traditional points in the meridians.

Sometimes, especially if pain is mostly in the muscle-tenden system, we also use needles around the painful spot or on the spot. This technique has been developed into a trigger point treatment as well.

Whether to use only the traditional acupuncture points, the extra-ordinary points, the spot points, or a combination of them, depends on the type of disease, and the experience and habit of the acupuncturists.

1.1.2 Time-Circle Acupuncture Style (子午流注针法)

This style of acupuncture also uses the acupuncture points in the traditional meridians, but the way of choosing the acupuncture point is different (www.epochtimes.com/b5/16/2/9/n4636499.htm).

It is believed in TCM that the life energy in the body is in dynamic flowing as a circle. At a given point in time, the life energy flow is stronger in one meridian and weaker in another meridian. The intensity of the life energy in the meridians is related to the year, the day and the hour of the day. For example, the life energy is overwhelming in the Lung meridian between 3 am and 5 am and, at the same time, it is weak in the Urine bladder meridian (Fig. 1). The acupuncture points are chosen based on the time of the month, the day, or the hours of the day.

There are more than 10 ways to apply this time-circle theory in acupuncture practice. To use it, firstly we need a meridian diagnosis to identify the disease and meridian it belongs to. Secondly, we need the knowledge of the Chinese expression of the year, the month, the day and the hour of the day, Five-element theory, Five-shu points, and more.

The easiest and most popularly used method is the Na Zi (time of day) method. For example, chronic cough is diagnosed as a disorder in the Lung meridian. The energy in the Lung meridian is overwhelming between 3 am and 5 am, so we can stimulate acupuncture in the Lung meridian every day between the 3 am and the 5 am. Similarly, for the treatment of insomnia (poor sleep), if it is diagnosed as a disconnection between the Heart and the Kidney, the acupuncturist can stimulate

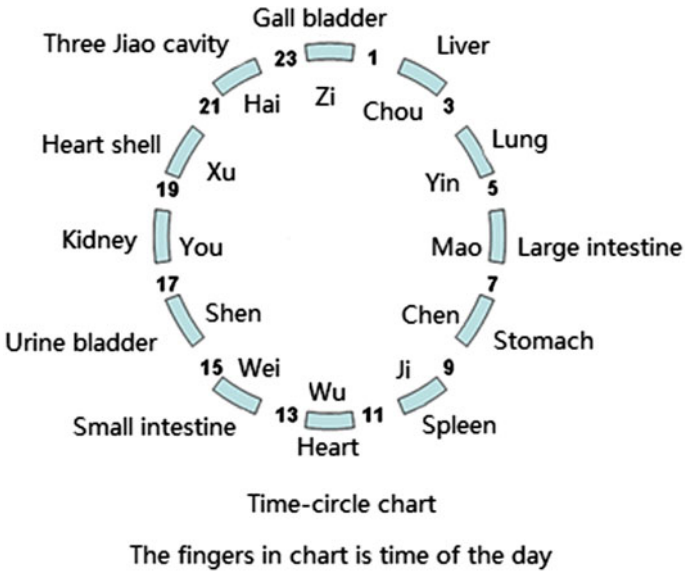

Fig. 1 Time circle of life energy flow in body during a day (www.qgren.com/qigong/lilun/384.shtml)

any acupuncture points in the Heart meridian between 11 am and 1 pm, and in the Kidney meridian between 5 pm and 7 pm.

More specifically for the chronic cough, if it is diagnosed as Lung Qi deficiency, the acupuncturist can follow the Five-element theory with the Five-shu acupuncture on the given meridian (Fig. 2). This acupuncture also is performed every day between the 3 am and 5 am. For the Lung Qi deficiency, the acupuncturist can stimulate the Soil point in the Lung meridian (every meridian has five points, which belong to one of the five elements: Wood, Fire, Soil, Metal and Water), which is the Taiyuan point (with nourishing technique of needle manipulation). However, if the cough is diagnosed as Lung excess, the acupuncturist stimulates the Water point on the Lung meridian with depleting technique, which is the Chize point. To nourish the Lung (Metal) meridian, the acupuncturist can also chose to stimulate the Soil point in the Soil meridian (Spleen meridian), which is the Taibei (Soil point). To deplete the Lung meridian (Metal), the acupuncturist can also deplete the Water point in the Water meridian (Kidney meridian), which is the Yingu point (Water point).

If it is difficult for patients to have acupuncture during the optimal time period, or if it is hard to diagnose the excess or deficiency of the disease, or if the disease is acute, the acupuncturist can just stimulate the Self point or the Primary point of the meridian.[2] For example in the same cough treatment, the acupuncturist can stimulate the Self point (Metal) or the Primary point (Metal) of the Lung meridian, both of which, in the Lung meridian, are the Taiyuan point (Metal).

[2]Every meridian has its Self point and Primary point.

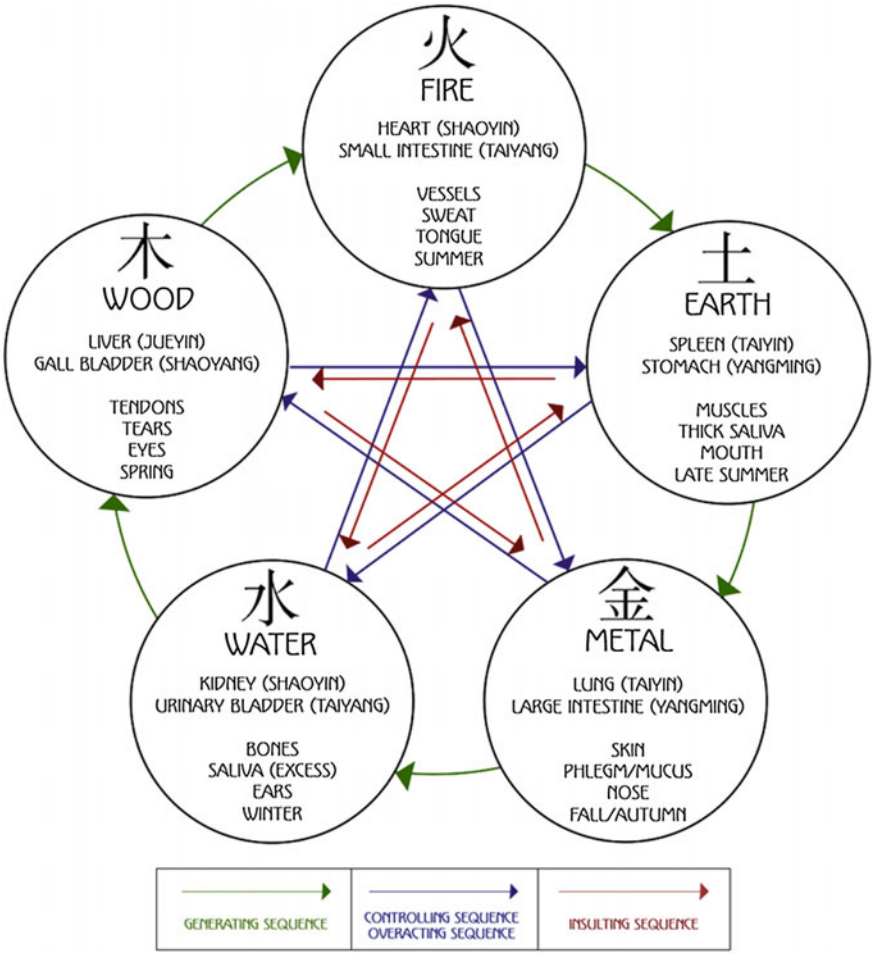

Fig. 2 Relationship between five elements in traditional Five-element theory (http://blog.sina.com.cn/s/blog_6383a68a0102e3sg.html)

This way of choosing acupuncture points is not used popularly among acupuncturists either in China or in the Western world, though it is traditionally introduced in the textbook of acupuncture. However, there are experts in the use of this Time-circle acupuncture (www.wfas.org.cn/lunwen/wfas10/201109/3346.html; Guan et al. 2003; Zhou 2004; http://blog.sina.com.cn/s/blog_ead9736c0102wix1.html). Though there is doubt from some acupuncturists about its certainty and usefulness in acupuncture practice (www.tcmforum.com/forum2.php?forumID=522; http://cntcm.39kf.com/shtml/2317-b-8.shtml; http://yannan.byethost5.com/health/health04.htm), several acupuncture clinical studies suggested that when using either the Time-circle acupuncture along with textbook acupuncture (Yuan et al. 2014; Liu et al. 2009), or

when using the Time-circle acupuncture alone (Han et al. 2008; Zhang 2013; Guan et al. 2005; Zhang et al. 2004), compared with using textbook acupuncture alone, the Time-circle acupuncture worked better than the textbook acupuncture.

1.1.3 Wang Wen-Yuan Balancing Acupuncture (王文远平衡针法)

This style of acupuncture (http://www.100md.com/index/0h/d1/0a/16/index.htm) can be called Dr. Wang Wen-Yuan Balancing acupuncture style because it was developed by Dr. Wang Wen-Yuan. The acupuncture points are also selected from the whole of the body following Mirror theory, most of the time. It is said that 80% of diseases can be treated with only one acupuncture point. Totally it needs only 38 acupuncture points. The locations of the points do not need to be exactly correct, but needles should be on the correct distributing line of the correlated nerve.

The Dr. Wang Wen-Yuan style utilizes the acupuncture Deqi sensation by pulling-inserting technique, so there is no need for nourishing-depleting technique. The needle is taken out once it is felt by the patient. Retention of the needle is not required.

With this style of acupuncture, insertion is fast, and take-out is also fast. Whole treatment is within 3 s.

1.1.4 Tan Wu-Bian Balancing Acupuncture (谭无边平衡针法)

This style of acupuncture was developed by Dr. Tan Wu-Bian (http://bbs.iiyi.com/thread-2548630-1.html; www.siyuanbalance.com/). It uses meridian diagnosis (not traditional organ diagnosis of TCM). Acupuncture points are chosen from the same meridian or other meridians, on the same side of the body or the other side of the body, but do not use the diseased spot.

For example, if the pain is on the lower part of the right front arm, the acupuncturist diagnoses that the pain is on the right Hand Yangming meridian. Therefore, the acupuncturist could choose a positively active point on the Left Foot Yangming meridian (e.g. the same name but on Foot and on opposite), or choose a positively active point on the Left Foot Jueyin meridian (e.g. the By-pass meridian),[3] or choose the positive point on the Taiyin meridian on the left arm (e.g. the Surface-inside relationship between the sick meridian and the treated meridian).

The location of the point on these chosen meridians follows the mirror theory. It is to stimulate the active point, not the traditional acupuncture points on the meridians. The active points are the points at which the patient feels pain when pressed by acupuncturists. This style of acupuncture also uses Time-circle theory to choose active points for the treatment.

[3]The Yangming and Jueyin, the Shaoyin and Shaoyang, the Taiyin and Taiyang, are bypass meridian relationships.

After each treatment, the painful active spot might disappear (the original pain usually becomes much less), but may have a new painful spot later. It is necessary to re-evaluate the meridian and stimulate the active spot. Repeat each time until the original pain completely subsides. This rule is similarly used with Jing Fang (e.g. the herbal formula introduced in book *Shang Han Lun*) where the symptoms are removed one by one as layer after layer.

1.1.5 Li Bai-Song Eight-Words Acupuncture (李柏松八字疗法)

This style of acupuncture was developed by acupuncturist Li Bai-Son (1938–2010). The eight Chinese words are 阴阳、相对、平衡、反应. The words mean Yin and Yang, relativity, balance, and reaction. These are the characteristics of this style of acupuncture (www.360doc.com/content/10/0818/09/840524_47041342.shtml).

This style of acupuncture separates the body into several units: head, neck, trunk and limbs (both arms and both legs are each one unit). First, the acupuncturist needs to determine the painful (or sick) part of the body. Second, it is necessary to find reflecting zone (or reflecting spot(s)) of the painful spot in the same unit (Figs. 3 and 4).

For example, if the pain is on the lower back, it is necessary to find the reflecting area on the body trunk. If the pain is on arm, it is necessary to find the reflecting zone in the limb unit. If there is headache, it is necessary to find the reflecting zone in the head (not on the truck or limb unit).

The principle in finding the reflecting zone is that "the reflecting zone is crossly opposite on other side of the unit". To find the reflecting zones for head, neck and body trunk, follow the "reverse mirror" theory, and for limbs, follow the "mirror theory".

For example, if the pain is on the right and inner side of the front of the arm, the reflecting zone would be on back side of calf of left leg.[4] If the pain is on the lower back, its reflecting zone would be on the upper part of sternum. The exception is that the reflecting zone for the top of the head is on the perineal region. For the treatment of cervical spondylopathy, the reflecting zone could be on or around the synchondroses pubis. The reflecting zone for prostatitis, dysmenorrhea, and uterus fibroid, is on or around the spinous process of the seventh cervical vertebrae.

Again, it is necessary to find a sensitive spot(s) in the reflecting zone. This can be done by rubbing the zone with alcohol on cotton, in order to find a red color spot. This sensitive spot may or may not be located on traditional meridians. Generally speaking, the sensitive points will only work for diseases in the same unit. This means that acupuncturist does not try to find a reflecting zone on the arms or legs to solve diseases on the head or body trunk. Note, the active spot in this style of acupuncture is the color spot after rubbing, not the painful spot upon pressing by acupuncturist (e.g. not the pain spot as in the Tan Wu-Bian Balancing acupuncture above).

[4]For the yin and yang zones in the body, refer to: http://blog.sina.com.cn/s/blog_6383a68a0102e3sg.html.

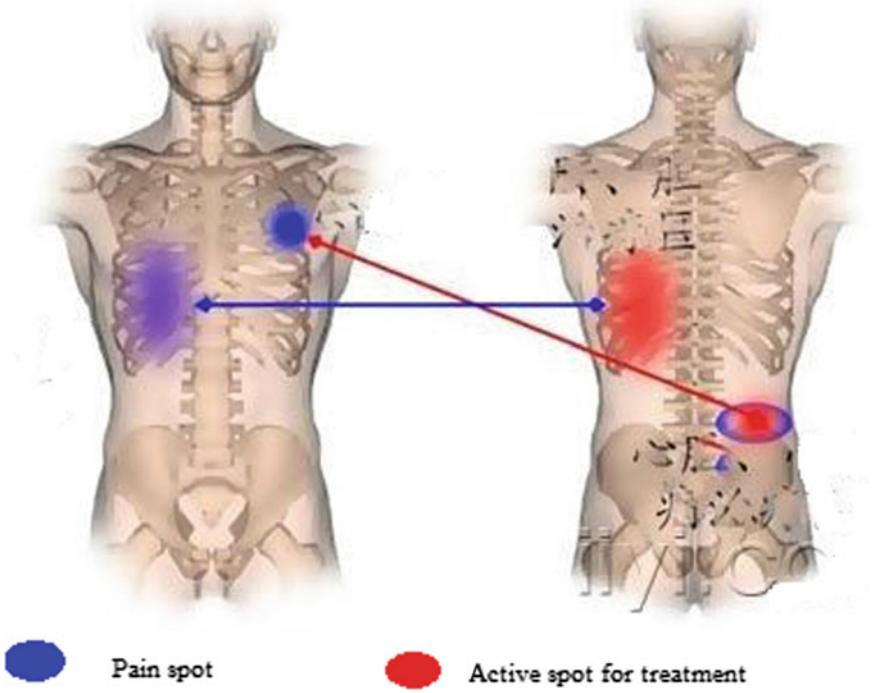

Fig. 3 Treatment of pain in the heart and liver area in the Li Bai-Song Eight-word balancing therapy (http://blog.sina.com.cn/s/blog_6383a68a0102e3sg.html)

Along with treatment and improvement of the disease, the sensitive spot may change its location and numbers. Therefore, it is said that any part of the body may be an acupuncture point and that acupuncture points are dynamic points.

After locating sensitive spots, use acupuncture to stimulate them.[5] Basically, it is necessary to stimulate so deep as to touch the bone membrane (except to treat shallow skin diseases, in which the stimulation is shallow too). It is painful stimulation.

To enhance the healing effect, it is necessary to also stimulate some "high energy" acupuncture points, such as Dazhui, Baihui, Qugu, Shenshu, Changqiang, the Common-Cold-three-needle points, and several points around the inner side and outer side of ankle.

It has been admitted that treatment as such could reduce the pain within a very short time, but also that the pain may come back again (rebound). To solve this problem, it has been suggested that the acupuncturist also includes a traditional Chinese medicine diagnosis and performs acupuncture on the related reflecting zone. For example, if a

[5]The points can also be stimulated by moxibustion, finger press, Guasha, herbal patch, etc.

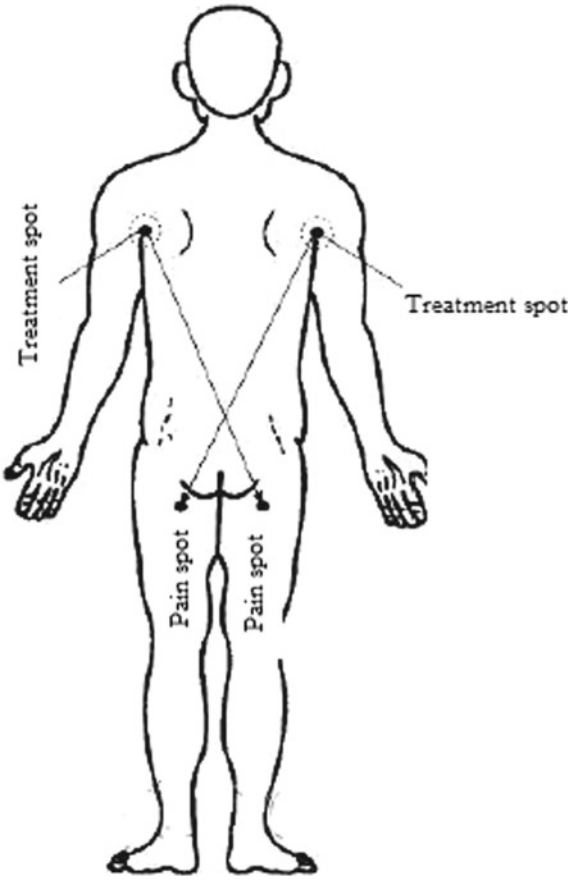

Fig. 4 Treatment of pain in the rear of hip area in the Li Bai-Song Eight-words balancing therapy (http://blog.sina.com.cn/s/blog_6383a68a0102e3sg.html)

pain on the leg is diagnosed by TCM as a Liver problem, the acupuncturist will also stimulate the acupuncture points on the liver reflecting zone.[6]

1.1.6 Chen Zhao Crane-Pine Yi Xue[7] Acupuncture (陈照鹤松易学针法)

This acupuncture style was created by Dr. Chen Zhao (http://sjzlu.blog.sohu.com/130194866.html; http://www.sanwen8.com/p/u4fectdo.html) There are several ways to choose acupuncture points for treatment:

[6]The liver zone however is designed according to the anatomic organ location, not TCM concept of liver.

[7]Yi Xue also means Yi Jing. It is a knowledge system for prediction of changes.

(1) Surface-inner related meridian (八卦成列). For example, if the pain is on the Yuji point (thenar muscles) on the left hand, which belongs to the Hand Taiyin meridian, the acupuncturist chooses the Hegu point on the right hand. Hequ belongs to Hand Yangming meridian, which has a surface-inner relationship with the Hand Taiyin meridian.

(2) Same-name meridian of the surface-inner related meridian (刚柔相摩). For example in the same case with pain in the Yuji point on the left hand, which belong to Hand Taiyin meridian, the acupuncturist can choose acupuncture points on the Foot Yangming meridian. Hand Yangming has a surface-inner relationship with the Taiyin meridian, so the acupuncturist chooses Foot Yangming meridian, rather than the Hand Yangming meridian.

(3) Same-name meridian (八卦相荡). In the same example above, the sick meridian is the Hand Yangming, so the acupuncturist then chooses the Foot Yangming meridian. The two meridians are the same name: Yangming.

(4) Four-diagram acupuncture (四局针法). The three meridians in the inner side of the arm are called Fire diagram; the three meridians in the outside of the arm are called Wood diagram; the three meridians in the inner side of the leg are called Metal diagram; and the three meridians in the back and outside of leg are called Water diagram.

The principle for the choice of meridian for the treatment is this: if the sick meridian is in the Fire diagram, use acupuncture points on the Metal diagram; if the sick meridian belongs to the Metal diagram, choose acupuncture points in the Fire diagram.

Similarly, if the sick meridian is in the Wood diagram, the acupuncturist chooses acupuncture points in the Water diagram and if the sick meridian is in the Water diagram, chooses acupuncture points in the Wood diagram. All in all, it means that if the sick meridian belongs to the Yin meridian in the arm, the acupuncturist chooses acupuncture points also in the Yin meridian but on the leg. If the sick meridian is on the Yang meridian on the arm, the acupuncturist chooses acupuncture points also in the Yang meridian, but on the leg. Just pay attention that if the sick meridian is on the hand, the acupuncturist chooses to treat the meridian on the leg, and, if the sick meridian is on the left, the acupuncturist choose to treat the meridian on the right side.[8]

(5) Eight-diagram theory. It has been summarized by other acupuncturists (http://www.sanwen8.com/p/u4fectdo.html) that this acupuncture style has principles in the selection of acupuncture points which mostly follow Eight-diagram theory.[9]

[8]It can also be understood as: the three Yang meridians treat disease in three Yang meridians in opposite (arm vs. leg, left side vs. right side).

[9]It was summarized to have more than 13 ways of choosing acupuncture points.

1.1.7 Liu Ji-Ling New One-Needle Acupuncture (刘吉领新一针疗法)

This style (https://v.qq.com/x/page/v0191de3sdh.html) is similar to Wang Wen-Yuan One-needle style. The acupuncture points are chosen from the opposite meridian. The acupuncture points are mostly located on traditional meridians. It does not require Deqi sensation. The needle sensation is very mild.

This style is suitable for the treatment of various symptoms such as headaches, spondylosis, neck-shoulder syndrome, tennis elbow, numbness in hands or feet, lumber spondylosis, lumber strain, pyriformis syndrome, various knee arthritis, ankle pain, and various bruise or strains (http://wtoutiao.com/p/6e5eHWU.html).

1.1.8 Zhang Xian-Chen Hand-Foot Three-Needle Acupuncture Style (张显臣手足三针疗法)

This style of acupuncture only uses three needles, either on the hands or feet each time (and rarely uses six needles on both hands and feet) (http://www.360doc.com/content/13/0526/09/11980212_288236524.shtml). The tree acupuncture points on the hand are: Jiangu, Zhongzhu, Houxi. The three points on the foot are: Taichong, Neiting, and Zulinqi (Fig. 5). It would be better to find and use sensitive or tender spot(s) around these acupuncture points. The needle tip for Zhongzhu is towards the finger. Those for Taichong, Neitin and Zulinqi are towards the ankle. The hand's three needles are used to treat disease over the hip. The foot's three needles are for disease below the hip level. Select the acupuncture points on the sick side of the body. If the pain is in middle of the body, select left side points for male and right side points for female. If the pain is in the middle (such as on the spine line), use acupuncture points on both sides.

Find the most sour-pain spot on or around these points (press the skin with a hard material, such as a probe) on the sick side of the body. Stimulate the sensitive spot with acupuncture needles.

It is necessary that the needle is inserted very fast. Twist (three times in either direction) and pull once very quickly. Repeat this depletion technique twice to get Deqi sensation. Then pull up on the needle until it is nearly out of the skin (but not out of the skin). Change the direction of the needle tip to another direction that is parallel to the meridian, so as to stimulate the neighbor acupuncture points on the same meridian. Repeat the depletion technique twice for the acupuncture point on each direction. The patient could feel a lot of pain during the treatment. Most of the needles are inserted at oblique angles (1°–30° to skin), except for Jiangu and Houxi, which should be inserted vertically.

Deqi sensation occurs very fast. Once the Deqi sensation occurs from the last point, the needle is taken out. The whole treatment lasts for only one to two minutes. For this acupuncture style, the Deqi sensation is very strong. After taking out the needle, ask the patient to move the sick part of the body. The three acupuncture points are used one by one. If the pain is gone completely with the first needle, do not continue with the second acupuncture point.

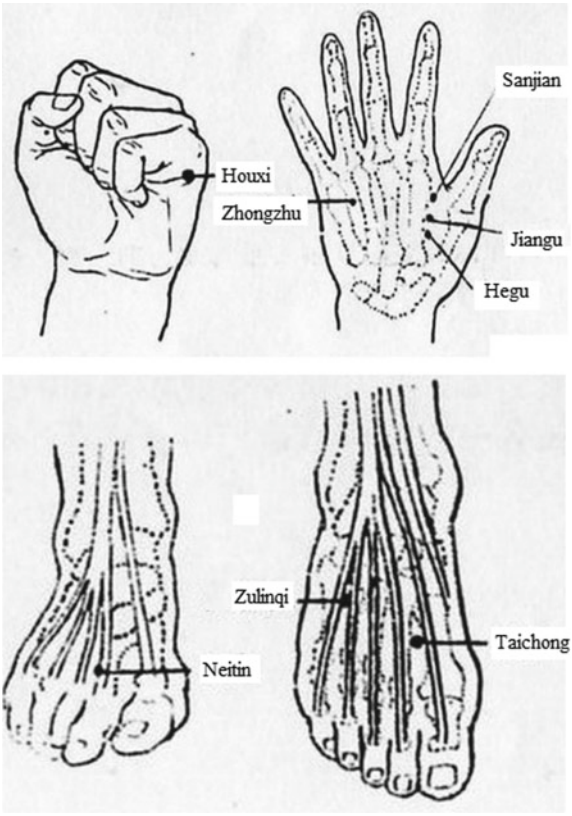

Fig. 5 Hand three needles and Fee three needles in Zhang Xian-Chen three needle acupuncture (http://www.360doc.com/content/11/0606/21/533142_122106761.shtml)

1.1.9 Jin Rui Three-Needle Acupuncture Style (靳三针疗法)

This Three-needle acupuncture was developed by Dr. Jin Rui (http://baike.baidu.com/view/640926.htm). It uses three needles as a group in each small part of the body for the treatment (Fig. 6). For example, there are feet three-needle, hand three-needle, eye three-needles, brain three-needle, intelligence three-needle, and so on.

Fig. 6 Eye three-needles in the Jin Three-needle group (http://baike.baidu.com/view/640926.htm)

In the treatment, the different three-needle groups may be combined. For example, for the treatment of arthritis in both hands, the three-needle in the left hand is used with another three-needle in the right hand. For the treatment of dizziness, the sedation three-needle is combined with the dizziness-pain three-needle. For the treatment of paralysis, the shoulder three-needle, hand three-needle, and the brain three-needle might be used the same time.

The acupuncture points belong to the traditional meridians. The Deqi sensation is required.

1.1.10 Fu Zhong-Hua Floating Acupuncture Style (符中华浮针疗法)

This style of acupuncture was developed by Dr. Fu Zhong-Hua in year 1996 (http://www.fuzhen.com.cn/xnew.asp?nid=868). It is also called Fu's Subcutaneous Needling (FSN).[10]

The selection of the acupuncture point also follows the meridian system. However, after being inserted into the skin, the body of the needle should be only between the skin and the fiber membrane that folds the muscle, and does not at all penetrate into the muscle (Fig. 7). In other words, the needle is within the loose connective tissue.

The needle, which is thicker than and ordinary acupuncture needle, is mostly applied around the painful spot (the tip of the needle points towards the pain spot). The needle is manipulated but does not aim to let the patient feel anything (e.g. no typical Deqi acupuncture sensation is desired). The needle is retained in the loose connective tissue for a longer time,[11] usually 6–24 h (Tao et al. 2014). With the needle in the loose connective tissue, the patient is asked to move the affected body

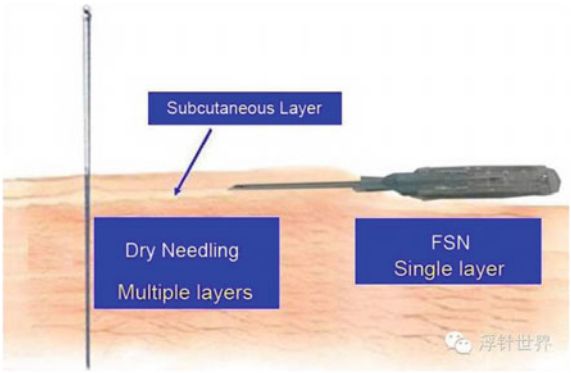

Fig. 7 Working layer of Fu Zhong-Hua subcutaneous needle acupuncture (http://www.haodf.com/zhuanjiaguandian/drheqingtao_1458384285.htm)

[10] This type of acupuncture system has been translated as Floating Acupuncture, Fu's Acupuncture, Fu Needling, Floating Needling, and now, mostly as Fu's Subcutaneous Needling.

[11] The pain can subside very quickly. However if the needle is released after that, the pain may come back again (rebound pain), so that retention of needle (or plastic tube) in the subcutaneous layer is required.

part to increase the healing effect. Each treatment needs only one to two needles. For chronic pain, we need only 3–4 times of treatment.

Generally speaking, the diseases that can be treated by FSN are similar to most of traditional acupuncture, such as chronic headache, cervical spondylosis, periarthritis of the shoulder, tennis elbow, peritendinitis, carpal tunnel syndrome, prolapse of lumbar intervertebral disc, lumbar muscle degeneration, gonarthritis, old injury of the ankle joint, femoral head necrosis, ankylosing spondylitis, cholecystitis and gallstone, chronic stomach pain, urinary stone, chronic accessory inflammation, cervicitis, dysmenorrhea, intractable facial paralysis, and so on.

The hypothesis for the FSN is that the loose connective tissue in between the skin and muscle is the main channel for the transportation and movement of material, energy and signal-information in the body. Any block to the channel would affect the transportation of these life element movements in the loose connective tissue. The block would decrease the threshold of the nerve to cause painful feelings. Removing the block with a TSN needle would re-open the channel, and restore the pain threshold and stop the pain. This is pretty much the same mechanism used to explain the function of various local therapies, such as trigger point therapy, anti-trigger point therapy, small needle-knife, as well as the Wrist-ankle acupuncture therapy.

Because the needle is different from traditional acupuncture needle and the needle is moved in the loose connective tissue in a swipe manner, rather than the vertical insertion of the needles typical in traditional acupuncture, the FSN therapy can be regarded as a mild surgical operation, similar to the small needle-knife therapy.

It is said that FSN therapy may not work properly if the painful limbs are swelling, or if the pain occurs only in some special position (positional pain), or if there is no clear location of the pain.

1.1.11 Zhao Wu-Rong Flying Acupuncture Style (赵武荣飞针针法)

This acupuncture style was developed by Dr. Zhao Wu-Rong and his father (Zhao 2011). It also depends on meridian diagnosis and TCM diagnosis, as well as the disease local zone selection. The uniqueness of this style is that it works more on meridian as a line or lines, and less on individual acupuncture points. According to the TCM diagnosis, one or more zones or meridians might be stimulated.

The acupuncturist uses needles to stimulate the meridian very quickly without leaving the needle in the points. The needle is mostly inserted only into the skin layer, or under the skin, but not into the muscle. The technique can use a single, ordinary needle, or a bundle of needles (bundle-needle acupuncture).

For example, in the treatment of chronic lumber back strain, the technique uses mass stimulation with needles on the lower back area and the rear part of the knee. It may also use a needle to stimulate the Foot Taiyang meridian (because this meridian passes through the lower back), plus bleeding therapy on the Weizhong points behind the knee (Fig. 8). The treatment can be done once or even twice a day, and at least once every other day.

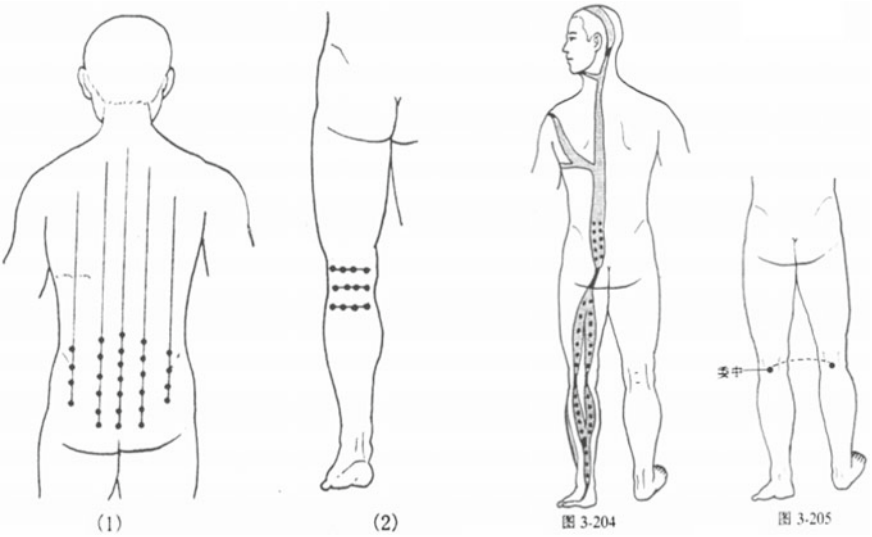

Fig. 8 Acupuncture points used by the Flying needle acupuncture style for the treatment of chronic lower back strain (Zhao 2011)

There are some other similarities to quick acupuncture styles in use in China (zy.china.com.cn; http://www.wujue.com/zljs/zljs/zhenci/201104/42664.html).

1.1.12 Li Jin-Niu Five-Element Acupuncture Style (李金牛五行生克针灸)

Traditionally, the original Five-element acupuncture says that each meridian has five acupuncture points that are named after the five elements: Wood, Fire, Soil, Metal, and Water. Also, the 12 body meridians are allocated into one of the five elements. For example, the Heart (small intestine) meridian belongs to Fire, the Spleen (Stomach) meridian belongs to Soil, the Lung (Large intestine) meridian belongs to Metal, the Kidney (Urine bladder) meridian belongs to Water, and the Liver (Gall bladder) meridian belongs to Wood.

The relationship between the elements is as follows: each meridian (and each acupuncture point in the Five element system) gets help from its previous mother meridian (or the mother element point), each nourishes and helps the following meridian (element point) (called son meridian or son point) and each inhibits the grandson meridian (or the grandson element points) that follows the son meridian (or the son element point).

For example, for Liver (Wood) meridian, Kidney (Water) meridian is its mother meridian, Heart meridian (Fire) is its son meridian and the Spleen meridian (Soil) is its grandson meridian. The Liver meridian gets help from the Kidney (Water)

meridian, and it helps its son meridian the Heart (Fire) meridian, but counteracts its grandson meridian (the Lung, the Metal meridian). For the five element point in each meridian, this is the same rule.

Traditionally, if any meridians is sick, the acupuncturist can correct the life energy flow in the sick meridian by adjusting the life energy flow in its mother meridian (point) or son meridian (point). If the life energy is overwhelming in the sick meridian, it is necessary to deplete the life energy at the acupuncture point with the same element nature, on its son meridian. If the life energy flow is weak in the sick meridian, it is necessary to nourish the acupuncture point with the same element nature, on its mother meridian.

For example, if the life energy is overwhelming in the Liver meridian, the acupuncturist has two choices: (1) to deplete life energy of the Fire element point on the Liver meridian and (2) to deplete the Fire element on the Fire meridian (the Heart meridian). If the life energy is weak in the Liver meridian, we can also (1) nourish the Water element point on the Liver meridian or (2) nourish the Water element point on the Water (Kidney meridian).

Based on the traditional Five-element acupuncture therapy above, Dr. Li Jin-Niu (2009) (Li et al. 2009) further developed modern Five-element acupuncture, taking into the consideration of the reverse-counteract relationship between the five elements.

His idea is that when one element is sick, it will also affect its relationship with other meridians in different ways from those noted above.

If one meridian is overwhelming in life energy flow, it would counteract its grandson meridian (as it normally does), and also reversely counteract its grandmother meridian (normally it is inhibited by its grandmother meridian).

If the life energy flow is weak in one meridian, it would be counteracted by its grandson meridian (which normally is counteracted by the weak meridian), and also be counteracted by its grandmother meridian (normally it has already been counteracted by its grandmother meridian).

For the treatment, if the life energy flow is overwhelming in one meridian, it is necessary to (1) nourish the Element points on the same meridian, which are the same element nature as its grandson meridian and grandmother meridian and (2) nourish the element point on the grandson (grandmother) meridian, which is the same element nature as the grandson (grandmother) meridian.

Let's take an example with the Liver meridian.

If the Life energy flow is overwhelming in the Liver (Wood) meridian, the acupuncturist can either nourish the Spleen point (Taichong) and the Metal point (Zhongfen) on the liver meridian or nourish the Wood point (Taibai) on the Spleen (Wood) meridian and nourish Metal point (Jingqu) on the Lung (Metal) meridian.

If the life energy flow is weak in the Liver (Wood) meridian, the acupuncturist can deplete the Wood point (Taichong) and Metal point (Zhongfen) on the Liver meridian or deplete the Wood point (Taibai) on the Spleen (Wood) meridian, and deplete the Metal point (Jingqu) on the Lung (Metal) meridian.

For any meridian, follow the same rule.

1.1.13 Ma Xiao-Ping Five-Element Acupuncture Style (马小平补北泻南法)

This method is another way of using Five-element theory (Ma 1990). It said that one element can make its mother element (point or meridian) overwhelming in life energy but weak in life energy in its son element (point or meridian).

For example a Liver-overwhelming-Lung-weakness condition, which is common in clinics,[12] can be treated by depleting Heart (Fire) and nourishing the Kidney (Water) to solve the imbalance. This can be done by depleting the Jing point (the Fire point) while also nourishing the He point (the Water point) on the Heart meridian, or by depleting the Heart meridian (Fire meridian) (or Heart shell meridian, also the Fire meridian), while also nourishing the Kidney meridian (Water meridian).

A similar acupuncture style to this one is the He acupuncture style in Korea (Ding et al. 2006).

1.1.14 Yangming Wuxing Acupuncture (阳明五行针法)

This Five-element style is used by Dr. Ding Li–Li (Ding et al. 2016a) for the treatment of obesity. The five element acupuncture points are not the same as the traditional five element points, for which the five element points are on the lower limbs of the 12 meridians (below the elbow and the knee). Its Five-element points are on the whole arm (from shoulder to wrist), whole leg (from hip to ankle), and also on abdomen.

1.1.15 Mang Acupuncture Style (蠭针,芒针)

Mang needle acupuncture is described in older TCM books (http://baike.baidu.com/view/5335366.htm) but was almost lost for a long time in history in most parts of China. Dr. Wang Shi-Gu learned it from a monk named Shaling, and then expanded on it. Later it was found that it had been used for a long time in a small section of China, known as Yao.

This acupuncture style follows traditional meridian system (http://blog.39.net/zhouxin54/a_16530628.html; https://www.youtube.com/watch?v=XXUGN31CBIw; https://www.youtube.com/watch?v=-ASKxsCJCGo), but uses very thick (at least 1 mm in diameter) and very long needles (can be as long as 30 cm or even longer) (Fig. 9). It requires very strict disinfection of the needles, the hands of acupuncturist, and the skin. The needle is manipulated under the skin horizontally, and very deeply. The needle is manipulated with either nourishing or deleting techniques. The intensity of the stimulation is said to not be as strong as might be expected. It is also interesting in that it rarely causes bleeding.

[12]Here, the weak lung can be regarded due to the reverse counteract from the overwhelming Liver. Therefore, the aim of the Five-element theory is to reduce the life energy in the Liver side, so as to release the reverse counteraction from the Liver.

Fig. 9 Mang needles (http://bj.dekunyy.com/html/yaoyi_488_1.html)

1.1.16 Guo Zhi-Chen Eight-Point Acupuncture Style (郭志辰八穴针法)

This acupuncture style was developed by Dr. Guo Zhi-Chen (1943–2011) (http://hopeyoubetter.blogspot.ca/2014/11/blog-post_41.html). It is a supplementary therapy to his Small-formula herbal therapy (草药小方疗法). Both therapies were developed during his Qigong practice. The main idea is that there is big energy in the body, the orbit of the big energy flow is along the middle of the body, from perineal region moving up (in the front of the body) to the top of head, then flowing down through the back of the body, along the spine (the Du meridian), to the perineal region again. It means than the energy flows from the perineal region, along the Ren meridian up to the top of the head, then down along Du meridian to the perineal region.[13] There are also smaller energies moving horizontally in the body too, but the most important energy flow is the big flow circle.

Diseases can be distributed in either the Upper Jiao cavity (Heart and Lung), the Middle Jiao cavity (Liver, Spleen, Stomach, Intestine), Low Jiao cavity (Kidney, Urine bladder), or Outer Jiao cavity.[14] To maintain the normal energy flow from the Low Jiao, up to the Middle Jiao, to the Upper Jiao, then over the shoulder to the Outer Jiao, or from the Outer Jiao back to the Low Jiao (though the perineal region), it is necessary to clear the front of the sick cavity and to create more energy in the back of the sick cavity, so that we can push the energy flow from the sick cavity further forward to complete the energy circle.

For example, if the disease is in the Upper Jiao, it is necessary to clear the Outer Jiao first, to allow the energy in the Upper Jiao to flow (move) further to front of the Outer Jiao cavity. To enhance the healing, we can also bring more energy from the Middle Jiao cavity to force the energy in the Upper Jiao to move.

Such energy movement therapy can be achieved by using the Small Formula herbal therapy, and also via the eight acupuncture points. The eight acupuncture points are Baihui, Dazhjui, Neiguan, Hegu, Changqiang, Zusanli, Sanyinjiao, and Zhiyin. The eight acupuncture points belong to the traditional acupuncture meridian system, but the function of them in this eight acupuncture style is completely different from traditional acupuncture theory.

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[13]The direction of the major energy flow is different from that of the energy flow in the traditional meridian system, in which the energy flows from perineal region, along the back of the body—the Du meridian, up to the top of the head, to the upper mouth lip, then down the front the body, along the Ren meridian, to the lower abdomen, then back to the perineal region again.

[14]In the Guo medical system, disease is diagnosed mostly from observation of the tongue.

According to Dr. Guo, the points Neiguan and Zhiyin work to clear the Upper Jiao, Hegu clears the Middle Jiao, Changqiang and Sanyinjiao clear the Outer Jiao, and Dazhui clears the energy in the head. Baihui moves energy from the top of head to the back of the body (along Du meridian, the Outer Jiao), and Changqiang moves energy from the Outer Jiao (through the perineal region) to the Lower Jiao. Baihui is the upper outlet of extra energy in the three Jiao cavities, and the Zusanli is the lower outlet of the extra energy in the three Jiao cavities.

In this acupuncture style, it is not necessary to get the Deqi sensation.

1.1.17 Pan Xiao-Chuan Classical Acupuncture Style (潘晓川古典针灸)

Classical acupuncture style was developed by Dr. Pan Xiao-Chuan (http://www.360doc.com/content/16/0808/11/11285146_581635215.shtml). It is different from what is commonly called Traditional acupuncture style. To distinguish this style of acupuncture from the commonly mentioned Traditional acupuncture styles, Dr. Pan named his acupuncture style the Classical acupuncture style.

In this style, the selection of acupuncture points follows meridian, but is based on pulse diagnosis.

For example, if the pulse diagnosis tells us that the heart meridian is weak, the acupuncturist stimulates acupuncture points based on the Primary-Branch relationship of the acupuncture points (原穴络穴), or Five-element theory, etc.

Pan believes that the human body consists of both an energy body (Qi concept in TCM) and a physical body (http://clasictcm.com/archives/257). For a disease, in most cases, the energy body becomes sick before the physical body. The improvement of condition in the physical body can be achieved by improving the energy body.

The aim of the pulse diagnosis is to detect the status of life energy in the body (in each meridian). The pulse acts like a window and is the easiest way to detect the status of life energy in the body. The acupuncture treatment aims to adjust and balance the pulse to a calmed and even level. If the pulse becomes calm, the disease will subside.

Acupuncture can stimulate the flow of the life energy (through feeling on pulse). The energy can be healthy Qi, which feels slow and soft. It can also be an aggressive Qi (disease Qi), which feels fast and aggressive. For a healthy Qi, use the nourishing technique of acupuncture; for the aggressive Qi, use the depleting technique to expel it out of body.

For the pulse, the acupuncturist only needs to identify if the pulse is big or small, deep or floating, slow flowing or fast flowing, and smooth or unsmooth. It is said that it is much simpler than any other currently available pulse diagnosis system.

During treatment, the Deqi sensation is not necessary. Dr. Pan feels that it is strange that the concept of acupuncture treatment depends on Deqi sensation. There is no indication in traditional Chinese medicine books that acupuncture depends on Deqi to exercise its healing effect.

The effective mark for acupuncture treatment is calming of the pulse. If the pulse is not improved (by acupuncture) into a calm status, the disease's symptoms may

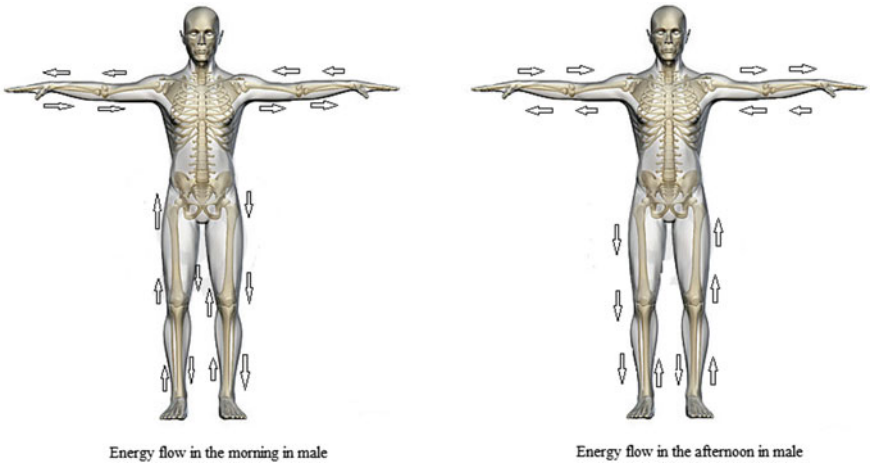

Fig. 10 Energy flow direction in the morning and afternoon in male

recur later. If the pulse has been calmed, then the disease would be improved for the long term, even if pain or other discomfort remains and is not corrected yet during the time of the treatment.[15] To get a consistently calm condition of the pulse, a longer time of acupuncture treatment is necessary. It is better to have acupuncture in the morning time and retain the needle for 25–30 min.

It should be mentioned that, because the energy flow in the body is believed to be different in the morning and in the afternoon, and that it is also different for male and female, the meanings of the pulse in the left and right wrists are different too (https://www.youtube.com/watch?v=e8ALXACZsfA). For example, the energy flow for male in the morning is along the left three Yin meridians from chest to the left hand, then along the three Yang meridians from left hand to the upper back, from there along the three Yang meridians to the right hand, then along the three Yin meridians from the right hand to the chest (Fig. 10). At the same time, the energy flows along the three Yang meridians in the left leg down to the left foot, along the three Yin meridians in the left leg up to the body trunk, from the body trunk it runs along the three Yin meridians in the right leg down to the right foot, along the three Yang meridians in the right leg up to the body trunk. In the afternoon (from noon), the flow direction is the opposite.

The meaning of the pulse for male in the morning is in the left wrist: Heart (cun position), Liver (guan position) and Kidney (chi position). On the right wrist it is therefore the Lung, Spleen and Life gate. In the afternoon, the pulse in the left wrist becomes Lung, Spleen and Life gate, while the right wrist becomes Heart, Liver and Kidney.

[15] It is said that no change in symptoms during treatment does not mean that there is no healing effect yet.

For female, the flow direction is opposite of the male in both morning and afternoon.

1.1.18 Korea Sha-Am Five-Element Acupuncture (韩国舍岩五行针法)

This Five-element acupuncture style (Youn 2010) also came from China, but was developed and applied more by Korea acupuncturists. There are some similarities between the Sha-am acupuncture style and the Five-element introduced above. For the purpose of this article, we omit the details of application.

1.1.19 Korea Li Ji-Ma Four-Diagram Acupuncture Style (李济马太极四象针灸)

The Tai-Ji Four-diagram acupuncture (李济马太极四象针灸) was developed by Dr. Li Ji-Ma and later further developed by Dr. Li Bing-Xin (李炳幸) in Korea (Jin 2009). This style of acupuncture diagnoses the body condition of a patient into four kinds: Taiyang, Taiyin, Shaoyang and Shaoyin. For the Taiyang, the Lung is stronger and the Liver is weaker. For Taiyin, the Liver is stronger and the Lung is weaker. For Shaoyang, the Spleen is stronger and the Kidney is weaker. For Shaoyin, the Kidney is stronger and the Spleen is weaker.

For the treatment, we use the Five Shu points in the Heart meridian and take into consideration the Five-element nature of the five points. The style also uses the Primary points of the traditional meridians for the treatment, based on the Five-element theory.

1.1.20 Nora Five-Element Acupuncture Style (Nora 五行针法)

Nora Five-element acupuncture style (http://www.laozongyi.com/zhongyi/284197.html) originated in China a long time ago. It was discontinued for a long time in China but survived in Korea and Japan. Later it was re-developed in England by J. R. Worsley and Nora Franglen.

This Five-element acupuncture style separates humans into five elements. Any person has one element that dominates his or her physical body function and emotional status. The dominant element stays with the person forever. Disease or symptoms cause an imbalance of the elements. The doctor needs to find out the dominant element of the patient and restore it via acupuncture treatment.

To find out the dominant element of the patient, the acupuncturist needs to collect information from the four major aspects of the patient: voice, color, smell/odor and emotional status. The acupuncturist also needs to collect other, broader information about the patient such as life style and emotional relationship with others. We need a very close relationship between the doctor and the patient to get sufficient and correct physical and emotional information about the patient (http://www.360doc.

com/content/16/0614/13/20849286_567684411.shtml). It is therefore claimed that this acupuncture style is not only able to treat the physical illness but also to improve the emotions of patients.

For pulse diagnosis, it is admitted that it cannot be used to help find the dominant element for the patient, but it can find the pulse indicating a poor relationship between husband and wife, and the pulse indicating energy flow blockage in the connection with two meridians (http://blog.sina.com.cn/s/blog_7da0ca120102vwto.html).

The acupuncturist also touches the body (the chest, the upper abdomen and lower abdomen) to find any imbalance within the Three Jiao, presses the Mu point to find any imbalance in each organ, and to touches the middle vertical line of the abdomen to find position changes of the abdominal aorta.[16]

The acupuncturist also uses the Akabane test[17] to find energy flow imbalances in the Jing points (the acupuncture points that are located on the fingers or toes) between the left and the right side of the body. If there is an imbalance, we must do acupuncture on the weak side of Jing point (using nourishing technique). Then we must test it again. If the imbalance remains, we do acupuncture on the Origin point of the meridian on the stronger side (also using nourishing technique). This treatment procedure needs to be repeated several times until the warm sensation on the Jing points on both sides of the body becomes equal.

After set up of the element diagnosis, the treatment might be relatively simple, because each element body has its own specific and co-related acupuncture points to stimulate. The whole treatment course is separated into different phases. Each phase has its own specific treatment goal. In the beginning, the acupuncturist mildly stimulates the 12 meridians. It works almost as a test period to see if the diagnosis of the dominant element is correct or not.

Here is an example for the treatment:

If a patient is diagnosed as Element Metal, on the first treatment, the acupuncturist will do acupuncture on Hegu and Taiyuan (both are the Primary point of the Lung meridian).

During the second treatment, the acupuncturist uses point Jingqu (to clear the garbage on the Lung meridian), Wood point Quchi and Taiyuan (to nourish the Lung meridian: mother meridian to nourish the son meridian: using Quchi and Taiyuan), Fire point (Fire counteract the Metal, using point Yuji), and Wood point (using Taiyuan, Yinbai, Yuji, or Zhongchong).

During the third treatment, the patient complains of some discomfort, poor digestion, and stiffness in the sinuses. It is found from pulse diagnosis that the pulse on the

[16] If there is position change with the abdominal aorta, the acupuncturist uses his hand to correct it.

[17] Akabane test: test the warm sensation of each Jing point on fingers and toes (total 12 such points) to see if the warm sensation on the Jing points on the left and right hands, and the left and right feet, are the same or not. If the sensation on one side is different from other side, it indicates imbalance of Qi flow between the two points. Use a burned line moxi to move close to the point and ask the patient if the patient feels warm at the point. The acupuncturist makes a record of how many times the patient starts to feel warm after the burned moxi moves over a spot. Most of time, the Jing points on the feet need about 10–20 times to feel warm and the Jing points on the hands need about 3–10 times.

Metal is stronger than the Wood, indicating an energy flow block in the large intestine and stomach. The acupuncturist uses point Yingxiang and Chengqi to remove the block. After removal of the block, it is necessary to decide if the treatment needs to use Primary point, or some other points, to improve energy flow in the meridians.

During the forth treatment, the patient feels a little better overall, but still feels depression. Acupuncture is performed on the Shenque point (Use moxi only. If there is hypertension, use Juque point only.). Again, it is necessary to decide if the treatment needs to use Primary point or some other points to improve energy flow in the meridians.

During the fifth treatment, use corresponding body back Shu point to the Metal, the Large intestine Shu point and the Lung Shu point. After treatment, again it is necessary to decide if the treatment needs to use Primary point or some other points to improve energy flow in the meridians.

It is emphasized that if the treatment above is performed in the fall, it is necessary to also use the Season point once. For Metal, the Season points are Shangyang (the Metal point on the Large intestine meridian) and the Jingqu point (the Metal point on the Lung meridian). These use the universe's energy to nourish the body energy.

During treatment, the body condition of the patient can show more clearly whether the person belongs to the Metal element. If so, the treatment can go further into the next phase. If it is not clear yet, the above treatment procedure has to be repeated to test for other Elements.

For the following treatment phase, the acupuncturist performs acupuncture on points that belong to the Metal meridian. Based on body condition, some points on the other meridians may also be stimulated, such as points on the body back (Urine bladder meridian), Du meridian and Ren meridian.

In the Five-element acupuncture style, we emphasize the use of Season circle and Daily circle of the energy flow in the meridians. It requires Deqi sensation. For nourishing technique, the needle is removed after getting the Deqi sensation. For depleting technique, the needle remains in spot for 20 min. Overall, the needle is inserted shallower than most of other acupuncture styles.

For such a treatment plan, we need at least 8–10 sessions of treatment. Acupuncturists in this style do not emphasize the importance of each acupuncture point. They tend not to stimulate the patient with a large number of acupuncture points, nor with stronger stimulation, so as to prevent the disturbance to the energy flow in the body. They do not aim to get quick improvement. They do not know what may happen next with their treatment, because each patient is different and the reaction of patient to the treatment is also very complex. It is claimed that the highest goal for such treatment is to change the life of the patient.

For treatment frequency, acupuncture is usually performed once per week. Once there is a sign of clear and constant improvement, acupuncture sessions can be changed to once every ten days, then once every two weeks, then once every two months.

(1) Aggressive Energy: This style also pays attention to the treatment of Aggressive energy (AE). Removal of the AE is the basic work before applying the typical

Five-element therapy. We use the body back Shu points for the treatment.[18] According to Five-element theory, the AE passes from the mother meridian to the son (counteracting the relationship between meridians). Without stopping its pass, the AE will damage all the meridians. To remove the AE, use the following body back Shu points: Heart Shell Shu, Liver Shu, Spleen Shu, Lung Shu, Kidney Shu.[19] The needles should be inserted shallowly and also at an oblique angle. If indeed there is AE in the body, there will be a pink color around these needles. It is necessary to wait and not to pull out the needles until the skin color disappears.[20]

(2) Attached energy body: the patient is affected by an extra energy body. The patient who is affected by the extra spirit body may behave strangely. In severe cases, the patient may appear to have a mental disease. For the treatment, the acupuncturist uses Inner-Seven-Dragon points: Jiuwei, Tianshu, Futu, and Jiexi. If the treatment does not work, the acupuncturist uses Outside-Seven-Dragon points: Baihui, Dazhu, Shenshu and Pucan.

(3) Imbalance of left-right pulse: if the pulse on the left side (called the husband side) is weaker than that on the right side (called wife side), there is a Wife-Husband imbalance.[21] For the treatment, we transfer the energy from the right side to the left side using the Five-element theory and the Primary-point theory.

(4) Meridian energy flow block: the energy flow is blocked from one meridian to next. The block happens mostly in the area where the two meridians connect. Such blocks can only be diagnosed by pulse, or by some physical illness sign around the blocked area. The most severe block is the block between the Du meridian and the Ren meridian, showing as weak pulse on both hands. For treatment, nourish the outlet point of the first meridian and the inlet point of the following meridian (both with nourishing technique).

(5) Scar tissue. Scar tissue could block the energy flow through meridian. For treatment, the acupuncturist stimulates the points located on both side of the scar tissue, with nourishing technique.

It is said that the treatment starts when the acupuncturist meets the patient and starts to have communication, not only from the use of needles. We can predict that this style needs a longer time to correct disorders of the body. Along with treatment (and personal relationship), the acupuncturist may change his diagnosis again and again. This style might be regarded more as emotional re-balance. Physical disorders can be corrected through the improvement of emotional/spiritual aspects.

We have not practiced this Five-element acupuncture yet, but we have concerns about it:

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[18] Other acupuncture systems may use Five Shu points to removal the AE out of body.

[19] Heart Shu is used only when there is AE in the heart.

[20] It may take 20 min to 2 h. But if the pink color does not disappear after some time, it may not mean that there is AE in the body. However, our own experience is that if there is pink color around needles on the back of the body, the healing effect of acupuncture is very good. We do not regard it as aggressive energy; it means that the body is sensitive to acupuncture stimulation.

[21] It may not really mean the poor relationship between the husband and his wife.

(1) It requires the acupuncturist to have good communication skills to talk with patients, and requires the acupuncturist to communicate the way that the patient prefers.
(2) It might be too simple to separate human beings into only the five elements, because, as we understand, the body elements of most people is a mixture of two or three or even more types of elements. For example, a person's body element might be mixture of Wood and Fire constitution, or Metal and Water elements. For a mixed body constitution, one element might be more dominant than another.
(3) It would be difficult to get correct information for elemental diagnosis if the patient refuses to reveal his or her personal information (http://blog.sina.com.cn/s/blog_7da0ca120102vwto.html; http://zhong1.org/2228.html).
(4) The acupuncturist needs to keep his or her own emotions in a balanced and have a peaceful status (as a mirror), so as to be sensitive enough to understand the emotional status of the patient.
(5) What if the acupuncturist's own dominant elements are Metal and Water?[22]
(6) We might spend unnecessary time on patients if the patient only wants to stop the pain as soon as possible.

Because this Five-element acupuncture style has greater emphasis on communication with patients, it seems more dependant on the psychological aspect of the treatment. The healing effect might be relatively more depending on a psychological effect, which might be doubted as a placebo effect.

It might be difficult to test if this Five-element acupuncture style is mostly dependant on a placebo effect, given current strategies of acupuncture research in Western countries, in which communication between acupuncturist and patient is restricted. Without communication between the acupuncturist and patient, how could the Five-elements of this style of acupuncture work? Currently, we can only find someone exploring the theoretical possibility to use this style of acupuncture to treat post-stroke depression patients (Ni 2015). Such a study might be difficult since patients are usually hesitant to communicate.

Overall, we feel that this type of so-called Five-element acupuncture is not an individual acupuncture style, but mixes acupuncture methods in the practical environment of an acupuncture clinic.

Knowing the dominant element of patients seems to have nothing to do with the treatment of their physical illness. The healing effect of this style of acupuncture can

[22]Theoretically, Element Metal shows as cool, and inner-forwarded, and people are not good at social communication but are good at job techniques. Element Water is quiet (as winter), and such people are also not good at social communication. During communication with patients, doctors who practice the Five-element therapy need to meet the needs of patients to know the doctor's personal information. A Metal and Water element doctor might be hesitant to share such personal information with patients. So, we predict that the proper element of a doctor who participates in such Five-element might best be Fire - Wood - Soil - Metal - Water combined. But, even so, if the patient is of the Water element, he or she might not like to meet a doctor who is too warm (a Fire element doctor). The co-relationship between the element of the doctor and that of the patient is important.

be attributed to various acupuncture methods used during treatment: (1) during the Akabane test, the moxi used has stimulated the acupuncture points (the Jing points of all the 12 meridian); (2) continuous stimulation of the Primary acupuncture points during different steps of the treatment; (3) in the release of block due to scar tissue; (4) in the treatment of aggressive Energy; (5) in the treatment of the attached energy body; (6) in the use of Spiritual Window points (to open the heart/emotion of a patient to the outside environment/world); (7) routine use of moxibustion before every needle stimulation; (8) frequent use of the Primary points during every treatment step.

In all of these treatment courses, the acupuncturist does not apply the Five-element theory for the treatment.

Once coming into Five-element therapy, it seems that the acupuncturist only believes that the principle problem for every patient is that his dominant element is weak and the dominant Element needs to be nourished. Therefore, the nourishing technique is principally used, which includes non-retention of the needle in the acupuncture point (if the needle is left for 20–30 min, it is regarded as a depleting technique).

If so, it seems that the acupuncturist does not follow the typical principle for the use of the Five-element theory. In typical Five-element acupuncture styles, in the case of the deficient Element/meridian, the meridian condition should be corrected by stimulating its mother Element. If the meridian is in an overwhelming status, we need to stimulate its son Element/meridian. At the same time, the Element or the meridian that resists the sick meridian, should not be stimulated because to stimulate this resisting meridian would make the sick Element/meridian weaker (one of the reasons for its weakness is due to suppression from another Element/meridian).

An example is given: the patient's body Element is diagnosed as Metal. It said that all of the treatment should be with a nourishing technique to support the Metal meridian (the Lung meridian and the Large intestine meridian). This means that the acupuncturist believes that the energy in the Lung meridian and the Large intestine meridian is weak.

In the first treatment, the acupuncture points Taiyuan and Hegu are used. The point Taiyuan is the Soil point in the Lung meridian. This is a correct use, according to Chinese Five-element theory, but the point Hegu is the Fire point in the Large intestine meridian. The Fire suppresses the Metal, so the use of Hegu may not be a proper choice. The acupuncturist uses it just because it is the Primary point of the Large intestine meridian. It seems that the primary point can be used at any time, without need to consider its element nature in this style of acupuncture.

From the second treatment, they emphasize the use of other acupuncture points to connect the life energy from other meridians to the Metal meridian. The points used are:

(1) Quchi and Taiyuan. The use of Taiyuan is fine because it is the Wood point in the Metal meridian. The use of Quchi is also fine, because it is the Wood point in the Large intestine meridian. The Wood point/meridian is the mother of the Metal point/meridian and it nourishes the Metal;

(2) Yuji. The Yuji point is the Fire point in the Lung meridian. It is not a proper point because the Fire suppresses the Metal;
(3) Yinbai or Zhongchong. The Yinbai point is the Wood point in the Spleen meridian (Wood meridian). Normally the Metal point/meridian suppresses the Wood. If the Metal is weak, the Wood would be able to suppress Metal in turn, especially if we stimulate the Wood to make it stronger. This is not a good acupuncture point choice. It is better to use the Taibai (Wood point) in the Spleen meridian (Wood meridian). The Wood nourishes the Metal. The Zhongchong is the Soil point in the Liver meridian (Wood meridian). It is hard to understand what would be the result of stimulating the Soil point in the Wood meridian on the energy status in the Metal.

Five-element is already complex for most of beginners in acupuncture. The use of the Five-elements in this style of acupuncture seems even more complex and difficult to understand according to traditional Five-element theory. According to the author, they use, at the same time, both the assistance relationship between the mother point/meridian (相生) and the son point/meridian, and the resistance relationship between the given point/meridian and its grandmother point/meridian (相克). They use the Yin and Yang points in either meridian to balance the life energy among the meridians. The idea is that, when the dominant meridian is weak, the acupuncturist can transfer energy from other meridians to support it. Once the energy is sufficient in the dominant meridian, it would likely and willingly share its energy with other meridians too.

It is also strange that the acupuncturist refuses to stimulate the acupuncture points on the Heart meridian, for the worry that it may otherwise disturb the emotion and spirit of the patient. This is absolutely unaccepted by the traditional Chinese acupuncture community. One of the Korean acupuncture styles also separates the body into Elements, but uses the Five element points in the Heart meridian to correct the imbalance among the four elements of the body.

We also ask why acupuncture always starts from the left side of the body.

Acupuncturists in this acupuncture style emphasize having a long treatment schedule. They believe that the whole treatment needs a long time to complete, and they do not expect quick improvement of body condition with their treatment. They worry that acupuncture stimulation may disturb the Qi and Blood environment of patients, so they recommend using the least possible number of needles, and have the fewest possible treatments. They cannot expect or predict what may happen to the patients with their treatment because they feel that each patient is different in the reaction to the treatment. However, they still claim that the highest goal of the treatment is to help the patient change their life.

This type of Five-element acupuncture is mostly practiced by acupuncturists in the UK, where there are several acupuncture schools that teach it.

1.1.21 Japanese Acupuncture

There are many different acupuncture systems in Japan (Xiao et al. 2011). One of the interesting characteristics of acupuncture in Japan is that some acupuncturists do not pay attention to the meridian diagnosis, and use the abdomen touching diagnosis instead. They find the painful spot in the abdomen (the A Shi point) and stimulate it during treatment. They insert the needles at a very shallow angle. Needles are very thin and they use large number. Deqi sensation is sought (http://www.zhifayixue.com/zhongyaolunwen/425.html).

One style of Japanese acupuncture is the Japanese Meridian acupuncture system (Keiraku Chiryo) (http://www.100md.com/Html/Dir0/15/16/23.htm; http://www.pacificcollege.edu/sites/default/files/PS2016Notes/3/KobyleckaM_PS2016_SaturdayAM_Handout.pdf). It emphasizes the diagnosis using the pulse on the wrist. It is believed that the imbalance in the distribution of the Qi in the meridians is the cause of disease. Stimulation of the meridian could restore the normal distribution and circulation of the life Qi in the meridians. They also use acupuncture needles, but the needles are inserted very shallowly (1–2 mm, or not even penetrating the skin). They do not aim to induce the Deqi sensation and the patient does not feel anything, or only feels a very mild stimulation. However, they emphasize that the acupuncturist should feel the energy in the meridians.

Another Japanese acupuncture style is the Kiiko Matsumoto Japanese Style (https://bconroytc.wikispaces.com/Fertility+Support+-+Kiiko+Matsumoto+Japanese+Style), which is currently available in US. It emphasizes the use of palpation on the abdomen to find the reason for a disease. In the treatment, the needle insertion is very shallow.

1.1.22 Various Special Manipulating Techniques of Acupuncture

There are also some more acupuncture styles that are used mostly in China. They usually choose acupuncture points from the traditional meridians but use a special way of manipulating needles for better treatment results. Examples for such special acupuncture are as follows:

Xing Nao Kai Qiao method by Dr. Shi Xue-Min (石学敏醒脑开窍针刺法) (He and Li 2012; Shen and Shi 2010);

Fei Jing Zou Qi method by Dr. Zhen Kui-Shan, Li Yu-Lin, Lu Shou-Kang, and Wang Fu-Chun (郑魁山, 李毓麟, 陆寿康, 王富春之各种飞经走气法) (Yu et al. 2014; Lou 2003; Wang 2009; Chen et al. 2001; Yang 1982; Xu and Wang 2008);

Big Meridian-connecting method by Dr. Zhang Yuan-Su (张元素大接经法) (Wu 2016);

Governor Vessel-regulating and brain-unblocking acupuncture method by Dr. Gao Yu-Pei and his father Dr. Gao Yu-Chun (调督通脑针刺法) (Zhang et al. 2016);

Target acupuncture by Dr. He Tian-You (何天有靶向针刺法) (Mao et al. 2015);

Tong Luo An Shen by Dr. Li Ming-Yue (李明月通络安神针刺法) (Li et al. 2016);

Yi Shen Tong Qiao by Dr. Yu Chuan (于川益肾通窍针刺法) (Yu et al. 2016);

Tian Kun acupuncture method by Dr. Li Ji-Chun (李济春乾坤针法) (Hao et al. 2016);

Lifting and pressing method by Dr. Ding Bang-You (丁邦友抽添针灸疗法) (Ding et al. 2016b);

Tong Du Tiao Shen acupuncture method by Dr. Li Ping (李平通督调神针法) (http://www.wfas.org.cn/lunwen/wfas20/201108/2871.html);

Shallow stimulating acupuncture techniques (各种皮下浅刺法[23]) (Gao and Fu 2016; Huang et al. 2012; Yan and Yu 2016; Liu and Fu 2016);

Motivating-tendon acupuncture by Dr. Chen De-Cheng (陈德成动筋针法) (Chen 2016);

Nou Yun Zhi Zhen acupuncture by Dr. Lou Mei (路玫努运滞针法) (Guan et al. 2013);

Zhu Tong Yi Ten acupuncture by Dr. Wen Hong (文洪教授"住痛移疼"针法) (Zhang et al. 2014);

Around acupuncture technique (围刺法) (http://baike.baidu.com/view/3508557.htm).

1.2 Acupuncture Styles Only Partly Following Traditional Meridian

1.2.1 Dong Jing-Chang Extraordinary Point Acupuncture Style (董氏奇穴疗法)

This style of acupuncture (http://www.tungs.net.cn/zh-tw/) was developed by Dr. Dong Jing-Chang (1916–1975). Later it was further developed by his students Yang Wei-Jie, Hu Wen-Zhi, Li Guo-Zhi and others.

The acupuncture points are distributed all over the body, but in most cases the points do not follow the traditional meridians. Instead, the distribution and the selection of the acupuncture points partially follow the Holographic theory.

Holographic theory (全息理论) states that any one part of the body contains the information about the whole body. Therefore, stimulation on a local spot can influence the co-related part of the whole body. For example, one front arm can be regarded as the whole (small) body. If the far-end (e.g. the wrist) part of the arm represents the head of the whole body, the near-end (e.g. the elbow part) of the arm would represent the foot of the whole body. If a person has pain on their foot, we can choose acupuncture points (belonging to meridians or not) near the wrist.

This style of acupuncture also partially follows a Mirror theory (镜像理论). This means that one part of the body can be regarded as a mirror part of another part of the body. For example, the head and foot have a mirror relationship. If a person has a headache, we can stimulate acupuncture points (also on the meridian or not) on the

[23] Mostly in the dermis layer, e.g. 2–3 mm from surface of skin, aimed to have Deqi sensation. If the needle is in the hypodermis, there is no aim to induce the Deqi sensation.

foot. If a person has pain on their left hand, we can perform acupuncture on the right hand (on a similar pain spot) or on the right foot too. Here the left hand and right hand have a mirror relationship, as do the left hand and the right foot.

Five-shu theory (五腧穴理论).

In this style of acupuncture, the acupuncture points are selected and based on the function of five Shu points on the 12 meridians. For example, for all the Jing points,[24] they can be used to treat stroke and other brain diseases (especially for acute diseases), or to treat bloating in the abdomen.

This style of acupuncture also has a special Five-element system (五行理论). Many of the acupuncture points are directly named as either Wood, Fire, Soil, Metal or Water, or in combination, such as Wood point, Fire-lian point, Wood-Fire point, and Soil-Metal point. The five elements can be distributed on a line, such as the Minghuang, Tianhuang and Qihuang (inside of thigh), all of which belong to Liver (the Wood line), or the Tianhuang, Renhuang, Dihuang (in the inside of calf), which belong to Kidney (Water line). The five elements can also be distributed as a zone in the body, such as the Fire zone, Metal zone, Soil zone and Wood zone on the upper back, or the Fire zone and Water zone, on the feet. From the name, acupuncturist should be able to realize what kind of disease these acupuncture points can work for.

The Five-element usage in this style of acupuncture is one of the greatest contributions to the Chinese acupuncture system.

Organ-bypass theory.

Additionally, acupuncture point selection follows Organ-organ bypass theory (脏腑别通). This theory states that life energy can also flow to other specific meridians that do not belong to the Surface-inside relationship (for example, the Gall bladder meridian and the Liver meridian have a Surface-inside relationship). In the Organ-organ bypass theory, for example, the Large intestine meridian is not connected (bypassed) to the Liver meridian.[25] This can explain how several acupuncture points on or close to the hand Yangming meridian (such as Dajian, Xiaojian, Waijian, Fujian points) can be used to treat diseases in testicle, hernia, urethritis and the perineum area. This is because the Liver meridian passes and goes around the perineum. It is said that the function of at least one third of the acupuncture points in this style can be explained with the Organ-organ bypass theory (http://www.360doc.com/content/11/0903/18/7644441_145527152.shtml).

Structure-corresponding structure theory (体体相应).

This theory states that we can stimulate a tendon to treat tendon-related diseases, stimulate bone membrane (bone) to treat bone-related diseases, stimulate muscle to treat muscle-related diseases, stimulate skin to treat skin disorders.

Structure-corresponding phase theory (体象相应).

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[24] Each of the 12 traditional meridian systems has one its own Jing point, which is believed to be the beginning of life energy in each meridian.

[25] In the bypass theory, Yangming meridian connects with Jueyin meridian; Taiyang meridian connects with Taiyin meridian; and Shaoyang meridian connects with Shaoyin meridian.

This theory states that the stimulation of a tendon can treat Wind disease, the stimulation of muscle can treat Wetness, stimulation of bone (membrane) can treat Cold disease, etc.

Depth-effect theory (深度效应).

It is believed that on a given acupuncture point, shallow needles work for shallow diseases (such as disease on the skin, or on the upper part of the body) and nearby diseases. Deeper needles work for distant diseases or inner organ diseases. For example to perform acupuncture on the Zusanli point, shallow needles treat diseases on leg, middle-deep needles work for diseases in the stomach-intestine, and deep needles work for diseases in the heart and lung. For facial paralysis, the needle has to be 2 cun deep and with needle tip pointing towards the head.

In this style, we do not emphasize the nourishing-depleting technique of the needle. Instead, we may apply two or more needles close together (in special sequence), for example in what they call the reverse-horse needle technique to enhance the healing effect. We can also apply the moving technique to enhance the healing effect. The style also uses penetrating needle (e.g. one needle penetrates two or more acupuncture points), such as from Linggu point to Dabai point.

This is a very complex and comprehensive acupuncture style.

1.2.2 Ke Shang-Zhi Distance-Meridian Acupressure Therapy (柯尚志远络疗法)

Distance-meridian acupressure therapy was developed by Dr. Ke Shang-Zhi (http://blog.xuite.net/peterjo/diary/69247612-%E5%9F%BA%E7%9D%A3%E4%B8%AD%E8%A5%BF%E9%86%AB%E5%AD%B8-%E9%81%A0%E7%B5%A1%E9%86%AB%E5%AD%B8). It only partially follows the traditional Chinese meridian theory. For this technique, we need to find the diseased (sick) meridian first, and then decide which will be the treating meridians. There are three meridians used usually to balance the sick meridian: the same name meridian,[26] the bypass meridian, and the surface-inner relationship meridian.

For example, if the sick meridian is the Hand Yangming meridian, the treatment meridian by the same name would be the Foot Yangming meridian. For the bypass meridian, the treatment meridian would be the Foot Yueyin meridian. And for the surface-inner relationship meridian, the treatment meridian would be the Hand Taiyin meridian on the other arm.

After identifying the sick meridian, the acupuncturist presses the Luo point on the meridian with a finger or with something hard, pressing tightly against the bone under it. At the same time, the acupuncturist presses the treating point on each of the

[26]There are differences in how to decide the same-name meridian in traditional Chinese meridian theory and this distance-meridian therapy. In the former, the three Hands Yang meridians match the three Foot Yang meridians and the three Hand Yin meridians match the three Foot Yin meridians. In this distance-meridian therapy, the three Hand Yang meridians also match the three Foot Yang meridian, but the Hand Taiyin (lung) matches Foot Jueyin (liver), Hand Jueyin (Heart shell) matches Foot Shaoyin (Kidney), and Hand Shaoyin (Heart) matches Foot Taiyin (Spleen) meridian.

treating meridians with either nourishing technique (press and moving along the flow direction of the life energy in the meridian) or depleting technique (press the treating point towards the opposite direction of the life energy flow in that meridian, with the speed of the patient's heart beats).[27] Therefore, this is a two-point acupressure technique.[28]

The Luo point is claimed to open the connection of energy flow between the sick meridian and the three treating meridians (traditionally it only connects with the other meridian that has a surface-inner relationship to the sick meridian). There are 14 Luo points in this style, not the traditional 15 Luo points. Among the 14 Luo points, only 4 Luo points are in the same position as in the traditional acupuncture meridian system (http://blog.xuite.net/hannah716/twblog/158411212-%E9%81%A0%E7%B5%A1%E7%99%82%E6%B3%95%E7%B5%A1%E7%A9%B4%E5%92%8C%E5%82%B3%E7%B5%B1%E4%B8%AD%E9%86%AB%E7%B5%A1%E7%A9%B4%E6%87%89%E7%94%A8%E7%9A%84%E5%B7%AE%E5%88%A5). The Luo point on the sick meridian needs to press hard against the bone without movement.

Treatment points on the other meridians can be found and decided according to parallel-mimic theory of the Holographic theory. This theory means that information on a whole arm is equal to a whole leg, or to that in the trunk of the body (Fig. 11). The arm, the leg, or the body trunk is separated into zones a, b, c, and 1–6. The wrist and the ankle are the separating line, marked as a. The hands and foot are b and c. Over the wrist and ankle are separated into 1–6. According to the pain spot on the sick meridian, it is necessary to find the treatment spot on the treatment meridians in the corresponding zone.

If the patient fears the pain pressing, the Luo point and the treatment points can be stimulated by finger (or by acupuncture needle).

Though it has been claimed that this style of acupuncture can eliminate the pain of various disorders (http://wwwu.tsgh.ndmctsgh.edu.tw/ane/pain/enrac.html), it has also been pointed out by others (http://windfix.pixnet.net/blog/post/316721364-%E6%9F%AF%E6%B0%8F%E9%81%A0%E7%B5%A1%E7%99%82%E6%B3%95%E7%B0%A1%E4%BB%8B) that it works mostly for functional disorders, such as various traumas, chronic pain (in the shoulder, neck, back, limbs), dizziness, migraines, and lingering pain after Herpes Zoster. It does not work properly for structural disorders, such as carpel channel syndrome, trigger finger, frozen shoulder, or sciatica pain due to piriformis syndrome. If the pain is due to a structural disorder, the passive movement of the body part would be restricted and limited, or the pain comes and goes after the distance-meridian therapy treatment. In this case, it is recommended to use small knife-needle therapy for treatment.[29] The clinical

[27] If the treatment meridian is the Yin meridian, press the meridian that is opposite to the sick meridian (except for the Liver meridian). If it is the Yang meridian, press the meridian that is on the same side of the sick meridian (except for the Heart meridian).

[28] Two-point treatment technique can also be found in the Moving acupuncture technique in Dong's extra-ordinary acupuncture system.

[29] But proponents of distance-acupressure therapy claims that the advantage of using it is to not touch the painful spot causing local damage.

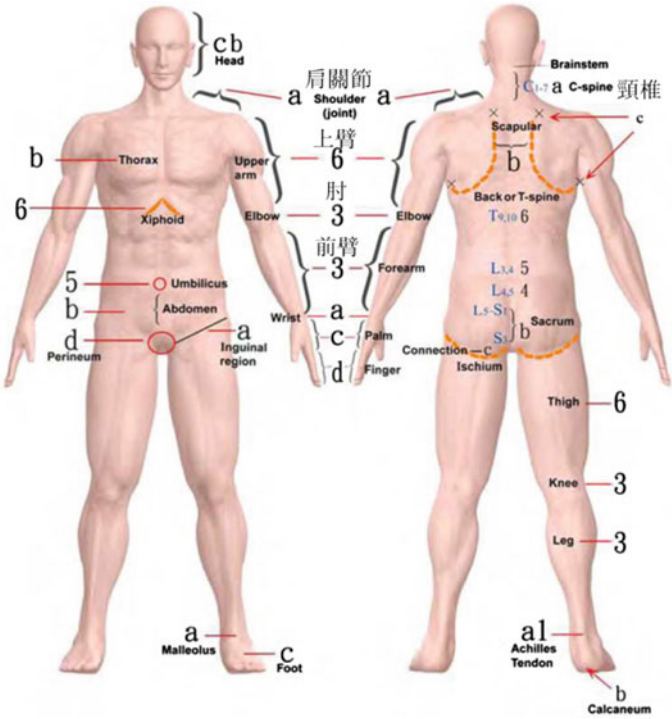

Fig. 11 Mirror distribution and location of pain spots and treating zone in Ke Shang-Zhi Distance-meridian acupressure therapy (http://blog.xuite.net/peterjo/diary/69247612-%E5%9F%BA%E7%9D%A3%E4%B8%AD%E8%A5%BF%E9%86%AB%E5%AD%B8-%E9%81%A0%E7%B5%A1%E9%86%AB%E5%AD%B8)

efficiency of the Distance-meridian therapy has been tested, but with acupuncture on traditional Luo pints and needle stimulation, not with acupressure or with hard materials (Guo et al. 2016).

It has also been summarized that this style of acupuncture may not work properly in the following conditions:

(1) If a disease is in central nerve system, this acupressure technique does not work as well if the pain is caused by local damage to muscle or tendon. Knowledge of Western medicine is needed to identify if the pain is due to local or to central nerve system.

(2) If the Five-element nature of the sick meridian is the same as the nature of the seasons, the healing effect might be low. For example, if the sick meridian is the Gall bladder meridian, then the Wood meridian, the treatment meridian for the sick Gall bladder meridian (as well as the Liver meridian) would be hard in spring. Similarly, the Fire nature meridian (the Heart meridian and Small intestine meridian) would be hard to improve in summer (Summer belongs to Fire). The Water nature meridian (Kidney meridian and Urine bladder meridian)

would be hard to improve in winter (winter belongs to Water). The Soil nature meridian (the Spleen meridian and Stomach meridian) would be hard to improve in June, July and August (these three months belong to Soil element).

(3) Acute pain would re-occur more readily than chronic pain. Pain in younger patients is easier to re-occur than in elderly patients.

(4) If the local inflammation is severe, then the inflammation needs to be under control before using this acupressure technique for the treatment.

The major weakness for this style of acupuncture is the pain that is created by acupuncturist when the acupuncturist presses the Luo point and the treatment points, though some people claimed that the technique does not touch the original pain spot of the body. The users of this style of acupuncture also claim that this technique is the combination of knowledge from both Chinese medicine and Western medicine. Difficulties arise if the acupuncturist does not have knowledge of Western medicine to find out, and to choose, the Luo points and the treatment points for the treatment.[30] As pointed out above, this technique does not work properly if the Five-element nature of the sick meridian and that of the season is the same (even if the developer of this style of acupuncture claimed that he had found new explanation and new usage of the Five-element theory). For example if the patient suffers from sick Liver meridian and the patient comes for treatment in Spring, the healing effect might not be good.

Overall, it seems that this style of acupuncture works more as a short-term pain killer. It may surprise the patient with its quick pain-reduction effect (for some kinds of pain), but may create new troubles in the future for the acupuncture as a whole. If so, patients may be hesitant to come back again, just because they could use a regular pain killer, which does not create more pain during treatment as this technique does.

There are some similarities between this acupressure technique and the Li Bai-Son Eight-word acupuncture style (李柏松八字疗法). In this acupressure style, the Luo points are pressed hard against the bone, and in the latter, the bone membrane is stimulated with needles. Both stimulate the bone membrane very strongly.

1.2.3 Han Wen-Zhi One-Needle Acupuncture Style (韩文治一针疗法)

This acupuncture style was developed by Dr. Han Wen-zhi (Taiwan) (Wu 2008a). This style is very different from traditional acupuncture style. It has its own meridian system, called Qi-Jing-Liu-Mai (e.g. extraordinary meridian and six meridian systems). The meridians are called Heart-Lung meridian, Liver-Gall-bladder meridian, Spleen-Stomach meridian, Large-Intestine-Small-Intestine meridian, and Kidney-Du-Ren meridian. The locations of these meridians and the spot or connections between two meridians are also very different from the traditional meridian system. Beside this difference, there are 14 special acupuncture points in use (though some points belong to the traditional acupuncture system too).

[30] Dr. Ke also explained how our body feels pain, with his rich knowledge in Pathophysiology in Western medicine. It is difficult for us to understand the usefulness of such knowledge in using this technique for the treatment.

Basically, each treatment session uses only one acupuncture point. Needles are inserted slowly. Acupuncture techniques of nourishing or depleting are needed. Deqi is needed. The needle is usually retained for 20–30 min, with manipulation from time to time.

There are another 12 special acupuncture points in use, which are named after the commonly used 12 animal signs for birth years in China: the mouse point, cow point, tiger point, rabbit point, snake point, horse point, sheep point, etc. For most of these points, the needles are inserted as deep as 2–3 body cun, but one needle is used only (Wu 2008b). For the treatment of some special diseases, more needles are used the same time, such as for the treatment of hypertension (http://www.hkjtcm.org/journals/2011%E5%B9%B4%E7%AC%AC%E5%85%AD%E5%8D%B7%E7%AC%AC%E4%B8%80%E6%9C%9F/18.%20%E5%8F%B0%E7%81%A3%E9%9F%93%E6%96%87%E6%B2%BB%E9%87%9D%E6%B3%95%E6%B2%BB%E7%99%82%E9%AB%98%E8%A1%80%E5%A3%93%E7%97%85%E7%9A%84%E7%B6%93%E9%A9%97%E5%BD%99%E7%B2%B9.pdf).

1.2.4 Zhang Xin-Shu Wrist-Ankle Acupuncture Style (腕踝针法)

Wrist-ankle acupuncture style was developed by Prof. Zhang Xin-Shu in year 1972 (Zhang 2003). In this style, needles are inserted in a spot on the front arm 2 finger lengths[31] from the wrist, or 3 finger lengths from the ankle. There are six spots on each front arm and also six spots on each shin (Fig. 12). The arm and leg are separated into six zones (Fig. 13). Each spot responds for the treatment of disease that are located in that zone. For example, if there is pain on the leg, which is located in zone A, the acupuncturist can stimulate the acupuncture spot that works for that zone. In this style, we prevented any feeling of the needle. If the patient feels pain, or tingling, or bloating, the healing effect would be lower than if the patient feels nothing.

For diseases that are located above the diaphragm, use points on wrist. If the disease is in the wrist or hand, the tips of the needles point towards the hand. Otherwise, point towards the shoulder direction.

If the disease is located below the diaphragm, use the points on the ankle. If the disease is on the ankle or foot, the tips of the needles point towards the feet. Otherwise they point towards the hip.

If the disease is in both upper and lower part of the body, choose the acupuncture points on both wrist and on ankle, such as for the treatment of paralysis. If it is hard to decide which side the disease is, such as with depression or poor sleep, use both sides.

All the treatment zones are vertically distributed on the body, either from hands to the chest, or from the feet to the body trunk (Fig. 13).

[31] Cun is a Chinese medicine way of measure length. One cun equals one inch.

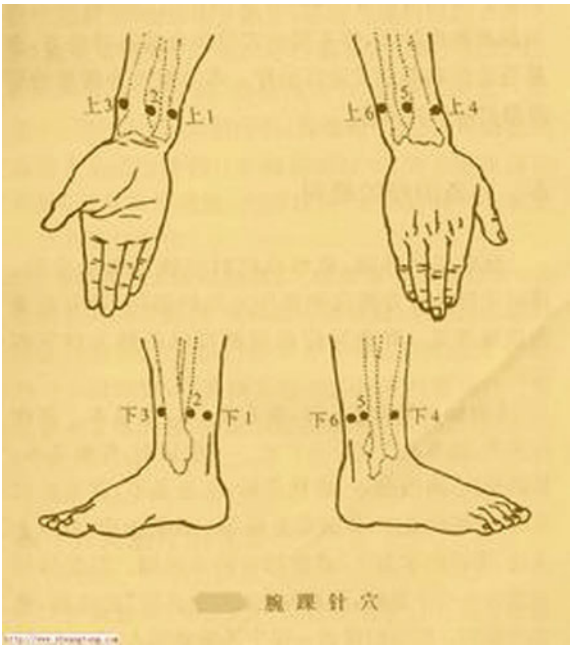

Fig. 12 Acupuncture points used in the Wrist-ankle acupuncture style (http://www.baike.com/wiki/%E8%85%95%E8%B8%9D%E9%92%88%E6%B3%95)

1.2.5 Western Style of Medicine Acupuncture

Finally we have to mention a modified style of acupuncture that is used mostly in Western countries.

White (2009) introduced the following: Western medical acupuncture is a therapeutic modality involving the insertion of fine needles. It is an adaptation of Chinese acupuncture using current knowledge of anatomy, physiology and pathology, and the principles of evidence based medicine. While Western medical acupuncture has evolved from Chinese acupuncture, its practitioners no longer adhere to concepts such as *Yin*/*Yang* and circulation of *qi*, and regard acupuncture as part of conventional medicine rather than a complete "alternative medical system". It acts mainly by stimulating the nervous system, and its known modes of action include local antidromic axon reflexes, segmental and extrasegmental neuromodulation, and other central nervous system effects. Western medical acupuncture is principally used by conventional healthcare practitioners, most commonly in primary care. It is mainly used to treat musculoskeletal pain, including myofascial trigger point pain. It is also effective for postoperative pain and nausea. Practitioners of Western medical acupuncture tend to pay less attention than classical acupuncturists to choosing one point over another, though they generally choose classical points as the best places to stimulate the nervous system. The design and interpretation of clinical studies is constrained by lack of knowledge of the appropriate dosage of acupuncture, and the likelihood that any form of needling used as a usual control procedure in "placebo

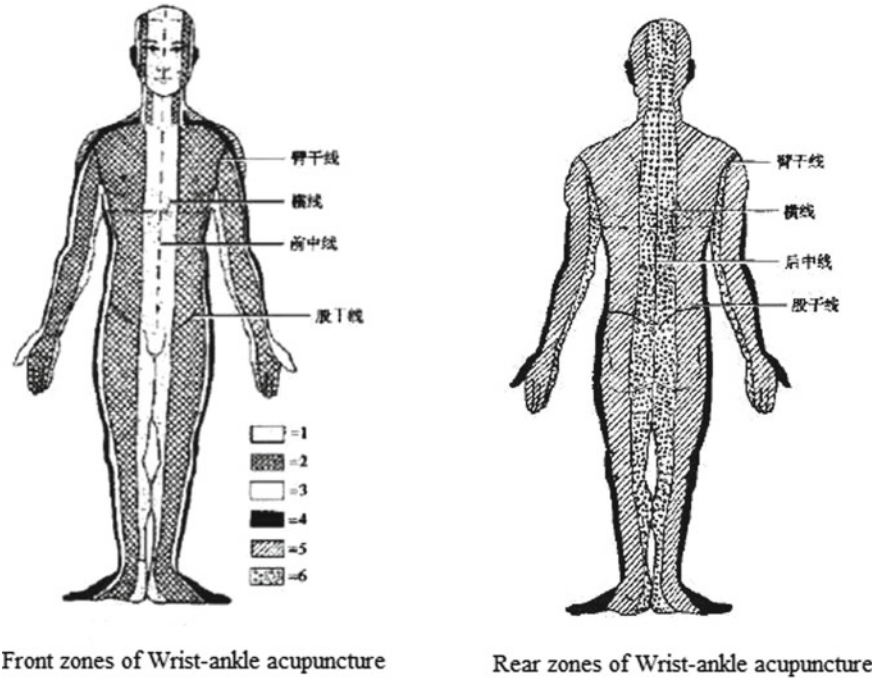

Fig. 13 Front zones and rear zones of Wrist-ankle acupuncture style (http://mp.weixin.qq.com/s?__biz=MzA3MTMxNjMwOA==&mid=2694210277&idx=8&sn=73001420a2cea562b5174e37448338d2&scene=0#wechat_redirect)

controlled" studies may be active. Western medical acupuncture justifies an unbiased evaluation of its role in a modern health service.

1.3 Local Acupuncture Style (局部针法)

In all of the following local acupuncture styles, the acupuncture points used are located on the local part of the body. These styles follow the Holographic theory. This means that one part of the body contains information for the whole body. Stimulating one spot can influence the function of a correlated part of the whole body.

1.3.1 Auricular Acupuncture Style (耳针)

Auricular acupuncture style (http://www.wfas.org.cn/tcmtools/therapy/820.html) stimulates points on the ear. The idea is that the ear contains information about the whole body. Each small spot on the ear is related to the function of a specific

part of the whole body (e.g. the Holographic theory) (Fig. 14). During treatment, the acupuncturist stimulates the exact co-related part of the ear to solve the disorder of the body. For example, for cervical spondylosis, the acupuncturist stimulates the spot for neck, elbow, and wrist points on the ear. But for inner organ diseases, a Western medicine concept is needed to decide the acupuncture points that need to be stimulated. For example for the coronary heart disease, we need to choose the heart point, but also have to stimulate the kidney point, sympathia point, endocrine point, adrenal gland point, and subcortical aphasia point on the ear.

The acupuncturist may also need TCM diagnosis to select proper points to stimulate. For example, for the treatment of conjunctivitis, the acupuncturist needs to stimulate not only the eye point, but also the liver point on the ear, because in TCM, the eye is associated with the Liver system in the body.

The points on the ear can be stimulated by various means, such as acupuncture needle, magnetic beards, imbedded needle, warm needle, electro-acupuncture, point injection, ion penetration, moxibustion, bleeding, etc.

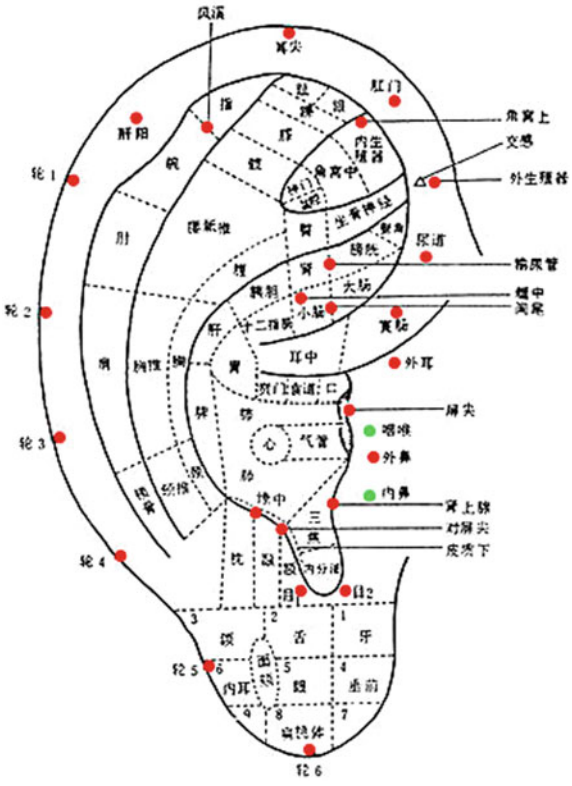

Fig. 14 Acupuncture points on ear (http://lwk.yes1798.com/lwk/search/view.asp?RecordNo=50943&NAME=%C2%A6%C3%95%C2%A5%C3%9E%C2%B9%C3%8F)

1.3.2 Scalp Acupuncture (头皮针)

There are as many as ten kinds of scalp acupuncture styles (Zhao et al. 2016). In some, acupuncture points are selected based on the projection of brain functional zones on the scalp, some using the traditional acupuncture meridian system, or a combination. The scalp acupuncture introduced in most acupuncture textbooks is modified from the Jiao's scalp acupuncture style (see below).

Jiao Sun-Fa Scalp Acupuncture Style (焦顺发头皮针)

This style was developed by Dr. Jiao Sun-Fa (http://baike.baidu.com/view/832430.htm). He believes that the functional regions of the brain are reflected and projected onto the scalp (Fig. 15). Stimulating the corresponding area of the scalp can treat diseases that are associated with the functional region of the brain. The style is mostly used to treat brain-associated diseases. For example, to treat motor disorders, the acupuncturist can stimulate the motor region on the scalp. For the treatment of tremor paralysis and chorea, the acupuncturist stimulates the dance-tremor region. The functional regions of the brain are separated into the motor region, sensation region, dance-tremor region, dizziness-hearing region, feet motor-sensation region, vision region, and balance region.

Fang Yun-Peng Scalp Acupuncture Style (方云鹏头皮针)

This acupuncture style was founded by Dr. Fang Yun-Peng in the 1970s. It separates the surface of the scalp into four major regions (called Face-down diagram, Face-down organs, Reverse-diagram, Reverse organs) and eleven functional stimulation zones (for thinking, memory, speaking, motion, signal, hearing, vision, balance, breath and circulation) (Fig. 16). It works much better for diseases in the nerve system (such as migraine, paralysis, and stroke) and also for rheumatic arthritis.

During the acupuncture treatment, the needle is inserted very quickly and vertically into the scalp and touches the bone membrane. This style of acupuncture emphasizes pulse diagnosis to decide which scalp regions to stimulate.

There is another scalp acupuncture style called Zhu Long-Yu scalp acupuncture. The distribution of the body on the scalp is similar to the Fang style, but it is opposite: the head region is on the rear of the scalp but the tail part is on the front. Both styles work well. This is not hard to understand, because in body acupuncture styles, the acupuncture points on the feet can be used to treat headache, suggesting that the head and the foot are correlated.

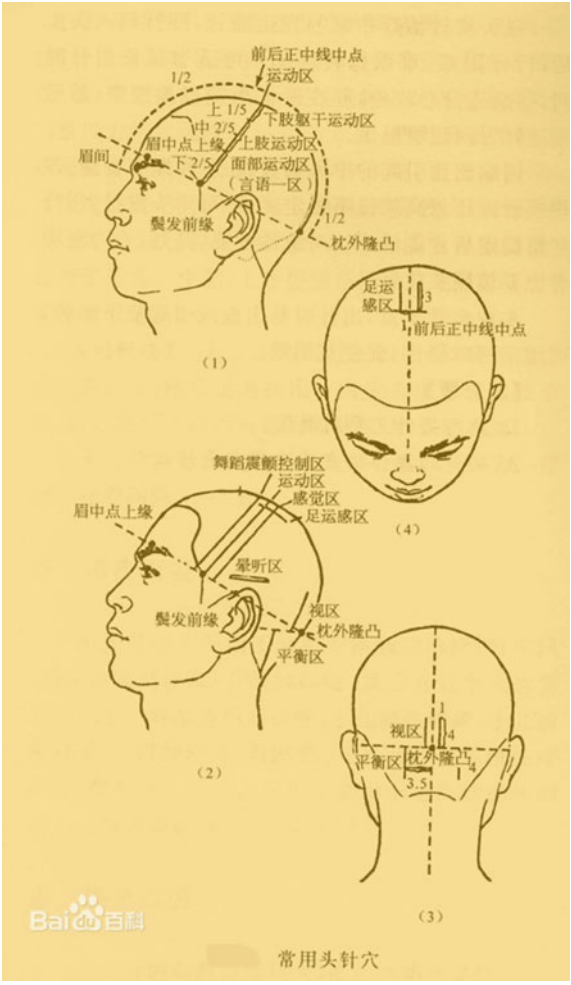

Fig. 15 Acupuncture zones in scalp (Jiao's scalp acupuncture) (http://big5.huaxia.com/hxjk/zhyx/zjtn/2009/06/1453618.html)

Zhu Ming-Qing Scalp Acupuncture Style (朱明清头皮针)

This style was developed by Dr. Zhu Ming-Qing. He found that there are nine treatment belts on the scalp (Fig. 17): Forehead-top belt, beside forehead I belt, beside forehead II belt, Top-temporal belt, Top-Occipital belt, Top-knob front belt, Top-knob rear belt, Front-temporal belt, Behind-temporal belt. Each belt is related to one part of the body. The acupuncture points chosen depend on the location of the sick part of the body. For example, for the treatment of sciatic pain, the acupuncturist stimulates the Top-knob front belt, because this belt is associated to the back part of the hip and the leg.

The following examples show the functions of each region on the scalp for acupuncture treatment:

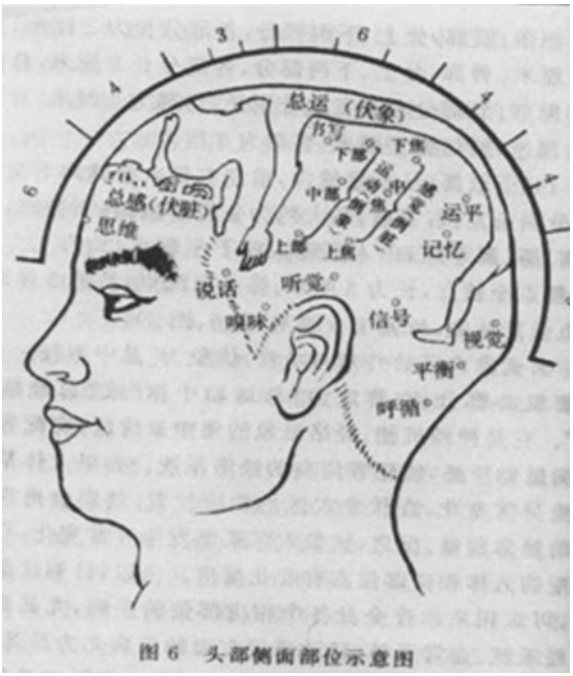

Fig. 16 Acupuncture points on scalp (Fang's scalp acupuncture) (http://blog.xuite.net/strokeonline/info/154742430-%E9%87%9D%E7%81%B8%E6%B2%BB%E7%99%82%E4%B8%AD%E9%A2%A8+-+%E9%A0%AD%E9%87%9D%E7%AF%87)

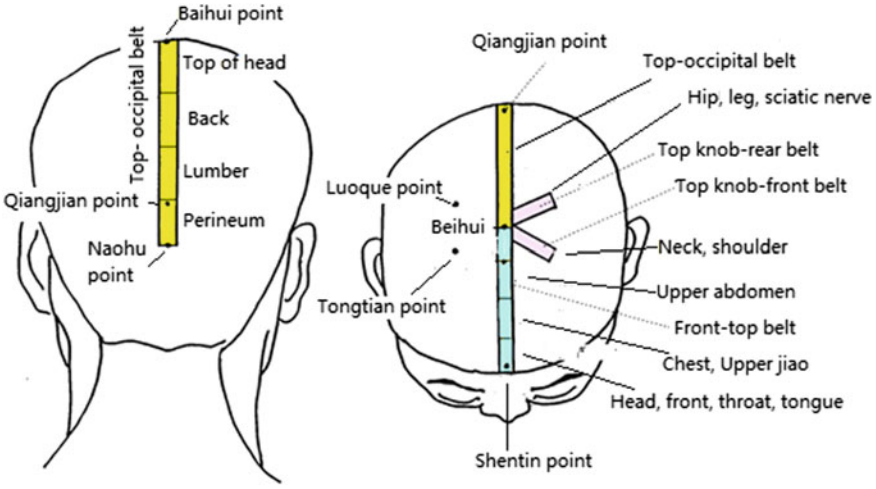

Fig. 17 Acupuncture points on Scalp (Zhu's scalp acupuncture) (http://www.guanliao.net/terminfo.asp?id=16)

The Forehead-top belt can be further separated into the first ¼, the second ¼, the third ¼ and the back ¼ part. The first ¼ part corresponds to diseases in the face, throat, and tongue. The second ¼ part corresponds to diseases in the chest (respiratory and heart). The third ¼ part corresponds to diseases in the upper abdomen (liver, gall bladder, stomach, spleen). The last ¼ part corresponds to diseases in the lower abdomen (kidney, urine bladder, prostate, uterus, ovary, anus).

The Beside forehead I belt corresponds to acute diseases in the middle Jiao (stomach, spleen, liver, gall bladder, pancreas).

The Beside forehead II belt corresponds to acute diseases in the lower Jiao (kidney, urine bladder, and reproductive system).

The Top-temporal belt is further separated into the upper 1/3 part, middle 1/3 part and lower 1/3 part. The upper 1/3 part corresponds to the diseases in lower limbs. The middle 1/3 part corresponds to the diseases in upper limb. The lower 1/3 part corresponds to the diseases in the face.

The Top-occipital belt, from the head top to the occipital, is for the diseases in the head, neck, back, lower back, and perineal part.

This is also a straight-forward scalp style that chooses acupuncture points on the scalp that correspond to the anatomic parts of the body. For example, for the treatment of lower back pain, the acupuncturist can stimulate the lower 1/3 part of the Top-occipital belt (back of head). During acupuncture, pulling-inserting technique is used.[32]

Liu Bing-Quan Scalp Acupuncture Style (刘炳权八卦头针)

This is a style used by Dr. Liu Bing-Quan. Choose several acupuncture points on the scalp, then insert needles around the spot using the Eight-diagram (all the diagrams around) (Fig. 18). The distance from the edge needles to the center of the Eight-diagram is different; there is both a small and bigger Eight-diagram in the scalp. This is similar to the Around Acupuncture technique. For the treatment, we may need only one Eight-diagram acupuncture (big or small Eight-diagram), or use two or three Eight-diagram circles on the scalp. Apparently it is not a typical Eight-diagram as we use it in other part of the body. For example, when the Eight-diagram is used on the abdomen, the spots on the diagram have to take into consideration their related meaning to the disease we are treating.

Tang Song-Yan Scalp Acupuncture Style (汤颂延头针)

This scalp acupuncture was developed by Dr. Tang Song-Yan (Ye and Tang 2010). He found that the projection of body parts on the scalp is as in Fig. 19. Stimulation on that part on the scalp can treat the disease on the corresponding part of the body.

[32]Most scalp acupuncture styles use twist technique, not the pulling-inserting technique.

Fig. 18 Head Eight-diagram acupuncture (http://www.uuchatroom.com/zhenjiu/3363223.html)

Fig. 19 Acupuncture point distribution in Tang's scalp acupuncture style

Lin Xue-Jian Scalp Acupuncture Style (林学俭头针刺激新区)

This scalp acupuncture style was developed by Dr. Lin Xue-Jian (http://wenku.todgo.com/nonglinmuyu/59949791ede54.html). It works on several regions on the scalp (Fig. 20): Temporal-three-needle region; Fronthead-five-needle region; Front-motor region; Attached-motor region; Depression region; Small-brain region (two needles on left side and tow on right side); and Small-brain-seven-needle region (on rear of head).

Yu Chang-De Scalp Acupuncture Style (俞昌德头针)

This scalp acupuncture style was developed by Dr. Yu Chang-De (Yu et al. 2002). The acupuncture needles are inserted mostly along the skull gap.

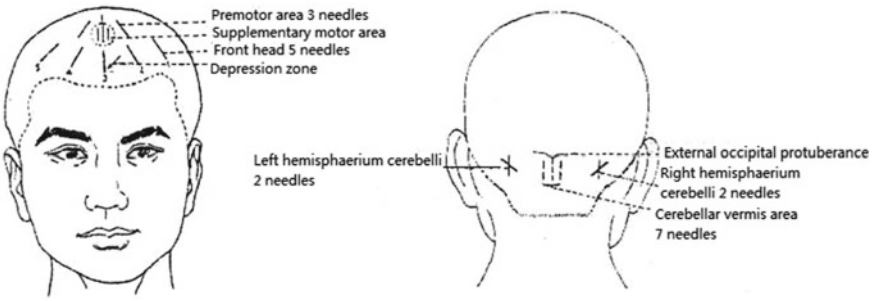

Fig. 20 Acupuncture point distribution in Lin's scalp acupuncture style (http://www.wfas.org.cn/tcmtools/therapy/820.html)

Jin Rui Scalp Acupuncture Style (靳瑞头针)

This scalp acupuncture style was developed by Dr. Jin Rui (靳瑞 1932–2010) (http://journal.9med.net/html/qikan/lcyx/zhxdlcyxzz/2005131/zyzy/20080901061327145_66342.html). Similar to his three-needle group of acupuncture on other parts of body, he also uses three needles as a group on the scalp for treatment. The acupuncture points are the traditional acupuncture points for the scalp. For example, for the treatment of poor intelligence, the needles used are the following: two needles on the Benshen acupuncture points (one on left and another on the right side). This three-needle group is called intelligence three-needle. For the treatment of a motor disorder, and poor balance, the three needles used are the Naohu and the Naoshi (one on the left and another on the right). It is called Brain-three-needle acupuncture.

Toshikatsu Scalp Acupuncture Style (山元敏胜新头针)

This scalp acupuncture style was developed by Japanese acupuncturist Toshikatsu Yamamoto (http://lib.cintcm.ac.cn:8089/opac/book/314985). He uses acupuncture on several lines in the front of the head (Fig. 21). Most of the acupuncture points are on the edge of the hair. There are points A, B, C, D, and E.

Point A: for the treatment of spondylosis, stiff neck, rear headache.
Point B: for the treatment of shoulder pain.
Point C: for shoulder and upper limb.
Point D: for lower back and lower limb.
Point E: for problems in the chest.

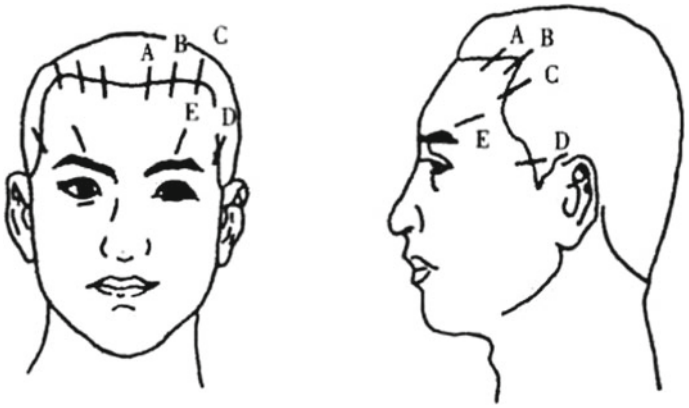

Fig. 21 Acupuncture point distribution in Toshikatsu's scalp acupuncture style (http://big5.huaxia.com/hxjk/zhyx/zjtn/2009/06/1453618.html)

1.3.3 Face Acupuncture Style (面针)

There two types of facial acupuncture styles, traditional facial acupuncture and new facial acupuncture style. The major difference between them is the distribution of acupuncture points on the face. For traditional style, the acupuncture points are distributed across whole face, while in the new style, the points are distributed mostly in the middle part of the face.

Traditional Facial Acupuncture (传统面针)

Facial acupuncture style separates the face into seven regions (Fig. 22) (http://baike.baidu.com/view/6935328.htm). They are front head region, nose region, eye region, mouth region, ear region, cheek region and cheekbone region.

There are two ways to select acupuncture points. Firstly, the points can be chosen as the corresponding acupuncture point on the face for the body part. For example, if there is stomach pain, the acupuncturist can stimulate the stomach point on the face. Secondly, we can choose based on TCM diagnosis. For example for the treatment of insomnia, if it is diagnosed as a Liver and Kidney Yin deficiency, the acupuncturist stimulates the liver point and the kidney point.

The facial points are mostly used to stop pain, however, they are also used for acupuncture anesthesia. For example, for total gastric resection, the acupuncturist stimulates the stomach, lung, heart and spleen points on the face. Facial acupuncture also works for the treatment of neurosis, hypertension, arthritis, and asthma.

Facial acupuncture must induce the Deqi sensation.

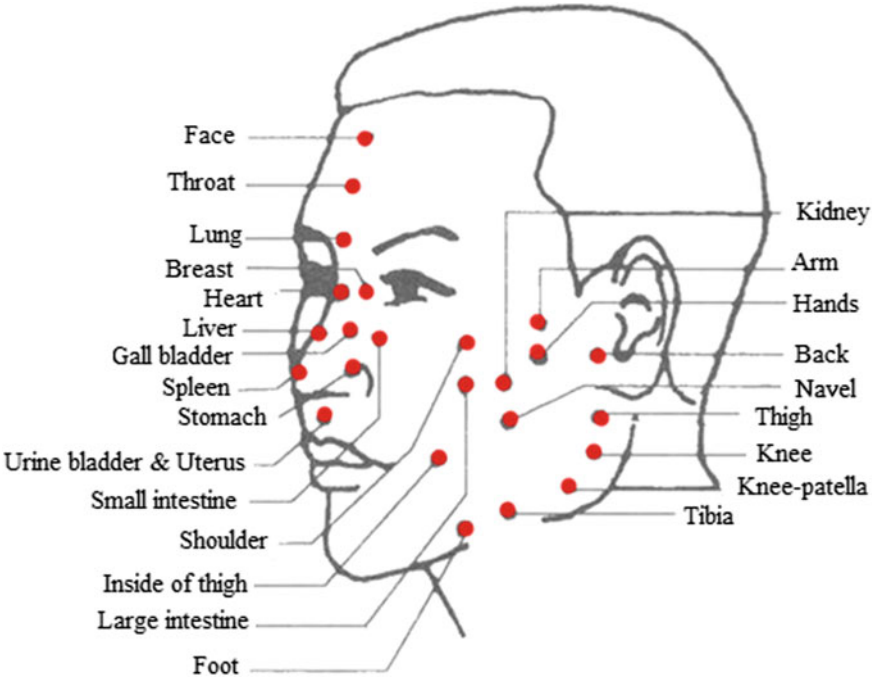

Fig. 22 Acupuncture point distribution in traditional facial acupuncture style (http://blog.xuite.net/strokeonline/info/154742430-%E9%87%9D%E7%81%B8%E6%B2%BB%E7%99%82%E4%B8%AD%E9%A2%A8+-+%E9%A0%AD%E9%87%9D%E7%AF%87)

New Facial Acupuncture (新面针)

New facial acupuncture was introduced by Dr. Huang Ying-Li (http://www.cdutcm.com/post/1532.html). The acupuncture points are selected with the corresponding relationship between the name of the points on the face and the name of the body part (Fig. 23). The acupuncture points can also be decided according to TCM diagnosis (as with traditional facial acupuncture).

Clinical experience shows that new facial acupuncture works both for painful syndromes and for post-stroke syndromes.

1.3.4 Peng Jin-Shan Eye Acupuncture Style (彭静山眼针疗法)

Eye acupuncture style was originally founded by Dr. Peng Jin-Shan, and later further developed by Dr. Tian Wei-Zhu (http://www.guanliao.net/terminfo.asp?id=16).

Each eye is separated into various regions (Figs. 24 and 25). There are several ways to choose acupuncture points around the eye. First, choose the point according to the meridian. If the pain is in the Lung meridian, stimulate the point on the Lung

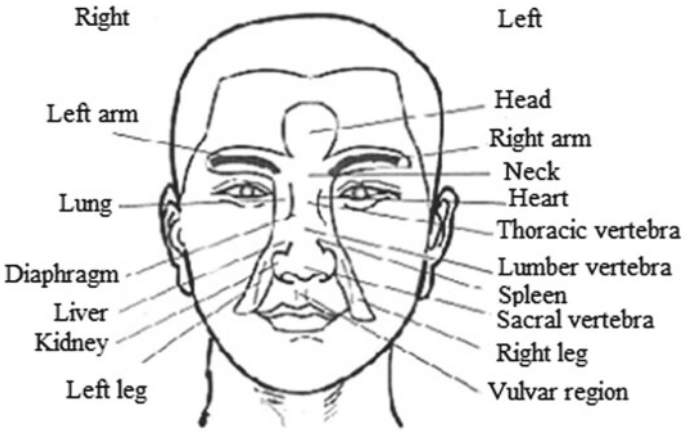

Fig. 23 Acupuncture point distribution in traditional facial acupuncture style (http://www.guanliao.net/terminfo.asp?id=16)

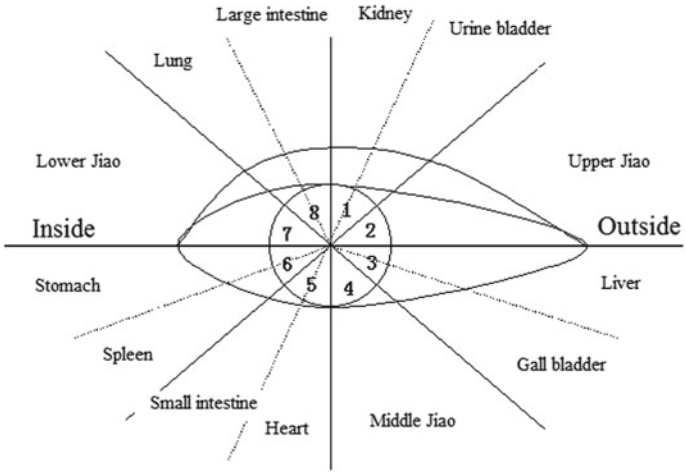

Fig. 24 Acupuncture zones in left eye (http://www.hnzjxh.com/onews.asp?id=26)

point on the eye. Second, choose it according to the local branch blood vessel, by seeing which region has more red-colored blood vesicles. Lastly, choose according to which Jiao cavity the disease is in. If the disease is in the upper Jiao cavity (inside the chest), stimulate the Upper Jiao point on the eye. If it is in the Middle Jiao, such as with stomach pain, stimulate the Middle Jiao on the eye. The points can also be chosen according to Eight-diagram in the eyes (Fig. 26).

The problem with eye acupuncture is that it is easy to cause bleeding. To prevent this, it is recommended to use thin and short needles and to use an ice-cold compress on the eye before acupuncture. Sensation of Deqi is required.

Fig. 25 Eye acupuncture (http://www.360doc.com/content/14/0227/17/9774604_356208274.shtml)

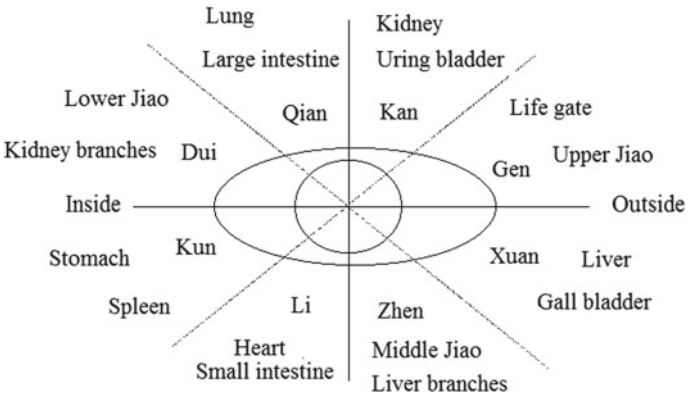

Fig. 26 Eight-diagram distribution in eye (left) (http://www.360doc.com/content/09/0817/21/203041_4999945.shtml)

It is summarized that eye acupuncture is good for both the treatment of pain syndromes and post-stroke syndromes too.

1.3.5 Nose Acupuncture Style (鼻针)

For this acupuncture style (http://www.baike.com/wiki/%E9%BC%BB%E9%92%88%E7%96%97%E6%B3%95), the acupuncture points are on the nose in three lines, with 23 stimulation points (Fig. 27). The principle in the selection of acupuncture points on the nose for the treatment is the same as for facial acupuncture.

The sensitive spot on the nose can be found by pressing with a probe on the nose, or by electric detecting tip. This works better to stimulate the sensitive spot.

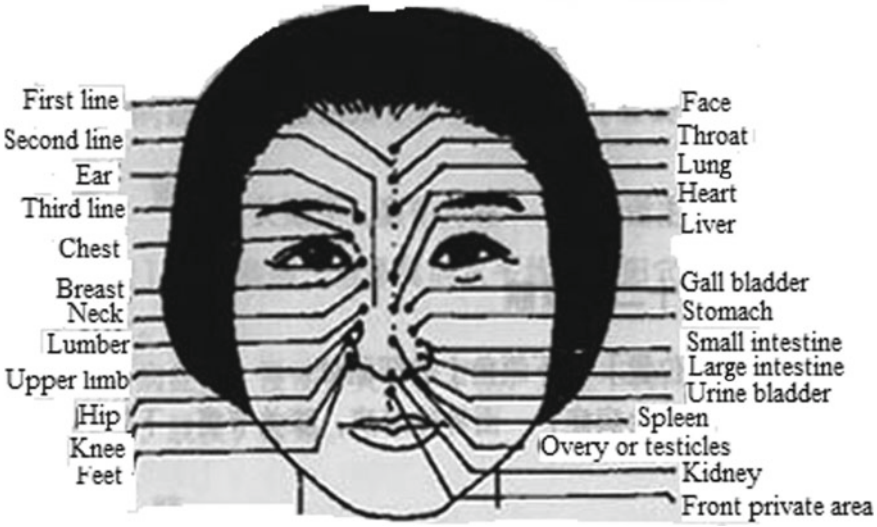

Fig. 27 Acupuncture point distribution on nose (http://book.th55.cn/a/200903/6456.html)

Nose acupuncture is used for acupuncture anesthesia. The basic points are the ear and lung points. Depending on the part of the surgery, other points are also used in combination.

1.3.6 Tongue Acupuncture Style (舌针)

There are acupuncture points on the top of the tongue and beneath it too (Fig. 28) (http://www.baike.com/wiki/%E8%88%8C%E9%92%88%E7%96%97%E6%B3%95). The TCM diagnosis, in consideration of the color, the shape, the wet or dryness, and the flexibility, of the tongue, is needed in selection of acupuncture points for the treatment.

For example, for the treatment of poor sleep, the heart point, the kidney point and the front head point are chosen from the tongue for the acupuncture. Because there are no points corresponding to the limbs, shoulder or back, to treat diseases in the muscle and joint pains in these areas of the body, acupuncture points outside of the tongue must also be used.

The acupuncture points on the tongue may be pierced with acupuncture needles, or pouched for bleeding therapy. With needle acupuncture, the Deqi sensation is needed, with the twist technique or the pulling-inserting technique.

Tongue acupuncture is mostly used for the treatment of tongue-related diseases, or body motor disorders, such as tongue numbness, tongue skew, tongue stiffness, ulcer in tongue, bad smell from mouth, post-stroke syndrome, and paralysis, though it is also used for the treatment of disorders in the circulation system, hypertension and spondylosis.

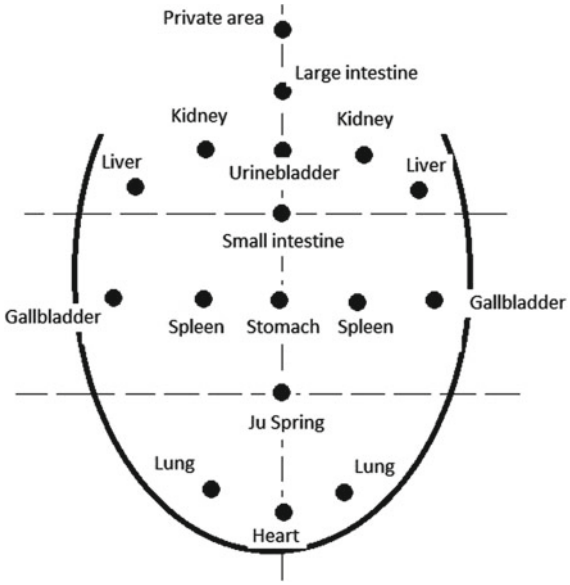

Fig. 28 Acupuncture point distribution on tongue (http://baike.baidu.com/view/6935328.htm)

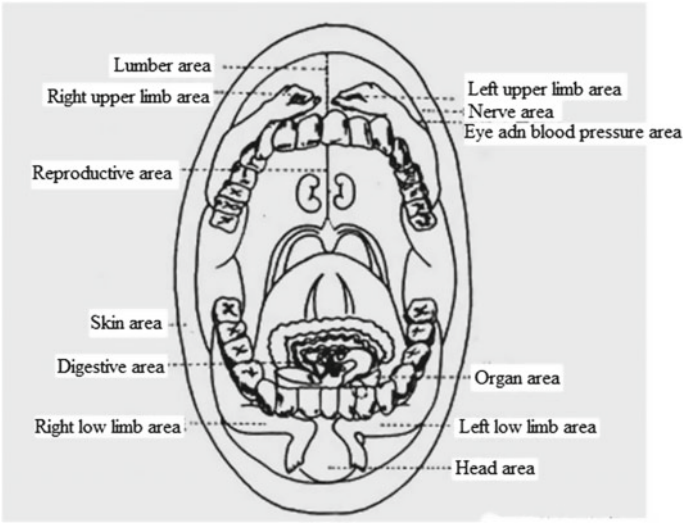

Fig. 29 Acupuncture point distribution on mouth (http://www.cdutcm.com/post/1532.html)

1.3.7 Mouth Acupuncture Style (口针)

Mouth acupuncture was developed by Dr. Liu Jin-Rong (http://blog.sina.com.cn/u/1559311971). The acupuncture points are distributed on the mucus of mouth, under the tongue (Fig. 29).

The acupuncture points on the mouth are selected for treatment in a similar way as for facial acupuncture and nose acupuncture. For example, for the treatment of sciatic pain, the sciatic point plus the hip point are selected for stimulation. The points are cross selected. For example, if the pain is in left side of the body, the right point in the mouth is selected.

This acupuncture requires the Deqi sensation. It works better for various pain syndromes, such as sciatic pain and acute strain on the lower back. It also works well for paralysis (http://www.documentsky.com/752668353/).

1.3.8 Ren-Zhong Acupuncture Style (人中针)

This acupuncture style aims to stimulate acupuncture points on the Ren-zhong groove (e.g. the nasolabial groove) (http://www.baike.com/wiki/%E4%BA%BA%E4%B8%AD%E9%92%88%E7%96%97%E6%B3%95). There are nine acupuncture points in the groove. From the mouth lip up to the nose are points 1–9, all of which can work for diseases in the face and head. Also, points 1–3 can work for diseases in the Upper Jiao part of the body. Points 4–6 are for the Middle Jiao of the body and points 7–9 are for the Lower Jiao part of the body.

If the needle tip tilts to the left side, treatment works better for the diseases on the left side of the body. Similarly, if the tip leans towards the right, it works more for the diseases on the right side of the body. If it leans towards the head, it works for the diseases along the Du meridian, such as in the face, head, neck, and back. If it leans towards the stomach, it works more for diseases along the Ren meridian, such as with chest pain or stomach pain.

Usually only one needle is used on the groove. If needed, treatment would be combined with body acupuncture, unless it is used for a stroke, for which more needles may be used in the groove.

1.3.9 Foot Acupuncture Style (足针)

Besides the acupuncture points that belong to traditional acupuncture style, there are different acupuncture styles in the foot (Fig. 30) (http://www.acucn.com/college/technique/200704/3032.html; http://www.wiki8.com/zuzhenliaofa_119798/).

The acupuncture points for this style are selected for treatment in a similar way as for palm acupuncture, nose acupuncture, etc. For example, for the treatment of a headache, the acupuncturist can stimulate the head point on the foot. For the treatment of stomach pain, the acupuncturist uses acupuncture on the stomach point on the foot.

The point chosen can also be selected according to TCM diagnosis. For example, for the treatment of dizziness, if it is diagnosed as Liver-kidney Yin deficiency, the

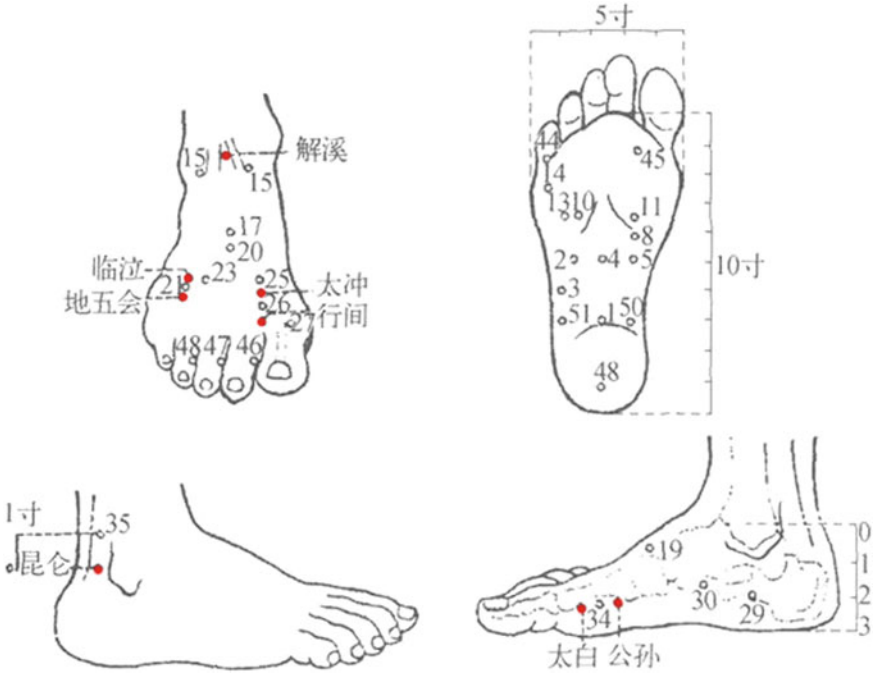

Fig. 30 Acupuncture point on Foot acupuncture style (round and the numbered dot). Red dots mean the acupuncture points belong to traditional acupuncture style

acupuncturist needs to use acupuncture on the head point, and the liver and kidney points as well. The Deqi sensation is required.

1.3.10 Fang Ben-Zheng Foot Region Acupuncture Style (足象针)

Foot region acupuncture and Hand region acupuncture (see below) were developed by Dr. Fang Ben-Zheng (http://www.360doc.com/content/17/0112/23/20699624_622105952.shtml). Similar to ear acupuncture, the acupuncture points in the feet can also be distributed roughly as a human being figure (Fig. 31).

1.3.11 Hand Acupuncture (手针针法)

There is also an acupuncture style for hands (Figs. 32 and 33) (http://www.wuji8.com/meta/429084912.html). Stimulation of the acupuncture points on the hands works for the treatment of various diseases.

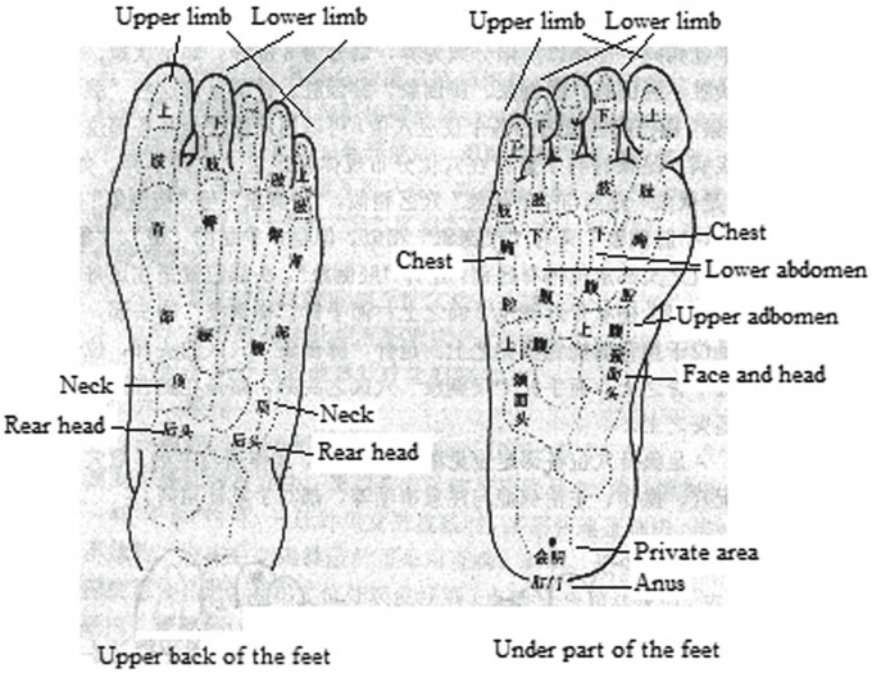

Fig. 31 Foot diagram picture (http://book.th55.cn/a/200902/4194.html)

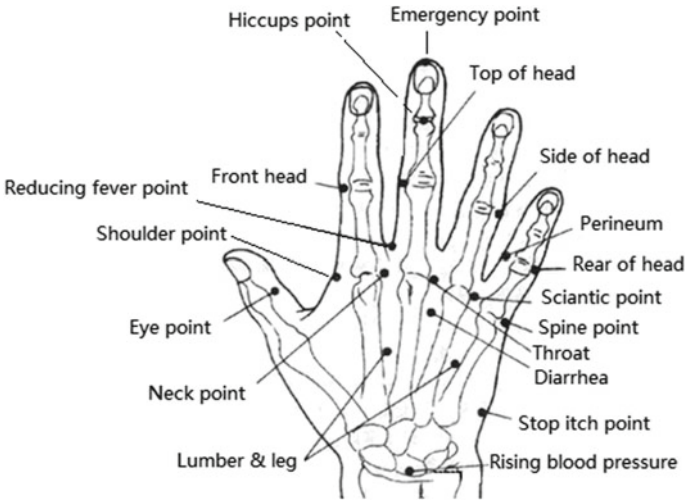

Fig. 32 Acupuncture points on back of hand (http://www.ddcd120.com/content/?777.html)

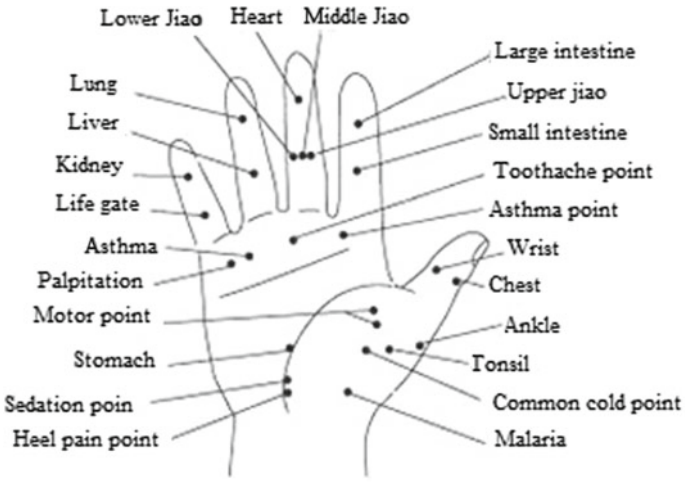

Fig. 33 Acupuncture points on palm side of hand (http://blog.sina.com.cn/u/1559311971)

1.3.12 Hand Region Acupuncture Style (手象针针法)

There is different distribution pattern for acupuncture points on hands. This is called Hand region acupuncture (Fig. 34) (http://blog.sina.com.cn/u/1559311971).

1.3.13 Yu Hao Yin-Yang Nine-Acupuncture Style (余浩阴阳九针)

This style was developed by Dr. Yu Hao (http://www.51yam.com/thread-256316-1-1.html; http://www.360doc.com/content/16/0628/12/5620517_571355557.shtml). The needles are mostly applied on fingers (For male, use left hand, for female, use right hand). The primary theory of this style is that a hand contains information for the whole body, as does a finger (Figs. 35, 36 and 37).

There are basically nine kinds of acupuncture techniques used with this style of acupuncture. Pulse diagnosis is used to facilitate diagnosis and the decision of which acupuncture technique to use.

For example, if a patient suffers from a stiff neck, the acupuncturist can use acupuncture on the spot on the thumb where it represents the neck (the second thumb finger joints). The needle can be in either direction, either from the thumb tip to the thumb root, or from the root to its tip (Fig. 38).

1.3.14 Ma Chun-Hui Small Six-He Acupuncture (马春晖小六合针法)

This acupuncture style was created by Dr. Ge Qin-Fu (葛钦甫) (http://baike.baidu.com/view/2509798.htm) and developed by Dr. Ma Chun-Hui. It also works

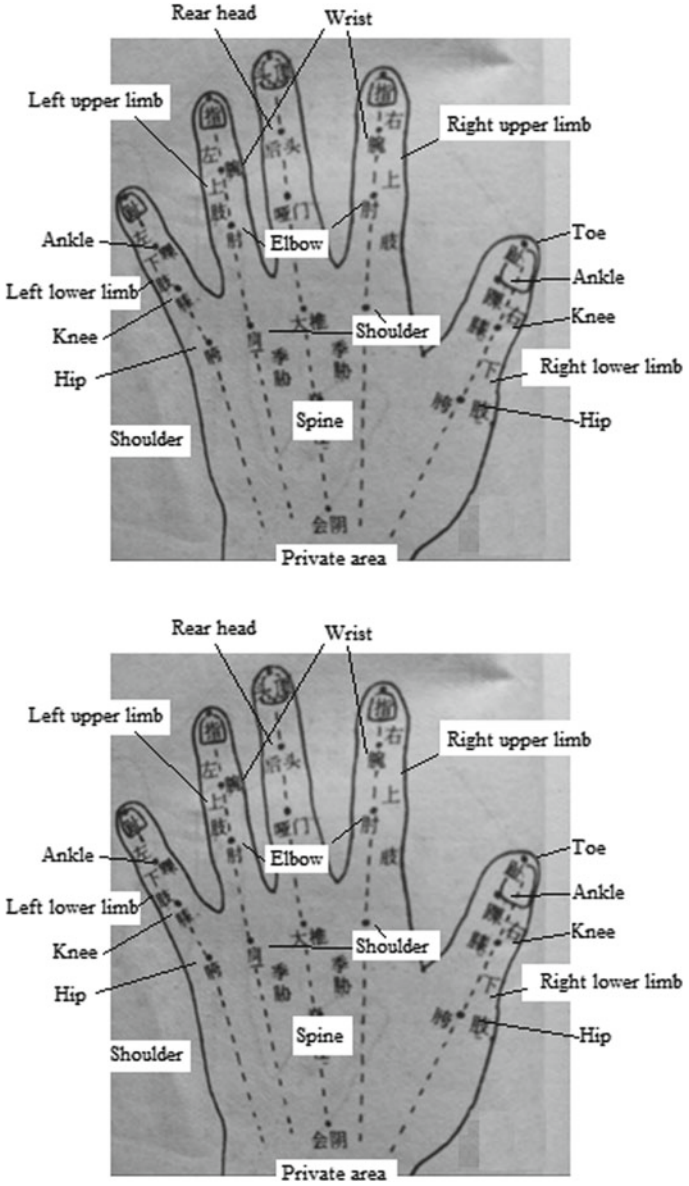

Fig. 34 Acupuncture points and zones in hand (both sides) (http://www.baike.com/wiki/%E8%88%8C%E9%92%88%E7%96%97%E6%B3%95)

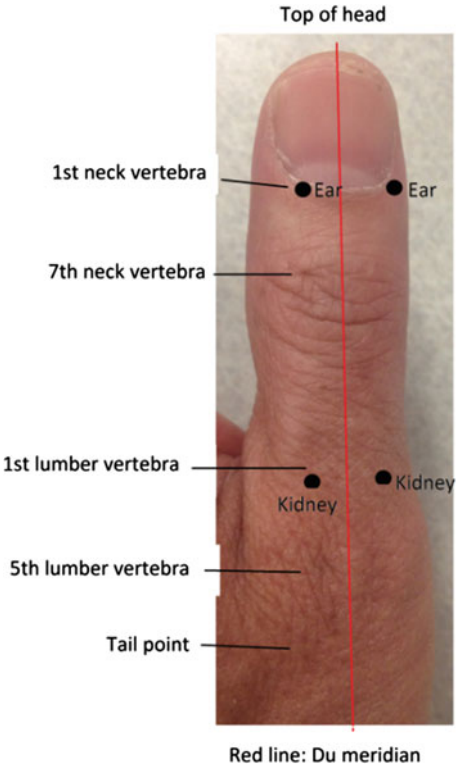

Fig. 35 Acupuncture zones on back of thumb in Yu's acupuncture style (modified) (http://www.documentsky.com/752668353/)

in palm (http://www.helpweixin.com/html/229496.html; http://www.360doc.com/content/14/1211/15/11285146_432153121.shtml). The acupuncture point is selected according to the Eight-diagram theory on the palm (Figs. 39 and 40). It usually uses only one needle and is called One-needle acupuncture technique.

It does not require the Deqi sensation. There is almost no pain.

1.3.15 Ge Qin-Fu Taiji Si-He Acupuncture Style (葛钦甫腹部太极六合针法)

This style was developed by Dr. Ge Qin-Fu (http://www.acucn.com/college/technique/200704/3032.html). This style of acupuncture uses the Eight-diagram theory in the abdomen. There are three levels of the Eight-diagram diagrams (Fig. 41). Two Eight-diagram diagrams are in the abdomen and the third expands to the whole body. In the abdomen, the diagrams are called Inner Eight-diagram diagram, and Middle Eight-diagram diagram, both are centered with the navel. The Inner Eight-diagram is a square with1.5 body cun from the center of the navel, and the Middle Eight-diagram is also a square of 4 body cun from the center of the navel.

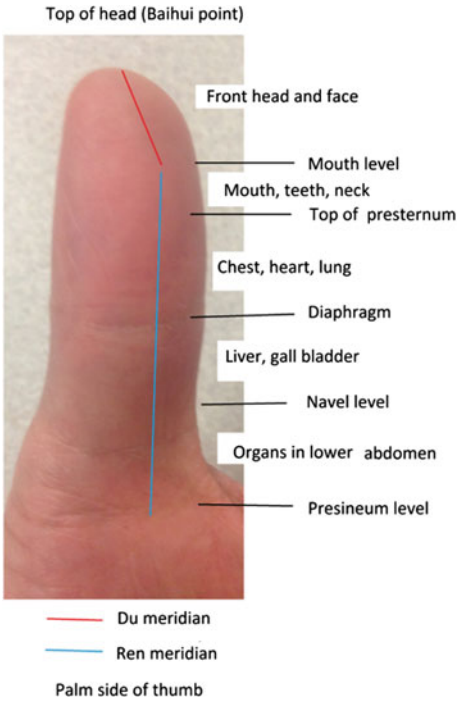

Fig. 36 Acupuncture zones on palm side of thumb in Yu's acupuncture style (modified) (http://www.documentsky.com/752668353/)

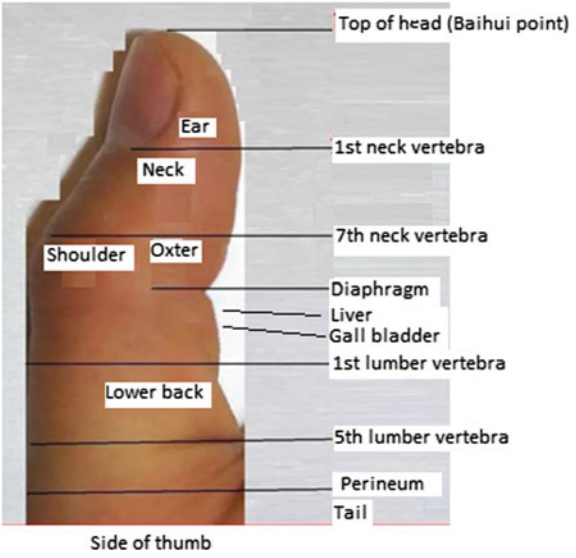

Fig. 37 Acupuncture zones on side of thumb in Yu's acupuncture style (modified) (http://www.documentsky.com/752668353/)

Fig. 38 Acupuncture zones on side of thumb in Yu's acupuncture style (modified) (http://www.documentsky.com/752668353/)

Fig. 39 Distribution pattern of palm Eight-diagram (http://e1689.blogspot.ca/2012/07/blog-post.html)

For treatment, the acupuncture points are chosen depending on the relationship and association of the diagram zone and the body parts (the head, neck, limbs), as well as the function of the body parts. For example, if a patient has pain on the right arm, the acupuncturist can insert a needle in the Zhen and Xun diagrams. This is because the two diagrams mimic the direction of the right upper part of the body (the right arm). This is also because the diagram is associated with body tendon and nerve. Both diagrams maintain the normal function of the tendon and nervous system. If a patient has a mouth ulcer, the acupuncturist can chose to do acupuncture on the Dui diagram, because the Dui diagram is responding to the normal function of mouth.

Fig. 40 Finger Eight-diagram pattern (http://www.hyt2000.com/resource01.php?pid=44&PHPSESSID=c7b5e5bc18baaef601efbe35d7fe5f4e)

Acupuncture points are selected based on several theories. For example, they can be selected simply with the space/geographic correlation of the diagram and the body part (as above) or as functional correlation of the diagram and the meridians. For example, if the sick meridian is detected as Hand Yin meridian, the acupuncturist can select the Gen and the Zhen diagrams, because these two diagrams are associated with the Yin meridian. The acupuncture points can also be selected as a time circle of Zi Yu Liu Zhu theory, the Five-element theory, etc.

Having chosen the diagram(s), insert needles into the diagram (the exact point is not so important, but should be within the diagram/zone), with needle tips pointing towards the edge of the body (away from the middle vertical line of the body). Deqi sensation is not emphasized. The patient does not feel very much pain. The needle can be left in place for about 30 min. The needle in the Inner Eight-diagram is needed. To enhance the healing effect, another needle is inserted into the Middle diagram but in the same diagram as in the Inner Diagram (It is called a directive needle. One needle is enough). Sometimes, acupuncturist even use more needles on the Outer Eight-diagram (accepting needle), or in the sick part or sick meridian (enhancing needle), to enhance the healing effect. This is called the four-step acupuncture program (四部通调).

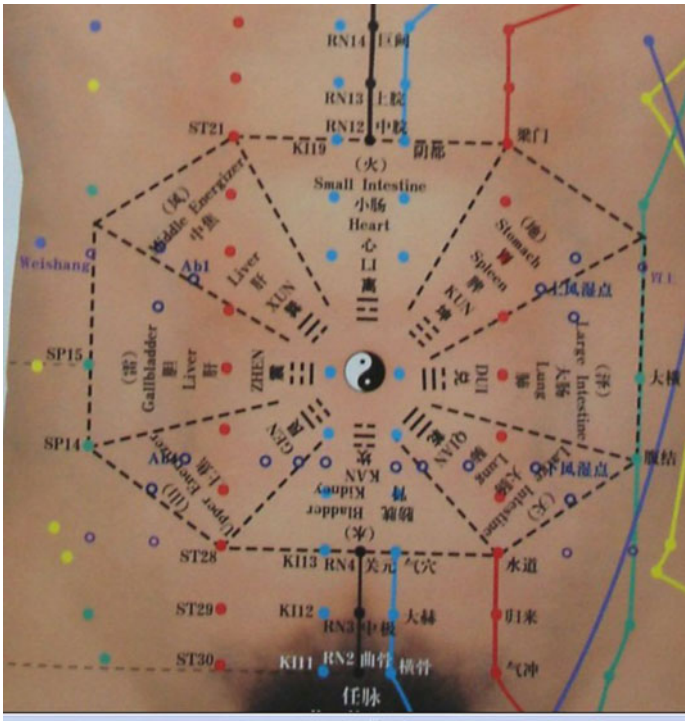

Fig. 41 Distribution of abdominal Eight-diagram around the navel (http://www.360doc.com/content/11/0218/19/619786_94138035.shtml)

1.3.16 Dr. Bo Zhi-Yun Abdominal Acupuncture Style (薄智云腹针疗法)

This abdominal acupuncture was developed by Dr. Bo Zhi-Yun (http://www.360doc.com/content/10/0716/21/474297_39512983.shtml).

In this style, acupuncture points are, most of the time, the same as in traditional meridians, but the needle is inserted very shallowly (Fig. 42). The patient does not feel any typical Deqi sensation.

This style of acupuncture needs very precise location of acupuncture points on the abdomen and precise sequence of needle insertion and removal. The needles are manipulated only with twist (not pulling up and down), or with slight twist and very slow pulling up and down. To remove the needle, the needles that were inserted first will be removed first (do not insert them deeper before removing).

For example, in the treatment of a stiff neck, the acupuncture points used are Zhongwan, Shangqu and Huaroumen, all of which belong to the traditional meridian system. It is necessary to insert the needle into Zhongwan first, then Shangqu, followed by Huaroumen last. The needle on Zhongwan needs to be inserted

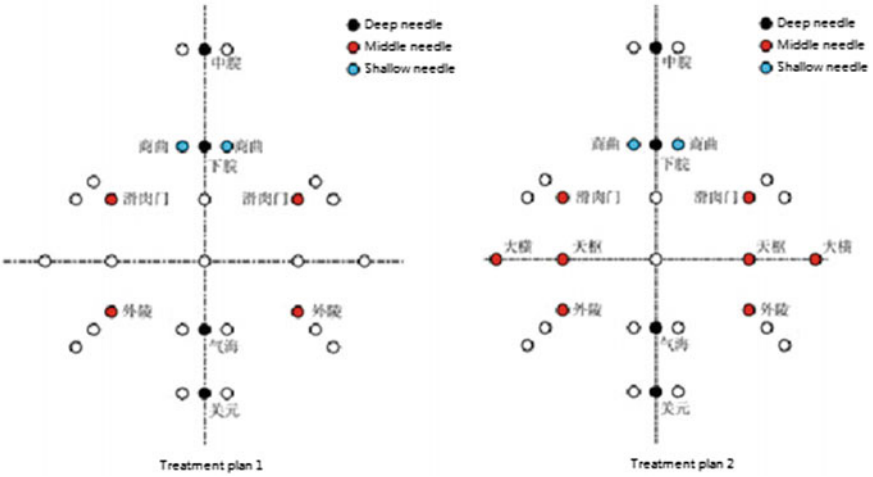

Fig. 42 Example of acupuncture points used in Bo's abdominal acupuncture style, with deep, middle deep or shallow acupuncture insertion (http://www.360doc.com/content/15/0224/15/11605768_450478906.shtml)

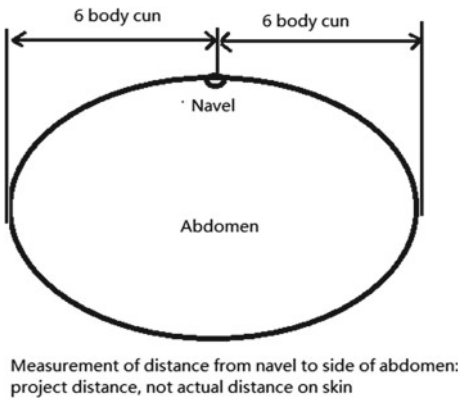

Fig. 43 Illustration of the way to measure distance on abdomen in the Bo's acupuncture style

deeply, Shangqu shallowly, and Huaroumen at middle depth (http://www.360doc.com/content/16/0816/23/29553696_583739407.shtml).

Needle retention time is usually 20–30 min. It can be a longer time for chronic disease or if the body constitution is stronger. Acupuncture should be performed once a day for three days, then changed to once every other day. Six to ten sessions are one healing course.

It should be mentioned that the measurement of the distance on the abdomen in this style of acupuncture is unusual: it is the project distance, not the actual skin surface distance (Fig. 43).

Generally speaking, Abdomen acupuncture is used for inner-oriented diseases, chronic diseases, or complex diseases. It is not recommended for acute abdominal

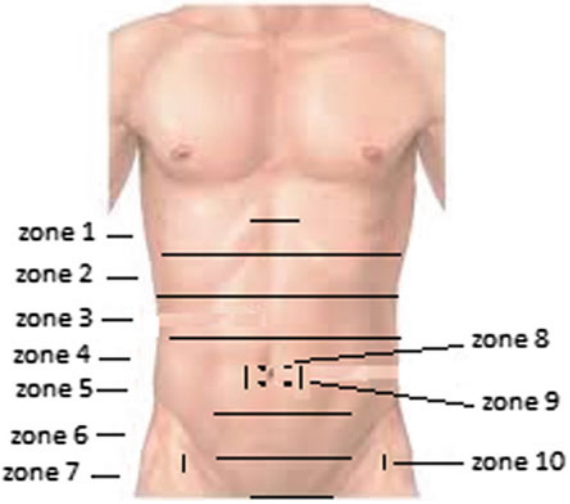

Fig. 44 Acupuncture zones in Sun's Abdominal Acupuncture style

syndrome, varicomphaius, neoplasm metastasis in abdomen, pregnancy for more than 3 months, or if the patient is very weak in body condition.

One of the special characteristics of Abdomen acupuncture is that there is fixed acupuncture formula for each disease. For example, the location and the number of acupuncture points, and the depth of the needle in each point, are all standardized. These requirements have to be followed exactly.

1.3.17 Sun Shen-Tian Abdominal Acupuncture Style (孙申田腹针疗法)

Sun's abdominal acupuncture style was developed by Dr. Sun Shen-Tian (Xu 2006). It separates the abdomen into ten zones (Fig. 44). Zones 1–4 are located in the upper abdomen; zones 5–7 are in the lower abdomen; zones 8 and 9 are around the navel; and zone 10 is on the anterior superior iliac spine.

The zones are separated as follows: along the middle vertical line from metasternum to navel, four horizontally zones are separated equally. Zone 1 is on the top next to the metasternum. Zone 2 follows, then zone 3, and zone 4 is next to the navel. Similarly, the area from the navel to the synchondroses pubis, is also equally separated into 3 horizontal zones. Zone 5 is next to the navel, zone 7 is next to the synchondroses pubis, and zone 6 is in between zones 5 and 7. In zone 1, there are 3 acupuncture points. In zones 2–7, each zone has two points (0.5 body cun to the middle vertical line of abdomen, middle to the upper and lower board of next zones, one point on each side of the abdominal middle line). In zone 8, there are 4 points. They are 0.5 body cun around the navel: left, right, top and bottom of the navel. Zone 9 is 0.5 body cun above the navel, then 1 body cun to the left and right, then from this point draw a vertical line 2 cm long. For zone 10, from the anterior superior iliac spine, draw a vertical line (parallel to the middle line of the abdomen).

Zone 1: There three acupuncture points in this zone. This is the emotional zone. It works for anxiety, depression, cravings, poor sleep, heavy dreams, poor memory.
Zone 2: This zone is for adjustment of autonomic nerve and endocrine functions (2 points, left and right side). It works for primary hypertension, diabetes, menopause syndrome, etc.
Zone 3: This zone is for vocal paralysis. It works for Parkinson's disease, tourettes syndrome, chorea.
Zone 4: This is the motion zone. It works for disorders of motor functions and post-stroke syndrome.
Zone 5: This zone is under the navel, and is the sensation zone. It works for various disorders in body sensation, such as pain and numbness.
Zone 6: This is also a motion Zone. It works for paralysis.
Zone 7: This is the vision zone. It works for disorders in vision.
Zone 8: The functions here are similar to zone 1.
Zone 9: This is the Foot Sensation-Motion zone. It works for restless leg, lower limb pain, urinary diseases, and diseases in perineal position area.
Zone 10: This is the Balance zone. It works for disorders of balance due to a small brain.

For most acupuncture points, the needles are inserted obliquely, except for needles in zone 8, in which the needles can be inserted vertically. Deqi sensation is required.

Sun's abdominal acupuncture is a newly developed acupuncture style. Currently, it is used in combination with other acupuncture styles (Sun and Yu 2014; Shen et al. 2014).

1.3.18 Qi Yong Navel Acupuncture (齐永脐针)

Navel acupuncture style was developed by Dr. Qi Yong (http://blog.sina.com.cn/s/blog_60a4a9bb0100e30a.html). There are several ways to select acupuncture points in the navel acupuncture style (Fig. 45) (Dong and Qi 2002). Points can be selected by locating a pain spot under pressure, by finding a knob under the skin, by using Luoshu Holographic distribution, by using Eight-zone Holographic distribution, by using Five-element distribution, and by Earth-branch Holographic distribution.

(a) Painful spot navel acupuncture

Find the painful spot around the wall of the navel. Stimulate the painful spot with a needle for several minutes. The tip of the needle points towards the wall (not vertically towards the bottom of the abdomen). About 20% of patients can have such painful spots. It is easier to find the painful spot with acute diseases.

(b) Knob navel acupuncture

Find a subcutaneous knob. The patient could feel pain upon pressing that spot. The skin color should be normal and the size of the knob should be about the same as a grain of rice. We only need to press the knob several times a day. Such subcutaneous knobs can be found in many patients with chronic diseases.

(c) Navel Luoshu Holographic acupuncture (洛书全息)

The navel contains information for the whole body. Distribution of the information in the navel is as follows (Fig. 46):

Look at the small human being figure inside the picture. It represents the correlation of the direction of navel wall to the body. For example, the top wall of navel is related to the head, the bottom to the feet, the left side wall to the left arm (upper left) and left leg (lower left). If there is pain in the left shoulder, the acupuncturist stimulates the upper left wall of navel. If the pain is in the right hip, the acupuncturist stimulates the lower right wall of the navel. This style of acupuncture is often used for the treatment of muscle-joint disorders.

(d) Navel Eight-diagram navel acupuncture (后天八卦脐针)

The distribution of organs is based on the Eight-diagram picture (Fig. 47). For example, in the treatment of respiratory diseases, the acupuncturist uses a needle to stimulate the left wall of the navel (left means the direction of left hand of the patient, though the spot is on the right of the following picture). For liver disease, the acupuncturist stimulates the right wall of the navel of patient.

(e) Five-element navel acupuncture (五行脐针疗法)

Make TCM diagnosis first, then perform acupuncture treatment, following the principle of the Five-element theory (following the Fig. 46).
Using Co-relation theory of the Organ relationship (脏腑关系).
This means to directly stimulate the corresponding position on the navel wall, which has the same nature as the TCM diagnosed disease. For example for a liver disease, which belongs to Liver Wood in TCM, the acupuncturist stimulates the navel wall on the right side of the patient's trunk (it is the Zhen diagram, which belongs to Liver Wood). The acupuncturist can either stimulate the Gall bladder Xun position on the navel wall, which belongs to the Gall bladder position, because the Gall bladder and the Liver have a surface-inner relationship. In this example, it is called gross co-relation (大比合) to stimulate the diagram of the diseased diagram, and it

Fig. 45 Navel acupuncture (http://www.360doc.com/content/11/0218/19/619786_94138035.shtml)

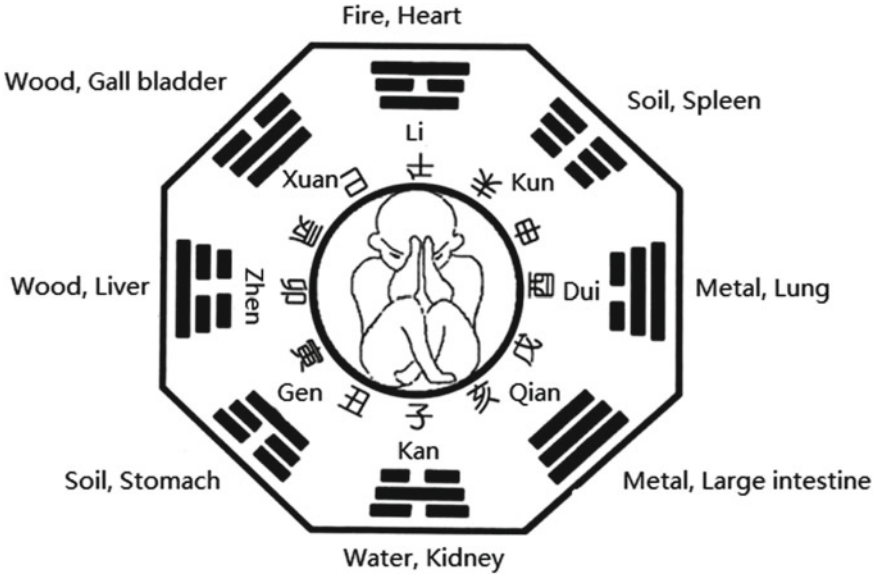

Fig. 46 Diagram in Luo Shu style. The small figure in the center represents the direction of the body to each diagram

Fig. 47 Earth-branch time circulation chart (http://baike.haoyun666.com/index.php?doc-view-629.htm)

is called small co-relation, (小比合) for the stimulation of another diagram, which has a surface-inner relationship with the diseased diagram.

Using mother-son theory of the Five-element theory (五行生克关系).

If the disease belongs to weakness, perform acupuncture on its month diagram (previous meridian) position on the navel; and if the disease belongs to overwhelming condition, the acupuncturist stimulates the son diagram (following diagram). The acupuncture can also be performed in another way: for the overwhelming condition

in a diagram, for example, Lung Fire, the acupuncturist can stimulate the Heart Fire diagram (with the needle tip pointing towards the head of the patient), because Heart Fire counteracts the Lung Metal. If the condition belongs to weakness, for example, Lung Weakness condition, the acupuncturist can stimulate the navel wall of the left hand direction of the patient (the Kun diagram/position/direction, which belongs to Spleen Soil), since Spleen Soil nourishes Lung Metal. Similarly, the acupuncturist can also stimulate the middle bottom, the navel wall on the right leg direction of the patient (both belong to Soil).

If the needle is inserted vertically from the middle of the navel, it is balanced nourish-depletion technique and it is used to treat diseases of the digestive system (TCM spleen and stomach). If the needle is placed a little bit towards the up direction (the head direction), it is used for the treatment of heart disease and eye disease. If it is placed towards the foot direction (the Water and the Kidney direction), it is used for the treatment of diseases in the urinary system. If it is placed towards the right direction (the direction of the right hand of the patient, the Wood, the Liver direction), it is used for the treatment of liver disease. One needle and one spot can treat many kind of disease.

(f) Earth-branch of Eight-diagram based time navel acupuncture (地支八卦脐针)

Earth-branch Holographic acupuncture system (Fig. 47) was developed by Dr. Guo Chang-Dian and Chen Wen (郭常典和陳文). It is mostly used for those diseases that show a very clear time-related onset pattern (http://www.360doc.com/content/16/0412/02/14001169_549872594.shtml; http://www.hkama.hk/journal/journal0901/content06/c6_01.htm). This means that the disease recurs at a fixed time of the day, month or year.

According to the Chinese bio-clock, the bottom of the clock is midnight, the right side is 6 am, the top is 12 pm, and the left is 6 pm. For example, if the diarrhea happens always at 3 am, the acupuncturist can use a needle to stimulate the 7 pm position of the navel. The needle should be inserted horizontally or obliquely, but not vertically. If a cough always occurs at 5 pm, which is the 酉time zone of Chinese clock and it located on the 3 pm of the ordinary clock, the acupuncturist can stimulate the 3 pm position of the navel wall. To stimulate the time-matched position, use the nourish-depletion technique of acupuncture.

For weak diseases, it is necessary to use nourishing technique by stimulating the next time zone on the navel wall. For the same cough patient, the acupuncturist needs to stimulate the navel wall of the patient in the 4 pm position. For overwhelming disease condition, the acupuncturist needs to use a depleting technique by stimulate the previous time zone. In the same cough example, the acupuncturist needs to insert the needle on his navel wall in the 2 pm position. This is position nourish-depletion technique.

The acupuncturist can also use handle technique for the nourish-depletion: strong stimulation belongs to depletion; keeping the needle in place for a while (retention) is nourishing. The position of nourish-depletion and the manual nourish-depletion technique can be combined at the same time.

(g) Four-diagram Navel acupuncture (四局针法) (http://www.shanyuankang.com/html/zwll/zjcx/2707.html)

In Fig. 47 above, if the acupuncturist uses three needles together in the combination pattern shown, the procedure can create different healing effects. For example, if the acupuncturist stimulates the navel wall on the Shen (Urine bladder), Zi (Gall bladder) and Chen (Stomach) position, it is called Water diagram (the yellow lines), which is used for the treatment of diseases that belong to Foot Yangming Stomach, Foot Shaoyang Gall bladder, and Foot Taiyang Urine bladder meridians.

If the acupuncturist stimulates the Ji (Spleen), You (Kidney) and Chou (Liver) (the blue lines), the procedure creates a Metal diagram, which is used for the treatment of diseases that are distributed in the range of the Foot Taiyin Spleen, Foot Shaoyin Kidney and Foot Jueyin Liver meridians.

If the acupuncturist stimulates the He (Three Jiao), Mao (Large intestine) and Wei (Small intestine) positions on the wall of navel (the green lines), this is the Wood diagram, which is used for the treatment of diseases that are distributed in the range of the Hand Taiyang Small intestine, Hand Shaoyang Three Jiao and Hand Yangming Large intestine meridians.

If the acupuncturist stimulates the Yin (Lung), Wu (Heart) and Shu (Heart shell) positions on the navel wall, the procedure creates a Fire diagram, which is used for the treatment of diseases that are distributed in the range of Hand Taiyin Lung, Shaoyin Heart and Jueyin Heart shell meridians.

Among these local acupuncture systems, the Auricular acupuncture, Scalp acupuncture, and the Abdomen acupuncture system are used more often. The Foot acupuncture system has been developed and used more in Western countries as reflexology.

The specific difference with the Abdomen acupuncture style is that it requires no feeling from the acupuncture needle by patients (similar to the Floating acupuncture and Wrist-ankle acupuncture systems above).

1.3.19 Holographic Acupuncture System (全息针灸体系)

Holographic acupuncture system was created by Dr. Zhang Ying-Qing (http://blog.sina.com.cn/s/blog_5ff306380102uwd8.html). The main idea of the theory is that any small part of the body contains information for the whole body (Figs. 48, 49 and 50). Indeed it has been found that many small parts of the body can be stimulated to treat diseases in other parts of the body. The distribution of the points in the small part of the body can cover the anatomic structure of the whole body. The smallest part of the body is found to be as simple as a single bone (Fig. 29). The Holographic theory is frequently used to explain the function of some acupuncture points in the treatment.

Another example is the second and the fifth Metacarpal bone holographic acupuncture.

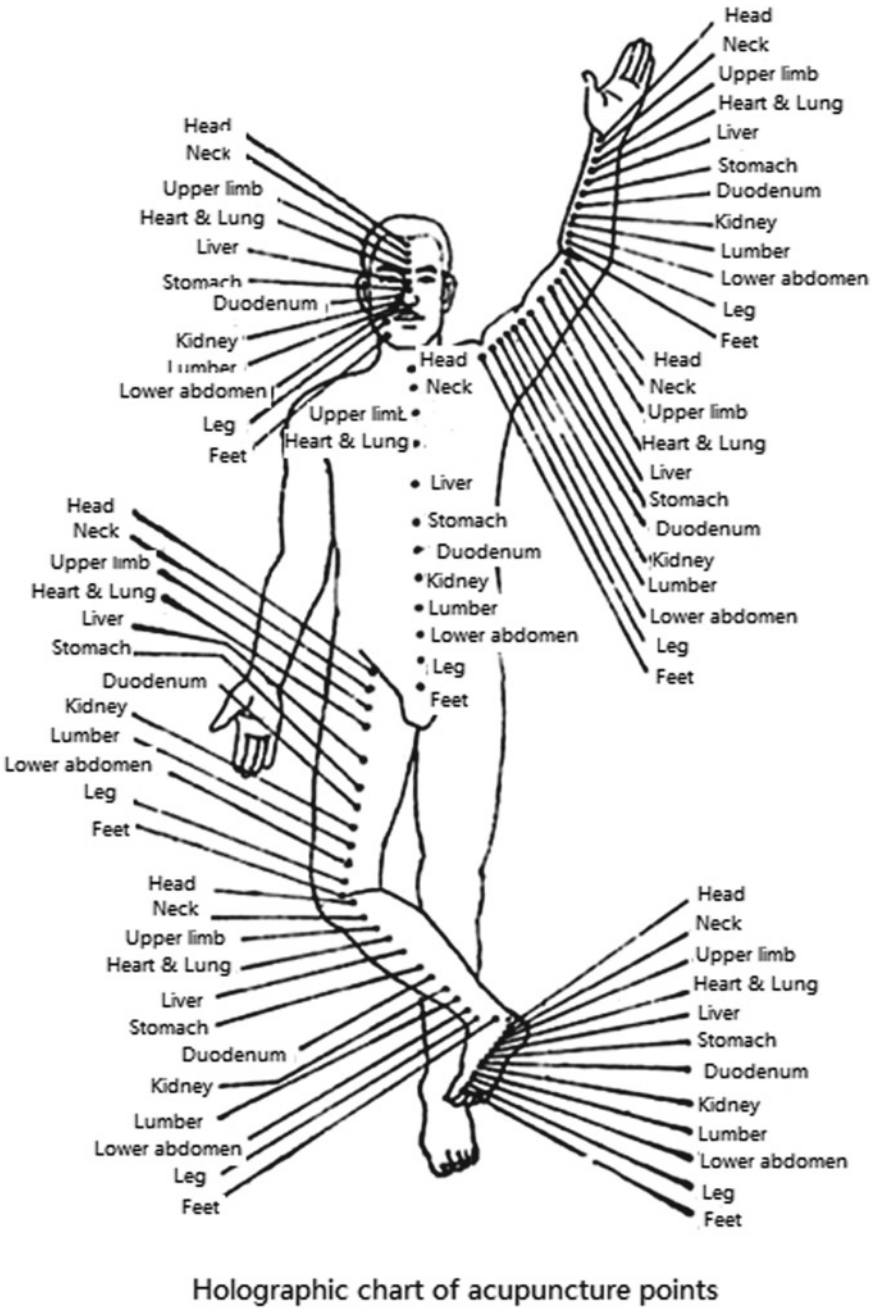

Fig. 48 Holographic chart of acupuncture points (Sun and Yu 2014)

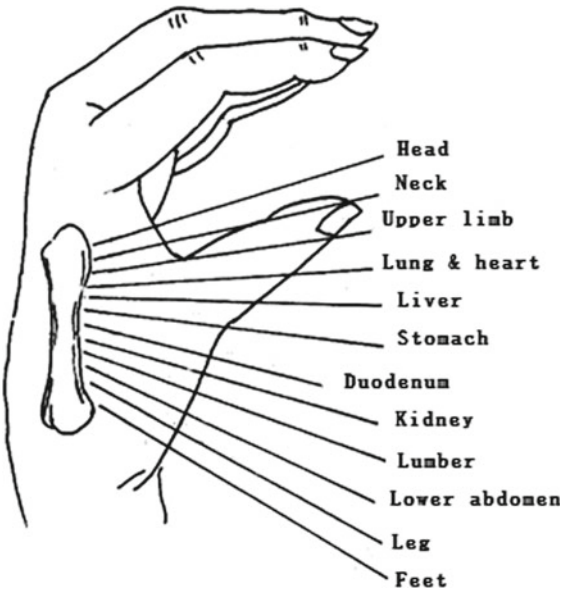

Fig. 49 Holographic chart for second metacarpal bone (http://www.360doc.com/content/09/0326/17/73907_2926067.shtml)

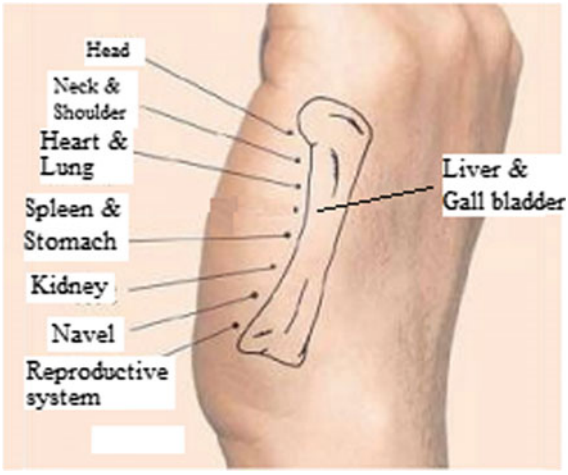

Fig. 50 Holographic chart for the fifty metacarpal bone (http://www.med66.com/new/42a206a2010/2010111zhangf165224.shtml)

1.3.20 Feng Ning-Han Nine-Place Acupuncture Style (冯宁汉九宫针法)

This acupuncture style was developed by Professor Feng Ning-Han. The idea came from the book "*Zhen Jiu Da Cheng*". In treatment, choose and find the sick point on the body first. This point will be the middle point (Middle Palace). Then select eight other points around the middle point (so called nine palaces), about 2–5 cm from the middle point. Insert the first needle on the middle point. For the remaining needles, insert them in the sequence of upper palace first, then lower palace, left,

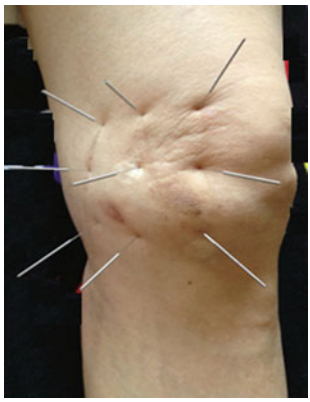

Fig. 51 Acupuncture illustration of Nine-palace acupuncture style (http://blog.sina.com.cn/s/blog_89da3dfe0101b4aj.html)

then right, upper-left, upper-right, lower-left, and finally lower-right (Fig. 51). The sequence can be understand as a clock: middle needle first, then insert the needle at 0 am (12 pm), then 6 am, then 3 am, then 9 pm, then 1.5 am, then 10.5 pm, then 4.5 am, and finally 7.5 am.

There is no need to manipulate the needle to induce Deqi sensation. We do acupuncture on the lower limb (to nourish or balance the Jing, e.g. micro essence material), the middle body (to nourish the Qi) and the head (to nourish the Spirit), no matter if the disease is mild or severe, and no matter if the diseases are caused by inner or outer reasons (http://www.hztjt.com/MEMBER/Views/1387).

赵梅 (2012) (Zhao and Wang 2012) treated 100 cases of prolapse of lumbar intervertebral disc by using the Nine-palace acupuncture (Deqi session was induced), plus traditional acupuncture points, herbal paste, TDP lamp, middle-frequency treatment machine, and an ion-inducing machine. After the treatment, 57 cases were cured, 35 cases were much improved, and only 8 cases had no improvement. To cure, as little as 10 days and as many as 20 sessions were needed.

1.3.21 Guan Zhen-Zai Nine-Palace Acupuncture Style (管正斋九宫针法)

This style of acupuncture was developed by Dr. Guan Zhen-Zai (http://zhongyibaodian.com/yianxinde/76005.html). This way of acupuncture is similar to the above style, but is mostly used on the spine. It requires the retention of needles for 30 min and the manipulation of needles three times during the session. It is said that this technique of acupuncture works mostly for diseases that are related to disorders of the spine: various spondylarthritis, spinal trauma, injury of supraspinal ligament, cervical spondylopathy, lumbar hyperosteogeny, thoracic vertebrae hyperosteogeny, prolapse of lumbar intervertebral disc, lumbar sprain, lumbar degeneration.

Chen (2008) treated 526 cases of prolapse of lumbar intervertebral disc with the Nine-palace acupuncture (Deqi session was induced), plus traditional acupuncture

points and cupping. After treatment, 35 cases were cured, 251 cases were much improved, and 240 cases were improved. The authors did not report how many sessions were needed.

There is another acupuncture style called Nine palace-twelve way style, which was developed and used by Dr. Yin Xue-Chen (http://www.jzsef.com/view.php?ID=227; http://www.huaxiamingyi.com/mylt/20130407/105437.aspx). It uses nine special needles for the treatment though detailed information is not available.

1.3.22 Along-Spine Acupuncture Style (脊针针法)

There are acupuncture points along the spine, independent of the traditional Jia Ji point. The style used here is called Ji needle acupuncture (Along spine acupuncture). The acupuncture points are on 0.5 body cun on the both side of the spinal spinous process, from cervical spine (7 pairs), thoracic (12 pairs), and lumber (5 pairs), to the sacral spine (4 pairs).

The points in the cervical pairs work for the diseases in the head, face, neck and upper limbs, such as nerve pain, spondylosis, tonsillitis or stiff shoulder.

The points in the thoracic pairs work for diseases in the upper limb (thoracic pair 1–3), such as shoulder pain, cough, asthma, chest pain; in the chest (thoracic pair 4–9), such as palpitation, angina pectoris, stomach pain; and in the stomach (thoracic pair 10–12), such as pain in liver region, biliary colic, biliary ascariasis.

The points in the lumber pairs work for diseases in the stomach, lower lumber and lower limb, such as stomach pain, abdomen bloating, appendicitis, enteritis, pain in the leg, paralysis, and pain in the lumber-sacral region.

The points in the sacral pairs work for diseases in the urinary and reproductive systems, such as impotency, spermatorrhea, enuresis, prolapse of the anus, uterine prolapse, dysmenorrhea, amenorrhea, paralysis in leg, pain in leg, or lumbosacral strain.

The acupuncture points are chosen based on where pain is felt by pressing, or on the known connection of the anatomic relationship between the level of spine and the organs connected via nerves.

Acupuncture on spine pairs requires Deqi sensation and is usually combined with body acupuncture treatment.

1.4 Local Acupuncture Styles for Local Diseases

1.4.1 A Shi Point Acupuncture (阿是穴療法)

A Shi point acupuncture belongs to traditional Chinese acupuncture. It is one of the ways to select acupuncture points for treatment. We press the body surface to find the painful spot, then to stimulate the painful spot for treatment. It is called the A Shi point because the patient would yell out “A” when pressing this point.

The A Shi point can be stimulated by acupuncture needle, by fingers (called finger press acupressure), or with electric machines, such as TENS, Hans machine, etc. For diseases in the muscle (soft tissue), such treatments apparently work pretty well.

If the local disease is on the skin, the acupuncturist can just insert the needles on and around the skin lesion. The number of the needles can be as little as four needles (Yang ci acupuncture), or as many as more than ten needles. The needles can evenly distributed on and around the skin lesion (branch needles), or can be one circle or even two circles around the skin lesion.

For severe muscle diseases, the acupuncturist may also use a small tool, called Needle-knife, which is inserted into the skin to losen the stiff tissue under the skin (the Small Needle-knife technique).

Sometimes, the acupuncturist may also pouch the painful spot to release some drops of blood, and then cover the spot with a cupping cup (called Bleeding Cupping technique).

All of these therapies indicate that a local disease can also be treated with local stimulation, without consideration of traditional meridian diagnosis or TCM organ diagnosis.

1.4.2 Release Point Acupuncture (反阿是穴療法)

Release point acupuncture (反阿是穴) is the opposite style to A Shi point style. It was developed by Dr. Zhang Wen-Bing and Dr. Huo Ze-Jun (Zhang and Huo 2005).

This style of acupuncture is also mostly used for the treatment of soft tissue damage. The release point means that, upon pressing some point on the muscle, the original pain in the affected muscle becomes released or disappears, although under the Release point, there is somehow pain or discomfort upon being pressed.

The location of the Release point is opposite to the A Shi point but they are basically on the same group of muscles. If the A Shi point is located on the starting point of the muscle, the Release point is on the middle or the end of the muscle. If the A Shi point is located on the middle of the muscle, the Release point is on the starting or end part of the muscle group. If the A Shi point is on the end point of the muscle, the Release point is on the starting part of the muscle.

There is usually tightness under the Release point. Upon pressing the Release point and letting the patient move the affected limb or joint, the patient would feel much release of the pain on the original pain spot. This is a very important way to find the Release point.

Similar to the treatment of the A Shi point, the Release point can also be stimulated with acupuncture needle, finger press, point injection, or fire needle, and so on.

Some acupuncturists (http://blog.sina.com.cn/s/blog_6383a68a0102e50g.html) believe that the use of this method works better for acute soft tissue damage. For chronic and repeated soft tissue damage, it can be used as an alternative choice.

1.4.3 Trigger Point (扳机点療法)

The concept of the Trigger point was firstly described comprehensively by Dr. Janet G. Travell. A Trigger point is a spot on the surface of the body (http://weibo.com/ttarticle/p/show?id=2309404025714667093284). Touching it could cause pain, cause a local muscle twitch, or cause pain in another place (referred pain). A patient may have more than 2 Trigger points and the Trigger points can be located on the primary pain spot, near it, or far away from it.

On the Trigger point, the acupuncturist can usually find a painful knob or tight muscle mass. Once the Trigger point is identified, then the acupuncturist can use acupuncture needles, point injection, or electric stimulation (such as TENS) for the treatment.

It should be pointed out that the Trigger point is not at all the acupuncture point, the A Shi point or the Release point noted above (http://blog.sina.com.cn/s/blog_5433aa7b0100m1wx.html).

1.4.4 Liu Nong-Yu Sinew Acupuncture (刘农虞筋针疗法)

Tendon acupuncture was developed by Dr. Liu Nong-Yu (Liu et al. 2015). It is mostly used for the treatment of soft tissue diseases. We select places about 2–3 cun from a painful spot or knob along the affected tendon as acupuncture points, e.g. along-tendon diagnosis. There is no need to have any TCM or meridian diagnosis. The needle is inserted shallowly (penetrating subcutaneously under the skin, not in the muscle layer). The technique only stimulates the membrane of the tendon. There should be no apparent pain or strong discomfort during acupuncture. It is reported that at the first treatment, the pain level can be reduced by more than 50%. Generally only one to three needles are needed for each session.

Tendon acupuncture is used for treatment of the following diseases: acute neck spasm, cervical spondylosis, intercostal neuralgia, acute lumbar sprain, lumbar muscle degeneration, periarthritis of shoulder, post-stroke shoulder pain, tennis elbow, carpal tunnel syndrome, loose tendon in the finger, trigger finger, soft tissue damage, heel pain, gout, and so on. For these diseases, the more pain there is, the better the healing effect is.

2 Characteristics of Current Acupuncture Styles

2.1 Acupuncture Points to Be Stimulated

In current acupuncture practice, not all the acupuncture points belong to the traditional meridian system. Points could also be chosen according to Holographic theory,

Table 1 The ways of choosing acupuncture points

Meridian-based acupuncture style	Traditional acupuncture style (Textbook acupuncture)
	Time-circle acupuncture
	Tan Wu-Bian Balancing acupuncture
	Liu Ji-Ling new one-needle acupuncture
	Zhang Xian-Chen Hand-Foot Three-needle acupuncture
	Flying acupuncture
	Zhao Wu-Rong Flying acupuncture
	Li Jin-Niu Five-element acupuncture
	Ma Xiao-Ping Five-element acupuncture
	Yangming Five-element acupuncture
	Mang acupuncture style
	Guo Zhi-Chen Eight-point acupuncture
	Pan Xiao-Chuan Classical acupuncture
	Korea Sha-Am Five-element acupuncture
	Korea Li Ji-Ma Four-diagram acupuncture
	Nora Five-element acupuncture
	Some Japanese acupuncture
	Bo Zhi-Yun abdominal acupuncture style
Holographic theory-based acupuncture style	Most kinds of scalp acupuncture styles
	Facial acupuncture style
	Eye acupuncture style
	Nose acupuncture style
	Mouth acupuncture style
	Tongue acupuncture style
	Ren-zhong acupuncture style
	Some Palm acupuncture styles
	Foot acupuncture style
Mirror theory-based acupuncture style	Wang Wen-Yuan Balancing acupuncture
	Tan Wu-Bian Balancing acupuncture
	Li Bai-Song Eight-words acupuncture
	Chen Zhao Crane-Pine Yi Xue acupuncture
	Ke Shang-Zhi Distance-meridian acupressure therapy

(continued)

the Eight Diagram theory, the Mirror theory, the Extra Point system, the nerve distribution zones and the positive point on the body (Table 1).

Table 1 (continued)

Meridian-based acupuncture style	Traditional acupuncture style (Textbook acupuncture)
Eight diagram or Nine palace theory-based acupuncture style	Navel Eight-diagram style
	Abdominal Eight-diagram style
	Liu Bing-Quan Eight-diagram scalp style
	Chen Zhao Crane-Pine Yi Xue acupuncture
	Peng Jing-Shan eye Eight-diagram acupuncture
	Feng Ning-Han Nine-Palace acupuncture style
	Guan Zhen-Zai Nine-Palace acupuncture
	Yin Xue-Chen Nine-Palace acupuncture
Extra point-based acupuncture style	Dong Jing-Chang Extra point acupuncture style
	Han Wen-Zhi One-needle acupuncture style
	Zhang Xin-Shu Wrist-ankle acupuncture
Nerve distribution zones	Along-spine acupuncture style
Pain spot-based acupuncture style	A Shi acupuncture
	Release point acupuncture
	Trigger point acupuncture
	Liu Nong-Yu Tendon acupuncture
	Western Medical acupuncture

2.2 Diagnosis Directing the Selection of the Acupuncture Point

Acupuncture points can be selected according to meridian diagnosis, traditional TCM organ, Qi-Blood diagnosis, Four-Jiao space diagnosis (the Upper Jiao, Middle Jiao, Lower Jiao and Outer Jiao, 四焦辩证), the Four-region diagnosis (四象辩证, e.g. the corresponding location of the diseases), the Four Diagram diagnosis (四局辩证) and the location diagnosis (such as for the treatment of headache, choosing the corresponding "head" point in various Holographic acupuncture systems), or by just touching the local tissue for positive points.

2.3 Steady Point Versus Dynamic Points

Acupuncture points can be steady, such as in the traditional acupuncture systems. The points can also be dynamic. This means that the points show up only during disease conditions, such as the positive reactive point in Tan Wu Bian Balancing acupuncture, Li Bai-Song Eight-words acupuncture, A Shi acupuncture, Release

acupuncture style, Trigger point acupuncture, and Liu's Sinew acupuncture. They target the positive reactive points requiring stimulation. The points do not exist in normal and healthy body condition.

2.4 Accuracy of Acupuncture Points

Some acupuncture styles require very accurate locations of the acupuncture spots, such as the Bo Zhi-Yun acupuncture style. Some do not require so much accuracy, such as various Eight-Diagram and Nine-Palace acupuncture styles, in which the acupuncture works under the condition that the needles are inserted in the correct diagram (or in a zone). Some acupuncture styles do not need precise acupuncture points, but need the precise positive points (Tan Wu-Bian Balancing acupuncture, Li Bai-Song Eight-words acupuncture, the A Shi points, the Release point, the Trigger points and the Liu Nong-Yu Sinew acupuncture).

2.5 Depth of Needle Insertion

The needle used in treatment can be very deep in the body, such as the Mang acupuncture style, in which the needle can be inserted into the body (horizontally) for more than 30 cm; or the Han Wen-Zhi One-needle acupuncture style, in which most of the needles are inserted for 2–3 body cun. The needle can also be very shallow, such as in some Japanese acupuncture styles, in which the needles are inserted into the skin for only 1–2 mm. Some Chinese shallow acupuncture styles insert needle at least to the hypodermis layer and aim to induce the Deqi sensation too (Yu et al. 2016). Some acupuncture styles insert the needle only in the subcutaneous layer, not into the muscle, such as Liu Ji-Ling new one-needle acupuncture, Fu Zhong-Hua subcutaneous acupuncture, Bo Zhi-Yun abdominal acupuncture, Wrist-ankle acupuncture, and Liu Nong-Yu Sinew acupuncture.

2.6 Intensity of Treatment Stimulation

The intensity of the acupuncture stimulation can be very strong, such as in the Dr. Shi Xue-Ming style of acupuncture, in which the needle needs to touch the nerve, in Ke Shang-Zhi Distance-meridian acupressure therapy, in which skin might be pressed hard to blue-purple color (bruise), in the Li Bai-Song Eight-words acupuncture and in the Zhang Xian-Chen Hand-Foot Three-needle acupuncture style. The needle feeling can also be very mild or almost nothing, such as in the Liu Ji-Ling new one-needle acupuncture, Bo Zhi-Yun Abdominal acupuncture, Eight-Diagram abdominal

acupuncture, Wrist-ankle acupuncture, Liu Nong-Yu Sinew acupuncture, or in some Japanese acupuncture styles.

2.7 Healing Efficiency of Acupuncture Styles

This is a very sensitive question in discussion. The answer might not be proper if there is no direct comparative study with the experts in each acupuncture style in the study. But each acupuncture style could have its own favorite and relatively not-so-favorite disease spectrum. For example, the various scalp acupuncture styles are commonly used for the treatment of nerve-affected disease, or brain-originated diseases, such as stroke, chorea festinans, paralysis, Bell's palsy, migraine, child cerebral palsy, supranuclear paralysis, epilepsy, dystaxia, epileptiform neuralgia, and sciatic pain, though it is also used for the treatment of other kinds of diseases.

Bo Zhi-Yun Abdominal acupuncture works relatively better for inside organ-related diseases, whereas various Positive point-related local acupuncture styles (such as A Shi point acupuncture, Release point acupuncture, Trigger point acupuncture, Tendon acupuncture, Fu Zhong-Hua subcutaneous acupuncture, etc.) work relatively better for local muscle-tendon originating diseases, such as shoulder pain, tennis elbow, carpal tunnel syndrome, lower back pain, and various muscle spasm (including sciatic pain).

Some acupuncture styles work better for acute pain than for chronic pain, such as the Wang Wen-Yuan Balancing acupuncture style. Some other acupuncture styles can work for even severe conditions (such as stroke), such as the Shi Xue-Ming Enhancing acupuncture style. Some acupuncture styles even work better for time-related disease (e.g. the onset of the disease is with fixed time of the day, the month, or the season), such as various Time-circle acupuncture styles.

For us as acupuncturists, we need to know the advantages and disadvantages of the various acupuncture styles. The acupuncture style to be applied is not only based on the nature of the diseases, but also on the patient. If the patient cannot tolerate much pain, we may consider the Zhang Xin-Shu Wrist-ankle acupuncture, the Liu Nong-Yu Sinew acupuncture, the Bo Zhi-Yun Abdominal acupuncture style, the Eight-diagram abdominal acupuncture, or the Qi Yong Navel acupuncture.

2.8 Whole Body Acupuncture Versus Local Acupuncture

One of the characteristics of Chinese medicine is that it emphasizes viewing disease from a whole body perspective. For this, acupuncturists believe that a local disease could influence the whole body, and that the treatment from the whole body aspect could also help to solve the local disease (such as carpal tunnel syndrome or ankle strain) and the whole body acupuncture would work much better than a local acupuncture.

This view may not always be true.

That a local can influence the whole and the whole can also influence the local is a philosophic idea. In practice, we need to know how much influence there might be. The local disease may or may not clearly influence the whole body and cause detectable structural and functional change. A structural and functional change in the whole body may or may not influence a local part of the body very much either. For example, a traffic accident on one street in the city of Edmonton may not dramatically influence the traffic of the whole city. A sick person with a whole body disease, such as hypertension, coronary heart disease, still has functional normal movement of their arms and legs.

In acupuncture practice, this means that some local diseases can be cured with a local treatment, such as A Shi point acupuncture, Release point acupuncture, Liu Nong-Yu Sinew acupuncture, and Wrist-ankle acupuncture. The acupuncturist does not really need to test the Five-element nature of the patients, or to solve the local pain or swelling by adjusting the pulse. Under such local pain, especially for a chronic pain, the pulse may not be clearly abnormal. Also, if the patient also has other chronic diseases, the pulse would be too variable to allow clear diagnosis. If so, the adjustment of the pulse would be difficult and it tends to fail in the treatment. In such instances, we have tried traditional acupuncture but the patient still felt a high level of pain. After, we used the TENS (or fire needle technique, or bleeding-cupping) locally, and the pain subsided much more.

3 Acupuncture Research

There are many ways to practice acupuncture. The acupuncture point can be chosen in different places; the points may be chosen from meridians, or not; the number of needles used can be only one or more than 10, 20 or even 30; the depth of the needle can be as shallow as just into the epidermis, or it can go into the hypodermis, deep into muscle or even touch the bone membrane; the Deqi sensation is required in some acupuncture styles, while it is prevented in some other styles.

There are still questions that the acupuncture researchers must answer:

First, are all or some of the acupuncture styles actually a placebo effect? Given the large variation in acupuncture methodology, it is very easy to suspect that acupuncture might be just a placebo effect.

The most questionable acupuncture style is the Nora Five-element acupuncture style, in which it is said that the most important part of the treatment is the good relationship between the acupuncturist and their patients, and that the influence of the acupuncture technique is less important. Such characteristics are very rare in Chinese styles of acupuncture.

Another questionable style is Japanese acupuncture in which the needles are inserted very shallowly into the skin (1 mm) (http://www.zhifayixue.com/zhongyaolunwen/425.html). The healing effect of very shallow acupuncture, such as some Japanese acupuncture styles, has been questioned long time ago by

some Chinese acupuncture masters (http://www.360doc.com/content/11/0601/21/840524_121045242.shtml). Not many acupuncture studies have been done in Japan. In one review (1978–2006) (Itoh and Kitakoji 2007), the reviewers could find only 57 papers on the subject, among which only 20 are full papers and the remaining 37 are case reports. Conditions examined were headache (12 trials), chronic lower back pain (9 trials), rheumatoid arthritis (8 trials), temporomandibular dysfunction (8 trials), katakori (8 trials) and others (12 trials). Applying the 5-point Jadad quality assessment scoring style, the mean score was 1.5 ± 1.3 (SD). The reviewers concluded that "there is limited evidence that acupuncture is more effective than no treatment."

This is very strange. In fact, even if we questioned whether the Chinese style of acupuncture is just a placebo effect, the researchers have to admit that the healing effect of acupuncture done in the hands is almost always significantly higher than no treatment (though it may not be higher than in placebo groups). We are therefore strongly interested in knowing whether the shallow-inserted needle acupuncture of the Japanese style is mostly a placebo effect.

The second big question for acupuncture researchers is that it seems that anywhere on the body can be stimulated as an acupuncture point for the treatment of disease. Although, for a given disease, we still needs to stimulate specific points, or regions, or zones of the body for the treatment. For example, for the treatment of headache, we can stimulate some spots on the head, the face, the eye, the nose, the feet, the hands, the arm, the stomach, or the navel, but in each region, we still needs to follow some rule to find the proper spots to stimulate. The function of some points can be explained by meridian theory, but some cannot.

The third question regards the relative advantages and disadvantages of each style of acupuncture. Each of acupuncture style should be compared with textbook acupuncture. The recommended diseases that should be compared are the following:

(1) nonspecific lower back pain;
(2) migraine;
(3) IBS;
(4) facial paralysis;
(5) post-operative nausea/vomit (acupuncture starts 30 min before operation and lasts to the end of the surgery);
(6) post-stroke paralysis or post-stroke depression;

All of these disease conditions are within the dominant advantage pattern of Chinese acupuncture.

In the study of acupuncture, it is better to separate Western medical acupuncture from the Chinese style of acupuncture. It has been recognized that there exists such Western styles of acupuncture that use needle for treatment but do not follow the traditional meridian diagnosis or TCM organ diagnosis to guide the choice of acupuncture points. Any reviewers should be aware of this fact and indicate which acupuncture style is reviewed in their review articles.

In the acupuncture comparison study, the exact practical procedures for the given style of acupuncture should be followed and are best performed by the expert in that

style. For example, in the study of Nora Five-element acupuncture, the acupuncture should be performed as once a week for 6–8 sessions. However, if we are comparing that style to the Chinese style of acupuncture, then the acupuncture should still be performed once a week for 6 or 8 sessions, with 2 days break before each course for a total of 6–8 weeks. In this way, we can compare the healing effect within the same treatment period (6 or 8 weeks), and also the same sessions (6–8 sessions).

The most difficult question is the mechanism of the acupuncture. Any theory needs not only to explain one style of acupuncture, but, at best, be able to explain all of the acupuncture styles.

There are several hypotheses regarding the mechanism of acupuncture. With a big picture of current acupuncture styles in mind, it is easy to find that Blood vessel theory, the Nerve reflection theory and the Fibro-membrane theory might work for the local acupuncture styles (A Shi point acupuncture, Release point acupuncture, Trigger point acupuncture, Liu Nong-Yu Sinew acupuncture), the Fu Zhong-Hua subcutaneous acupuncture and the Wrist-ankle acupuncture, but it is difficult to explain all the Holographic theory-based and the Eight-diagram theory-based acupuncture styles.

Currently, it seems very difficult to find a single theory to explain the mechanism of all styles of acupuncture (http://www.360doc.com/content/14/1223/13/7470776_435154741.shtml; Fei et al. 2011; Zhang 2012).

It has been pointed (http://blog.sina.com.cn/s/blog_6383a68a0102e50g.html) out that the meridian is a complex network structure in the body. It consists of at least seven kinds of bio-network structures, such as the collagenous fiber network, the polysaccharide/aquagel fiber net, and the tissue fluid transportation network, etc. The acupuncture point is imbedded in the soft connective tissue. Meridian phenomenon is the holistic biological phenomenon of these net structures. It might be that studying acupuncture mechanisms is as difficult as the study of telepathy. The mechanism of acupuncture might involve the transfer of information, which is another parameter of the concrete physical material world, besides the material, space location, time, and so on.

4 Conclusion

The aim of this paper is to supply basic information about various acupuncture techniques currently in practice, not only in Western countries, but also in China. We need to know that the textbook acupuncture style is only one style in use, and that it is used mostly in Western countries or in China. This is simply because this style was introduced in textbook form to many people. It does not mean that it is the best style of acupuncture, though the textbook has also introduced some other way of acupuncture, such as Time-circle acupuncture and Eight-diagram acupuncture, etc.

Currently in the US, for example, the most used acupuncture styles are textbook acupuncture, Dong's extraordinary point acupuncture, Five-element acupuncture, Tang's Balancing acupuncture, some Japanese acupuncture, Korea acupuncture, and

Western medical acupuncture (Zhen 2012). Acupuncturists must know the realities of the acupuncture profession and know different ways of acupuncture, so as to apply the proper style of acupuncture to each patient.

For acupuncture research, we may still have a long way to go to understand the precise mechanism of acupuncture, but this should not prevent researchers from finding out if acupuncture really has its own unique healing effect, beyond the placebo effect.

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Acupuncture Treatment for Chronic Fatigue Syndrome

Fei Yao, Yanli You, Xuan Yin, Dhea Khiati and Ying Xia

Abstract Chronic fatigue syndrome (CFS) was firstly defined in 1988 by the US Center for Disease Control and Prevention. The prevalence of chronic fatigue syndrome has ranged from 0.4 to 1% in the general population. Its pathophysiology remains unknown despite of intensive research on several pathological factors (e.g. infection, immune systems, neuroendocrinology, autonomic activity, and neuromuscular dysfunction). Its complex clinical manifestation may stem from physical, biopsychosocial and many other causes. On the other side, the therapeutic treatment for CFS is very limited in clinical settings. Recently, acupuncture treatment for CFS has gradually attracted physicians' attention. Based on Chinese medicine theory, acupuncture can promote the circulation of "meridian qi", regulate "qi" and "blood", balance "yin" and "yang", and thus restore the function of "Zang-Fu" organs via acupuncture signals generated from acupoints. Indeed, clinical practice has shown that acupuncture significantly relieves the clinical symptoms of CFS patients and improve the quality of their life. Simple acupuncture at appropriate acupoints or combined with electro-stimulation, blood-letting acupuncture, acupoint catgut

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embedding, acupoint injection, auricular acupuncture therapy, abdominal acupuncture, moxibustion and cupping treatment haven been used in the treatment of CFS with satisfactory outcomes. This chapter systematically reviews the progress in this field based on a broad search in the literature and our experiences.

Keywords Chronic fatigue syndrome · Acupuncture · Acupoints · Traditional Chinese medicine

1 Introduction

With increasingly fierce competition in our modern society, an increasing number of people are living with chronic physical and mental tension, or fatigue. Consequently, the incidence of chronic fatigue syndrome (CFS) has continued to rise year after year. CFS is not life threatening in the short-term, but its high incidence and long duration has serious negative impacts on people's work, studying, and quality of life. This has attracted great concern and attention in medical, psychological and sociological fields around the world.

Currently, modern medicine has not yet clearly defined the etiology and pathogenesis of CFS. Thus, there is a lack of effective therapeutic treatments available clinically for the treatment of CFS. In Traditional Chinese Medicine (TCM), it is believed that it is the qi transformation dysfunction of the "Five Zang" organs along with a decline in "Zang-Fu" functions that makes people unable to maintain their normal physiological functions, psychological states, and social activities, which leads to CFS. The patients with CFS often suffer from an imbalance among several "Zang-Fu" organs and have the disharmony between "qi" and "blood" and between "yin" and "yang". It is a disease of multi-organ and multi-system dysfunction caused by the consumption of "qi" and "blood".

In recent years, acupuncture treatment for CFS has gradually attracted attention. Chinese medicine theory and practice show that acupuncture treatment can promote the circulation of "meridian qi", regulate "qi" and "blood"and "yin" and "yang", and restore the function of "Zang-Fu" organs by stimulating acupoints. It has practical significance in improving the clinical symptoms of CFS patients and enhancing their quality of life.

In this chapter, we will tell readers about the methods, ideas, effects, and other related clinical practices of acupuncture treatment for CFS, we will outline basic research on acupuncture treatment for CFS, we will explore the mechanism of acupuncture treatment for CFS, and we will analyze advantages and problems of acupuncture treatment for CFS.

2 Clinical Symptoms of CFS

CFS is a syndrome that includes persistent or recurrent severe fatigue as its main feature with fatigue being the most important symptom. Fatigue is a subjective feeling, which brings about difficulties when attempting to accurately and reasonably evaluate CFS. Therefore, it is necessary to analyze the concept of fatigue.

2.1 Fatigue

Fatigue is a common phenomenon that almost everyone has experienced. Due to difficulties in describing and measuring fatigue, as well as the diversity and complexity of the effect factors, the definition and classification of fatigue has not yet been unified. "Ci Hai" refers to fatigue as the phenomenon of illness and a decrease in working efficiency caused by persistent tiredness or being overworked. In the *"Occupational Hygiene and Pathology of Chinese Medical Encyclopedia"*, fatigue refers to the phenomenon of the decline of working capacity due to excessive physical or mental work. There are various causes, such as high work intensities, long working durations, fast operating frequencies, lack of sleep, monotonous work, negative job morale, and a poor working environment (Liu 1992: 181).

Many scholars have defined and classified fatigue through different aspects. Japanese scholar Oshima Masako believed that fatigue involves three dimensions: physical symptoms, psychiatric symptoms and neurosensory symptoms (Masako 1979). In physiology, Lewis classified fatigue as the maximum loss of strength and capacity during the process of muscular activity (Lewis and Haller 1991); Sharpe et al. points out that fatigue is a subjective feeling, and that it has both a mental and a physical component (Sharpe et al. 1991a, b); Schwartz regarded that fatigue is a sensation of tiredness, insufficient energy, or exhaustion (Schwartz et al. 1993). Chalder et al. also said that fatigue includes two dimensions: mental fatigue and physical fatigue (Chalder et al. 1993). Others considered that fatigue contains five dimensions, but that the dimensions themselves differ. The former includes "general fatigue, physical fatigue, decreased activity, lack of motivation, and mental fatigue" while the latter contains "lack of energy, physical fatigue, physical discomfort, lack of motivation, and sleepiness "(Smets et al. 1995; Ahsberg 2000). Finally, Helen thought that fatigue is a single dimension of physical disease (Helen et al. 2003).

As mentioned above, scholars have done lots of studies about the definition and classification of fatigue but haven't yet reached a concensus. The relatively approved classification of fatigue is that fatigue includes psychological fatigue and physiological fatigue. Psychological fatigue refers to inattention, retardation of thinking, mental tension such as fickleness, anxiety, irritability, being consciously bored with work, etc. Physiological fatigue includes physical fatigue and mental fatigue. Physical fatigue is the phenomenon of decline or even loss of working ability due to repeated muscle contraction and diminished energy. Mental fatigue is the phenomenon caused

by excessive consumption of energy so that brain cells are damaged and brain activity is forced to slow down or even stop. Fatigue can be considered a temporary protective physiological response that can protect people from experiencing exhaustion.

2.2 Chronic Fatigue Syndrome

CFS is a syndrome that exhibits persistent or repeated severe fatigue (more than 6 months) as its main feature, and is often accompanied by a variety of physical and neuropsychiatric symptoms including memory loss, headache, muscle pain, joint pain, sleep disorders, and depression.

CFS is a systemic syndrome highlighting long-term extreme fatigue as the main manifestation. Furthermore, this long-term extreme fatigue cannot be relieved after rest. CFS is also accompanied by a series of physical symptoms and cognitive disorders, such as a sore throat, memory disorders, inattention, headache, and other clinical manifestations. It should be emphasized that these clinical manifestations are symptoms rather than signs. If tonsillitis or enlargement of lymph nodes is present, other diagnoses should be found in time.

3 Diagnosis of CFS

The diagnostic criteria for CFS have developed throughout history, and there is no gold standard for worldwide diagnosis of CFS. In 1988, **the US Center for Disease Control (CDC)** developed diagnostic criteria for the first time (Holmes et al. 1988), and revised it in 1994 (Fukuda et al. 1994). At the same time, Britain, Australia, Japan and other countries also developed diagnostic criteria suited to the characteristics and symptoms of CFS in their own countries.

3.1 Diagnostic Criteria of US CDC in 1988

The US **CDC** first outlined the criteria necessary for diagnosing CFS in 1988 and based diagnostic criteria on the presence of certain signs and symptoms. Signs and symptoms were divided into main and secondary diagnostic criteria.

3.1.1 Main Diagnostic Criteria

(1) Persistent or repeated fatigue for more than six months that cannot be significantly alleviated with bed rest. Fatigue may even be severe enough to reduce or impair average daily activity to below 50% of the patient's premorbid activity level.
(2) Before CFS can be diagnosed, other chronic diseases that could explain fatigue (such as cancer, autoimmune diseases(AID), chronic subacute bacterial infections, endemic infectious diseases, fungal diseases, parasitic diseases, chronic mental illness, neuromuscular disease, endocrine disease, drug dependency or abuse and other pulmonary, cardiac, gastrointestinal, hepatic, renal, or hematologic disease, etc.) must be ruled out.

3.1.2 Secondary Diagnostic Criteria

Symptoms or Medical History: Persistent or Recurrent Symptoms for Six Months or More Than Six Months

(1) Mild fever: oral temperature 37.5–38.6 °C;
(2) Sore throat;
(3) Enlargement or pain of the neck or armpit lymph nodes;
(4) Muscle weakness;
(5) Muscle discomfort or myalgia;
(6) Prolonged (24 h or greater) generalized fatigue after levels of exercise that would have been easily tolerated in the patient's premorbid state;
(7) Generalized headaches;
(8) Migratory arthralgia without joint swelling or redness;
(9) Neuropsychological symptoms: photophobia, transient visual scotomata, forgetfulness, excessive irritability, depression, inability to concentrate, and difficulty thinking;
(10) Sleep disturbance (hypersomnia or insomnia);
(11) Acute or subacute in onset.

Physical Criteria

(1) Mild fever (oral temperature between 37.6 and 38.6 °C, or rectal temperature between 37.8 and 38.8 °C;
(2) Nonexudative pharyngitis;
(3) Palpable or tender anterior or posterior cervical or axillary lymph nodes (diameter < 2 cm).

3.1.3 Diagnostic Basis

(1) 2 items of main criteria + 6 or more items of symptoms criteria + 2 or more items of sign criteria;
(2) 2 items of main criteria + 8 or more items of symptoms criteria.

The following are the main deficiencies of the diagnostic criteria in 1988:

(1) The standard is too strict and difficult to be used in practice, which will probably cause some CFS patients to be missed;
(2) The diagnosis mainly relies on subjective symptoms and clinical features and lacks objective laboratory parameters. Thus, there may be potential diseases or reasons to explain the chronic fatigue in patients diagnosed with CFS;
(3) Other diseases that consider chronic fatigue as the main manifestation (such as nerve disorders, fibromyalgia) can meet this criteria, and therefore can cause overlapping diagnoses;
(4) The standard does not explicitly classify the cases with different differences.

3.2 Diagnostic Criteria of US CDC in 1994

Diagnostic criteria:

A. Persistent or repeated chronic fatigue that cannot be explained by clinical assessment. Fatigue is newly-onset or has a clear start (not a lifelong occurrence); it is not the result of continuous physical work; it can't be significantly relieved with bed rest; it leads to an obvious decrease in levels of work, educational, social or individual activity.
B. 4 items or more of the following symptoms occur simultaneously; these symptoms are persistent or repeated for six months or longer, but they should not predate fatigue;

   (1) Memory loss or impairment in concentration;
   (2) Sore throat;
   (3) Tender cervical or axillary lymph nodes;
   (4) Muscle pain;
   (5) Multi-joint pain without joint swelling or redness;
   (6) Headaches of a new type, pattern, or severity;
   (7) Unrefreshing sleep;
   (8) Post-exertional malaise lasting more than 24 h.

Diagnostic basis:
Item A is a prerequisite, and 4 or more symptoms are required in item B.
Evaluation criteria/standard and process:

(1) Comprehensive and detailed medical history taking that includes: whether or not medical and psycho-social events occurred before fatigue, whether depression

or other mental illnesses are present, whether there is a history of symptoms that can't be explained by current medicine, whether there is a history of abuse in alcohol or other substances, types of medication taken, diet, etc.

(2) Checking of mental state: Confirm that there is no abnormity with emotion, intellect, memory, or personality. Pay special attention to possible symptoms of depression or anxiety, self-destructive thoughts, and observable signs such as psychomotor retardation. For mental or neurological abnormalities, a proper mental, psychological, or neurological assessment needs to be done.

(3) A comprehensive physical examination.

(4) A minimum amount of routine laboratory tests including: full blood count(CBC) and WBC classification, erythrocyte sedimentation rate(ESR), serum glutamic pyruvic transaminase(GPT/ALT), total protein(TP), albumin(ALB), globulin(GLB), alkaline phosphatase(AKP), calcium, phosphorus, blood glucose(GLU), blood urea nitrogen(BUN), electrolytes, creatinine(Cr), Thyrotropin, urine routine.

Symptoms of chronic fatigue need to be excluded if:

(1) There is a primary disease that could explain the chronic fatigue, such as hypothyroidism, insomnia, or iatrogenic fatigue caused by side effects of medicine;

(2) The chronic fatigue is caused by diseases that are clearly diagnosed clinically but difficult to treat under current medical conditions, such as acquired immunodeficiency syndrome (AIDS) or systemic lupus erythematosus (SLE);

(3) There is a past or present diagnosis of a severe major depressive disorder, bipolar disorder, dementia, anorexia nervosa, or neuropathic bulimia;

(4) Various bad habits are exhibited within 2 years before symptoms such as smoking or alcohol abuse;

(5) Severe obesity is present, BMI > 45.

3.3 Diagnostic Criteria in Other Countries

3.3.1 The Diagnostic Criteria of Canada in 1990 (Lloyd et al. 1990)

(1) Persistent or repeated systemic fatigue, aggravating after slight activity, results in a significant impact on daily activities, and lasts for more than 6 months;

(2) Neuropsychiatric dysfunction including impairment in concentration, manifested as difficulty in mental activity that was easily completed before; new short-term impairment in memory;

(3) Must exclude other diagnoses by medical history, physical examination, and investigation.

3.3.2 Diagnostic Criteria Britain Established in 1991 (Sharpe 1991)

(1) Fatigue is the main symptom;
(2) Clear occurrence time, its duration is less than a life cycle;
(3) The fatigue is severe, incapacitating, and affects the body and brain functions; fatigue symptoms should last at least six months; if it is intermittent during this period, the fatigue should be present at least 50% of the time;
(4) Accompanied by other symptoms, especially myalgia, mental and sleeping disorders;
(5) There are other diseases that can cause chronic fatigue and can be determined through medical history and physical examination. Exclude patients with the following conditions: patients with schizophrenia, manic depression illness, substance abuse, eating disorders or encephalosis. Other mental diseases need not be excluded (including depressive illness, anxiety, and hyperventilation syndrome).

Britain regards CFS as a disease, which appears after infection or a disease, which is connected to a current infection, and can be considered a post-infection fatigue syndrome. Post-infection fatigue syndrome is a subtype of CFS, whose diagnostic criteria meet the CFS's diagnostic criteria, and simultaneously meets the following additional criteria: the disease is definitely caused by infection, and infection was confirmed by laboratory evidence; this syndrome occurs after infection and persists for six months or more.

3.3.3 Diagnostic Criteria That the Ministry of Health and Welfare of Japan Established in 1992 (Kitani et al. 1992)

Diagnostic criteria:

A. An essential condition

(1) Severe fatigue symptoms that greatly affect life, persistent or recurrent for six months or more (severe fatigue refers to the fatigue that can't be restored after short-term rest; patient cannot do housework, and must often stay in bed).
(2) Other disorders must be ruled out.

B. Secondary condition

(1) The following symptoms persist or recur for more than 6 months: (1) mild fever; (2) sore throat; (3) enlargement of the neck or armpit lymph nodes; (4) unexplained decreased muscle strength; (5) muscle pain or discomfort; (6) general tiredness for more than a day after slight work; (7) headache; (8) migratory joint pain; (9) mental, neurological symptoms; (10) sleep disorders (drowsiness or insomnia); (11) the main symptoms occur within days or hours from the onset of an attack.

(2) Physical signs (appear at least twice in a month): (1) mild fever; (2) exudative pharyngitis; (3) the enlargement of neck or armpit lymph nodes.

Diagnostic basis:
A diagnosis: 2 items of A + more than 6 items of B (1) + 2 items of B (2); or 2 items of A + more than 8 items of B (1).

B suspicious: with 2 items of A but the conditions of B does not meet the criteria.

Since the diagnostic criteria of CFS; established by the CDC in l988, were first put on trial, they have since been adopted by researchers to various degrees. However, due to the fact that some of the content in the criteria are difficult to understand or operate based on, and that there are disagreements on the classification of chronic fatigue cases with mental illness, the criteria is modified frequently in practice. Countries like Japan, Britain, and Australia loosen the criteria or give more detailed instructions using the epidemiological and clinical studies carried out in their countries, combined with the characteristics of their countries. Because of the non-specificity of the clinical manifestations of CFS, it is easy to have overlapping symptoms with other diseases, which may cause difficulties in diagnosis. Currently there is no clear sign, examination or laboratory indicators to support its diagnosis, and its diagnosis relies mainly on clinical symptoms and medical history. Thus, there are some differences in the diagnostic criteria for different countries.

In 1994, some international CFS researchers and doctors (including some from the United States, Australia, Britain, Italy, and Sweden) modified the previous criteria, and the modified criteria became the most widely accepted diagnostic criteria. It is a diagnosis of exclusion in most cases, and the definition and diagnosis of CFS remains to be further defined and improved.

To be clear, the above examinations are only meant for research, not for the diagnosis of CFS. Based on this, further examinations are needed in practice according to the circumstances of the particular patient, such as serological tests (EB virus, rotavirus, enterovirus, and Candida albicans), immune function tests, imaging studies (including magnetic resonance imaging and radiation scans of head), etc. to assist diagnosis and to exclude other diseases with clear causes.

3.4 Current Diagnostic Criteria

Currently there are no golden diagnostic criteria for CFS, so most researchers are using the diagnostic criteria of the US CDC established in 1994.

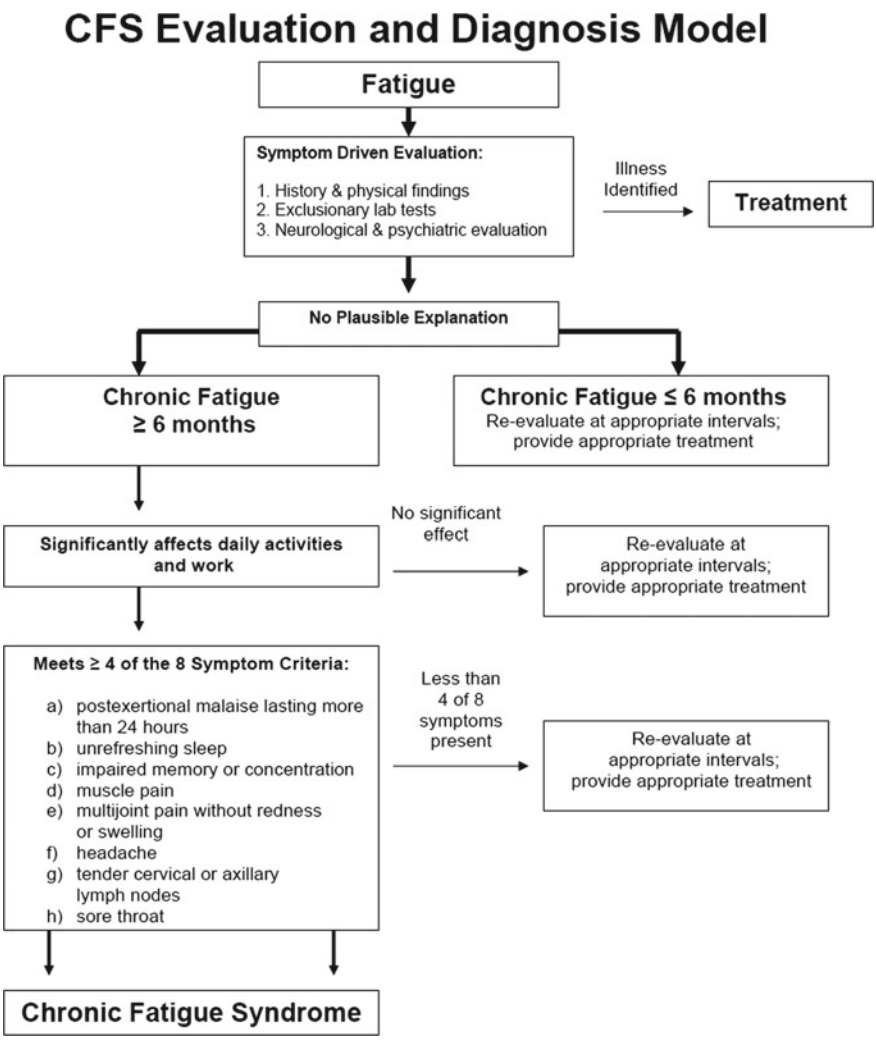
(1) Persistent or repeated chronic fatigue that can't be explained by clinical assessment, the fatigue is newly-onset or has a clear start (not as long as life cycle), it is not the result of continuous physical work, and it can't be significantly relieved with bed rest:
(2) Patients have an obvious decrease in the levels of work, education, social, or individual activity.
(3) 4 items or more of the 8 following symptoms appear simultaneously:

a. Obvious memory loss or impairment in concentration;
b. Headache of a new type, or severity;
c. Sore throat;
d. Tender cervical or axillary lymph nodes;
e. Muscle pain;
f. Joint pain without joint swelling or redness;
g. Unrefreshing sleep;
h. Post-exertional tiredness lasting more than 24 h.

The diagnosis of CFS is a diagnosis of exclusion, and should be made based on the exclusion of other diseases. The clinical manifestations of CFS is non-specific, and has no clear manifestation upon examination,, no abnormal laboratory tests or physical examinations, which all make diagnosis difficult due to symptoms overlapping with other diseases. When diagnosing a patient with CFS, we should have a comprehensive understanding of the patient's medical history, including the assessment of the factors that may cause fatigue such as the physical and psychological symptoms, social factors, medicine, etc; a comprehensive physical examination and mental status test; routine laboratory tests in order to exclude chronic fatigue due to other diseases such as chronic fatigue due to neuropsychic diseases, endocrine diseases, infectious diseases, and chronic wasting disease.

3.5 The Diagnosis Model of CFS

The recommended CFS diagnosis model by the American Chronic fatigue and immune dysfunction syndrome Committee (Chronic fatigue and immune dysfunction syndrome, CFIDS) is as follows:



4 Epidemiology

CFS was once described as "yuppie's flu", because it had high incidence among people in there 30 s or 40 s with high-income and a good educational background. Nowadays, due to fast working paces, eventful social lives, and fiercely competitive and highly challenging environments, people experience high levels of stress. Consequently, more and more people are troubled by CFS.

Fatigue is a very common symptom of CFS; a large survey done outside of the United States shows that more than 50% of people suffer from symptoms of fatigue

(Pawlikowska et al. 1994). The survey, which was performed from 2001 to 2002, showed that 12186 people out of 10 million suffered from chronic fatigue for at least six months (Bierl et al. 2004). In 2003, Reyes (Reyes et al. 2003) investigated\ 7162 people from 18 to 69 in the Wichita area of the United States and the results showed that 373 women and 83 men suffered from CFS in every 100,000 people. In 2004, Solomon's (Solomon and Reeves 2004) community survey found that middle-income people have a higher incidence of CFS than low-income people. Njoku (Njoku et al. 2007) conducted research in developing countries, and the results show that the incidence of CFS in Nigeria is higher than in the epidemiological investigation results of US communities.

Lorusso's survey in 2009 (Lorusso et al. 2009) shows that: the worldwide incidence of CFS is about 0.4–1%, the patients' peak age of onset is between 20 and 40 years old, the ratio of female-to-male patients is about 6:1, and the average duration is 3–9 years. It is estimated that over 800,000 people in the United States are suffering from chronic fatigue syndrome, and that there are about 240,000 CFS patients in the UK.

As the study progressed, western scholars launched epidemiological studies among different groups. Social changes, diversity of thoughts, stress of entrance examinations, and concern about the future places severe physical and mental burdens on young people and causes the incidence of CFS to increase. The survey Jones conducted in 2004 (Jones et al. 2004) shows that the prevalence rate of CFS in young people is approximately 338 per 100,000. Rimes's investigation on 842 ordinary British teenagers and their parents in 2007 (Rimes et al. 2007) found that 30.3% of them have symptoms of fatigue, 1.1% have symptoms of chronic fatigue, 0.5% have manifestation of CFS.

Chinese scholars have begun epidemiological investigations as well. Yuan's survey in 2001 showed that 202 subjects out of 923 might have CFS; the CFS incidence in scientific and technical personnel is relatively high, accounting for 26.23% (Yuan 2001). In 2002, Zhang conducted a survey of 2000 residents in Beijing and Baotou. 39 cases met the diagnostic criteria for CFS, accounting for 1.95%, and the prevalence ratio of male-to-female was approximately 1: 2.8, suggesting that occurrence in women is higher than that in men (Zhang et al. 2004). Mao's research in 2003 showed that 37.7% of medical workers often feel fatigue, and that the prevalence of CFS among them was 19% (Mao et al. 2006). In 2004, Yao conducted a random survey of 1,013 cases aged from 20 to 50 in Hong Kong, among which there were 65 people with chronic fatigue syndrome, accounting for 6.4%, 118 people with idiopathic chronic fatigue; accounting for 11.6%, 92 people with prolonged fatigue; accounting for 9.1%, 310 people with general fatigue; accounting for 30.6%, 215 people with mild fatigue; accounting for 21.2%, and 213 people without fatigue; accounting for 21%. The prevalence in women was 7.00%, while the prevalence in men was 5.29%, but there was no statistically significant difference between the two genders (Yao and Qiu 2005).

A survey in 2005 showed that 68.4% of university teachers have varying degrees of fatigue. Also, the prevalence of CFS was 13.8%, suggesting that university teachers are at a high risk of developing CFS (Wu et al. 2005). Wu's research in 2006 shows

that 76.7% of medical workers have varying degrees of fatigue and the prevalence of CFS amongst the medical workers was 14.1% (Wu et al. 2006a, b). Furthermore, in 2007, Sheng-jie Zhang's survey, of nurses in operating rooms showed that people with fatigue accounts for 85.26% of nurses. This study confirmed the large number of literature reports that claimed that Chinese medical workers; especially nurses, are a high risk group for developing CFS. This may be related to occupational stress, workload, medical risks, as well as other factors (Zhang et al. 2007a, b).

5 Etiology and Pathogenesis

CFS has a high rate of incidence, it is a syndrome with severe and persistent fatigue as the main manifestation, and cannot be diagnosed without the exclusion of other chronic organic diseases or mental illnesses. The occurrence may be caused by a variety of factors. Up until now, the etiology and pathogenesis of CFS have not yet been fully elucidated; however, scientists have proposed different possible hypotheses through research, which are shown below.

5.1 Stress Factors

Stress is the sum of the non-specific responses of the body to various external or internal stimuli, it is a self-protective mechanism by the body to adapt to changes in the external and internal environment and to maintain a stable internal environment. Modern medicine thinks that stress is an important factor leading to or inducing chronic fatigue. Experiments and clinical studies have both indicated that long-term chronic stress is more likely to affect physical and mental health than acute stress. Moreover, it causes behavioral changes, functional disturbances, or even changes in tissue structure. It also speeds up the occurrence of diseases and the aging process (Shi et al. 2005). Between the two types of chronic stress, unexpected stress is more likely to have adverse effects on the body than predictable stress (Xiao and Mibofeny 1996; Luo et al. 1996). Scholars' investigations have found that CFS is closely related to stress (Korszun et al. 1999). With the constant changes in pace that occur in modern times, psycho-psychiatric stress due to various causes has an increasingly recognizable effect on CFS. Studies have found that many people had stressful events a year before the onset of CFS in a CFS group. In addition, three or more stress sources could more easily induce the occurrence of CFS, indicating that the risk of CFS disease is related to the number of stress sources (Steele et al. 1998).

5.2 Infection

Studies show that the occurrence of CFS is related to the EB virus (Epstein-Barr virus, EBV), Coxsackie virus, human herpes virus 6, human lymphotropic virus II, hepatitis virus, enterovirus and retrovirus (Jason et al. 2000; Sogolow et al. 2008). However, there has not been sufficient evidence to prove that CFS is caused by the microbial infection of a specific virus. In fact, many patients have no clinical or laboratory evidence of viral infection upon examination. Further research is needed in order to draw firm conclusions.

5.3 Abnormities in the Immune System

Some researchers found that CFS patients have an abnormal immune function, including the increase in surface activation markers of T-lymphocytes (Klimas et al. 1990). Ogawa found that L- arginine can significantly enhance the activity of natural killer cells in a healthy group, while CFS patients have no reaction to L-arginine, suggesting that CFS patients are defective in their modulation function (Ogawa et al. 1998). Bounous thinks the response of CFS patients' lymphocytes to cytokines is weak. Therefore, some people call CFS "chronic fatigue immune dysfunction syndrome."

Despite numerous studies on the relationship between the immune system and the onset of CFS, only a few of them showed abnormal results, and some of these studies lacked control groups (Bounous and Molson 1999).

5.4 Abnormalities in the Nervous and Endocrine Systems

Some researchers have found that there are abnormalities in the nervous system and the endocrine system in CFS patients, and this is supported by the related experimental research and clinical studies.

The hypothalamic-pituitary-adrenal axis is an important human neuroendocrine system. It has been found that the negative feedback regulation of the hypothalamic-pituitary-adrenal axis in CFS patients is poor, this might be caused by a decreased activity of corticotropin releasing hormone (CRH), or might be a response to stress.

Scott's study shows that the reaction of adrenal glands to the corticotropin-releasing hormone decreases in CFS patients, and that the right and left adrenal glands shrink in size by 50% as well (Scott et al. 1999). Chen's research confirms that the amount of norepinephrine and dopamine tends to increase in the hypothalamus and pituitary gland in rats with chronic fatigue, and that the amount of 5-hydroxytryptamine decreases significantly. The increased dopamine and decreased

5-hydroxytryptamine may be related to chronic fatigue to some extent (Chen et al. 2000).

Chronic fatigue syndrome and depression have many similar symptoms, which brings about difficulty in distinguishing them from each other. However, the two illnesses have differences in cerebral regional blood flow and glucose metabolism. Siobban uses ROI (region of interest) and SPM (statistical parametric mapping) to assess the blood flow of CFS patients with no depressive symptoms, and patients with depression. The results show that, other than the similar increase in the cerebral perfusion to the right thalamus, globus pallidus and putamen, CFS patients also experience an increase in the cerebral perfusion to the left thalamus, while patients with depression have relatively low perfusion to the left prefrontal gyrus cortex (Siobhan et al. 2000). Tirelli's study suggests that the right central frontal cortex and the brain stem of CFS patients have significantly low metabolisms, and that the bilateral caudal medial frontal cortex of patients with depression has an extremely low metabolism while the brain stem is normal. Therefore, low metabolism in the brain stem is an indicator of CFS (Umberto et al. 1998).

5.5 Psychological and Social Factors

Psychological and social stress factors are important factors that can cause and impact CFS. Theorell's study finds that a high proportion of negative life events in CFS patients occur a few months before the onset of the disease (Theorell et al. 1999). The survey of outpatients conducted in Beijing in 2000 found that the incidence of CFS patients is context-specific; CFS occurs more easily in muggy environments, in people under stress, in people with prolonged laziness, or people feeling down. On the other hand, comfortable and cool environments and doing something happy and meaningful can reduce fatigue (Wang et al. 2000). A questionnaire survey of college students with CFS symptoms pertaining to exam stress found that college students' excessive attention to the results of exams, their subjective cognition of the exam content, and the chaotic rhythm of the life and learning environment are the most important factors that induce and impact exam stress. Many studies reveal that CFS occurs mainly in highly educated people, especially women (Zhang and Tang 2003).

5.6 Nutritional and Metabolic Disorders

Heap suggests that poor regulation of B-vitamins may be related to CFS (Heap et al. 1999). Liu's study demonstrates that the essential fatty acid level of red blood cell membranes in CFS patients is significantly lower than in the normal group (Liu et al. 2003). CFS patients are exposed to long-term stressful situations, and this may lead to the decreased activity of certain enzymes in the body, causing reduced synthesis

of essential fatty acids and decreased levels of essential fatty acids in cell membranes (Mills et al. 1994).

5.7 Heredity

Recent studies began to focus on the relationship between heredity and CFS. Some studies found that the expression of leukocyte antigen II in CFS patients was significantly different from the control group, suggesting that genetic factors have certain effects on inducing CFS (Walsh et al. 2001; Hickie et al. 1999). Alicia K recently used molecular biotechnology to study the traits of CFS and found that CFS patients may have differentially expressed genes (Smitha et al. 2008).

5.8 Allergic Factors

It has been reported that the incidence of CFS is related to allergic factors. Nawab reported that CFS patients are sensitive to exposure to chemicals, and found that many CFS patients suffer from allergic rhinitis and asthma, as well as significant irritable bowel syndrome (IBS), infectious mononucleosis syndrome, herpes, etc. (Nawab et al. 2000).

5.9 Other Factors

Medical scientists from Tezukayama University and Oxford University found that tryptophan can be a cause of CFS. Excessive uptake of tryptophan by the brain, inhibits body actions, and brings animals into a state of extreme fatigue. Thus, we should prevent uptake of tryptophan by the brain. However, the study also found that prematurely limiting intake of tryptophan might impact growth, so the intake of tryptophan should meet the physiological needs of the body (Wang et al. 2005).

6 CFS Treatment

Traditional Chinese Medicine believes that fatigue is a multi-organ, multi-system dysfunction disease caused by the consumption of “qi” and “blood”. Under the guidance of the Chinese medicine theory, acupuncture can regulate meridians and acupoints, the “yin- yang” balance of patients’ “Zang-Fu” organs, “qi” and “blood”, and emotions. It can also strengthen “healthy qi” to eliminate pathogenic factors, promote blood circulation, and enhance immune function; in order to adjust physical

and psychological changes, and to achieve a dynamic balance of the body functions. The specific methods of clinical acupuncture treatment include acupuncture, moxibustion, acupoint application, cupping, auricular acupuncture and scraping, etc. These methods can be used individually, or as a combination of two or three methods. They are easily accepted by patients due to advantages including less injury, significant effects, and simple operation, etc. Acupuncture can also be used as a preventive treatment not only for CFS patients, but also for sub-healthy and healthy people, which promises a wide application prospect.

"Qi" and "blood" are both basic elements indispensable to the body's physiological activity. They complement each other and are dependent on each other. The *Nanjing (the Canon of Difficult Issues)* states: "Qi invigorates and blood nourishes." The special pathways by which "qi" travels throughout the body along are called "meridians".

6.1 Acupuncture Treatments

Acupuncture, considered as a new alternative treatment in western cultures, has been practiced as a medical treatment for over 5,000 years. The primary function of acupuncture is to regulate "yin-yang" and to help the body restore its balance. Over the years, technological developments have taken place, and there are now a few related procedures that fall into the range of acupuncture treatments.

6.1.1 Simple Acupuncture

There are an increasing number of studies and clinical literature reports about acupuncture treatment for CFS, specifically because electro-acupuncture (EA) and comprehensive treatment are commonly used in its treatment. There is relatively less literature about simple acupuncture, and the existing literature is mainly divided into two parts: one observes the therapeutic effects before and after the treatment for CFS based on the related meridians and acupoints. The other chooses certain points first and then combines them with corresponding points or areas based on the different manifestations and patterns of CFS.

Shi used the rapid insertion method to treat CFS. She choose the acupoints Baihui (GV20), Danzhong (CV17), Zhongwan (CV12), Guanyuan (CV4), Neiguan (PC6), and Zusanli (ST36), and achieved good therapeutic effects according to clinical observation (Shi 2001). Zhang used acupuncture treatments on main acupoints Zusanli (ST36), Sanyinjiao (SP6), Guanyuan (CV4) and Baihui (CV20) to treat CFS, she then measured the contents of humoral immunity and cellular immunity indicators before and after treatment, and found that acupuncture treatment can correct abnormal levels of alexin and can regulate cellular immunity (Zhang 2002). Wang used acupuncture on acupoints Baihui (GV20), Danzhong (CV17), Zhongwan (CV12), Qihai (CV6), Guanyuan (CV4), Hegu (LI4), Zusanli (ST36), Sanyinjiao (SP6), Taichong (LR3),

Taixi (KI3), Liver Shu (BL18), Spleen Shu (BL20), Kidney Shu (BL23) and other points to treat 32 CFS patients, and set a control group that used acupoints not on the meridians (2 cm by the acupoints) for acupuncture treatment. Treatment was done three times a week, with a total of 14 treatments per patient, the World Health Organization Quality of Life Brief **(WHOQOL-BREF)** Scale was used to evaluate the survival quality of the patients in the 2 groups before and after treatment. The results demonstrated that the points for a person's physical condition, an individual's subjective feeling of health, and total points on the WHOQOL Scale of the acupoints group significantly improved after treatment, while the points for psychological and social relations, environmental areas, and individual's subjective feeling of life quality had no significant change. Furthermore, for the non-meridian acupoints group (the control group), the points of environmental area were significantly lower than before, while other areas showed no obvious changes (Wang et al. 2009). Chen used acupuncture treatment for CFS, and applied the fatigue scale to evaluate the therapeutic efficacy. The research found that applying acupuncture on patients' Renying (ST9), Fengfu (GV16), Baihui (GV20) and other acupoints can significantly decrease patients' mental fatigue score, physical fatigue score, and total score (Chan XH et al. 2010). Song chose acupoints Baihui (GV20), Danzhong (CV17), Zhongwan (CV12), Qihai (CV6), Guanyuan (CV4) and bilateral Hegu (LI4), Zusanli (ST36), Sanyinjiao (SP6), Taichong (LI3), Taixi (KI3), Liver Shu (BL18), Spleen Shu (BL20) and Kidney Shu (BL23) to treat CFS. Also, she performed reinforcing manipulation of rotation on the acupoints Zusanli (ST36), Qihai (CV6), Guanyuan (CV4), Spleen Shu (BL20) and Kidney Shu (BL23), and even-reinforcing and even-reducing manipulation on other acupoints. After 14 treatments, the score of patients' Visual Analog Pain Scale (VAS) was significantly reduced. Thus we believe that acupuncture treatment can effectively relieve pain for CFS patients (Song et al. 2010).

Yan and Li (2003) used Baihui (GV20), Neiguan (PC6), and Zusanli (ST36) as the main acupoints in their study, they added and subtracted acupoints based on syndrome differentiation to treat CFS. They found that acupuncture on Baihui (GV20), Neiguan (PC6), and Zusanli (ST36) can effectively improve the score of BELL's chronic fatigue syndrome (Yan and Li 2003). Chen considered nourishing the kidney to tranquilize the mind, reinforcing "qi", and nourishing "blood", as the principles for treating CFS. He chose the acupoints Baihui (GV20), Yintang (GV29), Neiguan (PC6), Shenmen (HT7), Qihai (CV6), Zusanli (ST36), Sanyinjiao (SP6), and Taixi (KI3), and demonstrated positive effects (Chen 2004). Tang used treatment based on syndrome differentiation, and selected Baihui (GV20), Zusanli (ST36), Sanyinjiao (SP6), and Guanyuan (CV4) as the main acupoints, and achieved satisfactory results (Tang 2005). Liu divided 110 patients into 5 patterns based on syndrome differentiation: the kidney deficiency and heart timidity pattern, the yin deficiency and yang hyperactivity pattern, the stagnation of the liver-qi and blood deficiency pattern, the dampness stagnancy due to spleen deficiency pattern, and the qi deficiency and blood stasis pattern. Liu et al. (Liu et al. 2009) chose acupoints based on syndrome differentiation, and applied acupuncture treatment once a day, 3–4 times per week for the acupuncture group, and applied decoction according to syndrome-types for the control group every day. The therapeutic effect was obvious

for most patients after two months of continuous treatment. It is considered that acupuncture therapy treatment demonstrates faster improvement of symptoms than the decoction, and that the recovery time for the acupuncture group is significantly shorter than the recovery time for the control group.

6.1.2 Electroacupuncture (EA)

Electro-acupuncture is a common method of clinical acupuncture treatments on CFS patients. It is a combined method of using acupuncture and electrical stimulation to treat diseases. Electro-acupuncture achieves the "de-qi" sensation after inserting the needle into acupoints, and then energizes the needles with a micro-electric current similar to human bioelectricity. Wang used electro-acupuncture on the Back-Shu points of the five Zang organs to treat 40 patients with CFS, and observed the score changes of the Fatigue Assessment Instrument (FAI) and Symptom Checklist (SCL-90) before and after treatment. The results showed that the scores of each factor in FAI and SCL-90 were significantly lower after treatment, and the difference between the two groups was of statistical significance ($P < 0.01$) (Wang and Xiong 2005). Therefore, Xiong believes that electro-acupuncture on the Back-Shu points of the five Zang organs is an effective method to treat CFS. The therapeutic effect of electro-acupuncture for CFS may be related to the improvement of patients' immunity; electro-acupuncture can significantly improve factors such as somatization, sleep disorders, depression, anxiety, psychosis, and interpersonal relationships (Xiong 2005). Yi-hui Zhu randomly divided 60 cases of CFS patients into the electro-acupuncture on acupoints group and the electro-acupuncture on non-acupoints group, with 30 cases in each group. After 2 courses of treatment, the Fatigue Severity Scale (FSS), physical and mental health reports (SPHERE), VAS Scale, and the Short Form Health Survey (SF-36) were used to evaluate the fatigue level, potential symptoms, pain degree and the life quality of patients. The results showed that after treatment, the scores of FSS, SPHERE, and the VAS scale of the two groups declined, while the scores of each SF-36 dimension rose significantly. This shows that, the EA on the acupoints group was better than the EA on the non-acupoints group ($P < 0.01$). The l month and 3 month follow-ups after treatment showed that the scores of FSS, SPHERE, and the VAS scale were higher than those after treatment, but the scores of the EA on acupoints group was lower than that of the EA on non-acupoint group ($P < 0.01$) and the scores of each SF-36 dimension for both groups were lower than those after treatment. Besides the general health dimension, other dimensions of the EA on the acupoints group are higher than those of the EA on the non-acupoint group ($P < 0.01$). These results suggest that EA has a clear effect to a certain degree on relieving clinical fatigue level and associated symptoms of CFS patients (Zhu et al. 2008a, b). Using "Huatuo Jiaji" points as the main points, Li energized the electro-acupuncture device after puncturing, then adjusted it to the condensation-rarefaction wave, and chose the appropriate intensity that patients could tolerate. Treatment was done for 30 min at a time, once per day. After EA treatment, the auricular application was done, using the auricular points Shenmen, sympathetic, and subcortex as the main

points. Patients were asked to press auricular acupoints regularly in the morning, afternoon and evening, 3 times a day, for 5 min each time. 10 days was considered the length of one course of treatment, and a total of 3 courses were used. The total effective rate was 93.75% (Li et al. 2005).

6.1.3 Blood-Letting Acupuncture

The plum-blossom needle tapping method, or the three-edged needle blood-letting method, is an effective method of treatment of CFS. Liao used the alternate tapping method on acupoints to treat CFS, and obtained satisfactory results after 18 courses of treatment. The specific selection of acupoints for the two groups were Taiyang(EX-HN4), Heart Shu(BL15), Lung Shu(BL13), Dazhui(GV14), and Zusanli(ST36). The operation steps were as follows: Start with routine cleansing, then taking the acupoint as the center perform plum-shaped scattered acupuncture on the point, 5 pricks for each point, and apply bloodletting combined with cupping. Alternate between two groups of acupoints, do bloodletting every three days, and a positive effect will be achieved (Liao 2004). Jiang used three-edged needles to stimulate the shoulders for CFS treatment. The procedure was as follows: choose the stimulation area in the upper central portion of the deltoid on the acromion and the humeral greater tuberosity, then ask patients to abduct arm to a horizontal position, find the area 5 cun posterior to the depression of the external acromioclavicular joint, and use a three-edged needle to continuously prick 3–4 times at various points with a minimal bleeding (Jiang 2005a, b).

Plum-blossom needle tapping is relatively superficial compared to the three-edged needle, so the stimulation site can be more extensive. Wang reported using the plum-blossom needle, and tapping Back shu points for the treatment of CFS. The procedure was as follows: tap point by point from Lung Shu (BL13) to Bladder Shu (BL28); tap until local skin flushing or slight bleeding, and then apply filiform needle acupuncture on Baihui (GV20) Sishencong (Ex-HN1), Taiyang (Ex-HN4), Neiguan (PC6), Shenmen (HT7), Qihai (CV6), Zusanli (ST36), and Sanyinjiao (SP6) as the control group. It is considered that the therapeutic effect of tapping on Back-shu is better than that of filiform acupuncture (Wang and Song 2005).

6.1.4 Acupoint Application

Acupoint application is a therapy theoretically based on the Chinese meridian theory, it is an acupoint treatment that grinds herbs into powder, then uses water, vinegar, rice wine, egg white, honey, vegetable oil, cooling oil, decoction or even saliva to make them into mush. Furthermore, it can also use solidified fat (such as Vaseline, etc.), yellow vinegar, rice, or jujube paste to either make them into ointments, pills or cakes. Decoct the decoction into cream, or scatter the herbal powder on the plaster, and then stick it to the acupoint or the certain part of the surface. Chen observed the effect of the application of Jiaweisini decoction to the back-shu points of the five Zang-organs

on CFS patients' fatigue symptoms and their endocrine function. They think that the application of Jiaweisini decoction to the back-shu points of the five Zang-organs can effectively improve the fatigue symptoms of CFS patients in liver stagnation and spleen deficiency patterns, and can improve their serum ACTH and CORT contents (Chen et al. 2014). Xue Chen observes the impact of the transdermal delivery of a "health-keeping medicine plaster" to Shenque (CV8) on the immune function of CFS patients in qi and blood deficiency patterns (Chen and Zhong 2012). Research shows that the application of a "health-keeping medicine plaster" to Shenque (CV8) has no clear effect on the immunoglobulin and NK cells, but can improve the C3, C4 contents, so the "health-keeping medicine plaster" can therefore, improve the cellular immune function of CFS patients in qi and blood deficiency patterns. Qiuhua Shan considered that acupoint application could treat CFS. Medicine application to the acupoint can make the medicine permeates quickly, more efficiently regulate the "Zang-Fu" organs and "qi and blood", strengthen "healthy qi" to eliminate pathogenic factors, improve immune function, and thus displaying anti-fatigue and sedation effects. It was reported that choosing herbs that can tonify "qi and blood", nourish "yin and yang", activate tendons and collaterals, and select the "back-shu" points of the five "Zang-organs" or Shenque (CV8) receives satisfactory results (Shan et al. 2003). Yuelin Zhang applied self-made "Fuzhengquxie" (strengthening "healthy qi" to eliminate pathogenic factors) plaster to the navel for 24 h to treat 32 patients with CFS. It was found that acupoint application can effectively relieve anxiety, improve sleep, and promote energy recovery (Zhang 2000).

6.1.5 Acupoint Catgut Embedding

Catgut embedding therapy is the combined therapy of acupuncture theory and modern physics, it works by transferring the stimulating information and energy of the physical-biological action, and the biochemical changes produced by the catgut embedded in the acupoints to the body by meridians in order to treat disease. Tan (Tan 2006) considers that acupoint catgut embedding can not only increase the weight of rat models in chronic fatigue, improve their emotional response, and increase their exploratory behavior, but also can reduce their glucocorticoid content, and can regulate neurotransmitter disorders of the hypothalamus, pituitary, and peripheral monoamine. Tan presumes that this might be the mechanism of catgut embedding therapy for CFS. Yang used the catgut embedding method and the traditional acupuncture method at the same acupoints, and found that the catgut embedding method has more advantages for treating CFS (Yang et al. 2008). Yang further reported using the catgut embedding method to treat the different patterns of CFS. Through clinical observation, he considered that the therapeutic effect of the catgut embedding method is more significant for deficient spleen qi pattern and liver qi stagnation pattern, while the effect on phlegm stasis pattern is not as good (Yang et al. 2007). Li chose Spleen shu (BL20), Liver shu (BL18), Kidney shu (BL23), Ge shu (BL17), Zusanli (ST36), Guanyuan (CV4), Baihui (GV20), and Danzhong (CV17) as the main acupoints, adding or subtracting acupoints based on syndrome differ-

entiation, and used acupoint catgut embedding therapy to treat 120 CFS patients. He used No. 000 catguts measuring about 1 cm-2 cm in length and achieved good results (Li 2011). Qu observed the impact of easy acupoint catgut embedding method and the traditional acupuncture method on the CFS patients' score of quality of life (WHOQOL-BREF), score of clinical symptoms, score of Fatigue Assessment Instrument (FAI), CD3, CD4, CD8, and CD4/CD8 contents in peripheral blood, as well as serum IgG, Iga, IgM contents. He compared the impact of these two methods on patients' life quality and clinical efficacy. Results showed that the easy acupoint catgut embedding method and the traditional acupuncture method can effectively improve the CFS patients' symptoms in both the physiological and the psychological fields, thereby improving the quality of life. They also demonstrated that (1) the results of the easy acupoint catgut embedding is better than that of the traditional acupuncture; (2) the impact of the embedding method on personal evaluation of general health is equivalent to that of acupuncture and (3) neither the embedding method nor acupuncture showed any improvement in the individual total score of life quality, the social relation field and the environment (Qu 2013).

6.1.6 Acupoint Injection

Acupoint injection, also known as "hydro-acupuncture", is a method where Chinese or western medicine is injected into the relevant acupoints to treat diseases. Most injection medicine used is modern purified medicine, so this therapy uses the advantages of traditional acupuncture combined with the efficacy of modern medicine. In recent years, there has been increasing concern about the clinical application of acupoint injection. Su observed the clinical efficacy of the astragalus and salviae miltiorrhizae injection to the Liver shu (BL18), Spleen shu (BL20) and Kidney shu (BL23). He randomly divided 180 CFS patients into 2 groups. For the 92 cases in the treatment group, he injected 2 ml astragalus and salviae miltiorrhizae to the bilateral Liver shu (BL18), Spleen shu (BL20) and Kidney shu (BL23). For the 88 cases in the control group, he injected 2 ml astragalus and salviae miltiorrhizae to the bilateral Zusanli (DT36), Shousanli (LI10) and Fenglong (ST40). The results showed that injecting astragalus and salviae miltiorrhizae injection to Liver shu (BL18), Spleen shu (BL20) and Kidney shu (BL23) is safe and effective (Su et al. 2009). Li used acupoint injection of astragalus to treat CFS patients with qi deficiency pattern, he chose Baihui (GV20), Zhongwan (CV12), Guanyuan (CV4) and bilateral Neiguan (PC6), Zusanli (ST36) Sanyinjiao (SP6), and Taichong(LR3), and alternated between the back-shu points of the five Zang-organs, and achieved good clinical efficacy (Li 2013). Nie used acupoint injection of Shengmai injection to treat CFS patients in yin deficiency pattern, he chose bilateral Zusanli (ST36), Sanyinjiao (SP6), Chize (LU5), Taichong (LR3), Taixi (KI3), Yinxi (HT6), and Zhongwan (CV12), and alternated between bilateral Heart shu (BL15), Lung shu (BL13), Liver shu (BL18), Stomach shu (BL21) and Kidney shu (BL23), and achieved good clinical efficacy (Nie 2014).

6.1.7 Auricular Acupuncture Therapy

Miao used auricular acupuncture therapy to treat 60 cases of CFS patients, he stuck tape with cowherb seed to the auricular points, the heart, lungs, spleen, liver, kidneys, sympathy, adrenal glands, shenmen, endocrine, subcortex, etc., and slightly rubbed them to trigger the sensations of heat, swelling and pain. The points were rubbed 3–5 times a day, 5 min each time. 7 days was considered one course of treatment. After four courses of treatment, the total efficiency was 96.7% (Miao 2012). Shan believes that the ears are closely related to the Zang-fu organs and meridians, so the auricular points distributed on the auricle can regulate the function of the Zang-fu organs and meridians to treat diseases. Therefore, the use of acupuncture or buried needles, or pressing on the auricular points with seeds can regulate body functions. The commonly- used points are shenmen, sympathy, endocrine, subcortex, and occiput, combined with the points heart, liver, spleen, kidney, stomach and others depending on the syndrome differentiation Shan and Sun (2003). Yuan observed the clinical efficacy of auricular acupuncture combined with acupoint catgut embedding therapy for CFS. He believed that it would be an effective clinical treatment for CFS (Yuan et al. 2014). Auricular acupuncture with acupoint catgut embedding therapy has fewer clinical side effects than traditional acupuncture, it is easy to perform and has a long stimulating time, so it is worthy of clinical application.

6.1.8 Abdominal Acupuncture

"Bo's abdominal acupuncture" is a new acupuncture therapy advocated by professor Bo in recent years. Bo regards that there is not only a circulatory system related to the qi and blood circulation of the whole body in the abdomen, but also an advanced general control system of the body that is regulated by stimulating the abdominal acupoints that centers Shenque (CV8). This system can regulate the imbalance of the "Zang-fu" organs to treat systemic diseases (Bo 1999). Yong Huang used abdominal acupuncture to treat 40 CFS patients and he selected the abdominal points Zhongwan (CV12), Xiawan (CV10), Qihai (CV6), Guanyuan (CV4) and bilateral Huaroumen (ST24), and Wailing (ST26). After inserting the needle, Bo either rotated the needle without lifting-thrusting manipulation or rotated the needle slightly with slow lifting-thrusting manipulation, he kept the needles in for 30 min, and treatment occurred once a day for 2 weeks. His results showed that abdominal acupuncture can significantly improve the CFS patients' fatigue, poor appetite, insomnia, forgetfulness, diarrhea, aches and pains, and can regulate both their physical and mental conditions, which shows that it has a positive role in regulating CFS (Huang et al. 2007). Da-yan Chen used scores of fatigue assessment instrument (FAI) to evaluate the efficacy of Bo's abdominal acupuncture to treat CFS, the results showed that the total efficiency of the abdominal acupuncture group is 94.34% (Chen et al. 2012), thus further confirming the therapeutic effect of abdominal acupuncture therapy for CFS.

6.2 Moxibustion

The moxa leaf (folium artemisiae argyi) is spicy, bitter to the taste and warm to the touch. It is a meridian tropism of the liver, spleen, and kidney meridians, having the effect of warming meridians to stop bleeding, and eliminating cold to stop pain. Also, it produces moderate heat when burned, which makes people feel comfortable and helps patients to avoid the pain and fear of acupuncture, so many patients accept its use.

Gou et al. observed the clinical efficacy of moxibustion treatment along meridians for treating CFS, and when used on a group of 60 random CFS patients the results showed that moxibustion along the Du meridian and the back-shu points increases clinical efficacy in treating CFS (Gou et al. 2004). The occurrence of CFS is closely related to the dysfunction of Du meridian and Bladder meridian. Using moxibustion along with meridians involves a wide range of operational acupoints/body parts and makes it more helpful and more efficient in terms of the treatment. Guo et al. selected two groups of acupoints (Guanyuan (CV4), Zusanli (ST36), Sanyinjiao (SP6), Liver shu (BL18), Spleen shu (BL20), and Kideny shu (BL23)) to perform mild moxibustion on with moxa sticks in CFS patients, with each acupoint being treated for 10 min. It illustrated that moxibustion on commonly-used tonifying acupoints and the "Back-shu" points can significantly improve the clinical symptoms of CFS patients. It can be used as a way in which patients can relieve fatigue and improve quality of life (Guo et al. 2007).

A clinical study by Zou showed that the efficacy of moxibustion on Shenque (CV8) to treat CFS is better than oral administration of fluoxetine (Zou 2011). Shenque (CV8), also known as the navel, is the "yang" point on the Ren meridian, it is connected from front to back to Mingmen (GV4) and is the place of life energy. Moxibustion on Shenque (CV8) is easy to operate because patients can operate on themselves.

Thermo-sensitive moxibustion is the process of suspended moxibustion, where the heat produced by burning moxa is directed onto the thermo-sensitive acupoints, so as to motivate the sensations of diathermy, heat expansion, heat transmission, distant heat with no (little) local heat, deep heat with no (little) superficial heat, non-thermal sensation, and the transmission of meridian qi, as well as to use individualized amounts of saturated non-sensitive moxibustion. It is reported that for now, this has been an effective treatment for CFS. Xiao-ming Rao chose Yintang (GV29), Shenmen (HT7), Taixi (KI3), Taichong (LR3), Sanyinjiao (SP6), and Zusanli (ST36), to treat with thermo-sensitive moxibustion. 63 CFS patients were randomly divided into the treatment group of thermo-sensitive moxibustion and the control group of herbal treatment. He then observed and compared the efficacy of thermo-sensitive moxibustion on CFS patients to the control group, the results confirmed that thermo-sensitive moxibustion has an effect on CFS (Rao et al. 2011).

Chen used mild moxibustion on Yongquan (KI1) to treat CFS, and had significant improvements in sleep disorder treatment (Chen et al. 2012). Gan-chen Xiao observed the clinical efficacy of moxibustion on the acupoints of the five "Zang-organs" to treat

CFS. He used acupoints of the five "Zang-organs" as the main points, and combined them with other corresponding acupoints depending on the syndrome differentiation. Results showed that both the scores of the clinical symptom scale and the laboratory tests had improvements (Xiao et al. 2014).

In addition to simple moxibustion, there are some treatments combining acupuncture with moxibustion. Zeng used warming needle moxibustion based on syndrome differentiation to treat CFS. For the CFS patients with the pattern of yang-deficiency of spleen and kidney as well as the pattern of deficiency of heart and spleen, moxibustion for 3–5 "zhuang" (unit of moxa cone) or 5–7 "zhuang" of moxa-cones was done after insertion of the needle. Both methods achieved satisfactory results (Zeng and Liu 1999).

Shan selected the back-shu points of the five Zang-organs, and Baihui (GV20), Guanyuan (CV4), and Zusanli (ST36) as the main acupoints, and applied warming needle moxibustion, moxibustion with moxa cones, and mild moxibustion (Shan et al. 2003). The selected acupoints have an effect on regulating qi movement of the Zang-fu organs and also play a role in tonifying the healthy qi. Combined with the warming and tonic effect of moxibustion, it can tonify "qi and blood", regulate the "Zang-Fu" organs which allows for sufficient qi and blood flow, and smoothens "qi" movement which can relieve CFS patients' fatigue, myalgia, sleep disorders and other symptoms, this makes it an effective method for the treatment of CFS.

Guo et al. explores the comprehensive efficacy of acupoints, herbal medicine and moxibustion for CFS treatment. The results show that clear moxibustion on the back-shu points of the five Zang-organs is effective in treating CFS, and also that moxibustion on "Bazhen" cake; (cake made by Chinese decoction called "Bazhen" decoction) a medicinal cake, has improved effects (Guo and Xu 2006). De-bin Zhang reports using warming needle moxibustion on the back-shu points for treating CFS (Zhang et al. 2007). He chose Huatuo Jiaji points as the main points, which are points that are 0.5 cun apart under the 4th, 5th, 6th, and 7th cervical spinous process and 0.5 cun apart under the 1st, 2nd, 5th, 6th, 7th, 9th, 10th, 11th, and 12th thoracic spinous process. Acupuncture manipulation was done at each point for 3 min, and moxa that was 1.5 cm in length was placed on the needle handle after achieving deqi sensation. The needle was kept in place for 30 min after burning out. The treatment combines acupuncture and moxibustion and achieved satisfactory results.

Yue used warming electro-acupuncture moxibustion on the back-shu points for treating CFS (Yue 2008). He chose needles 0.30 mm in diameter and 40 mm in length, and punctured the needle subcutaneously using the pricking method. He then used the sparrow pecking method 2–4 times to promote the arrival of qi due to quickly puncturing the back-shu points. He inserted the burning moxa stick that was 2 mm in length to the needle handle and combined it with the electro-acupuncture at the same time. The main symptoms of the reported CFS patients had significant improvements. Someone believed that non-scarring moxibustion on the acupoints of the five Zang-organs should make qi and blood sufficient, and could also make qi movements smooth by tonifying qi and blood, as well as regulating Zang-fu organs. All of these effects can combine to relieve CFS patients' fatigue, myalgia, sleep disorders and other symptoms (Lan and Feng 2011).

Liang observed the efficacy of acupoints catgut embedding method combined with in-box moxibustion method for CFS. The results showed that catgut embedding for Zusanli (ST36), Sanyinjiao (SP6), Guanyuan (CV4), Qihai (CV6), Xuehai (SP10), and Liver shu (BL18), combined with in-box moxibustion for the whole abdomen and lower back achieved good results (Liang and Liu 2014).

6.3 Cupping

Cupping is a type of therapy, which uses cups as tools and stimulates energy flow. The process works by keeping air from getting inside the cups using fire to create a negative pressure, so that the cup can be adsorbed and sticked to acupoints or any other part to be cupped on the body surface, causing stimulation that makes the skin hyperemic and congested, in order to prevent and cure diseases. Huang used moving cupping therapy to treat 30 cases of CFS patients, and after 12 rounds of treatment, the patients' conditions significantly improved, and other symptoms were relieved or even disappeared to varying degrees (Huang 2001). Lu combined cupping with acupuncture to treat CFS, he performed cupping on the Du meridian and the first and second lateral line of Bladder meridian on the back, and achieved satisfactory results (Lu and Wang 2001).

Chen's clinical research showed that multiple cupping on a patient's back can effectively relieve the symptoms of CFS, improve clinical symptoms, and improve scores on the fatigue assessment instrument (Chen et al. 2008). Guo-min Xiao regards that multiple cupping on the Huatuo Jiaji acupoints has a positive effect on improving CFS patients' quality of life during the treatment, and that the efficacy of cupping is not affected by the course of the disease (Xiao et al. 2011). Xiang-qiong Wu observed the therapeutic effect of multiple cupping on the back in CFS treatment. He divided patients into two groups. For one group, he used multiple cupping with Chinese medicine, he performed multiple cupping with the flash fire method along the first lateral line of Bladder meridian on both sides of the spine, from the cervical to the sacral vertebrae. For the other group, he used simple Chinese medicine. The results showed that the efficacy of the group using multiple cupping with Chinese medicine is significantly better than that of the group using simple Chinese medicine (Wu 2012).

6.4 Comprehensive Acupuncture Therapies

Compared to simple treatments, comprehensive therapeutic plans that use acupuncture combined with Chinese medicine, cupping, or tuina have broader application possibilities in the clinical practice of CFS treatment. Because of the mixed quality of literature and the various clinical treatment methods, it is difficult to generalize for one method. Here, we describe only some, of the combined methods of acupuncture

and Chinese medicine, the combined methods of acupuncture and cupping, and some characteristic methods.

6.4.1 Acupuncture Combined with Chinese Medicine

Acupuncture or catgut embedding method combined with Chinese medicine has obvious advantages in diagnosing and treating CFS based on syndrome differentiation. If the therapy is more convenient to perform, it will be accepted by more patients. Tian-wei Ma used acupuncture combined with Chinese medicine to treat CFS and received good results. He performed acupuncture on Zusanli (ST36), Sanyinjiao (SP6), and Dazhui (GV14), combined with Danggui (Angelica sinensis) blood-supplementing decoction and Chaihu (bupleurum) liver-soothing powder to treat 53 CFS patients. The total efficacy rate was 86.79% (Ma and Zhu 2003). Min Huang used capsules made by Codonopsis, Astragalus, and Schisandra, combined with acupoints catgut embedding to treat 40 CFS patients. He performed catgut embedding once every two weeks, he embedded 1.5 cm of catguts in the subcutaneous tissue or in the muscle of Spleen shu (BL20), Kidney shu (BL23), Liver shu (BL18), Guanyuan (CV4), and Zusanli (ST36), and received good clinical efficacy after 3 rounds of continuous treatment (Huang et al. 2010). Zheng Yang observed the efficacy of the catgut embedding method combined with Jianpibushen decoction from the perspective of strengthening the spleen and tonifying the kidney to treat CFS. He believed that the efficacy of catgut embedding therapy combined with Chinese medicine is reliable (Zheng Yang et al. 2011). Wei Zou used Banxiabaizhutianma (pinellia ternate, rhizoma atractylodes, and gastrodia) decoction with acupuncture on Baihui (GV20), Sishencong (EX-HN1), Taiyang (EX-HN5), Fengchi (GB20), Yintang (EX-HN 3), Taichong (LR3), Sanyinjiao (SP6), Neiguan (PC6), and Shenmen (HT7) to treat CFS, and achieved good clinical results (Zou et al. 2013).

6.4.2 Acupuncture Combined with Cupping

Zhang used acupuncture combined with cupping therapy to treat CFS and obtained satisfactory results. He selected Dazhui (GV14), Heart shu (BL15), Lung shu (BL13), Spleen shu (BL20), Liver shu (BL18), and Kidney shu (BL23), and then used a skin needle to tap on the back to cause slight bleeding, and combined this with cupping to allow bloodletting. It is regarded that tapping with a skin needle then cupping for bloodletting can improve immune function, and can cause anti-fatigue and can tranquilize the mind (Zhang 2004).

Ni reported using acupuncture combined with flash cupping method for the treatment of CFS (Ni 2012). The main points used were Baihui (GV20), Sishencong (EX-HN1), Neiguan (PC6), Zhongwan (CV12), Guanyuan (CV4), Zusanli (ST36), Sanyinjiao (SP6), and Taichong (LR3). The matching acupoints were 1–2 acupoints from Taixi (KI3), Shenmen (HT7), and Yinlingquan (SP9). Neiguan (PC6) was strongly stimulated with the reducing method, and the reinforcing method was used for Taixi

(KI3), Zusanli (ST36) and Guanyuan (CV4). The even-reinforcing even-reducing method was used for the other acupoints. After acupuncture, the flash cupping method was applied on the first lateral line of the Bladder meridian on the back, from Fengmen (BL12) to Kidney shu (BL23) until the skin on the back was flushed. The cups were held on Heart shu (BL15), Live shu (BL18), Spleen shu (BL20), and Kidney shu (BL23) for l0 min.

Liu observed 40 cases of CFS patients treated by acupuncture combined with the cupping method (Liu and Sun 2006). Using filiform needles, he punctured the skin at Dazhui (GV14), Zhiyang (GV9), Heart shu (BL13), Ge/Diaphragm shu (BL17), Mingmen (GV4), Kidney shu (BL23) and Changqiang (GV1). After withdrawing the needles, he chose the first and second lateral lines of Du meridian and Bladder meridian on the back to perform the moving cupping method. Efficacy was significant with a large stimulation area.

Xu regards that acupuncture combined with cupping for bloodletting therapy can effectively improve immune function, alleviate fatigue, and tranquilize the mind (Xu 2009). During treatment, he punctured the acupoints on the patient's back with slight bleeding and then performed cupping for the bloodletting method.

6.4.3 Acupuncture Combined with Psychological Music Therapy

Guo reported clinical studies of acupuncture with psychological therapy for treating CFS. He performed acupuncture on the "Back-shu" points, adding or subtracting acupoints depending on syndrome differentiation, and during needle retention, he used psychological counseling according to the variability of the individual, including transference therapy, trans-disposition therapy, emotion inter-resistance therapy, and situation therapy. The total effective rate of the acupuncture group was higher than that of the control group (Guo 2005). Li observed the clinical efficacy of eletro-acupuncture combined with music for CFS treatment. He chose Baihui (GV20), Zusanli (ST36), Neiguan (PC6), and Taiyang (EX-HN5) as the main acupoints, and chose (2–3) corresponding back-shu points and five emotions points based on the patient's symptoms, combined with a beautiful music environment. The results showed that this combined method demonstrated good clinical efficacy (Li 2014).

6.5 Other Treatments

Since both the etiology and pathogenesis of chronic fatigue syndrome are not yet clear, CFS has a lack of effective prevention and control measures. Currently, Western medicine has no specific approaches for CFS treatment. Treatments with medicine, cognitive behavioral therapy, and exercise are aimed mostly at treating the symptoms rather than the disease.

6.5.1 Medicine Therapy

From the perspective of medicine therapy for CFS, numerous studies have discussed from different angles, the efficacy of various drugs. A study suggests that the dysfunction and abnormal pain processing of the CNS (Central Nervous System), as well as the dysfunction of the ANS (Autonomic Nervous System), have a certain relationship with CFS, especially the CNS. CNS dysfunction is mainly related to pain, fatigue, sleep disorders, concentration, memory loss, and mood disorders (including depression and anxiety). Therefore, most clinical symptoms of CFS can be seen as a result of brain dysfunction (Gur and Oktayoglu 2008).

Research shows that acetylcarnitine can reduce physical and mental fatigue in elderly people, and can improve their cognitive status and physiological function (including muscle pain, persistent fatigue after exercise, sleep disorders, physical fatigue, mental fatigue, etc.) (Malaguarnera et al. 2008). Melatonin may improve sleep disorders of CFS patients and effectively regulate their circadian rhythm (Van Heukelom et al. 2006). Antidepressants can significantly reduce the severity of CFS symptoms, and improves five of the eight core symptoms (Amsterdam et al. 2008). Stimulants for the central nervous system can relieve CFS patients' degree of fatigue, as well as patients' difficulty in paying attention in the short-term, but no long-term efficacy was observed (Blockmans et al. 2006). Commonly-used anxiolytic and hypnotic medicine (such as doxepin, amitriptyline, Fluoxetine, etc.) and anti-inflammatory drugs (such as aspirin, ibuprofen, etc.) can be used to relieve fever and pain (Rose et al. 2001; Friedberg and Jason 2001). It is important that when CFS patients use medicine affecting the central nervous system, they should first start with a small dosage and then gradually increase the dosage.

Studies show that for CFS patients whose disease was caused by EB virus (Epstein.Barr Virus, EBV) infection, long-term (6–12 months) antiviral therapy (taking antiviral drugs such as acyclovir, famciclovir) may not only significantly improve their functional condition of physical activity to regain good status, but some patients may even experience a full recovery and no longer be diagnosed with CFS. Thus, in evaluating the effectiveness of any treatment, it is necessary to further divide CFS patients based on their characteristics into several sub-sets for research (Lerner et al. 2002, 2007). In Eastern Europe, it is reported that using antibiotics for treating CFS caused by Q fever (Post-Q-fever) is effective (Ledina et al. 2007), but further evidence is needed.

6.5.2 Psychological, Cognitive Behavioral Therapy

CFS patients not only have typical physical dysfunction, but also have significant mental and social adaptation dysfunction as well. Thus, psychological and social factors have a significant impact on CFS. Social-psychological factors may influence the autonomic nervous system, the endocrine system, neurotransmitters, and the immune system, thereby influencing the stability of the internal environment, damaging the body's defense system, and eventually leading to disease. Previous

studies on CFS emphasized the effects of biomedical factors, and hardly considered the impact of social-psychosocial factors, and with the ongoing revelation of the relationship between social-psychological factors and CFS, psychotherapies or adjuvant treatments of CFS have been inreasing. During treatment, we should consider biomedical factors as well as psychological and social factors. To strengthen CFS patients' psychological qualities and to improve their social endurance, psychotherapy may be an important means of treatment for CFS.

Studies show that CFS patients' main symptom; fatigue, is independently associated with depression. The relationship between fatigue and reduced psychosocial function is closely related to the severity of depression, and the relationship between fatigue and the reduced function of the other two fields is partially related to the severity of depression. This fact is a reminder that the severity of depression can affect the relationship strength between fatigue and the reduced functions of CFS patients through wider areas (Hadlandsmyth and Vowles 2009). Thus, if CFS patients can accept the fact that their mental function has some certain shortcomings, they can actively seek support from psychotherapy. This will help them to, correctly face all kinds of pressure, adjust attitudes, continuously improve their mental capacity and self-adjustment capacity, improve their psychological quality, and restore the overall balance of their mental state.

It has been recognized that CFS patients have cognitive disorders. Cognitive behavioral therapy (CBT), contributes to promote patients' cognitive changes, keeps them in a positive, optimistic and progressive condition, helps them maintain a happy, healthy, and stable mood, and relieves mental stress in real life. CBT has good results in relieving symptoms (Deale et al. 2001), and a number of studies show that CBT has a certain efficacy in CFS patients (Malouff et al. 2008; Deale et al. 1997; Huibers et al. 2004; Moss-Morris et al. 2005; O'Dowd et al. 2006; Powell et al. 2001; Prins et al. 2001; Stulemeijer et al. 2005; Wallman et al. 2004; Wearden et al. 1998). It can reduce patients' self-reported cognitive impairment, but it cannot improve patients' performance in neuropsychological tests (Knoop et al. 2007a, b). Self-education (a light degree of cognitive behavioral intervention) under the doctor's guidance is an effective treatment for CFS patients in less serious conditions, and can significantly improve the patients' fatigue degree and the degrees of other reduced functions (Knoop et al. 2008). A study points out that CBT may helps CFS patients gain a full recovery, if doctors share these positive messages with patients, it can increase patients' expectations for treatment and thus help to improve efficacy (Knoop et al. 2004).

6.5.3 Exercise Therapy

There has been a large number of debates about the etiology and treatment of CFS, including the relationship between exercise and CFS. Study shows that exercise decreases the pain threshold of CFS patients, and the myalgia after exercise is the main reason that causes CFS patients to lose normal activity (Whiteside et al. 2004). Excessive exercise may lead to immune function disorders, and may aggra-

vate CFS patients' symptoms. However, studies have found that CFS patients can obtain encouraging results from exercise, and there is no evidence that shows that exercise may worsen the disease (Edmondas et al. 2004). Limiting exercise intensity and duration can prevent some changes in CFS patients' health status after exercise (such as fatigue, body pain, decreased energy that may be persistent for more than 24 h after exercise) (Nijs et al. 2008a, b).

Cochrane Collaboration recommends that physicians should guide CFS patients to take graded exercise therapy based on the treating principle of cognitive behavior. Biological and clinical evidence suggest that graded exercise therapy is bearable for CFS patients; it is safe and has no adverse effects on the immune system. The graded exercise should be designed according to each patient's physical ability, and can be adjusted at any time according to changes in the patient's symptoms. When being treated using the Cognitive Behavioral Therapy (CBT) and graded exercise, patients should be instructed to strengthen self-management including, appropriately slowing down activity frequency, being fully aware of and accepting their own limits in physical and mental aspects, etc… In the long term, CBT helps CFS patients improve their daily functions (Nijs et al. 2008a, b). After at least six months of treatment, CFS patient show improvements in health-related aspects, both in quality of life and in psychosocial functions (Pardaens et al. 2006).

6.5.4 Diet Therapy

A previous report shows that CFS is related to the hyperplasia of candida albicans, so dietary adjustment is recommended as an alternative treatment for CFS. But the results of a RCT study about the correlation between dietary intervention and the CFS patients' fatigue degree, as well as their quality of life showed that the group with a low sugar low yeast (LSLY) diet showed no obvious difference when compared to the healthy eating (HE) group. From the perspective of improving CFS patients' fatigue degree and quality of life, the patients' compliance with the LSLY diet is worse. This illustrates that instead of advocating a low-sugar low-yeast dietary policy that is complex and difficult to adhere to, it is more effective to give some guidance to patients about the healthy dietary mode (Hobday et al. 2008). In addition, studies show that long-chain polyunsaturated fatty acids (such as γ linoleic acid) contribute to the rehabilitation of CFS patients (Puri 2006).

6.5.5 Other Therapies

Japanese studies show that hyperthermia (far infrared radiation) has a significant effect on improving CFS patients' physical symptoms (such as fatigue, pain, fever). Repeated hyperthermia has a relaxing effect, and can reduce the chief complaints and loss of appetite of patients with mild depression (Masuda et al. 2007). In addition, the study suggests that proper supplementation of vitamins (vitamins A, C, E, and especially B vitamins) and trace elements (minerals, magnesium preparation, etc.) is

necessary for CFS patients, but more studies must be performed to determine efficacy (Dotsenko et al. 2004).

6.5.6 Multi-modal Combined Therapy

In CFS patients, a simple intervention has a limited effect. Some researchers are turning to the complex interventions of combining cognitive behavioral therapy (CBT) with medication therapy. A randomized, controlled, double-blind, crossover trial with, a sample size of 72 cases, a duration of 24 weeks, and using the Fatigue Scale (FS) and the Clinical Global Impression Scale (CGIS) as the effect evaluation indicators, showed that the group of patients who first began using CBT treatment had the most significant efficacy until the 12th week. On the other hand, until the 24th week, the patients who took 12-week CBT treatment first and then accepted 12-week antidepressant treatment had better efficacy than other groups. The results suggest that multi-modal combined interventions have a positive therapeutic effect on CFS patients, and that the order of the interventions also plays an important role (Stubhaug et al. 2008). One Japanese study indicates that a special treatment plan combined with a variety of non-medicine treatments (including rehabilitation, lifestyle guidance and graded exercise therapy) and medicine treatments is important to the recovery of CFS patients. After the treatment above, if the patient's symptoms still persist, it is very necessary to invite psychiatrists or medical experts in the physical and mental fields (Yoshihara and Kubo 2007).

Currently, Western medicine is not clear about the pathogenesis of CFS, so there is a lack of effective treatment and specific evaluation indicators in the clinic. Therefore, finding practicable treatments in Chinese medicine becomes a direction in which we can actively explore in the research field of CFS.

6.6 Rules of Meridians and Acupoints Using in Acupuncture Treatment for CFS

We collected 40 clinical research papers about acupuncture treatment for CFS that were published in medical journals over the last 10 years, and analyzed the main acupoints of the selected papers which record clear acupoint prescription. There are 40 acupoints, and the main acupoints in the prescription belong to the 14 meridians, except the Sanjiao meridian and the Small intestine meridian. The selection of these acupoints has the following characteristics:

(1) In the order of the frequency of use of the meridians to which the main acupoints belong: the results showed 70 uses (7 acupoints) of the Bladder meridian, 48 uses (7 acupoints) of the Du meridian, 32 uses (6 acupoints) of the Ren meridian, 30 uses (2 acupoints) of the Stomach meridian, 28 uses (2 acupoints) of the Spleen meridian, 12 uses (3 acupoints) of extra-meridian points. Acupoints of other

meridians were also selected, but the most commonly used were the ones listed above.

(2) Among the selected acupoints, the more frequently selected acupoints chosen were: Zusanli (ST36) (29 times), Sanyinjiao (SP6) (25 times), Baihui (GV20) (19 times), Guanyuan (CV4) (15 times), Neiguan (PC6) (12 times), and Dazhui (GV14) (10 times), the back-shu points which were selected frequently were: Kidney shu (BL23) (17 times), Heart shu (BL15) (16 times), Liver shu (BL18) (11 times), Spleen shu (BL20) (10 times), Lung shu (BL13) (7 times), the extra-meridian points which were more frequently selected were: Sishensong (EX-HN1) (6 times), Huatuo Jiaji (EX-B2) (3 times), Taiyang (EX-HN5) (3 times). In total, there are 33 specific points, involving 10 kinds of the specific points.

6.6.1 Analysis of the CFS Acupoints Selection Based on Meridians and Collaterals Theory

(1) The Bladder meridian is the most commonly used of the 12 meridians: selecting the back-shu points of five Zang-organs can activate the meridian qi of the Bladder meridian, inspire the qi movement of Zang-fu organs, and regulate the brain functions, so it is chosen as the main meridian.

(2) The application of Ren meridian and Du meridian in CFS treatment: Ren meridian and Du meridian are the two sides of the body that produce "original qi", and are the sources of "genuine qi". the original qi runs with the meridians and spreads over the whole body. Ren meridian is the "sea of yin meridians", it regulates the yin qi of the whole body, and nourishes the Zang-fu organs of the whole body; Du meridian is the "sea of yang meridians", it regulates the yang qi, commands the yang of the whole body, strengthens the healthy qi, and improves immune function.

(3) Spleen meridian and Stomach meridian: The Spleen and stomach are the roots of acquired constitution and sources of qi and blood. CFS patients have a deficiency in qi and yin; or deficiency in spleen and heart, which is caused by mental tension or overwork. Choosing the spleen meridian and the stomach meridian can tonify and reinforce the after-birth sources of qi and blood. Balanced spleen and stomach functions promise sufficient food essence and essential qi, which makes Zang-fu functions strong and keeps people healthy and energetic.

6.6.2 Analysis of the CFS Acupoint-Selection Based on the Function of the Specific Acupoints

(1) **"He-sea" points**: The most commonly used acupoint is Zusanli (ST36); analysis of the data shows that it has the highest selection frequency in the prescriptions of matched acupoints, it also ranks No. l. In "*Ling Shu (Miraculous Pivot)*", and it proposes the theory that he-sea points can treat diseases of internal organs.

In "*Tong Xuan Zhi Yao Fu*", it points out that Zusanli (ST36) can eliminate fatigue and emaciation caused by the deficiency of the five Zang-organs. Modern medicine has proven that Zusanli (ST36) can improve the immune function of the body. It has a two-way adjustment effect, acupuncture on Zusanli (ST36) helps to mobilize the healthy qi to promote the harmonization of the internal environment and the external environment, to achieve yin and yang balance. In "*Su Wen (Plain Questions)*", it points out that staying healthy keeps the pathogenic factors away, and that the choice to use Zusanli (ST36) reflects the basic treating principle of strengthening healthy qi to eliminate pathogenic factors in traditional Chinese medicine.

(2) **"Back-shu" points**: from the obtained data, the acupoints of the Bladder meridian have the highest selection frequency amongst the "Back-shu" points, with a selection frequency which goes up to 70 times; the back-shu points of the five Zang-organs are commonly chosen, which can be explained by the theory of the back-shu points. According to the CFS feature that if there is a deficiency in qi and blood in the five Zang-organs and dysfunction of qi movement, the back-shu points of the five Zang-organs should be selected as the main acupoints; the back-shu points of the five Zang-organs are where the qi of the five Zang-organs infuses to the back, so they can regulate the qi movement of the five Zang-organs. The smooth qi movement of the Zang-fu organs promises, normal circulation of qi and blood, and the nutrition of limbs and bones, which prevents the body from experiencing fatigue. Acupuncture on the back-shu points of the five Zang-organs can inspire healthy qi, adjust qi movement, and can have a sedative effect. Based on the clinical syndrome differentiation, the treatment is combined with acupuncture on other acupoints to strengthen healthy qi to eliminate pathogenic factors, and to regulate the yin and yang. This helps the yin and yang to achieve relative equilibrium, and restoring the function of the five Zang-organs back to normal.

(3) **Crossing points**: a crossing point is the point where two meridians or more cross together, it can not only treat the disease of the meridian it belongs to, but can also treat the disease of the crossing meridians. Sanyinjiao (SP6) is usually chosen; it belongs to the spleen meridian, and is also the crossing point of Foot Taiyin, Foot Shaoyin and Foot Jueyin. It can be used to reinforce the spleen, to generate blood, to tonify the liver, and to nourish the kidneys.

(4) **"Yuan-source" points**: in "*the No. 66 problem of Nanjing (Classics on Medical Problems)*," it calls for the stimulation of "yuan-source" points of the "Zang-fu" organs when organs suffer from problems and Shenmen (HT7,) is the "yuan-source" point of the Heart meridian. According to the Chinese medicine theory, the heart, governs mental activities, controls blood circulation and is the commander of the "Zang-fu" organs. Furthermore, common symptoms of CFS such as fatigue, heart palpitations, insomnia, and forgetfulness are related to the abnormal function of the heart. Treatment by regulating the heart can be achieved by choosing the acupoint Shenmen (HT7). Hegu (LI4) and Taichong (LR3) are also frequently chosen. Hegu (LI4) is the "yuan-source" point of the Hand Yangming meridian, and the Yangming meridian is the meridian of

sufficient qi and blood. So Hegu (LI4) can be used to invigorate qi and blood, strengthen the spleen, and tonify the stomach. Taichong (LR3) is the "shu-stream" point and the "yuan-source" point of the Foot Jueyin meridian. In "*Su Wen (Plain Questions)*", it records that the liver is the root of endurance, that the liver governs tendons, and that the motor function of the tendons and joints in the body depends on the nourishment of the liver "essence qi", and if the liver "essence qi" becomes weak, tendons will lose nourishment and become flaccid.

(5) **"Luo-connecting" points**: a commonly used acupoint is Neiguan (PC6); Neiguan (PC6), is the luo-connecting point of the Pericardium meridian, the point connecting with the Sanjiao meridian of Hand Shaoyang, and the hui-influential point of the Yinwei Meridian. It is a point which connects three meridians, and has the special function of regulating meridians, Zang-fu organs, and qi and blood.

(6) **Non-meridian extra points**: the most commonly used are Sishencong (EX-HN1) and Huatuo Jiaji points (Ex-B2). Sishencong (EX-HN1) is located around the Du meridian, and two of their points are located on the pathway of the Du meridian. The Du meridian runs inside along the spine, and belongs to the brain. The brain is the house of mental activity, and all mental activity and qi movement of the human body are at its disposal. Regulating the Du meridian can have a mind-tranquilizing, heart-nourishing and sleep-promoting effect. Sishencong (EX-HN1) is at the center of the parietal and is the projection reflex zone of several nerves including the great auricular nerve and the auriculotemporal nerve, it can regulate the excitation-inhibition function of the cerebral cortex. Huatuo Jiaji points (Ex-B2) are at both sides of the Du meridian, and run along the Bladder meridian; they can adjust all the meridians, circulate qi and blood, tonify yin and yang, and nourish bones and tendons. Modern physiology and anatomy confirm that Jiaji points (Ex-B2) are closely connected to the spinal segments, acupuncture can not only influence the dorsal segments of spinal nerves, but can excite the spinal segments and then influence the cortex. Also, due to the close relationship between the Jiaji points (Ex-B2) and the former ramus, acupuncture can regulate the sympathetic nerve as well. Moreover, the Jiaji points are connected to the Zang-fu activities, and can regulate the Zang-fu organs as well as qi and blood.

According to the theory of TCM, the occurrence of CFS is mainly due to the weakness or injury of the "Zang-fu" organs and the deficiency of qi-blood and yin-yang. The spleen and the kidneys are the foundation of congenital and acquired constitution, and the core of the dysfunction of the Zang-fu organs. In Zhu YH et al.'s study, they chose the important acupoint, Zusanli (ST36) of the Stomach meridian of Foot Yangming and the "back-shu" point, Kidney shu (BL23) of Bladder meridian of Foot Taiyang for electro-acupuncture. Zusanli is the "he-sea" point of the Stomach meridian, and the "lower he-sea" point of the stomach, it can keep the spleen and stomach invigorated, regulate and tonify the five "Zang-organs" and harmonize "qi and blood". Kidney shu (BL23) is where the kidneys' "essence qi" is gathered, which can tonify kidney essence, and warm kidney "yang". The two

matched acupoints can regulate the spleen and kidneys, coordinate the five "Zang-organs", and harmonize "qi and blood". Electro-acupuncture is a kind of treatment that combines needle and electrical stimulation. After getting the "deqi" sensation when puncturing the acupoints, a micro current that is similar to bio-electricity is run through the acupuncture tools. EA helps with continuous needle manipulation rather than having to rely on manual stimulation, and can objectively control the amount of stimulation given, so it is widely used in the clinic. Yi-hui Zhu found that after doing electro-acupuncture treatment on Zusanli (ST36) and Kidney shu (BL23) in CFS patients, the scores of the fatigue severity scale, the physical and mental health report, and the visual analogue scale in the acupoint group significantly decreased compared to those in the non-acupoint group. Moreover, the scores of each dimension in the short form 36 health survey significantly improved, which indicates that EA on Zusanli (ST36), and Kidney shu (BL23) can significantly reduce the fatigue degree of CFS patients, reduce their potential symptoms, reduce pain, and improve their quality of life (Zhu et al. 2008a, b).

Zusanli (ST36) was firstly described in "Ling Shu (Miraculous Pivot)". It is the "He-sea" point of the Stomach meridian of Foot Yangming, the "lower he-sea" point of the stomach, and belongs to "earth" in the "five elements". It can regulate the spleen and stomach, tonify qi and blood, and is commonly used clinically as one of the tonifying acupoints. Yangming meridian is the meridian with sufficient "qi and blood", and has an exterior-interior relationship with the Spleen meridian of Foot Taiyin. The stomach and spleen are the foundations of acquired constitution, the sources of "qi and blood", and the basis of life activities. Ancient doctors have detailed records about Zusanli (ST36). For example, "*five evils of Ling Shu*" records that evil in the stomach causes muscle pain, and deficiency in "yin and yang" causes heat and cold pathogens, and that all of these can be regulated by Zusanli (ST36). "*Tong Xuan Zhi Yao Fu*" records that Zusanli (ST36) can eliminate fatigue and emaciation caused by a weakness in the five "Zang-organs". "*Chinese acupuncture*" also records that Huatuo says that Zusanli (ST36) governs the fatigue and emaciation caused by a deficiency of the five Zang-organs, and the weakness and fatigue caused by "seven damages" (seven kinds of impairments in TCM theory). In "*the source of acupuncture and moxibustion*", it regards that Zusanli (ST36) can treat all the deficiencies and weaknesses of limbs. Moreover, Gao believes that the main cause of CFS is excessive annoyance and fatigue, as well as improper diet, because of this the disease is located in the five Zang-organs, especially in the spleen. The general syndrome differentiation is the deficiency of spleen qi, and the main treating rule is to reinforce the spleen (Quan-guo Gao et al. 2005).

Kidney shu (BL23) comes from the "*back-shu points of Ling Shu (Miraculous Pivot)*", it is the acupoint of the Bladder meridian of Foot Taiyang. The back-shu point of the kidney is the place where kidney essence qi is gathered, and is a commonly used acupoint for tonifying kidney yin and yang, nourishing the essence and marrow, and strengthening the back and bones. It has important effects on maintaining the normal function of the five "Zang-organs", and is used to treat chronic wasting disease clinicaly. Ancient medical books have a lot of records about the effects of Kidney shu (BL23) on reinforcing the vital essence, tonifying deficiencies, and eliminating

fatigue. For example, in the "*Compendium of Acupuncture and Moxibustion,*" it records that Kidney shu (BL23) can be used to treat fatigue, weakness and thinness, deafness, and kidney deficiency, "five consumptions and seven damages". Also, in "*the Integration of Acupuncture and Moxibustion*", it records that Kidney shu (BL23) and other acupoints can be used to treat improper diet, exhaustion, limb laziness, irritability and somnolence. As well as this, in "*Lei Jing Tu Yi*", it records that Kidney shu (BL23) can be used to treat a consumptive disease of the five Zang-organs.

A scholar analyzed 78 published papers about the acupoints selected in the acupuncture treatment for CFS patients, and found that Zusanli (ST36) has the highest frequency of selection, up to 45 times, accounting for 57.7%, while Kidney shu (BL23) has the second highest frequency of selection, up to 39 times, accounting for 50% (Wang 2005a). This indicates that Zusanli (ST36) and Kidney shu (BL23) are the main acupoints for the treatment of CFS.

7 Mechanism of Acupuncture Treatment for CFS

Since the etiology and pathogenesis of CFS is unknown, there is still a lack of specific prevention and treatment for CFS worldwide, and there is no clear mechanism of treatment either, so various exploratory therapies are mainly targeted towards symptomatic treatment (Exley et al. 2009; Thomasa et al. 2008; Maquet et al. 2006). Acupuncture is a Chinese medical therapy, and traditional Chinese medicine has its unique understanding about the etiology, pathogenesis, and treatment of CFS. In recent years, the role the nervous system plays in the pathogenesis of CFS has been focused on, and to some extent, has provided the scientific basis for acupuncture treatment for CFS.

7.1 Understanding of Traditional Chinese Medicine

CFS is a group of diseases with unknown etiology, various symptoms, and few signs, which belong to the consumptive disease category in traditional Chinese medicine. In ancient Chinese medical books, it is often described as sluggishness, burnout, tiredness, heavy body, heavy limbs, "lily" disease and so on. For example, in "*Su Wen (Plain Questions)*", it says that the abnormal movement of kidney essence leads to heavy and weak limbs, also a deficiency of the liver, kidney and spleen makes the patient have a heavy body and a depressed mind. The manifestation of "lily" disease is that the patients intend to eat food, but find themselves unable to eat. In addition, they often keep silent, and intend to lie down, but cannot do so, and intend to walk but cannot walk. The patient sometimes has a good appetite, and sometimes loses it, the pattern is like cold syndrome but not actually cold, and like heat syndrome but not actually hot. In "Ten Books by Dong-yuan", it says that the deficiency of the spleen

and stomach cause laziness, sloth, drowsiness, and weakness of limbs. Moreover, in "the Theory of Spleen and Stomach", it says that a lack of healthy qi may cause fatigue, weakness, silence, insomnia, dullness, loss of appetite, aversion to heat, and laziness." The manifestation of a consumptive disease is usually insomnia due to dysphoria, aching limbs, restless fever of hands and feet, dry mouth and throat, etc. All of these signs and symptoms form a unique systematic fatigue theory of traditional Chinese medicine, and provide a theoretical basis for acupuncture treatment for CFS (Wang et al. 1994; Li et al. 2004, 2007; Pan and Wang (2003); Yuan et al. 2009; Lu et al. 2009).

In ancient TCM records, Zhang Zhong-jing not only suggested the word "fatigue", but also regarded that the treatment for a consumptive disease must use needles to lead yang, keep the pulse in gentle condition, so the disease can be cured when the pulse is not tight. "Fatigue" was first recorded in the "*Jinkui Yaolue Fanglun (Synopsis of Prescriptions of the Golden Chamber)* "(Huang 2005). The pulse is a little unsmooth, and a little tight at Cunkou and above Guan. For treatment, we can use needles to lead yang and keep the pulse gentle, and the disease can be cured when the pulse is not tight.

Fatigue is a multi-organ, multi-system dysfunction caused by under "consumption" of qi and blood. Therefore, acupuncture treatment for fatigue must be a treatment based on syndrome differentiation, which can regulate qi or blood according to the specific performance of the Zang-fu organs. In "*Taiyin Yangming Theory of Su Wen (Plain Questions)*", it says that due to spleen dysfunction, the spleen cannot help the stomach in circulating the body fluids, so bones and muscle become weak and useless because there is no source of spleen qi. The liver governs tendons, and is the root of endurance, in "*Zang-xiang Theory of Su Wen*", it records that the liver is the root of endurance and the site of mental activities. In addition, tendons are important parts of body movement, and liver dysfunction is an important cause of symptoms such as fatigue, lack of energy, and reduced movement, etc. The kidneys govern bones and generate marrow, which are the congenital foundation. The heart governs the mind, the lack of heart blood causes a lack of nutrition for the mind, and symptoms such as insomnia, forgetfulness, etc. follow suit. The lungs govern the qi of Ying-Wei. The lungs can command the skin and hair, and are the guards of the body, they also have a close relationship with the non-specific resistance of the body in modern medicine. In short, chronic fatigue syndrome is the disease caused by the dysfunction of qi movement in "Zang-Fu" organs, the declined organ functions make the body unable, to maintain the normal physiological and mental functions, and to perform social activities. A patient often shows an imbalance of multiple "Zang-fu" organs and an imbalance of "yin and yang". It is worthy of focus that many scholars regard that the main patterns of CFS are the patterns of "qi" deficiency and liver stagnation, and the important accompanied patterns are patterns of blood deficiency and blood stasis. During the treatment of CFS, it is necessary to relieve the patients' working stress, regulate their emotions, and smooth liver "qi" (Peng and Peng 2007; Li et al. 2009; Shi and Xu 2008).

A study found that gender and marriage are risk factors of CFS, and that unmarried women and married women with children are more susceptible to CFS. This may be

closely related to the physical characteristics of women and the dual pressures exerted on them by work and family. Medical workers, administrators, and teachers are under heavy workloads and daily stress, and are also highly susceptible to CFS. With the rapid development of modern science and technology, these people mentioned previously are facing increasingly more serious social competition, employment, work, and family pressures. Although CFS affects the five "Zang" organs, the liver is the major organ that is affected. On the basis of treatment by syndrome differentiation in traditional Chinese medicine, we should fully consider the characteristics of patients' emotions, and support them with proper emotional and psychological counseling in order to obtain a satisfactory therapeutic effect.

Acupuncture plays an increasingly important role in the prevention and treatment of CFS; the treatment is based on the holism concept and differential treatment, and advocates regulation of mental and physical activities. The principle of the treatment is to reinforce deficiencies and reduce excess, strengthen body resistance to dispel pathogenic factors, and treat both the symptoms and root causes which obey the content in "*Ling Shu (Miraculous Pivot)*", which states that it is necessary to reinforce the deficiency and reduce the excess, to regulate the deficiency and excess, to clear the pathways, and to eliminate the pathogenic factors for the treatment of CFS. Filling the essence of the five Zang-organs to nourish their spirits can regulate the yin-yang and qi-blood of the five Zang Organs. This helps to achieve a state where yin and yang are in equilibrium and to ensure balanced mental activities. During acupuncture treatment, we can respectively apply the treatments of supplementing qi and nourishing yin, relieving the liver and regulating qi, promoting blood circulation and removing stasis, and invigorating the spleen and kidneys according to the patients' different constitutions such as strong or brittle bones and tendons, hard or weak muscles, thick or thin skin, and loose or tight skin texture.

Chinese scholars have achieved some progress in studies of the mechanism of acupuncture treatment for CFS. Meng observed the effects of electro-acupuncture on Baihui(GV20), Zusanli (ST36), and Taichong (LR3) on hypothalamic endorphin (β-EP) content under the fatigue status induced by chronic stress. The results showed that the hypothalamus β-EP content of the model group increased at first, and later became normal after electro-acupuncture. It suggests that electro-acupuncture can reduce brain tissue damage caused by β-EP after stress-induced fatigue by reducing the content of β-EP, which may help CFS treatment (Meng et al. 2003). Jiang considers that electro-acupuncture can adjust the disordered state of CNS monoamine neurotransmitters NE, DA, and 5-HT in the CFS rat model with spleen-deficiency, and can regulate the increased cytokines IL-1β, IL-2 in serum of the model rat (Jiang 2005b). Tian studied the moxibustion effects on the immune function of CFS patients. By performing moxibustion on Qihai (CV6), Guanyuan (CV4), Zusanli (ST36), Kidney shu (BL23), and Mengmen (GV4), the NK cell activity and the IL-2 content in CFS patients significantly increased and reached normal levels. Due to these results, he believed that moxibustion used for tonifying acupoints can effectively improve the immune function of CFS patients (Tian et al. 2006). Wu measured the effect of electro-acupuncture on the monoamine neurotransmitters content in the hypothalamus of rats afflicted by chronic fatigue due to combined stress. He used the

chronic combined stress method to establish the rat model of chronic fatigue, he then performed electro-acupuncture on Baihui (GV20) and Taixi (LR3) and measured rat behavior, the changes in monoamine neurotransmitters content in the hypothalamus, and the acupuncture treatment effects. The results showed that the content of monoamine neurotransmitters in the hypothalamus in the model group was lower than normal, and that the changes in rat behavior supported the condition of chronic fatigue. Furthermore, electro-acupuncture was able to help rat behavior and the content of monoamine neurotransmitters in the hypothalamus increased to a normal level. Therefore Wu concluded that the reduced content of monoamine neurotransmitters in the hypothalamus of rats afflicted by chronic fatigue caused by combined stress may be involved in the occurrence and development of chronic fatigue, and that electro-acupuncture treatment is a good method of treatment for chronic fatigue (Wu et al. 2006a, b).

7.2 Experimental Research

Many clinicians believe that CFS is a "functional somatic syndrome"; that fatigue is just a mental abnormality, and that there is no real body-derived factor, so it is improper to attribute CFS as some serious illness. Researchers found that the central nervous system (CNS) plays a key role in the pathogenesis of CFS. De Lange tested 28 cases of CFS patients and matched healthy participants in two separate centers with high-resolution MRI, combined with morphometric techniques, and found that brain gray matter volume in the CFS patients was significantly reduced, which was associated with reduced physical activity (De Lange et al. 2005). Lange regards that the serious cognitive disorders of CFS may be related to the frontal lobe (Lange et al. 1999). Siemionow measured the EEG of CFS patients when they were doing the grip strength 50% MVC (Maximal voluntary contraction level), and found that the MRCNP (Motor activity-related cortical negative potential) of the CFS group was higher than that of the control group, and the difference in the MRCNP was more obvious in the fatigue test. This indicates that the CNS signals in CFS patients are different to those in normal patients when controlling voluntary muscle activity, and that the changes in EEG signals induced by physical activity may be the objective signs in physiology that can diagnose CFS (Siemionow et al. 2004). Ken found that when CFS patients were doing maximum sustained anterior tibial muscle exercises, the muscular arbitrary contractility decreased while the muscle excitation-contraction coupling, as well as the fatigue and metabolism at the cellular and systemic levels, were normal; this suggests that muscle fatigue of CFS is related to central nervous factors (Ken et al. 1993). Schillings observed CFS patients doing biceps MVC exercises, and found that the central activation of CFS patients was reduced, which may be related to cognitive changes, decreased attention, or physiological changes such as changes in corticospinal excitement and the concentration of neurotransmitters (Schillings et al. 2004). Henderson found that lasting muscle fatigue and pain may lead to the activation of zones of the ipsilateral anterior insular lobe and the con-

tralateral posterior insular lobe (Henderson et al. 2007). Clinical experiments suggest that the reduced synthesis of neurotransmitters in the cerebral frontal gyrus (Brodmann'S Zone 9/46), the temporal cortex (BA21 and BA 41), the anterior cingulate gyrus (BA24 and BA 33) and the cerebellum brain regions of CFS patients may reveal the subjective sensation mechanism of chronic fatigue. They further suggest that acetyl-L-carnitine may be the biochemical marker of CFS (Kuratsune et al. 2002). Some scholars found that the changes in CFS patients' cognitive function were closely related to the functional changes in the left front, tempus and parietal cortex (Pierre et al. 2010).

Acupuncture treatment has obvious advantages in helping with neurological mechanisms and in regulating nerve disorders. A feature of the nervous system in CFS patients is the overstressing of the central nervous system, or the excitement—-suppression disorder. Its pathophysiological basis is to weaken the function of the cerebral cortex, which causes a reduction in the regulation and controlling function of the subcortical region, and autonomic nervous system function, and thus leads to disorders in the nervous system and in mental activity.

The mechanism of acupuncture on the nervous system may be that acupuncture can enhance the sensing ability of the body, increase the excitability of the central nervous system through afferent nerves, improve the regulatory function of the cerebral cortex and neurohumour, and help the motor center of the cerebral cortex and the second information system stimulate the excitement center while other regions of the cortex are put in the inhibitory state to allow the brain rest. Alternatively, acupuncture can help the brain get more oxygen and nutrients, promote the secretion of a variety of neurotransmitters in the brain; causing the brain to have an agile thinking response, and can increase the capacity of cellular and humoral immunity to activate the reticular cortex system and to regulate nerve function disorders.

Chen observed the effect of electro-acupuncture on hypothalamic, pituitary, and adrenal indexes, as well as on the expression of corticotropin releasing hormone mRNA in the chronic fatigue rat models. The results showed that the hypothalamic, pituitary, and adrenal indexes of the CFS rat model increased, and that the expression of cRHmRNA increased as well. After the electro-acupuncture treatment, the condition of mental and physical fatigue improved significantly, the adrenal index decreased, the expression of cRHmRNA declined, and the hypothalamic index and the pituitary index decreased a little (Chen et al. 2007). In other words, electro-acupuncture may reduce the expression of cRHmRNA and the adrenal index to correct the dysfunction of the HPA axis in order to treat CFS. Yi-hui Zhu used electro-acupuncture on Kidney shu (BL23) and Zusanli (ST36) to treat chronic fatigue syndrome, and discussed the regulating effect of electro-acupuncture on the pathological rhythm of CFS. The study found that the CFS patients have circadian rhythm disorders in the core body temperature, heart rate, blood pressure and the peak of melatonin and that electro-acupuncture has a positive regulating effect on these factors (Zhu et al. 2008a, b). Zhu performed animal experiments to explore the effect of electro-acupuncture on Kidney shu (BL23), and Zusanli (ST36), on the spontaneous activity of rats with chronic fatigue. The pre-treated rats demonstrated abnormal spontaneous activity, electro-acupuncture helped to regulate the electro-acupuncture of rats with

chronic fatigue (Zhu et al. 2011). Lv studied the effect of acupoint catgut embedding on behavior and on hormone levels related to HPA-axis of chronic fatigue rats. He used the combined stress method of suspending the rats in cold water and making them swim in order to replicate the chronic fatigue rat model. For the catgut embedding group, he embedded the catgut in the bilateral Liver shu (BL18), Spleen shu (BL20), and Kidney shu (BL23) while modeling, the results showed that acupoint catgut embedding was able to inhibit the excessive secretion of hypothalamic CRH, plasma ACTH and CORT, and could correct abnormal HPA axis function in order to treat CFS (Lv and Lv 2009). Yang studied the effect of electro-acupuncture on the level of serum transforming growth factor-β1 (TGF -β1) in a chronic fatigue rat model, the results showed that acupuncture for Baihui (GV20), emotional area 1, and sensory area can significantly adjust the level of TGF-β1, thus leading to speculation that this effect may be one of the mechanisms of acupuncture treatment for CFS (Yang et al. 2014). He Sun observed the effect of moxibustion on Zusanli (ST36) and Lung shu (BL13), on the levels of serum IL-1β, LA and BUN in a CFS rat model. The results showed that moxibustion on Zusanli (ST36) and Lung shu (BL13), can reduce the levels of serum IL-1β, LA and BUN (He Sun et al. 2014). This may be the mechanism by which acupuncture exerts its effects for treating CFS.

8 Concluding Remarks

Currently, modern medicine is not clear on the etiology and pathogenesis of CFS, and there is a lack of effective treatments clinicaly. In recent years, acupuncture treatment for CFS has achieved relatively satisfactory clinical effects, and has gradually attracted people's attention.

However, current research is lacking in a unified syndrome differentiation standard, and a unified evaluation standard of efficacy as well. Thus, it is difficult to have reliability and comparability in clinical reports, and the effective treatment course of the clinical reports are not unified either. At this point in time, we should discuss the thought of acupuncture treatment for CFS based on the combination of clinical practice and experimental research, and it is urgent to do further studies on the selection of acupoints in the clinic.

The acupoints selection of acupuncture treatment for CFS should be based on Chinese acupuncture theory; selecting acupoints according to the guidance of syndrome differentiation of the Zang-fu organs and meridians, and by exploring its mechanism from a multi-perspective multi-level point of view on the basis of combined clinical and experimental research. During clinical studies, we should refer to extensive literature, and should vigorously carry out clinical research to determine the acupoints which are most frequently reported in literature, have the highest probability of being used in clinical application, and have the best efficacy. We should also observe the efficacy of different combinations of acupoints, and screen the best, matching main acupoints and then apply them in clinical practice. As well as this, the screening researches of acupoints selection prescription should strictly follow the

requirements of clinical randomized controlled trials, and should select a comprehensive evaluation system so as to objectively, comprehensively, and systematically evaluate the observed indicators of CFS clinical manifestations. Experimental studies should be done based on clinical efficacy, and deep and comprehensive research into the mechanism of matching acupoints with a reliable efficacy should be done as well. Through systematic and scientific clinical research and experimental studies to confirm the standard basic main acupoints, we matched points based on syndrome differentiation and acupuncture operation methods of CFS treatment, in order to determine the most systematic and effective acupuncture treatment.

In order to perform accurate experiments on acupuncture efficacy, we must strictly design the scientific protocols to reduce bias. Follow the principle of randomization, do good clinic random allocation concealment. If it is difficult to apply blind method, at least we should choose blinded-evaluator method, i.e., the evaluators do not know the treatment and grouping, thus avoiding selection bias. It is recommended to use newly recognized disease diagnostic criteria, as well as unified standard syndrome differentiation, to ensure the comparability of included cases. The treatment group should be adopted in one needling technique, do not mix with a variety of other treatments. The control group should be adopted in the placebo acupuncture or sham acupuncture, try to avoid using "ordinary acupuncture" or "normal acupuncture" as control.

The efficacy evaluation indicators should be as objective and standardized as possible. The main and secondary symptoms of CFS should be divided, and evaluated using tools such as the fatigue scale in order to objectively compare the total score changes of the main symptoms before and after the treatment. In addition, if using a dichotomous variable such as an efficacy grade constituent ratio to evaluate, then a relatively unified definition standard of efficacy grade such as Nimodipine method must be used. We must also pay attention to the evaluation of patients' quality of life and their reported results, by using the common QOL scale to assess their quality of life. As well as this, the evaluation of patients' reported clinical outcomes must be emphasized, and the treatment effect from the patient's point of view should be evaluated. CFS has a long course of treatment, and requires a certain period of time to observe the treatment and efficacy. The course of treatment must last at least for one month, after that a middle-term and long-term efficacy evaluation should be done, and a 3–6 months follow-up to observe the recurrence of the disease should be performed as well.

Since the etiology and pathogenesis of CFS is still not fully understood, some hypotheses proposed by researchers don't have enough evidence. Thus, at present the experimental studies on acupuncture treatment for CFS are limited to animal models.

The limitation of solely using animal studies for acupuncture treatment of CFS is that CFS is closely related to multiple stressors including long-term mental stress and physical overload, etc. Furthermore, these kinds of subjective factors including human emotions and personal thoughts are difficult to replicate in animal models. These factors become the bottlenecks of the animal studies on acupuncture treatment for CFS. A model of a single factor is easy to perform, and can have good

reproducibility, but it can only simulate human disease status from a single aspect; either physical fatigue or mental fatigue, and it cannot reflect the integrity of CFS. Currently, some people are trying to develop an animal CFS model with multiple stress factors, combining the physical fatigue caused by exercise like swimming and running with the mental or psychological fatigue caused by stimulations like bondage, sleep deprivation, suspension, and tail clamping, in order to simulate the occurrence and development of CFS, in a similar manner to a certain extent to the socio-psychological factors involved in the occurrence of CFS in humans. Generally speaking, CFS animal modeling is becoming more and more similar to the development of CFS in humans, providing validity to studies on the mechanism of CFS and the evaluation of the efficacy of anti-fatigue medicine. However there are still some problems, such as the fact that various modeling methods lack standardization and unification. Also, the choice of experimental animals lacks consistency, for example, most researchers use rats and mice, while some use rabbits and cats; this illustrates the lack of a clear standard for modeling. These issues need to be to be solved through further experimental studies.

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Acupuncture Cardiovascular Regulation: Translational, Clinical Studies and Underlying Mechanisms

Stephanie C. Tjen-A-Looi, Peng Li, John C. Longhurst and Shaista Malik

Abstract Mechanisms associated with the effects of acupuncture on cardiovascular health have been investigated in the recent decades. Although the precise mechanisms are yet unclear, a list of finding has been reported on acupuncture induced sympatho inhibition (Longhurst and Tjen-A-looi 2013) to support the promising effects of this therapy on cardiac and cerebral vascular diseases aggravated by hypertension. The common underlying mechanism, in part, relates to sympathoexcitation that occurs for instance with dietary sodium, physical and emotional stress and aberrant autonomic neuronal activity electroacupuncture (EA). We have observed that the acupuncture outcomes depend on well-defined specific EA treatment are influenced by responders and non-responders. Acupuncture may also modify ischemia in the heart and brain through angiogenesis and nerve fiber regeneration. Decreasing peak blood pressure with acupuncture could prevent these types of ischemia leading to myocardial ischemia and stroke. Alongside reduction in sympathoexcitation, acupuncture also decreases parasympathoexcitation during neurogenic syncope. Thus acupuncture has the capability to influence the cardiovascular function in patients with disease that are contributed by altered autonomic nervous system regulation, for example hypertension and hypotension.

Keywords Hypertension · Hypotension · Arrhythmia · Myocardial ischemia · Stroke

1 Introduction

Optimal cardiovascular regulation is achieved through circulating hormonal and autonomic nervous systems. Blood pressure can be viewed as the final outcome of complex interactions between genetic and environmental factors that influence the neural, renal and cardiovascular systems and ultimately blood volume, cardiac output and

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vascular tone. Neurophysiological and hormonal systems are regulated continually through feed forward and feedback mechanisms to maintain optimal homeostasis. However, in pathophysiological conditions, the neural and/or hormonal systems may be out of balance. Western medical therapy is used to restore balance for example with receptor blockade or surgical procedures, but frequently either incomplete restoration or unwanted side effect limits optimal management. Integrative medicine potentially provides an additional option for clinical treatment.

We are beginning to appreciate a potential role for acupuncture in treatment of several clinical cardiovascular conditions, including hyper- and hypotension as well as myocardial and cerebral ischemia. Elevated sympathetic activity contributes to hypertension in subjects with a genetic tendency toward developing high sympathetic tone as a consequence of repetitive psychological stress, obesity and high sodium intake, among other factors (Esler et al. 2001). Restoring physiological balance in hypertension using drugs or surgery can lead to unwanted responses (e.g., headache, dizziness, fainting, bradycardia, etc.), as a consequence to pharmaceutical antagonism of receptors or denervation of renal sympathetic nerves (Krum et al. 2009; Neale 2014; Esler et al. 2010). Thus, although western medical science has developed a number of treatment strategies to control hypertension, antihypertensive medical therapies are often associated with adverse side effects. In this regard, drug therapy indiscriminately blocks many receptors and can lead to unwanted responses (Mayer 2000; Macpherson et al. 2001; Diao et al. 2012), including serious injuries associated with falls in older patients (Tinetti et al. 2014). We need targeted approaches with limited side effects that aim at the underlying mechanisms of primary hypertension. Lifestyle changes and non-pharmacological treatments have been used that include integrative medical approaches like dietary and exercise strategies, and acupuncture, among others. To identify more effective approaches to achieve optimal control of hypertension, for the last two decades we have focused on the homeostatic actions of acupuncture (Ernst 2006; Li et al. 2015a) that restores aberrant autonomic neuronal activity underlying a host of cardiovascular pathologies (Tjen-A-looi et al. 2012; Chao et al. 1999).

A significant mechanism in the genesis of hypertension involves interaction between high dietary sodium intake and renal sodium excretion that is influenced by sympathetic renal activity and the renin-angiotensin-aldosterone system (Stocker et al. 2013; Zicha et al. 2011; Li et al. 1996). Increased sympathetic activity elevates secretion of renin, angiotensin and aldosterone, and promotes renal tubular sodium reabsorption and hence expansion of blood volume. In this regard, extracellular volume expansion and autoregulation of blood flow together with arterial vasoconstriction may underlie chronic increases in vascular resistance (Weber 2004) that, in turn, contribute to hypertension. Acupuncture modulates elevated renin in hypertension because this therapy decreases enhanced sympathetic activity (Li et al. 2009; Tjen-A-Looi et al. 2003; Li et al. 2015b; Zhou et al. 2006; Chiu et al. 1997).

Acupuncture also may have a role in treating hypotension (Morillo et al. 1997). The prevalence of dizziness has been reported to be about 29% (Xue et al. 2013). Dizziness is difficult to treat since this symptom is caused by many physiological and pathophysiological conditions, including those of cardiovascular origin (Sloane et al.

2001), mainly hypotension and bradycardia. A common cause for dizziness among patients 60 years and older is vasovagal syncope (Sloane et al. 2001). This problem (Kapa and Somers 2008; Calkins and Zipes 2008) potentially might be treated with acupuncture as demonstrated recently in experimental mechanistic studies (Tjen-A-Looi et al. 2012; Wang et al. 1987; Wang and Li 1988). In this regard, hypotension and bradycardia associated with experimental vasovagal syncope is partially reversed by acupuncture (Tjen-A-Looi et al. 2014).

During vasovagal syncope increased parasympathetic activity and depression of sympathetic activity decrease heart rate and blood pressure. Cardiopulmonary reflexes that induce vasovagal syncope (Sneddon et al. 1993) can lead to falls and fainting. With the exception of experimental animal studies from Tjen-A-Looi and

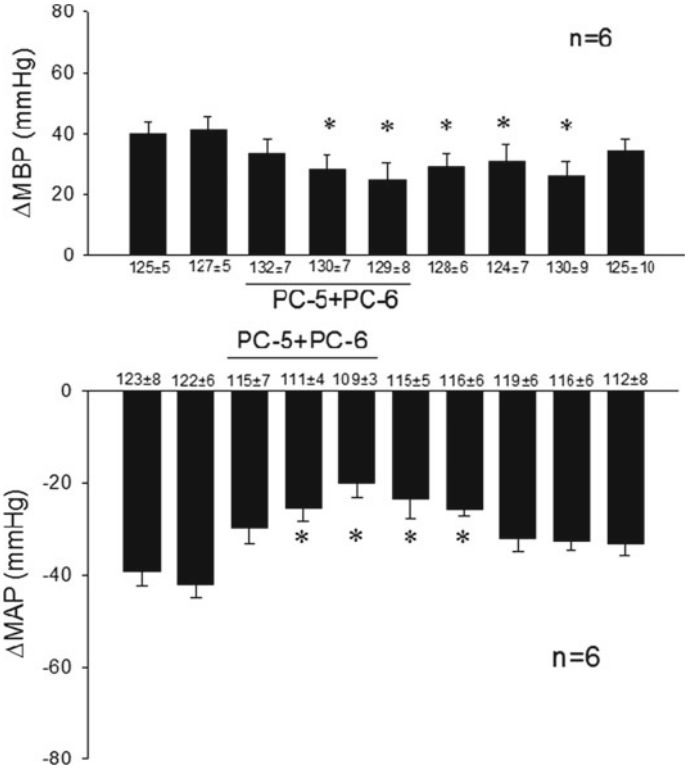

Fig. 1 Electroacupuncture (EA) applied for 30 min with low frequency and low intensity reduced reflex increases (top panel) and decreases (bottom panel) in blood pressures. Consistent changes in mean blood pressures (ΔMAP) prior to EA at PC-5 and PC-6 were reduced during and after application of EA. The effect of acupuncture started 20 min into application of EA. The acupuncture modulation of blood pressure responses persisted after end of EA treatment. Means and SEM associated with each bar indicate baseline MAP immediately prior to each blood pressure reflex response. * indicates significant difference in the blood pressure reflex response compared with prior to onset of EA. Figures modified from studies by Tjen-A-Looi et al. (2004, 2012)

coworkers (2012, 2013, 2014) little is known on the effects of acupuncture in modulating clinical neurogenic (vasovagal) syncope. Although not much has been reported with respect to reducing neurogenic syncope with acupuncture, one study has used this therapy to elevate blood pressure in patients with anesthesia induced hypotension (Sahmeddini et al. 2012) (Fig. 4.1).

Worth mentioning is that, in contrast to conditions associated with hyper- or hypotension, acupuncture does not influence blood pressure, heart rate or heart rate variability in normal physiological conditions when blood pressure and heart rate are within the range of normal (Chang et al. 2010; Li et al. 2004; Tjen-A-Looi et al. 2007). These observations suggest that acupuncture has little potential to cause unwanted side effects under normal conditions and underscore the notion that the potential importance of this treatment mainly is applicable to clinical significant situations (Fig. 4.2).

Cardiac and cerebral vascular diseases that lead to a relative lack of blood flow or ischemia in the heart and brain are associated with high mortality and morbidity (Ford et al. 2014; Mozaffarian et al. 2015). In fact, coronary artery disease (CAD) and stroke are the leading and the second most common causes of death in both men and women in the western world (Mozaffarian et al. 2015). Nearly two decades

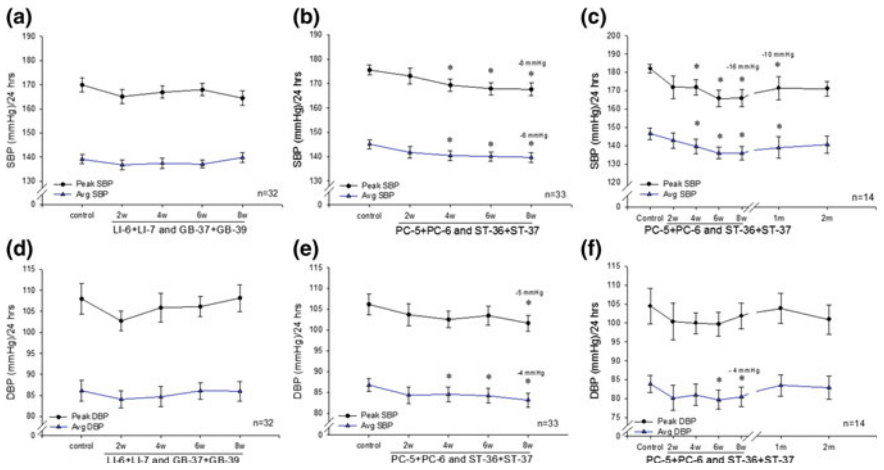

Fig. 2 Randomized prospective clinical trial using ambulatory systolic and diastolic blood pressure measurements demonstrates the efficacy of 30 min of weekly acupuncture treatment in patients with mild to moderate hypertension off medications. Electroacupuncture (EA) at control acupoints LI 6-7 + GB 37-39 did not reduce blood pressure in these patients (Panels A and D). Peak (●, black lines) and average (▲, blue lines) systolic blood pressures (SBP) evaluated during 24 h period were decreased with EA at PC 5-6 + ST 36-37 acupoints (Panels B and E). SBP decreased after four weeks (4w) of EA and lasted throughout the eight weeks (8w) of treatment (Panel B). The long lasting blood pressure lowering effect of EA persisted for at least another four weeks in a subgroup of patients who were followed for two months after completing eight weeks of therapy (Panels C and F). Both systolic and diastolic blood pressures were influenced by EA (Panels C, D, E, F). * indicates significant changes from control, pretreatment. Figures modified from Li et al. 2015b

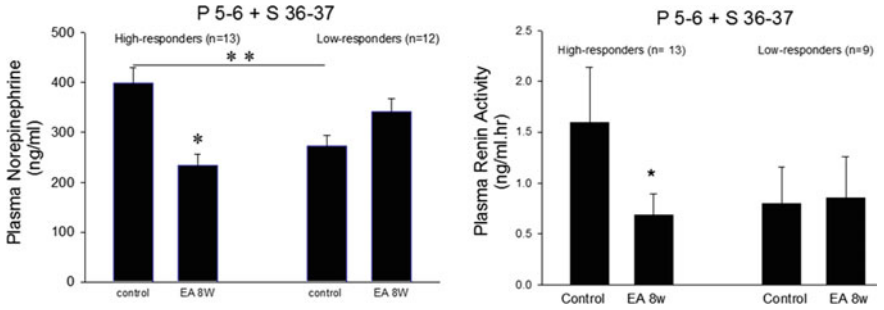

Fig. 3 Plasma levels of catecholamines and renin activities in patients with mild to moderate hypertension were reduced by the eight weeks of acupuncture treatment. High responders (70% of patients treated) to EA therapy (blood pressure Δ of ≥5 mmHg) demonstrated elevated baseline norepinephrine plasma concentrations and high renin activities and responded to EA compared to low-responders (blood pressure Δ of <5 mmHg), which had lower pretreatment hormone levels and did not respond to EA (Panels A and B; P is PC and S is ST). * significant difference compared with control. Adapted from Li et al. 2015a, b

ago Ballegaard reported that patients with angina due to CAD could benefit from acupuncture treatment (Ballegaard et al. 1986). Patients with ischemic heart disease experiencing an ischemic event in the heart manifest increased sympathetic activity, altered blood pressure and arrhythmias (Fu et al. 2008; Fu and Longhurst 2009b; Guazzi et al. 1971; Lombardi et al. 1984) that promote additional mortality and morbidity. In this regard, pharmacological therapy (e.g., β-adrenoceptor antagonists) by reducing activity of adrenergic receptors and thus decreasing sympathetic activity is commonly used to prevent recurrent ischemic attacks (Cleland and Pellicori 2013; Gottlieb et al. 1998). Experimental studies on acupuncture have focussed on its ability to decrease sympathetic activity and thereby modulate myocardial ischemia (Zhou et al. 2012; Li et al. 1998). Furthermore, acupuncture also may influence cerebral vascular disease, since pre-treatment with acupuncture may minimize cerebral ischemia (Wang et al. 2009). Clinically its combination with conventional medication has been suggested to offer significant improvement over medication alone (Tan et al. 2013). Thus, vascular diseases occurring in the heart and brain may benefit from acupuncture therapy (Fig. 4.3).

2 Clinical Application

2.1 Hypertension

Acupuncture significantly lowers blood pressure in patients on antihypertensive medications (Li et al. 2014a), but its efficacy is inconclusive in non-medicated hypertensive patients. Several studies have shown an adjunctive effect of acupuncture in

lowering blood pressure in hypertensive patients (Cevik and Iseri 2013; Flachskamp et al. 2007; Yin et al. 2007). However, trials in unmedicated patients have examined blood pressure outcome following treatment with acupuncture applied at numerous acupoints that have an unclear relevance to cardiovascular autonomic function (Macklin et al. 2006a). In this regard, a meta-analysis of 47 studies reported on four randomized and sham-controlled clinical trials. They concluded that acupuncture significantly decreases blood pressure in patients on antihypertensive medications opposed to patients not on antihypertensive drugs (Li et al. 2014a). This review included two studies in unmedicated patients. One study used manual acupuncture at a dozen acupoints while the second utilized manual acupuncture with needles at two acupoints (PC-6 and ST-36) left in place but not stimulated for 20 min (Macklin et al. 2006a, b; Kim et al. 2012). The acupuncture efficacy of lowering blood pressure in these patients likely would have been enhanced by applying acupuncture at points shown to have strong autonomic cardiovascular effects and by using continuous manual or electrical stimulation of acupoints as shown in recent study (Li et al. 2015b).

Traditional Chinese medicine promotes individualized stimulation of acupoints based on what is commonly referred to as pattern diagnosis employing meridians that are detected with skin resistance detector (Longhurst 2010; Cheung et al. 2001; Li et al. 1962). However, patients undergoing symptom-based individualized acupuncture therapy that employ numerous and different combinations of acupoints between patients may yield inconclusive findings because of the inconsistency of treatment. In this regard, a prospective double-blind randomized sham-controlled trial (Stop Hypertension with Acupuncture Research Trial), which treated patients with moderate hypertension over a 10-week period, demonstrated no influence on blood pressure over and above the response to an invasive sham control when blood pressure was measured intermittently with mercury sphygmomanometers (Macklin et al. 2006a). In another trial (Flachskampf et al. 2007), over 75% of the subjects medicated for hypertension were treated with acupuncture at many acupoints over a six week period. Although acupuncture decreased significantly 24 h ambulatory average systolic and diastolic blood pressures after treatment by 5.4 and 3.0 mmHg, respectively, it is unclear if in the absence of antihypertensive medications acupuncture applied at numerous acupoints effectively decreases blood pressure. An ongoing randomized controlled trial of patients with mild to moderate hypertension off medication is examining the combined effect of six treatment points (Li et al. 2013). This controlled trial includes three different control groups (non-meridian, invasive non-acupoint and wait listed) and employed cardiovascular-related acupoints. We will have to wait to see if this study confirms the findings reported by Li et al. that acupuncture at select cardiovascular-related acupoints decreases blood pressure in patients with mild to moderate hypertension (Li et al. 2015b).

Recently we have demonstrated that electroacupuncture lowers the blood pressure in patients with mild to moderate hypertension (Li et al. 2015b). This trial was restricted to four acupoints that have been shown experimentally to reduce elevated blood pressure and sympathetic activity (Tjen-A-Looi et al. 2003; Zhou et al. 2006; Tjen-A-Looi et al. 2004). Electroacupuncture was applied for 30 min once weekly

to stimulate a set of points that have been shown experimentally to exert strong influence over the cardiovascular system (PC-5, PC-6, ST-36 and ST-37) relative to control points (LI-6, LI-7, GB-37, and GB-39) that have little or no cardiovascular action. In this study electroacupuncture/significantly reduced both elevated systolic and diastolic blood pressures in 70% of hypertensive individuals who qualified for study (Li et al. 2015b). The onset of acupuncture's hypotensive action was slow, frequently requiring two to four weeks of treatment before sustained decreases in blood pressure were observed. The decreases persisted for up to four weeks following cessation of acupuncture. Stimulation of control non-cardiovascular acupoints did not influence the elevated blood pressure. This evidence suggests that acupuncture applied repetitively and particularly targeting cardiovascular active acupuncture points can reduce blood pressure in patients with mild to moderate hypertension. Ad hoc analyses showed a gender and age related differential efficiency to the acupuncture treatment (unpublished data). The study also found that patients most responsive to acupuncture displayed higher baseline plasma levels of norepinephrine and responded to electroacupuncture with decreases in circulating norepinephrine and renin activity (Li et al. 2015b). Thus, elevated norepinephrine and renin seem to set the stage for responsiveness to acupuncture in patients with mild to moderate hypertension . These findings support earlier observations that acupuncture works through its influence on sympathetic outflow and the renin-angiotensin-aldosterone system (Chiu et al. 1997).

2.2 Hypotension

Acupuncture has been used to restore low blood pressure in China for many years (Deng 1990; Huangdi Neijing 1983). Although, acupuncture therapy has been reported to be a useful treatment in syncope in number of individual cases (Deng 1990; Wang and Gao 2011), clinical trials are not available to confirm its efficacy. Orthostatic vasovagal syncope involving parasympathetic and sympathetic mechanisms (Morillo et al. 1997) potentially might be modulated by acupuncture treatment at the cardiovascular acupoints PC-5 and PC-6 (Tjen-A-Looi et al. 2011, 2013), which, as noted above, have also been used to lower high blood pressure in animals (Tjen-A-Looi et al. 2004) and human subjects (Li et al. 2015b).

Clinical studies on hypotension suggest that acupuncture may provide beneficial effects in anesthetized patients (Sahmeddini et al. 2012). Patients with end-stage liver diseases who undergo liver transplantation can develop hypotension during the surgical procedure (Kang et al. 1989; Jawan et al. 2014; Sahmeddini et al. 2012). Electroacupuncture at PC-5 and PC-6 acupoints appears to reduce the severity of hypotension in such patients during transplantation to a similar extent as conventional medicine (Sahmeddini et al. 2012). This study is limited by the fact that it did not compare the outcomes with control acupuncture such as needling at non-acupoint. Like acupuncture, high frequency transcutaneous electrical nerve stimulation (TENS) at PC-5 and PC-6 acupoints (30−70 Hz) has been reported to reduce

post spinal anesthesia-related hypotension in patients (Arai et al. 2008). Low systolic and diastolic blood pressures thus have been restored with TENS at PC-5 and PC-6 compared to no TENS treatment. Patients treated with TENS at PC-5 and PC-6 (active TENS group), but not patients who received non-acupoint TENS, showed significant increases in blood pressure. Both non-acupoint and no TENS treatment control groups required ephedrine medication to treat the hypotension in contrast to the group treated with active TENS (Arai et al. 2008). Thus, stimulation at PC-5 and PC-6 acupoints may reduce the incidence of hypotension post anesthesia but additional studies, particularly large randomized sham-controlled blinded trials are warranted.

2.2.1 Arrhythmias

Atrial fibrillation consequent to CAD is the most common cardiac arrhythmia in clinical practice in an increasingly aging population (Kannel et al. 1998). A meta-analysis that reviewed 571 studies found 10 that met inclusion criteria of randomized controlled acupuncture intervention clinical trials of cardiac arrhythmias (Kim et al. 2011). The responses of paroxysmal supraventricular tachycardia (PSVT), premature ventricular contractions (PVCs) and atrial fibrillation to acupuncture were evaluated in this analysis. The heart rate responses in patients with PSVT were similar with either acupuncture treatment or drug intervention in two studies that assessed the immediate effects following single application of acupuncture treatment (Dong 2006; Qi and Zhao 1993). Another trial demonstrated that a 10-day period treatment of PSVT with either repetitive acupuncture or Diltiazem led to conversion of the arrhythmia to normal sinus rhythm (Wu and Lin 2006). Two studies suggested a favorable response to acupuncture with respect to atrial fibrillation recurrence in two months (Lomuscio et al. 2011) and conversion from atrial fibrillation to normal sinus rhythm within approximately 40 min (Xu and Zhang 2007). One of these trails was a small clinical study of chronic atrial fibrillation, which demonstrated that over a period of 12 months acupuncture applied at acupoints PC-6, HT-7 and BL-17 was almost as effective as amiodarone, and acupuncture prevention of reoccurrence of atrial fibrillation after electrical cardioversion was much more effective than either no therapy or sham (needling outside meridians) acupuncture (Lomuscio et al. 2011). A study by Xu and Zhang on paroxysmal atrial fibrillation showed that acupuncture converted fibrillation to normal sinus rhythm within 40 min as opposed to the 50 min conversion time in a control group treated with amiodarone (Xu and Zhang 2007). Kim et al, 2011 concluded that although acupuncture may be an effective treatment for arrhythmias, the majority of studies in this area are low in methodological quality and many of the outcomes are based on small sample sizes. Higher quality studies in this area are needed to solidify current findings (Kim et al. 2011). Currently in Seoul Korea the effects of acupuncture in persistent atrial fibrillation (ACU-AF clinical trial), are being examined with a prospective, two-parallel-armed, participant and assessor blinded, randomized, sham-controlled clinical trial (Park et al. 2015). Both groups of patients on antiarrhythmic medication will be treated for 10 weeks once

weekly with either acupuncture or sham acupuncture. The primary outcome will assess the rate of occurrence of fibrillation (Park et al. 2015). The findings hopefully will provide new information on the adjunctive role of acupuncture in addition to conventional medication.

2.2.2 Myocardial Ischemia/Infarction

Clinical trials in patients with symptomatic CAD who were experiencing demand-induced myocardial ischemia have shown that acupuncture can reduce both the intensity and frequency of angina attacks (Ballegaard et al. 1986). Acupuncture also appears to improve the quality of life and lower the cost of treatment (Ballegaard et al. 1996 1999; Richter et al. 1991). Several clinical studies suggest that both TENS and acupuncture may reduce myocardial ischemia during pacing and exercise in patients with angina and electrocardiographic evidence of ischemia (Mannheimer et al. 1982, 1985, 1989; Emanuelsson et al. 1987; Ballegaard et al. 1990, 1991, 1996, 1995, 1999; Richter et al. 1991). A meta-analysis has examined the incidence of acute myocardial ischemia in patients treated with acupuncture in combination with conventional drugs or drugs alone. The analysis indicated that the number of ischemic events in patients treated with a combination of acupuncture and drugs was superior to medication alone. The time to onset of relief was improved in patients treated with acupuncture and medications. However, the onset of relief took longer in patients treated with acupuncture alone compared to drug therapy (Chen et al. 2012). Similarly, slow onset but long-lasting responses to acupuncture have been observed in a recent clinical trial of hypertension, an important risk factor for CAD (Li et al. 2015b; Rapsomaniki et al. 2014). Another clinical study involving a small group of patients with angina examined the possibility that electroacupuncture at PC-6 for 20 min improved cardiac function (Liu et al. 2014). Acupuncture improved cardiac function in these patients but did not influence cardiac function in normal controls. Inclusion of a control such as sham acupuncture (for instance needling outside a meridian) would enhance studies designed to confirm current findings.

Patients with stable ischemic heart disease have reduced heart rate variability (HRV) (Vaseghi and Shivkumar 2008). A recent clinical study evaluated cardiac autonomic function using HRV in patients with stable ischemic heart disease following acupuncture at eight acupoints vs. non-acupoints vs. no treatment (wait listed group). Compared to sham acupuncture, 12 weeks of acupoint treatment moderately modulated HRV in these patients (Mehta et al. 2014), suggesting that acupuncture may improve depressed HRV and therefore autonomic sympatho-vagal balance (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology 1996; Stein and Kleiger 1999). Additional clinical trials are warranted to solidify these findings.

2.3 Stroke

Scalp acupuncture is one of several specialized acupuncture techniques with specific point location, in which needles are applied to specific points on the scalp (Liu et al. 2012). Cranial acupuncture has been practiced for thousands of years and has developed into one type of treatment known as scalp acupuncture in recent decades in the western world (Wang et al. 2012; Liu et al. 2012), although little high quality data from adequately constructed clinical trials are available to support their use. Scalp acupuncture often is used to treat abnormalities of the central nervous system, in particular, stroke. The clinical efficacy and safety of scalp acupuncture for acute ischemic stroke has been evaluated in a systematic review that utilized six databases (Wang et al. 2012). Randomized controlled trials of acute ischemic stroke treated with either scalp acupuncture or western conventional therapy included in this review incorporated eight studies with a total of 538 subjects. It was concluded that treatment with scalp acupuncture improved neurological deficit scores and a new measure called the clinical effective rate. The clinical effective rate included favorable clinical outcome following general medical support, specialized support such as improvement of cerebral circulation with anti-platelet and anti-clotting drugs and treatment for acute complications. No adverse events were reported in any of the eight studies (Wang et al. 2012). However, the authors did conclude that the beneficial effect from treatment with scalp acupuncture was overvalued since the placebo or sham actions of acupuncture scalp needling in acute ischemic stroke were unclear. Hence, sham-controlled clinical trials are needed for further investigation of the value of scalp acupuncture in stroke.

In addition to the above studies of scalp acupuncture, a randomized controlled pilot study assessed motor function recovery in patients with acute ischemic stroke treated with either western medications or combined electroacupunctureand western medicine. Patients received medications or electroacupuncture and western medicine ($n = 32$) for 14 days. The combination of electroacupuncture and medication greatly improved motor function compared to patients treated with conventional medication (Tan et al. 2013). There was no sham acupuncture comparison of patients treated with medication. To verify the findings of this study a multicenter clinical trial with subjects and inclusion of sham acupuncture group is necessary.

3 Mechanistic Research

3.1 Hypertension

Experimental studies in animal models have shown that electroacupuncture inhibits sympathetic outflow and hence reduces blood pressure that is elevated during sympathoexcitatory reflex activation. The reduction of sympathetic activity is orchestrated by changes in signal processing in a number of interconnected cardiovascular

regions in the brain (Li et al. 2006, 2010; Moazzami et al. 2010; Tjen-A-Looi et al. 2006). A number of neurotransmitter systems activated by acupuncture are involved in stress and reflex-induced hypertension (see below) and facilitate reductions in elevated sympathetic outflow (Fu and Longhurst 2009a; Guo et al. 2004, 2008; Li et al. 2010; Tjen-A-Looi et al. 2007, 2009; Moazzami et al. 2010; Zhang et al. 2013). Experimental paradigms used to evoke sympathoexcitation and to test the influence of acupuncture include stimulation of sensory nerves in the visceral organs, such as the gallbladder with bradykinin (related to inflammatory pain) and distension of the stomach (related to food ingestion), spontaneously hypertensive rats and stress-induced hypertension in rats (Li et al. 2002, 2016; Tjen-A-Looi et al. 2007; Yao et al. 1982; Zhang et al. 2013). Sympathetic activity is chronically elevated in spontaneously hypertensive rats relative to non-hypertensive Wistar Kyoto rats (Jia et al. 2014) as well as in cold-induced hypertensive rats (Li et al. 2016; Papanek et al. 1991). Chronic elevation in blood pressure in conscious spontaneously hypertensive rats has been reduced by acupuncture at ST-36, a response that lasts for up to twelve hours (Yao et al. 1982). Sustained cold-induced hypertension in conscious rats is reduced by five weeks of electroacupuncture applied bilaterally twice weekly at ST-36 and ST-37 acupoints (Li et al. 2016). Furthermore, the blood pressure in cold-induced hypertensive rats treated with electroacupuncture at ST-36 and ST-37, in contrast to sham acupuncture, is decreased markedly during and after therapy, concurrent with elevation in the mRNA of preproenkephalin, the precursor of the opioid peptide enkephalin. Preproenkephalin remains elevated for up to three days after termination of the repeated acupuncture treatment. These findings demonstrate that through transcriptional regulation electroacupuncture increases modulatory opioid peptides in the rVLM to persistently reduce elevated sympathetic activity and blood pressure.

Electroacupuncture inhibits elevated sympathetic activity during exercise (Li et al. 2004). Exercise-evoked reflex increases in systolic and mean blood pressures are reduced by electroacupuncture at PC-5 + PC-6 and LI-4 + L-7 acupoints in about 70% of normal subjects while diastolic blood pressure and heart rate are unchanged. Additionally, the achieved exercise workload is increased following 30 min of electroacupuncture. The postulated mechanisms are reductions in cardiac afterload associated with vasodilation of exercising muscle to allow improved performance (Li et al. 2004). Furthermore, in patients with mild to moderate hypertension eight weeks of electroacupuncture applied weekly decreases blood pressure and norepinephrine, reflecting reduced sympathetic activity (Li et al. 2015b). Thus, in animals and humans, both reflex and sustained hypertensions are inhibited by single and repetitive electroacupuncture, respectively.

A number of neurotransmitters in the brain contribute to the reduction of sympathoexcitatory activity during electroacupuncture. In this regard, stimulation of somatic afferents by electroacupuncture alters central processing through the actions of γ-aminobutyric acid (GABA), opioids, nociceptin, glutamate, acetylcholine, cannabinoids and serotonin and their receptor subtypes to influence sympathetic activity (Li et al. 2010; Tjen-A-Looi et al. 1999, 2007, 2009; Crisostomo et al. 2005; Moazzami et al. 2010; Zhou et al. 2006). Immunoreactive expression of neuropeptide

apelin-13, a stress-related neuropeptide detected in cardiovascular rostral ventrolateral medulla (rVLM) of the brainstem, is decreased by electroacupuncture (Zhang et al. 2013). Daily intermittent electric foot shock for 14 days induces sustained elevations in blood pressure. Five days of daily electroacupuncture treatment for 30 min at ST-36 acupoints reduces the stress-induced elevated blood pressure, while the expression of apelin, but not its receptor, is decreased in the rVLM (Zhang et al. 2013). Future studies are warranted to better understand the importance of apelin in the rVLM during stress induced sympathoexcitation and acupuncture.

3.2 Hypotension

Acupuncture also appears to modulate hypotension underscoring its tendency to normalize blood pressure. In this regard, acupuncture is capable of reversing hypotension in experimental models of nitroprusside infusion and hemorrhage (Xiao et al. 1983; Syuu et al. 2003). The influence of acupuncture likewise has been studied during intravenous infusion of phenylbiguanide (PBG), a 5-HT_3 receptor agonist that stimulates cardiopulmonary vagal afferent endings (Coleridge and Coleridge 1980; Fu and Longhurst 1998; Jeggo et al. 2005) to evoke bradycardia and hypotension. This model has been used to simulate clinical neurogenic or vasovagal syncope, a common cause of syncope in patients (Kapa and Somers 2008; Calkins and Zipes 2008). Electroacupuncture significantly reverses PBG-induced bradycardia and hypotension, in part through the actions of opioids and GABA. In the nucleus tractus solitarius (NTS), GABA modulates glutamatergic and vagal preganglionic neuronal activity that influences the ventrolateral region of the nucleus ambiguus and, in turn, heart rate (Tjen-A-Looi et al. 2012, 2014). Anatomical studies have shown that preganglionic cholinergic vagal neurons in the nucleus ambiguus that process EA-evoked input are in close proximity to neuronal processes containing enkephalin, further confirming the role of this opioid neurotransmitter in electroacupuncture modulation of parasympathetic outflow and heart rate (Guo et al. 2012). Other studies suggest that opioid receptor activation in the NTS contributes to the reduction of hypotension with acupuncture (Tjen-A-Looi et al. 2014, 2018), likely through inhibition of sympathoexcitatory outflow from the rVLM. These data, in aggregate, show that acupuncture through its actions on a number of brain stem neuronal pathways normalizes heart rate and blood pressure when they are decreased by reflex cardiopulmonary input.

Transcutaneous electrical nerve stimulation (TENS) has been used as a surrogate for acupuncture. There are similarities between TENS and electroacupuncture (Melzack and Wall 1982), but there also are differences. Transcutaneous stimulation is not exactly equivalent to acupuncture since it uses stronger intensities of stimulation and often higher frequencies. High frequency stimulation with transcutaneous stimulation likely will not display identical hemodynamic outcomes as those achieved with electroacupuncture. For example, 100 Hz stimulation at ST-36, SP-6, LI-4 and LI-11 does not raise blood pressure during sodium nitroprusside-induced hypotension in

dogs (Zhang et al. 2014). However, this frequency of acupoint stimulation has been shown to increase blood flow to liver and stomach and reduce apoptosis in certain organs such as stomach and kidney (Zhang et al. 2014). On the other hand, another clinical study has documented reversal of spinal anesthesia-induced hypotension during TENS at 30−70 Hz (Arai et al. 2008). The mechanisms underlying TENS are not fully understood and may depend on the actions of different neurotransmitters than those that have been shown to underlie acupuncture's actions. More investigation is needed to better understand the mechanisms involved in TENS therapy.

3.3 Arrhythmias and Myocardial Ischemia/Infarction

The effectiveness of acupuncture in experimental arrhythmias during stimulation of the hypothalamus has been studied extensively (Li and Tjen-A-Looi 2013). Stimulation of the dorsal medial hypothalamic nucleus, ventral medial hypothalamic nucleus and fornix of the medial and posterior hypothalamus increases skeletal muscle blood flow, cardiac sympathetic activity and blood pressure, and induces premature ventricular contractions (PVCs), while bilateral stellectomy abolishes this arrhythmia and the associated pressor response (Lopes and Palmer 1977; Li and Tjen-A-Looi 2013). Low frequency and low intensityelectroacupuncture at ST-36 and PC-6 inhibited hypothalamically stimulated PVCs. Stimulation of cutaneous nerves, such as the peroneal or radial nerves, does not inhibit PVCs, indicating the importance of stimulating deep somatic nerves underlying ST-36 (deep peroneal nerve) and PC-6 (median nerve) (Guo et al. 1981). Bilateral vagotomy does not influence acupuncture-related inhibition of PVCs, suggesting that such therapy does not reduce ventricular arrhythmias through a parasympathetic mechanism.

Reperfusion-related ventricular tachycardia in rats following three minutes of coronary artery occlusion is reduced by electroacupuncture at PC-5 and PC-6 concomitant with a decrease in myocardial oxygen demand (Lujan et al. 2007). If acupuncture reduces myocardial ischemia, it is natural to suggest that this intervention also may reduce infarction. Two recent experimental studies examining the potential for electroacupuncture to reduce infarct size in models of ischemia-reperfusion injury have arrived at different conclusions. One study of rabbits subjected to 30 min of left anterior descending coronary artery occlusion, followed by 90 min of reperfusion reported that 30 min of low frequency (2 Hz) electroacupuncture at PC-5 and PC-6, but not sham acupuncture (needle insertion at active points without stimulation), decreased infarct size from 49 to 15% of the area at risk as well as the arrhythmia score (Zhou et al. 2012). These decreases were associated with a lower heart rate, double product, ST depression and interstitial norepinephrine concentration during reperfusion. Naloxone, which antagonizes opioid receptors, attenuated the beneficial response to electroacupuncture. A second study in rats utilizing low frequency (2 Hz) electroacupuncture at same points along the pericardial meridian, beginning 5 min before coronary occlusion and lasting for 40 min, demonstrated no reduction of infarction in the area at risk nor any alteration in arrhythmias

(Kloner et al. 2012). The investigators in the latter study observed no change in hemodynamic responses during ischemia-reperfusion in response to acupuncture. The different outcomes suggest that, in the absence of any hemodynamic changes that will reduce myocardial oxygen demand, electroacupuncture is unlikely to alter infarct size.

Cardiac norepinephrine spillover is increased in patients with sustained ventricular arrhythmias suggesting that cardiac sympathetic activation is associated with ventricular arrhythmias in some patients (Meredith et al. 1991). Electroacupuncture at PC-5 and PC-6 offers cardiac protection against myocardial ischemia and reperfusion through decreases in oxygen demand and cardiac norepinephrine as well as opioid and PKC-dependent pathways (Zhou et al. 2012), further suggesting that acupuncture inhibits sympathetic outflow to the heart (Li et al. 1998). It is conceivable that, when acupuncture decreases cardiac sympathetic activity to protect against cardiac injury following myocardial ischemia-reperfusion, it also modulates ventricular arrhythmia by modulating sympathetic tone.

Electroacupuncture also significantly decreases renal sympathetic nerve activity, inhibits capsaicin-induced cardiac sympathetic afferent reflex response, and lowers the blood pressure in rats with heart failure following coronary artery ligation (Ma et al. 2014). In heart failure, electroacupuncture for one week at PC-5 and PC-6, in contrast to stimulation of LI-6 and LI-7 acupoints, significantly increases left ventricular ejection fraction as well as fractional shortening, reverses left ventricular end-diastolic enlargement consequent to changes in end-systolic and end-diastolic dimensions and reduces infarct size (Ma et al. 2014). Moreover, 30 min of daily acupuncture at ST-36 for eight weeks increases heart rate and baroreceptor reflex sensitivity in rats with coronary artery ligation induced heart failure (Lima et al. 2015). In summary, electroacupuncture reduces sympathetic activity and inhibits cardiac sympathetic reflex responses, which are sensitized in chronic heart failure, decreases infarct size and improves baroreceptor reflex responses. Thus, acupuncture may serve a useful role in improving cardiac function, remodeling of the heart and reducing infarct size.

In addition to decreasing sympathetic excitation, acupuncture may promote angiogenesis after myocardial ischemia (Fu et al. 2014). Through acetylation of the gene for vascular endothelial growth factor (VEGF), angiogenesis is an important process for cardiac protection (Lorier et al. 2011). Acupuncture at PC-6 may influence angiogenesis mediated by increased VEGF gene expression that is directly regulated by H3K9 histone acetylation (Fu et al. 2014). Fu and coworkers have demonstrated that during myocardial ischemia acupuncture reverses S-T segment changes, reduces Q-wave area, and decreases the release of creatine kinase, creatine kinase-MB, and lactate dehydrogenase, mitigates myocardial remodeling and promotes microvessel formation (Fu et al. 2014). RNA-sequencing has demonstrated that electroacupuncture modifies a signaling pathway in VEGF-induced angiogenesis (Fu et al. 2014). Protein expression by western blot demonstrates that VEGF and its signaling factors, including Ras, phospho-p44/42 MAPK, phospho-p38 MAPK, phospho-SAPK/JNK and Akt are elevated significantly following electroacupuncture (Fu et al. 2014). Acupuncture treatment during myocardial ischemia increases H3K9 acetylation, sup-

porting the conclusion that H3K9 recruitment at the VEGF promoter may lead to angiogenesis and improve cardiac protection (Fu et al. 2014).

3.4 Stroke

Each year approximately 800,000 people experience new and recurrent strokes. In 2010, one of every 19 deaths was caused by cerebral vascular disease in the United States (Go et al. 2014). Acupuncture therapy following a stroke event has been suggested to reorganize surviving networks, assessed with single-photon emission computed tomography brain perfusion images in six patients with middle cerebral artery occlusion (Lee et al. 2003). Reorganization of neuronal network occurs following structural damage in the brain (Grefkes and Ward 2014). Corticospinal and brainstem pathways as well as interhemispheric connections influence cortical reorganization and functional recovery (Grefkes and Ward 2014). Acupuncture stimulation at cranial and somatic acupoints activates many regions in the brain, including the brainstem and hypothalamus (Tjen-A-Looi et al. 2003; Li et al. 2009), and in this fashion may contribute to recovery after an ischemic insult to the brain.

Although clinical studies are inconclusive, experimental electroacupuncture for 30 min at facial and scalp points (Du-26 and Du-20) within 5 min after the onset of middle cerebral artery occlusion (MCAO) in rats has been shown to reduce ischemic infarction, neurological deficits and survival. Cerebral blood flow also is increased during low energy acupuncture at frequencies between 5 and 20 Hz (Zhou et al. 2011). Angiotensin receptor stimulation may participate in the improved blood flow (Li et al. 2014b). Electroacupuncture at GV-26 decreases elevated AT-1, but not AT-2, receptors and associated receptor-mediated signaling pathway during MCAO. Such application of acupuncture improves cerebral blood flow and decreases ischemic injury in rats (Li et al. 2014b). However, inclusion of a control acupuncture group would help determine if the needling or simple manipulation of the animal reduces stroke injury.

Electroacupuncture at GB-20 scalp acupoint markedly improves behavioral responses, reduces ischemic injury and promotes neuroplasticity compared with an MCAO control group (Xu et al. 2013). Like pergolide, a selective dopamine D2-receptor agonist, acupuncture reduces the detrimental responses to cerebrovascular occlusion. Conversely, a D2-receptor selective antagonist, spiperone, reversed the beneficial effects of electroacupuncture Xu et al. (2013), suggesting that acupuncture modifies cerebral ischemic injury through a dopamine mechanism. Growth associated protein-43 (GAP-43), a marker of nerve fiber regeneration is increased in dopaminergic neurons following electroacupuncture or treatment of rats with a dopamine agonist. It is unclear, however, if acupuncture increased the number of dopaminergic neurons or simply the expression of GAP-43. Furthermore, control or sham acupuncture with ischemic injury group was not examined.

4 Conclusion and Perspectives

The last five to ten years a number of studies have reported on the usefulness of acupuncture on cardiovascular diseases such as hypertension, hypotension, cerebral ischemia and stroke, and other cardiac diseases and disease manifestations, including arrhythmias, myocardial ischemia and infarction. Acupuncture at somatic acupoints modulating sympathetic activity appears to reduce hypertension and arrhythmias, especially tachyarrhythmias, and parasympathetic outflow to increase blood pressure and heart rate during hypotension and often accompanying bradycardia To treat cerebral ischemia, acupuncture treatment at facial and cerebral acupoints may improve blood flow to the brain, although additional high quality studies are necessary. Importantly it has become apparent that an improved understanding of mechanisms associated with acupuncture-cardiovascular regulation demonstrated in experimental studies can help guide clinical studies to examine efficacy of this therapy in the treatment of cardiovascular diseases.

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Electroacupuncture Inhibition of Hypertension is Slow Onset and Long-Lasting

Peng Li, Stephanie C. Tjen-A-Looi and John C. Longhurst

Abstract Our recent study shows that electroacupuncture (EA) at P 5-6 + S 36-37 acupoints with low current and low frequency once a week for 4–8 weeks can effectively reduce systolic blood pressure (SBP) and diastolic blood pressure (DBP) in patients with mild to moderate HTN (BP: > 140 < 180/ > 90 < 110 mmHg). Thirty six hypertensive patients without medication were assessed with 24 h ambulatory BP monitoring, and EA at P 5-6 and S 36-37 given once weekly for 30 min for eight weeks. The 8-week treatment significantly decreased peak and average SBP/24 h in 25 patients (~70%). The peak and average DBP/24 h also decreased significantly. Heart rate was unchanged. After termination of EA treatment, SBP remained reduced for an additional four weeks but over the next four weeks returned to near pretreatment levels. Eleven patients (~30%) did not respond to the EA treatment. Both SBP and DBP/24 h were not reduced in 28 other patients treated with control acupoints (LI 6-7 + G 37-39). These data suggest that EA at select acupoints, performed once weekly for 8 weeks, significantly reduced BP. This beneficial effect was slow in onset but persisted for a prolonged period of time. The mechanism of the slow onset and long-lasting EA effect is complicated. It likely is related to opioids and GABA in rostral ventrolateral medulla (rVLM), neural circuit between arcuate nucleus in hypothalamus and rVLM, and preproenkephalin mRNA in rVLM. In subgroups of patients we measured plasma catecholamines (n = 25), renin (n = 22) and aldosterone (n = 18). After eight weeks of EA, plasma concentrations of nor-epinephrine, renin and aldosterone decreased significantly ($P < 0.05$) in the EA-responders in contrast to low-responders. Thus, the renal sympathetic function and renin-aldosterone system were related to the long-lasting effect of EA inhibition.

Keywords Opioids · γ-aminobutyric acid · Arcuate nucleus, ventrolateral periaqueductal gray · Rostral ventrolateral medulla · Preproenkephalin mRNA · Renin · Catecholamine, angiotensin · Aldosterone

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Abbreviations

SBP Systolic blood pressure;
DBP Diastolic blood pressure;
HTN hypertension;
GABA Gamma-aminobutyric acid;
rVLM Rostroventrolateral medulla:
vlPAG ventrolateral periaqueductal gray
NRP Nucleus raphé pallidus.

1 Introduction

Hypertension (HTN) or high blood pressure is one of the most common clinical disorders in the world. In the United States nearly a third of the adult population is hypertensive while the prevalence of hypertension increases with age. The lifetime risk of developing hypertension in middle-aged adults approaches 90% in the United States (Vincent and Richardson 1986). Many patients (46%) with known cardiovascular disease are hypertensive and 72% of them have experienced a stroke that accounted for approximately 15% of the 2.4 million deaths (Mayer 2000). In 2008 the estimated direct and indirect cost of hypertension was $69.9 billion.

Although western medical science has developed a number of treatment strategies to control hypertension, antihypertensive medical therapies are not perfect and are associated with adverse side effects. Drug therapy indiscriminately blocks many receptors leading to unwanted responses (Eisenberg et al. 1993, 1998; World health organization 2003).

2 Clinical Application

2.1 EA at Select Acupoints Reduces High Blood Pressure

Previous mechanistic laboratory studies have demonstrated that acupuncture modulates neurohumoral regulatory systems and hence cardiovascular function (Li and Yao 1992; Cheung et al. 2001). Using a point-specific approach to acupoint stimulation we have demonstrated that acupuncture at Neiguan–Jianshi and Zusanli–Shangjuxu (P 5-6 and S 36-37), in contrast to EA at Pianli–Wenliu and Guanming–Xuanzhong (LI 6-7 and G 37-39), modulates elevated blood pressure (Li et al. 1998; Zhou et al. 2005). We also have shown that low frequency, low intensity electroacupuncture, at an intensity that is just below motor threshold, causes the largest decreases in reflex induced hypertension (Li et al. 2002; Tjen-A-Looi et al. 2003). Repeated EA (P 5-6 + S 36-37) prolongs the lowering of blood pressure (Li et al. 2016; Li et al. 2015).

Our clinical study showed that weekly EA at P 5-6 + S 36-37 (active) but not LI 6-7 + G 37–39 (control) acupoints for 8 weeks decreases elevated blood pressure for a prolonged period of time in patients with mild to moderate hypertension. We used 24 h ambulatory blood pressure measurements to monitor EA-inhibition of peak and average SBP and DBP and to identify high and low responders to EA. About 70% of mild to moderate hypertensive patients, who are not on antihypertensive pharmaceutical therapy, responded well to EA treatment. This beneficial acupuncture effect is slow in onset but persists for a prolonged period of time (Li et al. 2015).

2.2 Slow Onset and Long-Lasting EA Effect

The slow onset and long-lasting EA effect also exist in animal experiments. In anesthetized animals, we and others have demonstrated that EA inhibition of sympathoexcitatory cardiovascular premotor rVLM neuronal activity lasts for over an hour after cessation of EA (Tjen-A-Looi et al. 2004). EA inhibition of cardiovascular excitatory reflex responses lasts between one to six hours in anesthetized rabbits, rats, and cats (Guo et al. 1981; Huangfu and Li 1985; Lovick et al. 1995). In conscious animals (dogs and spontaneous hypertensive rats), EA modulates blood pressure for 1 to 12 h (Lin and Li 1981; Yao T et al. 1982). Thus, inhibition of cardiovascular function by acupuncture cannot be explained with short-term neural occlusive response originating from somatic-visceral convergent. We have identified several mechanisms that likely are involved in the prolonged action of EA on cardiovascular function.

3 Mechanistic Research

3.1 Mechanism of the Long-Lasting Inhibition of EA in Animal Experiments

The inhibitory action of EA on rVLM sympathetic premotor neuronal responses to excitatory visceral input lasts for 30–40 min after the cessation of a single 30 min application of EA. This prolonged inhibition involves specific neurotransmitters. In particular, opioids and GABA but not nociceptin, are important during the long-lasting EA effect (Tjen-A-Looi et al. 2007).

The hypothalamus, midbrain and medulla participate in the action of acupuncture. Microinjection of the glutamatergic excitotoxic agonist, kianic acid (KA), into the hypothalamic region blocks EA inhibition of reflex-induced hypertension, including the prolonged action of EA in this hypertensive reflex response. The prolonged inhibition of rVLM neurons by EA requires an intact arcuate nucleus (Huangfu and Li 1985, 1987, 1988; Li P et al. 2006a). Furthermore, we have examined reciprocal excitatory projections between the arcuate nucleus and the vlPAG that form a rein-

forcing circuit contributing to prolongation of EA-cardiovascular regulation for as long as 30–60 min (Li et al. 2010b). Projections from the vlPAG to the NRP and then to the rVLM contribute to serotonin inhibition of rVLM neurons (Li et al. 2010c). Thus, the long-lasting inhibition of sympathoexcitation with acupuncture involves a long-loop neural supraspinal pathway that includes the arcuate nucleus, vlPAG, NRP and rVLM, important sites of neurotransmitter opioid synthesis (Huangfu and Li 1988; Li et al. 2006a; Li and Longhurst 2007).

Prolonged inhibition of blood pressure lasts for several days in patients with mild to moderate hypertension. In this respect, studies have suggested that acupuncture may increase mRNA expression of opioid precursors in the brain for 24 to 72 h (He et al. 1995; Guo et al. 1996). Recent data from our laboratory using real-time PCR demonstrated that preproenkephalin in the rVLM is increased by 90 min after completion of a single 30 min application of EA at P 5-6 acupoints of rats (Li et al. 2010a). Moreover, in conscious rats treated with repeated EA expresses increased preproenkephalin for over 24 h while the concentration of enkephalin is elevated for 48 h in the rVLM (Li et al. 2012). The roles of opioid mRNA expression and other neurotransmitter precursors, as well as neurotransmitters released in the hypothalamus, midbrain, and other regions of the medulla, particularly in studies involving repetitive EA in sympathoexcitatory conditions are worthy of further investigation.

3.2 Humoral Factors in EA Inhibition of HTN

Acupuncture reduces blood pressure modulation of the endocrine system that includes decreases in plasma renin, angiotensin II and aldosterone and increases in excretion of sodium (Yao 1993). Our recent clinical data in HTN patients showed that following EA at P 5-6 + S 36-37 acupoints for eight weeks influenced the concentrations of plasma catecholamine, renin and aldosterone (Li et al. 2015).

Plasma epinephrine was not influenced by EA (40 ± 6 to 38 ± 8 ng/ml, $P > 0.05$) in 25 patients. Plasma norepinephrine in the high responders was significantly greater than the low responders prior to EA treatment. Following eight weeks of EA treatment, norepinephrine decreased from 398 ± 32 to 234 ± 22 ng/ml in 13 high responders (Fig. 7, Li et al. 2015). Norepinephrine in the low responders remained unchanged with EA treatment. Plasma norepinephrine also was unchanged (274 ± 19 to 345 ± 25 ng/ml) in six patients subjected to stimulation of LI 6-7 + G 37-39 acupoints.

Plasma renin activity in 13 high responders to EA at P 5-6 + S 36-37 decreased from 1.8 ± 0.6 to 0.6 ± 0.2 ng/ml·hr after EA treatment. Treatment with EA at P 5-6 + S 36-37 acupoints did not alter renin activity (0.8 ± 0.4 vs. 0.9 ± 0.4 ng/ml·hr) in nine low responders. Baseline renin activity tended to be lower in the low responders than the high responders ($P = 0.102$) (Fig. 8, Li et al. 2015). Nine other patients treated with EA at LI 6-7 + G 37-39 points for eight weeks displayed an insignificant change in renin activity (1.5 ± 0.4 vs. 2.5 ± 0.8 ng/ml·hr).

Plasma aldosterone was reduced by EA from 143 ± 10 to 111 ± 11 pg/ml in five EA-responsive patients. Insufficient blood samples were available to assay aldosterone in the low responders to EA P 5-6 + S 36-37 acupoints. Plasma aldosterone was not altered (from 156 ± 43 to 161 ± 46 pg/ml) in seven patients treated with EA at LI 6-7 + GB37-39 acupoints.

3.3 CCK8 in Non-responders

Non responsiveness to acupuncture treatment occurs in about 30% of subjects. Han and Terenius (1982) in Beijing and Cao et al. (1983) in Shanghai reported that the EA analgesic response occurs in ~ 70% of patients (Han and Terenius 1982; Cao et al. 1983). We observe similar acupuncture effectiveness in sympathoexcitatory cardiovascular responses and hypertension (Li et al. 2004; Li and Longhurst 2015). Consequently, in rats we investigated the neurotransmitter that antagonizes the actions of opioid, the important neuromodulator in the actions of EA. We have shown that within the rVLM, cholecystokinin 8 (CCK8) reverses the effects of EA while blockade of its receptor converts EA non responsive subjects into EA responders (Li et al. 2013). Thus, neurotransmitter mechanisms cover a broad range of actions and influence the effectiveness of acupuncture.

4 Concluding Remarks and Perspectives

Our data demonstrate that EA at P 5-6 + S 36-37 once weekly for 4–8 weeks significantly inhibits systolic and diastolic blood pressures measured over 24 h who are not on medication in ~ 70% HTN patients. After stopping EA treatment, blood pressure remains low for one month and by two months the effectiveness of acupuncture has subsided and blood pressure increases toward original hypertensive level. In a small number of patients 6-month reinforcement therapy of once a month was provided reinforcement therapy of once a month was provided following the eight weeks EA treatment. The lowered blood pressure was maintained for at least six months. The 30% non- or low responsiveness to EA patients may have been influenced by neuronal CCK that antagonized the actions of opioids. However, the poor responsiveness to EA may also be related to the level of stress, including the emotional state, being over- weight, lack of exercise, among other factors. Further analysis is warranted.

We have not examined other acupoints used by other acupuncturists in treating symptoms related to hypertension. The acupoints such as LI11, LI4, and other acupoints located on the head also project to the arcuate nucleus and thus may inhibit sympathetic activity and reduce hypertension. Furthermore, the question remains on how frequently the patients should be treated to gain maximal acupuncture effect. Thus, we do not know if EA reduces high blood pressure significantly faster or leads

to a greater reduction in blood pressure if the therapy is applied twice or more times per week to hypertensive patients. These issues likewise need further study.

Although we have shown that EA modulates both sympathetic and parasympathetic systems in inhibitory cardiovascular responses, it is unclear if acupuncture also influences parasympathetic activity in treating HTN. Our data suggest that the long-lasting EA inhibition of hypertension is related to inhibition of sympathetic activity, in particular, the renal sympathetic nerve. The decreased release of renin, angiotensin and aldosterone suggests an increase in the excretion of sodium and water that leads to decrease in blood volume and reduced SBP. However, we also do not know how the decreased catecholamine, renin and aldosterone influence the central nervous system. Further studies are needed.

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Acupuncture Treatment for Pain: Clinical and Laboratory Research

Ting Wang, Zhiyan Sui, Terry C. Xia, Guoqiang Wen and Ying Xia

Abstract Pain is a complex feeling with emotional driving and vegetative nerve reactions, and is one of the most common symptoms in the clinic. Pain has dual meanings to the human body. On the one hand, pain serves as a warning sign of injury, disease, and abnormality. A person with a loss of congenital pain cannot quickly respond to internal and external insults that often cause trauma, scald, or other injury. Those that have no pain or are insensitive to pain cannot respond to visceral disorders in time, which delays or misleads the diagnosis and treatment. On the other hand, persistent or severe pain brings suffering to the patient, and needs to be treated. However, many issues remain unsolved in term of pain management, e.g., analgesics-induced drug addiction. An abundance of research has shown that acupuncture or electroacupuncture can induce a good analgesic effect with little side effects. This chapter will summarize clinical and laboratory research on this topic and update recent progress.

Keywords Acupuncture · Analgesia · Pain evaluation · Animal models · Neurotransmitters · Brain

Abbreviations

5 Hydroxytryptamine	5-HT
Acetylcholine	ACh

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Acetylcholinesterase	AChE
AMP-activated protein kinase	AMPK
Bio-breeding Zucker/Worcester	BBZDR/Wor
Blood brain barrier	BBB
Brain-derived neurotrophic factor	BDNF
Catecholamine	CA
Central Nervous System	CNS
Choline acetyltransferase	ChAT
Chronic compression injur	CCI
Chronic low back pain	cLBP
Chronic pelvic pain syndrome	CPPS
Chronic prostatitis	CP
Complete Freund's adjuvant	CFA
Delta-opioid receptors	DOR
Diabetic painful neuropath	DPN
Dopamine	DA
Dorsal root ganglion	DRG
Facial expression scoring	FPS
Gamma-aminobutyric acid	GABA
Goto-Kakizaki	GK
κ-opioid receptors	KOR
Irritable bowel syndrome	IBS
Long-needle acupuncture	LA
Lumbar disc herniation-induced	LDH
Manual acupuncture	MA
McGill pain questionaire	MPQ
Monoamine oxidase	MAO
Motor nerve conduction velocity	MNCV
Mu- opioid receptors	MOR
Neuropathic pain	NP
Norepinephrine	NE
Nuclei raphe magnus	NRM
Numeric rating scale	NRS
Painful diabetic neuropathy	PDN
Partial sciatic nerve injury	PNI
Periaqueductal grey	PAG
Postdural puncture headache	PDPH
Postherpetic neuralgia	PHN
Postoperative nausea and vomiting	PONV
Preproenkephalin	PPE
Prodynorphin	PDYN
Randomized controlled trials	RCTs
Raphe-spinal	R-S
Rostral ventromedial medulla	RVM
Spinal cord dorsal horn	SCDH

Spina cord injury	SCI
Spinal manipulative therapy	SMT
Spinal nerve ligation	SNL
State-Trait Anxiety Inventory-State	STAI-S
Streptozotocin	STZ
Submedius	SM
Substance P	SP
The quality of life	QOL
Total intravenous anesthesia	TIVA
Traditional acupuncture	TA
Trigger point acupuncture	TrP
Transcutanclus Electrical Acupoint Stimulation	TEAS
Transcutaneous electrical nerve stimulatior	TENS
Vascular endothelial growth factor	VEGF
Ventrolateral orbitalcortex	VLO
Vesicular acetylcholine transporter	VAChT
Verbal rating scale	VRS
Visual analogue scale	VAS
Zucker diabetic fatty	ZDF

1 Introduction

Pain is a clinically major problem, and a common cause for seeking physician consultation (Chen et al. 2014). As defined by the International Association for the Study of Pain and the World Health Organization, pain is an unpleasant sensory and emotional experience which is associated with actual or potential tissue damage, or described in terms of such damage (International Association for the Study of Pain 2014). Some of pain states are not fatal, but they always have a considerable negative impact on daily life, create a huge economic burden, and put a huge strain on the world's health care system (Chen et al. 2014). The pathophysiology of pain is extremely complex. Analgesics (opiates and nonsteroidal anti-inflammatory drugs), antispasmodics, antidepressants, and so forth are among the most common medications used to treat acute or chronic pain. However, they are not always optimal due to the obvious adverse effects such as addiction and constipation. In addition to, the development of analgesic tolerance, analgesic effect, and the long-term use of opioid hyperalgesia has become an unfortunate obstacle to their clinical application. (Joranson et al. 2000; Staahl et al. 2006; Chu et al. 2008; Chen et al. 2014).

Acupuncture therapy is an important part of traditional Chinese medicine (Xia et al. 2010, 2012; Xia 2015). Back in the ancient Stone Age, there were some records of acupuncture analgesia. Since modern times, the literature has been increasing. Besides manual acupuncture (MA), electroacupuncture has been widely used in clinic because of its unique characteristics, such as easy prescriptive operation and good repeatability of stimulus parameters.

The analgesic effect of acupuncture was discovered on the human body several decades ago. Then, an abundance of studies has been conducted in both clinical and laboratory sides to explore the underlying mechanism since 1950s (Chen et al. 2014). The research has covered various types of pain including neuropathic pain (NP) (diabetic painful neuropathy (DPN), spinal cord injury (SCI)-induced pain, sciatica, etc.), cancer-induced pain, visceral pain, inflammatory pain, and so on. Acupuncture-induced analgesia is at least partly a result of interaction of signals at different levels of neuraxis, from the dorsal root ganglion (DRG) to the cortex, of afferents originated from acupoints and injured somatic and/or visceral sites (Cervero 1983; Zhao 2008). Moreover, many investigations show that acupuncture inhibits pain via the regulation of multiple neurotransmitters such as endogenous opioids, serotonin, norepinephrine, gamma-aminobutyric acid (GABA), etc. (Chen et al. 2014; Zhang et al. 2014). Acupuncture also attenuates pain feeling, emotional driving and vegetative nerve reactions via other complex mechanisms. This chapter will briefly summarize the previous research and update recent progress in clinical and laboratory research.

2 Clinical Research on Acupuncture Analgesia

2.1 Clinical Evaluation Index of Acupuncture Analgesia

Pain is a subjective sensation caused by multiple factors, and is influenced by many factors including environmental, emotional, cognitive, or behavioral factors. It is important to use an objective tool for evaluating the pain, quantifying the subjective feeling and understanding the pain level of the patient, by which we can reliably and objectively evaluate the clinical efficacy of the intervention. At present, the commonly used clinical evaluational indexes of acupuncture analgesia are verbal rating scale (VRS), visual analogue scale (VAS), mcGill pain questionaire (MPQ), and numeric rating scale (NRS).

2.1.1 Visual Analogue Scale

VAS also known as visual analogue scale and is widely used in the assessment of pain in clinical practice. The characteristic of VAS is simple, relatively objective, and sensitive (Carlsson 1983; Jensen et al. 1986; Stephen 1996; Donoghue and Stokes 2009). It is used not only to measure changes in the intensity of pain, but also to measure the degree of pain relief and other aspects at emotional and functional levels (Wynne et al. 2000; Herr and Garand 2001). The method is to draw a line with a length of 10 cm on a piece of paper. The two ends are “0” and “10” respectively, in which “0” means no pain, and “10” represents the most severe pain that is unbearable (Wynne et al. 2000; Herr and Garand 2001). When used in clinic, the patient should indicate

the corresponding position of the pain level on the ruler, and the doctor evaluates the score according to the position indicated by the patient (Kahl and Cleland 2005). VAS was used as a pain assessment method in many studies of acupuncture analgesia, such as in the study of migraine headache, sciatica, labor analgesia (Feng et al. 2016), postherpetic neuralgia, cervical spondylosis, knee arthritis, and so on. The major disadvantage is that individuals with visual or cognitive deficits may not be able to use the scale accurately (Kahl and Cleland 2005).

2.1.2 Verbal Rating Scale

The VRS is used to describe different levels of pain as painless, mild pain, moderate pain, severe pain, and extremely severe pain (Williamson and Hoggart 2005). With this method, 0 is no pain, 2 is mild pain, 3 is moderate pain, and 4 or 5 is severe pain or extremely severe pain. VRS is mainly used based on the impact of pain on work and life, and the use of analgesics. In most cases (Williamson and Hoggart 2005), data collected using VRS can only be analyzed using non-parametric statistics.

2.1.3 Numeric Rating Scale

The NRS is an 11, 21, or 101 point scale where the end points are the extremes of no pain and worst pain (van Dijk et al. 2012). The NRS can be delivered graphically or verbally. When presented graphically, these numbers are typically enclosed in boxes which is called an 11 or 21 point box scale, depending on the level of discrimination presented to the patient. There is no published information about the distribution or error of data obtained using the NRS. However, the scale is at an interval level and can provide data for parametric analysis (Williamson and Hoggart 2005).

2.1.4 McGill Pain Questionnaire

MPQ is a multi-factor pain survey scoring method. Its design is more precise than above methods and it focuses on the relation between pain, the nature of pain, the characteristics of pain, the intensity of pain, and the various complex factors experienced by the patient after analgesia (Di Cesare et al. 2011). MPQ is conducted with a questionnaire form (Di Cesare et al. 2011). There are 78 words used to describe all kinds of pain in the table of the questionnaire, and they are arranged in increasing intensity and include four categories: sensory, emotion, evaluation, and nonspecific. In 1987, Melzack et al. simplified the MPQ to SF-MPQ (Melzack 1987). It can accurately evaluate the strength and properties of pain because it is characterized by the design of the patient's physiological feelings, emotional factors, and cognitive abilities of the pain. However, its disadvantages are that it is susceptible to the patient's cultural and emotional factors. The MPQ is usually used to evaluate treatment effects in the clinical study of acupuncture treatment.

In these pain evaluation methods, VAS, NRS, and VRS are one-dimensional pain evaluation methods, while MPQ is a multi-dimensional pain evaluation method. The one-dimensional method also includes facial expression scoring (FPS) (Li et al. 2007). FPS (Herr et al. 1998) is constituted by six facial expressions and 0–10 points (or 0–5 points) that represent the degrees of painless to painful pain; the patient chooses the image or number to reflect the degree of the nearest pain. FPS has a good correlation to VAS and NRS, and can be used when it is difficult to communicate with the patient.

It is important to keep standard procedures for all patients when using these methods. However, the clinical evaluations of acupuncture treatment for pain are largely based on individual observation. The evaluation standards are not consistent, which may lead to different or even controversial results. Therefore, it is important to unify quantification, make the evaluation tool internationally standardized, and establish scientific evaluations for acupuncture research.

2.2 Clinical Observations on Acupuncture Analgesia

2.2.1 Acupuncture and Anesthesia

Acupuncture has been used for more than 50 years during the perioperative period (Acar 2016). "Acupuncture anesthesia" was first used in Shanghai, China in 1958 (Zhang 1989). Perioperative acupuncture provides clinically meaningful benefits for patients. It helps to reduce consumption of anesthetics and analgesics, and to enhance postoperative analgesia. In addition, it can reduce complications of surgery, such as postoperative nausea and vomiting (PONV), hemodynamic instability, intubation-related complications, and so on (Gliedt et al. 2015). In view of the above facts, perioperative acupuncture can be used in all of the states of surgery including the preoperative, intraoperative, and postoperative (Acar 2016).

Preoperative Period

The clinical study of acupuncture treatment in the preoperative period involves a variety of surgeries, including caesarean operation, abdominal surgery, and so on. These studies focused on the prevention of preoperative anxiety, relief of postoperative pain and anesthetic tolerance of acupuncture treatment. These effects may interact with each other. For instance, one of the reasons of preoperative acupuncture effects of anesthetic tolerance may be the sedative effects of treatment because increased anxiety may be related to increased pain levels. In other words, the relief of preoperative anxiety may be the most important part of preoperative acupuncture.

Preoperative anxiety is the primary problem for anesthesiologists in the preoperative stage (Acar 2016). The first study about acupuncture for preoperative anxiety in Western literature was performed by Wang et al. (Wang et al. 2011; Acar

2016). In order to assess the effect of acupuncture therapy for preoperative anxiety, a meta-analysis (Bae et al. 2014) was conducted in 2014. It included 14 randomized controlled trial (RCT) publications (N = 1034) and revealed that acupuncture interventions result in a greater reduction in preoperative anxiety when compared to sham acupuncture assessed by the State-Trait Anxiety Inventory-State (STAI-S) in six publications (mean difference = 5.63, $P < 0.00001$, 95% CI [4.14, 7.11]) or by VAS in eight publications (mean difference = 19.23, $P < 0.00001$, 95% CI [16.34, 22.12]). They concluded that acupuncture can reduce preoperative anxiety in the meta-analysis. Some other studies confirmed the conclusion. In a single-center, prospective RCT (Wiles et al. 2017), 128 patients were randomly allocated to the acupuncture group [acupuncture at the Yintang (EX-HN3) point] or the control group (no intervention). The result showed that median (IQR [range]) anxiety STAI-S reduced significantly in the acupuncture group with no change seen in the control group, which revealed that acupuncture can reduce preoperative anxiety in patients. Karst et al. (2007) compared the effects of pharmaceutical agents and acupuncture on preoperative stress and revealed that auricular acupuncture and intranasal midazolam had similar effect on anxiety. In addition to relieved preoperative anxiety, Rosted and colleagues (Rosted 1998; Dias et al. 2010) observed that when segmentally administered acupuncture was given before a regional inferior dental block, the onset of a local anesthetic was quicker. The faster onset of local anesthetics may be related to increase the local blood flow after acupuncture (Blom et al. 1993).

There are other voices for the effect of acupuncture in the preoperative period. For example, several studies found no statistically or clinically significant differences in the efficacy of nonpharmacological methods, such as parental acupuncture (Wright et al. 2007; Strom 2012). Nevertheless, most clinical data suggested that acupuncture therapy aiming at reducing preoperative anxiety has a statistically significant effect compare with placebo or nontreatment conditions. Perioperative acupuncture can improve the rehabilitation in outpatient surgery populations and reduce morbidity and mortality in elderly patients after surgery (Lu et al. 2015). However, it is still unclear whether there is a difference in the efficacy of acupuncture therapy versus conventional premedication treatments. It needs well-designed and rigorous research, with a large sample size for further exploration.

Intraoperative Period

General anesthesia has three main features: loss of consciousness, muscle relaxation, and surgical analgesia (Acar 2016). Numerous studies have found that acupuncture can result in analgesia, but there is no evidence that acupuncture can relax muscle and loss of consciousness (Acar 2016). For these reasons, the studies of acupuncture anesthesia have focused on acupuncture as an adjuvant to general anesthetics in order to reduce the doses of anesthetics and/or opioids intraoperatively.

Early studies have indicated that intraoperative acupuncture could reduce anesthetic requirements to 70% of normal usage (Doenicke et al. 1976; Tolksdorf et al. 1980; Zhou 1984). However, these studies have a major limitation because of method-

ological quality since most of them were not double-blind, placebo-controlled studies. In recent years, new clinical research has shown that acupuncture can reduce the consumption of anesthetics and analgesics. In a clinical trial (Wang et al. 2014), 60 patients scheduled for sinusotomy were randomly assigned to Transcutanclus Electrical Acupoint Stimulation (TEAS) or control group. TEAS consisted of 30 min of stimulation (6–9 mA, 2/10 Hz) on the Hegu (LI 4), Neiguan (PC 6), and Zusanli (ST 36) before anesthesia. In the control group, the patients had the electrodes applied, but received no stimulation. The researchers found that patients in the TEAS group required 39% less remifentanil during surgery than that of the controls [0.0907 (SD 0.026) μg kg(−1) min(−1) vs. 0.051 (0.018) μg kg(−1) min(−1)]. In another blinded clinical trial (Liu et al. 2015), 92 supratentorial craniotomy patients were randomly allocated into a multipoint TEAS (n = 46) and a sham TEAS group (n = 46). They received total intravenous anesthesia (TIVA) with propofol and sufentanil, and TEAS was administered with 30 min before anesthesia induction in the TEAS group and this was maintained in four pairs of acupuncture points during the operation. The results indicated that sufentanil target plasma concentration in TEAS patients was significantly lower at some time points during supratentorial craniotomy, and total sufentanil consumption was significantly higher in the sham group ($P < 0.05$). In addition to these, preoperative acupuncture can reduce the intraoperative analgesics consumption.

These studies suggested that acupuncture might decrease the need for intraoperative anesthesia. However, acupuncture reduces drug usage in different degrees depending on the type of the drugs used. In a study with three groups, the patients underwent three treatments, respectively (Yang et al. 2014): the intravenous anesthesia group (A group, 30 cases) received sufentanil combined with propofol, the acupuncture-anesthetic composite anesthesia (AACA) group (B group, 32 cases) received sufentanil combined with acupuncture, and the acupuncture combined with intravenous anesthesia group (C group, 31 cases) received sufentanil and propofol combined with acupuncture. The authors found that the propofol consumption decreased in Group C ($P < 0.05$) compared to Group A, but the sufentanil dosage had no statistical difference. In a randomized, double-blind, placebo-controlled trial (Tsao et al. 2015), the two cohorts of acupuncture (n = 30) and sham acupuncture (n = 29) did not show any significant difference in the amount of opioid or the length of care after general anesthesia. In addition, controversial results have been reported, such as an increased demand for sevoflurane (MAC from 1.8 to 2.1%) (Kvorning et al. 2003). The main reason behind this is that the small sample sizes of these studies limited their power to provide strong evidence. It may be also related to the operation type, the body condition, needle type, needle insertion point, and so on. Therefore, more clinical data are needed to ascertain if acupuncture can reduce intraoperative anesthetic/opioid consumption (Chernyak and Sessler 2005; Gliedt et al. 2015).

Postoperative Period

In the postoperative period, postoperative pain relief is the most common challenge in clinical settings. Fortunately, a growing number of studies have demonstrated the effectiveness of acupuncture for this condition. Additionally, acupuncture treatment is also used for PONV, postdural puncture headache (PDPH) and postoperative sore throat.

The initial global interest in acupuncture stemmed from a report on James Reston, who was treated with acupuncture for postoperative pain after suffering from acute appendicitis in 1971 (Sun et al. 2008). Subsequently, more and more clinical studies have focused on the effect of postoperative pain of acupuncture. A review by Sun et al. (2008) included 15 RCTs conducted in 2008, showed 21–29% reduction in opioid consumption after acupuncture, which is considered to be clinically significant. The conclusion has been supported by some recent studies. For an example, in patients undergoing tonsillectomy (Yang et al. 2014), home surveys of patients but not of parents revealed significant improvements in postoperative pain control ($P = 0.0065$ and 0.051, respectively) and no adverse effects in the acupuncture group were reported. Another clinical study was conducted by Feng et al. (2016) which indicated that performing TEAS provides postoperative pain relief before and after surgical abortion. In this cohort, 140 nulliparae requesting pregnancy termination with intravenous anesthesia were recruited. They were divided into three cohorts (TEAS preoperation, postoperation, and both preoperation and postoperation), alongside a control group. TEAS was performed for 30 min before and/or after the operation while received no TEAS treatment in the control group. Pain levels were respectively assessed upon recovery at 10, 30, and 45 min after abortion. Both of them demonstrated that acupuncture can enhance the postoperative analgesia, which is agreed with many reports (Wu et al. 2009; Feng et al. 2010; Tong et al. 2010a, b; Ding et al. 2011; Li et al. 2012a, b; Chen et al. 2015; Liu et al. 2015).

The postoperative analgesic effect of acupuncture is dependent on electroacupuncture frequency. Lin et al. (2002) showed that the time of first analgesic requested was 10, 18, 28, and 28 min in the control, sham- (needle insertion without electrical stimulation), low- (2 Hz of electrical stimulation), and high-EA (100 Hz of electrical stimulation) groups. During the first 24 h, the total amount of morphine required was decreased by 21, 43 and 61% in the sham-, low- and high-EA groups, respectively. Their findings demonstrated that preoperative treatment with low-EA and high-EA reduced the need for pain relief after surgery with high-EA being better. This initial finding needs to be verified by more evidence.

The selection of acupuncture points is also important for the outcome. Gao and his colleagues (Gao et al. 2017) aimed to choosing a better stimulating method and most effective acupoints for acupuncture analgesia in thyroidectomy. They conducted a clinical study including 216 thyroidectomy patients, and the patients were randomized into 6 groups to receive the one of local anesthesia, Futu (LI 18)-EA, Hegu (LI 4)-Neiguan (PC 6)-TAES (transcutaneous acupoint electrical stimulation), LI 4-PC 6-EA, Yanglingquan (GB 34)-EA, non-acupoint (NA, about 1.5 cm latero-posterior to KI 9)-EA. Their results indicated that EA stimulation of both Xialian (LI 18) and

Hegu (LI 4)-Neiguan (PC 6) and TAES of Hegu (LI 4)-Neiguan (PC 6) combined with anesthetics have a better effect in inducing analgesia and need lower dosages of anesthetics for patients undergoing thyroidectomy, for which Xialian (LI 18) and Hegu (LI 4)-Neiguan (PC 6) are evidently superior to Yanglingquan (GB 34) and non-acupoint.

In the postoperative period, PONV and PDPH are the other common challenges. Indeed, acupuncture can relieve PONV (Wang et al. 2014). On the other hand, PDPH, though it does not have the severe complications of spinal anesthesia, may be very disturbing for patients. Some results suggest that PDPH patients might benefit from acupuncture treatment (Perera 1998; Sharma and Cheam 2009; Acar et al. 2013).

In conclusion, perioperative acupuncture is a promising intervention, but high-quality research is still needed, especially in the field of intraoperative acupuncture. The success of acupuncture treatment in perioperative period depends on some factors, such as the selection of points, duration of sessions, timing of acupuncture and selection of stimulation technique. For example, Nei Guan (PC 6), Yintang (GV 29), and Shenmen (HT 7) acupoints are the most studied and the most effective acupoints in reducing postoperative pain experiences, PONV and preoperative anxiety (Gliedt et al. 2015). Further studies are needed to assess the safety and effectiveness of perioperative acupuncture and to predict the subgroups that are most likely to respond positively to perioperative acupuncture.

2.2.2 Acupuncture and Neuropathic Pain

According to the 2011 International Association for the Study of Pain, NP is defined as "pain caused by a lesion or disease of the somatosensory system" (Jensen et al. 2011), which is a definition based on the previously agreed (Treede et al. 2008). The causes of NP vary, including postherpetic neuralgia (PHN), painful diabetic neuropathy (PDN), or NP after surgery, such as trigeminal neuralgia and SCI. Many people with NP are clearly disabled and experience moderate or severe pain for many years because NP often occurs in patients with joint pain (Soni et al. 2013).

Acupuncture and Sciatica

Sciatica is a common type of neuralgia characterized by pain which is radiating into the leg (Qin et al. 2015). It is usually caused by inflammation of the sciatic nerve or nerve root compression and irritation. For the treatment of sciatica, pharmacological approaches have associated side effects, and surgery is expensive which is not for every patient. Acupuncture is generally regarded as a safe and effective measure to alleviate pain, including sciatica (Chen et al. 2009; Li et al. 2012a). However, the effect of acupuncture to successfully treat sciatica is unclear, either as a monotherapy or as an adjunct to Western medicine (Qin et al. 2015).

In early years, many researchers conducted clinical studies to assess the therapeutic effect of regular acupuncture on sciatica. In the last decade, more and more

acupuncturists are using different types of acupuncture approaches for the treatment of sciatica, such as acupuncture stimulation of the sciatic nerve trunk versus routine acupuncture, ankle acupuncture versus traditional needle, electroacupunctureversus transcutaneous electrical nerve stimulator (TENS) and so on. In 2015, Qin and colleagues conducted a meta-analysis (Qin et al. 2015) by collecting RCTs published before 2014. This review revealed the efficacy and safety of acupuncture for the treatment of sciatica is generally considered to have clinical significant. The recent clinical research on acupuncture treatment for sciatica are following. A randomized controlled clinical trial (Qiu et al. 2016) of treatment of lumbar disc herniation-induced (LDH) sciatica indicated that in LDH patients, acupuncture stimulation of the sciatic nerve trunk is effective in relieving sciatica, and is superior to simple routine acupuncture in the clinical efficacy. In addition, a double-blinded, randomized controlled clinical trial is under way. In this clinical trial (Xiang et al. 2017), patients diagnosed with disc-related sciatica were randomly divided into 3 parallel groups (the treatment group receive ankle acupuncture, the 2 control groups either undergo traditional needle manipulation or sham acupuncture at the same point as the treatment group).

Furthermore, other research explored how acupuncture affects sciatica. In 2009, a clinical study (Chen et al. 2009) showed that the therapeutic effect of the warming needle moxibustion group was better than the control groups and pain threshold increase in the warming needle moxibustion group, significantly higher than that of other groups. The finding indicated that acupuncture can relieve the symptoms of sciatica by increasing pain threshold. The results are consistent with those of Chen's research reported in 2005 (Chen et al. 2005). For better clinical practice, more double-blind and randomized studies are needed to validate the acupuncture efficacy and optimal conditions for the best therapeutic results.

Acupuncture and Pain Induced by Spinal Cord Injury

Traumatic SCI causes multiple dysfunctions in the sensory systems, such as neuronal hyperexcitability in the Central Nervous System (CNS), which consequently lead to NP (Gerke et al. 2003; Hains et al. 2005; Gwak et al. 2010, 2013; Yague et al. 2011; Kim et al. 2012). It is reported that 70% of SCI individuals have persistent pain (Finnerup et al. 2001). It greatly impacts on the quality of life (QOL) patients including daily activities and emotion. However, the adequate treatment of SCI-induced NP is still an unresolved problem.

Currently, pharmacological approaches (such as opioids, neuropeptides, neurotrophins, anti-inflammatory cytokines, and some neurotransmitters or the pain-mediating signaling molecules) are the predominantly treatment of the SCI-induced NP (Zijlstra et al. 2003; Gwak et al. 2016). There is evidence suggesting that acupuncture treatment is a good approach to promote the pathophysiological recovery of the SCI-induced abnormal pathophysiology and is more effective than pharmacological treatment. The pain relief may be greater than that with morphine and placebo. In a systematic review and meta-analysis (Ma et al. 2015), the authors concluded that

acupuncture promoted neurological recovery, motor function, and function recovery following SCI. In clinical reports, the results showed that acupuncture can lead to 40% satisfaction in pain relief in SCI patients over up to 3 months (Boldt et al. 2014). However, the patients with severe pain did not experience pain relief in the report. Furthermore, acupuncture is a safe and useful technique for pain and NP therapy. According to the statistics, about 95% of the patients with SCI pain reported few or no side effects after acupuncture treatment while pharmacological therapy always had high occurrences of adverse effects (Richardson and Vincent 1986; Pariente et al. 2005; Wheway et al. 2012). Additionally, in a systematic meta-analysis of RCTs, it was revealed that the SCI patients who were treated with the approach of acupuncture combined with the conventional treatment (rehabilitation or medication) had better functional recovery (Heo et al. 2013). However, other researchers seem to have different views on the role of acupuncture in alleviating SCI-induced NP. According to some reports, although many people of SCI-induced NP have tried acupuncture to relieve pain (approximately 20–40%), only a few have found enough relief (Budh and Lundeberg 2004; Cardenas and Jensen 2006).

As the standardization of therapeutic parameters of acupuncture is still controversial, such as the duration, intensity, and methods of stimulation, it is needed to further clarify whether acupuncture is an effective alternative treatment for SCI-induced NP (Borsook et al. 2007; Baliki et al. 2013).

Acupuncture and Diabetic Painful Neuropathy/Painful Diabetic Neuropathy

Painful diabetic peripheral neuropathy occurs in about 25% of diabetic patients (Snyder et al. 2016). It usually causes burning pain, paresthesias, and numbness of the pattern, progressing from the feet and hands proximally (Snyder et al. 2016), which has a significant influence on patients' quality of life, mood, sleeping, working ability, interpersonal relationships, and so on (Corbett 2005). Clinicians should carefully consider the patient's goals, potential adverse effects of medication and functional status when choosing to treat for painful diabetic peripheral neuropathy (Snyder et al. 2016).

Acupuncture has successfully relieved PDN symptoms. In an earlier study, acupuncture analgesic therapy was performed on 46 diabetic patients with chronic painful peripheral neuropathy (Abuaisha et al. 1998). The result showed that their pain symptoms were significantly improved in 34 (77%) and completely cleared in 7 (21%) ($P < 0.01$) without side effects. However, the data may be questioned because this research did not set up a control group and was not a double-blind study. Fortunately, there have been some high quality clinical studies that have confirmed this view in recent years. In a single-blind, placebo-controlled RCTs (Garrow et al. 2014), 45 participants with PDN were randomly divided into receiving a 10-week course either of real (53%) or sham (47%) acupuncture. The results revealed that there were small improvements in the true acupuncture group with VAS −15 (−26 to −3.5). Another research conducted by Tong et al. (2010a, b). They found that the treatment of spontaneous pain and numbness of lower extremity by acupuncture was supe-

rior to the sham operation. In addition, there is even research on the influence of acupuncture related technique to PDN. In a crossover study, 5 participants with PDN were randomly divided into Traditional Transcutaneous TENS (80 Hz, 200 ms) or acupuncture-like TENS (2 Hz, 200 ms) which were applied daily for 30 min over ten days. Acupuncture-like TENS had a large effect size ($z = -1.625$, $r = 0.514$), while traditional TENS produced a medium effect size ($z = -1.214$, $r = 0.384$) and no adverse effects were reported which suggested that acupuncture-like TENS may be more effective for PDN than traditional TENS.

These data demonstrated that acupuncture therapy is a safe and effective long-term management of PDN, although its mechanism of action is still at the speculation stage. In conclusion, acupuncture is effective in PDN, but may be effective in SCI-induced pain and sciatica, under the conditions of the included studies. Further studies are needed to explore the potential therapeutic role in these population.

2.2.3 Acupuncture and Cancer Pain

According to the statistics, 40% of individuals suffer from early or intermediate stage cancer and 90% of cancer patients have moderated to severe pain (Payne and Paice 1998; Laird et al. 2008). Pain in cancer patients may be related to tumor growth, disease progression, bone metastases or the treatment of cancer itself (Strong 2002; Urch et al. 2008). Furthermore, as many as 70% of cancer-related pain patients do not get enough pain relief, which affects physical and psychological well-being and leads to a decline in QOL (Van den Beuken-van Everdingen et al. 2007a, b; Vallerand et al. 2007).

Acupuncture and related therapies are commonly used to treat cancer-related pain, however, their efficacy and safety are still controversial (Wu et al. 2015). In 2003, a high quality study (Alimi et al. 2003) provided strong evidence for acupuncture to treat cancer pain. In this RCT, 90 cancer patients were randomly allocated to three groups (one acupuncture group and two placebo groups). Patients in the acupuncture group received two courses of auricular acupuncture at special points while the other placebo groups at placebo points. Researchers found that pain intensity decreased by 36% after 2 months in the patients receiving acupuncture compared to baseline, while there was little change in the placebo groups (2%) ($P < 0.0001$). The results clearly indicated auricular acupuncture is benefit for the patients of cancer pain.

For pancreatic cancer pain, the result of a RCT (Chen et al. 2013a) illustrated that electroacupuncture is an effective treatment for relieving the pain through treating on Jiaji (Ex-B 2) points T8-T12 bilaterally by acupuncture for 30 min once a day for 3 days and pain intensity was assessed with NRS before the treatment (Baseline), after 3 treatments, and 2-day follow-up. For metastatic cancer pain, a research (Lee and Yoon 2014) in 2014 showed that pain intensity score and pain interference score significantly decreased in the TM (true moxibustion) group (TM vs SM (sham moxibustion): intensity, -0.82 ± 0.93 vs. 0.46 ± 0.87, $P = 0.020$; interference, -1.12 ± 1.31 vs. 0.24 ± 0.61, $P = 0.047$). The conclusion is that moxibustion could be a safe and feasible method to treat cancer pain in patients with metastatic cancer. Last

year, a report of Lam (Lam et al. 2017) agreed that acupuncture tends to be effective in reducing cancer pain, and more importantly, the effect is rarely accompanied by severe adverse reactions.

The stable analgesic treatment is a common treatment for cancer-induced pain. The above-mentioned studies with properly randomized evaluation demonstrated the efficacy of acupuncture for cancer-induced pain that is resistant to effective intervention. However, most of these studies had small sample sizes, which leaves them prone to bias, and a future multicenter study with a larger sample size is warranted.

2.2.4 Acupuncture and Visceral Pain

Acupuncture for Treating Pain of Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common chronic functional gastrointestinal condition characterized by abdominal pain, defecation disorders, accompanied by a psychological conditions (Ma et al. 2014). Its recurrent symptoms lead to a decline of QOL for patients. A great amount of research has revealed that acupuncture has a therapeutic effect on irritable bowel syndrome.

Some studies have indicated that acupuncture can enhance the pain threshold of IBS patients. In a study by Kuiken et al. (2005), patients with various subtypes of IBS and healthy volunteers were subjected to rectal harmful stimulation with balloons and water balloons. The experiment revealed that the abdominal discomfort threshold of IBS patients was significantly lower than that of healthy volunteers. The decreased pain threshold may contribute to abdominal pain of IBS with mild stimulation. In another clinical study (Xing et al. 2004), the threshold of the rectal sensation of gas (the sensation of pain) was significantly increased when TEAS at Neiguan (PC 6) and Zusanli (ST 36). The same results were obtained by Xiao et al. in the same year. The authors observed that after 2-month of TENS intervention in the D-IBS patients, the threshold rectal perception significantly increased and the pain intensity obviously decreased (Xiao and Liu 2004). There is a meta-analysis evaluation of the efficacy of acupuncture in IBS. It included 11 clinical RCTs with 969 patients showed the effective rate of acupuncture and moxibustion superior to conventional Western medication treatment (Pei et al. 2012). Another meta-analysis of 6 RCTs also confirmed that acupuncture can improve the symptoms of IBS, including abdominal pain (Chao and Zhang 2014). All of these results supported the efficacy of acupuncture for irritable bowel syndrome.

However, several new studies suggested no significant differences between true and sham acupuncture. One clinical trial was conducted by C. Lowe and his colleagues in 2017 (Lowe et al. 2017). In this trial, 79 IBS patients received real acupuncture twice a week for 4 weeks ($n = 43$) or sham acupuncture ($n = 36$) and followed up again 12 weeks later. The results were assessed by symptom severity scores, SF-36 and IBS-36 QOL tools, MPQ, and the Pittsburg Sleep Quality Index. They found that a total of 53% had successful treatment intervention in the true acupuncture group while 42% in the sham group, which did not differ significantly between the

two groups; the thresholds of rectal sensory were increased in both groups and pain scores decreased but the changes between the two groups also were similar. The clinical study revealed that acupuncture does not have a specific treatment effect in IBS, including pain relief. At the same time, a RCT of 2-year follow-up (MacPherson et al. 2017) revealed that there was no statistically significant differences between the acupuncture and the routine care groups in severity score of IBS symptoms at 24 months post-randomization, and the average differential estimate was about 80% of the statistically significant results at 6, 9, and 12 months.

Acupuncture has gained increasing acceptance in the treatment for IBS patients over the past few decades. However, the efficiency of acupuncture in IBS still remains uncertain. Further research should be conducted to accurately evaluate the efficacy and mechanism of acupuncture in treatment of IBS.

Acupuncture for Treating Renal Colic

In 85% of the patients with renal colic, renal colic is caused by renal-ureteral stones. For renal colic therapy, the purpose is to eliminate pain, eliminate the obstruction of excretory pathway and retain renal function. Many drugs are used to relieve pain, but always have side effects. Recently, there have been several reports on acupuncture treatment for renal colic.

Acupuncture can relieve renal colic. A RCT (Beltaief et al. 2018) by Beltaief K and his colleagues was reported in 2018. In the clinical trial, 115 patients with renal colic were randomized into the morphine infusion group (n = 61; 0.1 mg/kg morphines injected every 5 min until the pain index decreased by at least 50% of its baseline value) and the acupuncture group (n = 54; received 30 min of acupuncture treatment according to a pre-specified protocol). The result showed that the analgesic effect of the acupuncture group was better ($P < 0.05$ from the 10th min and above), and the analgesic speed was faster with the extension of time with the baseline VAS being decreased by 50% ($P < 0.001$). Only three patients in the acupuncture group had minor side effects, while 42 patients in the morphine group ($P < 0.001$) had side effects. There were no serious side effects observed in both groups. These results revealed that compared with titrated IV morphine, acupuncture has a faster and deeper analgesic effect with better tolerance. Before this research, Kaynar et al. (2015) and (Ju and Niu 2012) had made similar conclusions that acupuncture can relieve pain of renal colic as an alternative treatment modality with a low incidence of adverse reactions, and Ju, et al. also stressed that it is important to acupuncture at Neiguan (PC 6) and Zusanli (ST 36). Additionally, eye acupuncture was shown to be a rapid and effective way to treat renal colic when compared to morphine and bucinnazine (Lin et al. 2007). The effect of acupuncture on renal colic may closely be associated with an increase in endogenous opioid substances (Lee et al. 1992) and down-regulation of plasma SP and 5-hydroxytryptamine (5-HT) levels (Wang et al. 2013).

Therefore, use of acupuncture to treat renal colic may be a rational alternative, although it is needed to conduct more research with placebo or blank control.

Acupuncture and Other Visceral Pain

The research of acupuncture for visceral pain mainly involves IBS and renal colic; the rest are chronic cholecystitis, digestive tract ulcers, appendicitis, and especially chronic cholecystitis. The evidence is following. Acupuncture can effectively relieve shoulder-back pain and stomachache of chronic cholecystitis when stimulated of Jianjing (GB 21). In one research (Wen et al. 2012), 60 patients with chronic cholecystitis were recruited and randomly divided into a Jianjing (GB 21) group and a non-acupoint group. A filiform needle was inserted into Jianjing (GB 21) or the non-acupoint on the right side, operated for a period of time until "deqi", and kept for 30 min. The results show that the therapeutic effect of Jianjing (GB 21) was significantly superior to non-acupoints ($P < 0.05$). Last year in this study, Wang et al. made the same point (2011). In addition, the reports revealed that acupuncture can relieve pain of peptic ulcers (Niu et al. 2007; Meng and Qi 2016) and acute appendicitis (Nager et al. 2014).

2.2.5 Acupuncture Research on Chronic Pain

Chronic pain is usually defined as pain that lasts longer than 3 months or longer than the expected time of histopathologic healing (Turk et al. 2011). Chronic pain is caused by persistent stimulation or by changes in the nociceptive receptors caused by acute injury or disease (such as osteoarthritis), damage to the nervous system (peripheral or central), or both (Cheng 2010).

Several systematic reviews have discussed the effect of acupuncture on chronic pain. For example, a meta-analysis in 2012 (Vickers et al. 2012) analyzed data from 29 of 31 eligible RCTs with a total of 17,922 patients. Their results revealed that patients receiving acupuncture had less pain, with scores of 0.23 (95% CI, 0.13–0.33), 0.16 (95% CI, 0.07–0.25), and 0.15 (95% CI, 0.07–0.24) SDs lower than sham controls for back and neck pain, osteoarthritis, and chronic headache, respectively, and the effect sizes in comparison to no-acupuncture controls were 0.55 (95% CI, 0.51–0.58), 0.57 (95% CI, 0.50–0.64), and 0.42 (95% CI, 0.37–0.46) SDs. The conclusion of the meta-analysis is that acupuncture is a reasonable referral method for treating chronic pain. As described earlier in this chapter, SCI induced pain, sciatica, DPN, cancer-related pain are all in the range of chronic pain and acupuncture has a therapeutic effect on them.

Chronic low back pain. Chronic low back pain (cLBP) is located between the costal margin and buttocks and has lasted for more than 3 months (Yeganeh et al. 2017). The patient suffers physical disability and psychological pain at the same time. Various of non-pharmacologic therapies provided by different health care professionals are available for LBP patients. Many non-pharmacologic treatments, especially acupuncture, can be used to treat lower back pain (Yeganeh et al. 2017). There are some clinical studies supported the effectiveness of acupuncture in treating cLBP (Haake et al. 2007; Chou and Huffman 2007). High-quality evidence suggests that

acupuncture appears to be superior to conventional treatments for cLBP, though there is another voice.

In a prospective RCT (Weiß et al. 2013), acupuncture treatment was performed on 143 patients with cLBP to investigate the effectiveness of acupuncture. The pain relief in group A (acupuncture intervention) was superior to group B (controls). The result suggests that acupuncture is an effective, well-tolerated therapy and has no significant adverse reactions to cLBP. In 2014, Bahrami-Taghanaki et al. (2014) presented that accompanying routine acupuncture with time method acupuncture can enhance the efficacy of treatment and the persistence of its benefits in individuals with cLBP which measured by the VAS. Wand et al. (2013) found that the difference of the average pain intensity between after participants had received acupuncture with sensory discrimination training (2.8 ± 2.5) and when they received acupuncture without sensory discrimination training (3.6 ± 2.0) was statistically significant (after adjustment; mean difference $= -0.8$, 95% CI -1.4 to -0.3; $P = 0.011$). The results suggest that acupuncture may provide particular benefits, which do not depend on the precise position of the needle insertion, but rather on where the patient is paying attention.

Some researchers compared the effects between acupuncture and other non-pharmacologic therapies, e.g., instance acupuncture and spinal manipulative therapy (SMT). The results of a RCT feasibility study (Kizhakkeveettil et al. 2017) revealed that both had clinically meaningful improvements in the primary outcome measures; however, no differences in outcomes were apparent between groups.

In general, there is strong evidence showing that acupuncture may be a useful treatment for chronic pain. However, there are no strong recommendations because of a lack of research with low risk of bias. Therefore, future trials should involve clinical relevance of the results, including regression work as a result and long-term follow-up, with low risk of bias and adequate sample size (Yeganeh et al. 2017).

Chronic prostatitis/chronic pelvic pain syndrome. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is one of the most common chronic inflammatory diseases in adult males. Current evidence supports acupuncture as an effective treatment for CP/CPPS-induced symptoms, particularly in relieving pain. Recent evidence is as follows. In a prospective, randomized, nonblinded, clinical trial (Küçük et al. 2015), 54 patients with category IIIB CP-CPPS were randomly assigned to the medical treatment group (group 1, $n = 28$) and the acupuncture treatment group (group 2, $n = 26$). The patients in group 2 were intervened by electrical pulse generator bilateral to stimulate the sacral nerve on Ciliao (BL 32) and Zhongliao (BL 33) acupoints, twice a week for 7 weeks while group 1 took levofloxacin 500 mg daily and ibuprofen 200 mg twice a day for 6 weeks. The result is that reduction of pain was higher in the acupuncture group compared to the medical group, which suggested that acupuncture treatment is a safe and effective treatment of category IIIB CP-CPPS. Sahin et al. (2015) and Lee et al. (2008) published the same results when acupuncture group compared to the sham group. The effect may be related to acupuncture point and the type of the needle. Zhou et al. (2017) did a randomized controlled pilot study to demonstrate the view. In the study, 77 patients were randomly divided into long-needle acupuncture (LA) group and traditional acupuncture

(TA) group and the patients received six sessions of acupuncture for 2 weeks and a follow-up was scheduled at week 24. The conclusion of the research is that needling at the Baihuanshu (BL 30) and Huiyang (BL 35) using LA benefits patients with CP/CPPS when compared to TA.

There are some reviews to assess the effects of acupuncture for CP/CPPS. One review reported in 2018 (Franco et al. 2018) which included 38 unique studies with 3290 men with CP/CPPS across 23 comparisons, including three studies and 204 participants of acupuncture. The results revealed that acupuncture reduces prostatitis symptoms compared to the sham procedure and standard medical therapy, but acupuncture likely results in little to no difference in adverse events (moderate QoE). However, the other review (Liu and Wang 2016) concluded that acupuncture treatment of pain for CP/CPPS is effective and safe. In addition, Qin et al. (2016) thought that acupuncture might be similar to medicine (Levofloxacin, Ibuprofen, and Tamsulosin) in its long-term effects with rare and slightly adverse events in the same year.

Taken together, accumulating evidence supports acupuncture as an effective treatment to improve symptoms of CP/CPPS, especially relieving pain. In pain relief, real acupuncture leads to significant reductions when compared to sham acupuncture, and may be more effective when compared to conventional Western medicine. However, there is no significant difference between acupuncture and conventional Western medicine in terms of urinary symptoms and QOL. With regard to adverse events, acupuncture was linked to rare and slightly adverse events, and these resolved quickly and no other serious events have been reported. Current existing evidence allows limited conclusions, and additional trials are needed to improve the reliability of these findings (Qin et al. 2016).

Chronic knee pain. Knee osteoarthritis is a chronic disease with high morbidity and economic cost. There is little study about the efficacy of acupuncture treatment for chronic knee pain, and the most results were negative. For example, a randomized, double-blind, controlled trial (Chen et al. 2013b) revealed that improvement pain from combined therapy with no difference between true (31.6%) and nonpenetrating acupuncture (30.3%). Furthermore, the effect of acupuncture was no better than that of non-acupuncture. Another example (Hinman et al. 2014) also debates the benefits of acupuncture for knee pain. In the clinical trial, patients were divided into no acupuncture (control group, $n = 71$), needle acupuncture ($n = 70$), laser acupuncture ($n = 71$), and sham laser acupuncture ($n = 70$) and treatments were delivered for 12 weeks. Analyses showed needle and laser acupuncture did not significantly improved pain at 12 weeks compared to sham, but compared to the control, the pain was moderately improved compared with the control group. These findings seem not to support acupuncture with moderate or severe chronic knee pain for patients older than 50 years.

Chronic shoulder/neck pain. Although there is evidence that acupuncture is effective in treating chronic shoulder pain, it is not clear which type of acupuncture is most effective. Zhang et al. (2016) suggested that contralateral acupuncture has beneficial effects in the treatment of chronic shoulder pain, assessed by VAS scores. However, in a preliminary study (Itoh et al. 2014), 80 patients were randomized into

a trigger point acupuncture (TrP) group (received treatment at trigger points for the muscle) and a sham acupuncture group (received sham acupuncture treatment on the same muscle), each receiving five treatment sessions. The research revealed that TrP therapy appears more effective for chronic shoulder pain when compared to sham acupuncture therapy. In addition, acupuncture also has been shown to play a safe role in chronic neck pain (Zhang et al. 2013; Llamas-Ramos et al. 2014).

In conclusion, when compared to pharmacological therapy, acupuncture is likely to be effective for most pain without side effects or with rare and slightly adverse events. However, there is a lot of missing data. Further studies are needed to assess the long-term impact of these interventions on pain and clarify whether these reports raise the benefits of acupuncture relative to pharmacological treatment solely due to the patient's preference for acupuncture or the expectation of a greater improvement in patients with acupuncture related drugs (Manheimer et al. 2012). Future research should aim to minimize methodological deficiencies by incorporating appropriate subjects and investigator blinding, standardization of acupuncture intervention, use of validated, objective outcome assessments, a priori hypotheses with a proper sample and effect size calculations, and appropriate statistical analyses.

3 Laboratory Research on Acupuncture Analgesia: Animal Models

To explore the mechanisms of pain modulation and acupuncture analgesia, numerous animal models, mostly rodents, have been used to simulate specific human pain situations.

Pain studies accounts for about 25% of total studies, more than any other area of studies, according to studies published in flagship journals (Cata et al. 2008). The animal model of pain dates back to the late 19th century and plays a crucial role in our understanding of pain (Von Frey 1896). Since then, many animal disease models were developed in order to better understand the pain of a variety of diseases, including acute and chronic diseases, and has been shown to help further specific questions and process of disease (Woolf 1983; Schaible and Schmidt 1985; Bennett and Xie 1988; Berberich et al. 1988; Hargreaves et al. 1988). More and more obviously, the pain is a kind of heterogeneous phenomenon that varies greatly depending on the affected tissue (skin, muscle, joint, viscera, etc.) (Ness and Gebhart 1990; Sluka 2002; Magee et al. 2007) and the mechanism of injury (thermal, mechanical, inflammatory, neuropathic, etc) (Dewey et al. 1970; Milligan and Watkins 2009; Schmidt et al. 2010). Using the animal models of pain is a continuing necessity, despite the development of human imaging studies, such as functional MRI.

3.1 Models of Neuropathic Pain

NP is caused by injury or disease of the peripheral or central somatosensory system, usually secondary to diabetes, cancer, stroke, multiple sclerosis, spinal stenosis, HIV-AIDS, trigeminal neuralgia, phantom limb pain, radiculopathy, vitamin B12 deficiency, Charcot-Marie-tooth, post-herpetic neuralgia, and so on (Baron 2006; Heitmann et al. 2016; Van Den Kerkhof et al. 2016). The irreversible damage of NP in humans is difficult to evaluate, which results in the requirement of validated and easily reproducible animal models of NP (Huang et al. 2013). A variety of models have been designed which mimic the above disease conditions (Kumar et al. 2017). Therefore, it will help to further study the pathogenesis and treatment of various pain to the establishment and continuation of the neuropathic rational pain animal model.

3.1.1 Models of Spinal Cord Injury (SCI)

Several NP models have been simulated in rats with SCI. These studies have primarily focused on SCI caused by spinal contusion or weight loss, spinal compression, excitatory neurotoxins, photochemical-induced ischemia, spinal cord trafficking or spinal cord rupture.

Contusive or Hemicontusive Models: Spinal contusion is the oldest and most widely used animal model (Nakae et al. 2011). This injury elicits motor dysfunction and sensory dysfunction, including NP (Tanabe et al. 2009; Hoschouer et al. 2009). The unilateral spinal cord contusion model is made by cervical hemicontusion. Cervical vertebral contusions are often used for motor function analysis because of the difficulty in estimating pain related behaviors due to motor dysfunction in the forelimbs (Gensel et al. 2006; Tom et al. 2009). The thoracic spinal cord contusion model is the most popular research model of pain and is induced with impactors (Gruner 1992). In brief, the exposed spinal cord is injured by dropping a 10.0-g rod from a designated height (Crown et al. 2006; Nakae et al. 2008). After 2 or 3 weeks, motor dysfunction is recovered and pain behavior can be analyzed. The effects of injuries often vary. Therefore, especially in short distances from the rod to the spinal cord, pain behavior does not always occur. Following injury, motor function analysis should be performed to eliminate the possibility of unilateral paralysis and unilateral contusion. Abnormal sensations caused by mechanical, hot, or cold stimuli can be observed for weeks or longer (Kerr and David 2007; Hoschouer et al. 2009; Meisner et al. 2010), and all regions (at-, above-, below-level) of allodynia are analyzed (Nakae et al. 2011).

Transection or Hemisection Models: The model of complete spinal transection injury reflects the symptoms of patients with complete SCI (Nakae et al. 2011). Following laminectomy, spinal cord is transected with spring scissors. Occasionally, a sterile gel foam is placed between the two removed ends of the spinal cord in order to attach the two ends for regeneration (Nakae et al. 2011). At-level and below-level NP are then analyzed (Scheifer et al. 2002; Densmore et al. 2010). Many studies

have reported muscle spasms in the model of complete spinal transection (Crone et al. 2007; Murray et al. 2010), and musculoskeletal pain pathology during spasm helped to clarify the use of this model. The partial spinal transection injury model (hemisection) has been widely used in NP studies (Peng et al. 2006; Liu et al. 2008a, b; Marchand et al. 2009). Motor dysfunction occurs only on the injured side of the same side for 5 days to 4 weeks (Hains et al. 2003). Mechanical allodynia and thermal hyperalgesia are bilaterally observed in above-level and below-level cases (Bennett et al. 2000; Hains et al. 2000; Gwak et al. 2004; Lee et al. 2010).

Photochemical Model: Over the past two decades, the SCI photochemical model, developed by Watson et al. (1986), has proven to be one of the most reliable and reproducible graded experimental rat models of SCI (Hao et al. 1991; Erichsen et al. 2005; Hao et al. 2006) and has been widely used to study neurotrauma in mice. The biggest advantage of this method is that the resulting injury does not induce mechanical trauma to the spinal cord, because no laminectomy is required (Nakae et al. 2011). In contrast, intravascular photochemical reactions occur by using a dye activated by an argon ion laser to produce single oxygen molecules on the surface of the spinal vascular endothelium (Nakae et al. 2011). This leads to a strong platelet response, followed by vascular obstruction and parenchymal infarction (Hao et al. 1991); the pathology is of a purely ischemic origin. Motor deficits are related to irradiation duration, and mechanical anomalies (cold, not thermal), which lasts for several days (Hao et al. 1992). Following application of the von Frey filament to the trunk, behavioral analysis is performed according to vocalization threshold. Antiallodynic effects of analgesics have been determined using this model (von Heijne et al. 2001). However, the extent of the injury is difficult to control. Therefore, motor deficit scores, such as blood brain barrier (BBB) (Basso et al. 1995) and CBS (Gale et al. 1985), have been widely utilized.

3.1.2 Models of Sciatic Nerve Lesion

The chronic compression injury model: The chronic compression injury (CCI) model of the sciatic nerve was established by Bennette and Xie (1988) and is widely used in clinical animal experiments. This model combines nerve compression with wallerian degeneration, intraneural edema, and epineural inflammatory lesions (Costa et al. 2005). The injury is induced by the ligation of the relaxed contraction around the sciatic nerve trunk at the mid-thigh level (Bennett and Xie 1988)). An incision between the femoris muscles and gluteus exposes the sciatic nerve of hind paw. At a distance of 2 mm from the trigeminal branch of the sciatic nerve, sciatic nerves are ligated with 4-0 chromic gut or silk to 4 sections with each section spaced 1 mm apart which are placed avoiding any interruption to avoid any disruption of the epineural circulation and pain allergy progression within 24 h of surgery (Muthuraman et al. 2008). CCI model is simultaneously sensitive to both A- and C-fibers and is used as a reliable NP method (Gabay and Tal 2004). The CCI model produces unilateral peripheral mononeuropathy, and symptoms in this rat model have

been observed to correspond to the patient's burning pain or complex regional pain syndrome (Kumar et al. 2017).

The partial sciatic nerve injury model: The partial sciatic nerve injury (PNI) model was developed to incorporate features Seltzer et al. (1990) developed this model in rats that only 1/3 to 1/2 of the sciatic diameter is tied off by tight ligation with an 8-0 silk suture either on the peroneal nerve, tibial nerve, or both (Kim and Chung 1997). The behavioral changes similar to CCI occur within 1 week after surgery and last up to 6 weeks (Kumar et al. 2017). There have been many attempts to simplify and standardize the procedures of the PNI model. For example, the one modified by Malmberg and Basbaum (1998) with less severe motor paralysis is more useful than CCI (Kumar et al. 2017). The PNI models can help to understand NP injury, as the PNI is the main cause of causalgiform pain in humans (Kumar et al. 2017).

The spinal nerve ligation (SNL) model: Another approach designed to standardize the procedure for partial nerve lesions is the spinal nerve ligation (SNL) model, which is designed by Kim and Chung (1992). In this model, spinal nerves L5 and L6 are tightly ligated distal to the DRG (Komori et al. 2007). In the SNL model, signs of spontaneous pain develop quickly and usually persist for 4 months (Kumar et al. 2017). This pain is sympathetically mediated (Xie et al. 1995) and is supported by sympathectomy. Ligation of L4 results in motor deficits as it has a lot of motor fibers which interferes with a behavioral test (LaBuda and Little 2005). Ligation of L5 alone is a highly reproducible method with less surrounding tissue damage (LaBuda and Little 2005) and ligation of L7 has similarity to pain in humans. Kiso et al. (2008) observed large and stable pain behavior in mice by replicating SNL with symptoms lasting for 2 months. The NP symptoms in the SNL model imitated the symptoms of human patients suffering from causalgia that developed after an injury to the peripheral nerve (Kumar et al. 2017).

When comparing these models, it was found that the inflammatory cell count and proinflammatory cytokine levels were increased at the lesion site 14 days after surgery and that the inflammatory response correlated with tactile hypersensitivity in the CCI and PSL animals. This finding is important since it implies that inflammation may play a role in the genesis of neuropathy in these models. Inflammation may also be a confounding factor producing symptoms and pharmacological responses not exclusively related to neuropathy when animals are tested within a few weeks of the original injury. A study comparing the CCI, PNI, and SNL models found that mechanical hypersensitivity was more pronounced in the SNL and least pronounced in the CCI model whereas behavioral signs indicating ongoing pain were more prominent in the latter. Surgical skill and procedure may have a significant impact on the outcome of neuropathy models and contribute to variability between surgeons and laboratories. Another factor shown to play a role is genetic differences between strains of animals, which represents a significant source of variability in model outcome. Taken together, these factors may be more important than the differences between the specific models.

3.1.3 Models of Diabetic Neuropathic Pain

Systemic neuropathies that are associated with conditions such as diabetes have also been examined. Diabetic neuropathy is caused by genetic modification of mice or injection of streptozotocin (STZ) (for the full review, see Feldman et al. 2008). After subcutaneous injection of STZ (50 mg/kg), C-fibers hyperresponsivity and hyperalgesia occurred within 2–3 weeks (Ahlgren and Levine 1993). There have been concerns that STZ itself may have neurotoxic effects that directly induce neuropathy, rather than through an induced diabetic state. However, there is evidence that STZ does not cause neuropathy except in combination with hyperglycemia (Davidson et al. 2010). In addition, transgenic animals of type I and II diabetes showed long-term diabetic complications including PDN (Kumar et al. 2017). The models of type II diabetes include Zucker diabetic fatty (ZDF) rats, Goto-Kakizaki (GK) rats, db/db mice, leptin-deficient (ob/ob) mice, and Bio-breeding Zucker/Worcester (BBZDR/Wor) rats (Kumar et al. 2017). GK rats show stable hyperglycemia without ketosis and obesity (Goto et al. 1988). The characteristic of ZDF rats is characterized by decreased sensory and motor nerve conduction velocity (MNCV) reduce and thermal hyperalgesia lasts for 6 weeks (Li et al. 2006). BBZDR/Wor rats show mild axonal atrophy and fiber loss without neuropathy (Schmidt et al. 2004). Ob/ob mice show transient hypothermia of thermal pain, which was observed in people with diabetic neuropathy (Calcutt 2002) in contrast to BBZDR/Wor-rats and ZDF rats where a persistent thermal hyperalgesia is observed (Dyck et al. 2000). Ob/ob animals have been shown to develop PDN (11-week-old) characterized by sensory as well as MNCV deficits, thermal hypoalgesia, tactile allodynia, and epidermal sensory fiber loss, characteristic features in humans with diabetes (Kumar et al. 2017).

3.2 Inflammatory Pain Models

Large amounts of inflammatory mediators are released after injury, which can lead to peripheral and central sensitization (Ji et al. 2014). The subsequent inflammatory responses usually recede after tissue healing, but in some cases, initial acute inflammation may persist and develop into chronic inflammatory pain (Burma et al. 2017). The models of inflammatory pain are built by injecting multiple irritants into the animal's skin, paw, muscle, joint, and visceral organs (Gregory et al. 2013) to induce the localized inflammatory responses. The inflammatory stimulants include those that induce acute inflammatory pain associated with neutrophil recruitment as well as more persistent pain responses associated with a macrophage infiltration (Gregory et al. 2013), such as formalin, complete Freund's adjuvant (CFA; Stein et al. 1988), or carrageenan (Martin et al. 1984). Every kind of chemical irritant produces a unique pain reaction time, ranging from a few minutes (e.g., formalin) to a few weeks (e.g., CFA), allowing for short- or long-term studies of local inflammation (Zhang and Ren 2011; Burma et al. 2017). They are commonly used to model conditions with acute

and chronic inflammation, and all have been validated by showing the effectiveness of opioids and NSAIDs.

The pain model of Carrageenan: Carrageenan is a commonly used inflammatory irritant (Gregory et al. 2013). Injection of carrageenan into the paw, muscle, and joint results in an acute inflammation initially, which could be converted into a chronic inflammation by 2 weeks (Hargreaves et al. 1988; Radhakrishnan et al. 2003). Carrageenan injection is associated with increased sensitivity to both thermal and mechanical stimuli at the site of injury (primary hyperalgesia) and external injury (secondary hyperalgesia) (Gregory et al. 2013). Additionally, there is strengthened protection of hind limbs, reduced weight of hind limbs, avoidance behaviors (PEAP), spontaneous pain behaviors, and reduced running activity (Hargreaves et al. 1988; Radhakrishnan et al. 2003; Sluka and Rasmussen 2010). The model has been shown to be helpful in understanding the conditions associated with acute inflammatory pain and may be associated with tissue damage such as sprains, strains, and myositis (Gregory et al. 2013).

The pain models of Complete Freund's adjuvant: CFA has been injected into the tail, paw, muscle, and joint of the experimental animal and causes a more chronic inflammation than carrageenan (Gregory et al. 2013). Thermal and mechanical hyperalgesia can be caused at around and beyond the injection site. At the same time, the weight of the hind limbs of the experimental animals reduced, and the spontaneous pain behaviors and non-reflexive pain behaviors enhanced, as well as wheel running decreased (Ren et al. 1992; Feldman et al. 2008; Parvathy and Masocha 2013). CFA is used to simulate chronic inflammatory pain that might occur in rheumatoid arthritis or tendonitis (Gregory et al. 2013).

The pain models of capsaicin: Injection of capsaicin into the skin, muscle, or joint activates TRPV1, which contains pain receptors, produces local neurogenic inflammation, and causes pain (Szolcsanyi et al. 1985; Tominaga et al. 1998). Capsaicin injection causes a change in reflexive behavior, including thermal and mechanical hyperalgesia around the site of the injury (the site itself becomes analgesic) and mechanical hyperalgesia outside the site of injury (Simone et al. 1989; Sluka 1997). These changes correspond to the primary and secondary areas of pain mediated by pain receptors and central nervous sensitization, respectively (Willis 2009; O'Neill et al. 2012). Capsaicin can also be used as an experimental pain model for experimental subjects (O'Neill et al. 2012), allowing for translation between animals and humans (Gregory et al. 2013).

3.3 Cancer Pain Models

Cancer pain associated with cancer may be the result of the cancer itself or the treatment used against cancer (Gregory et al. 2013). Cancer related pain has been modeled by local xenograft in the orofacial region to model orofacial pain, or to model metastatic bone pain in bone xenograft. Mouse femur bone cancer pain model: The model is modeled to a painful osteosarcoma via inoculation of osteolytic fibrosar-

coma (NCTC 2472) cells into the femur of mice (Kumar et al. 2017). The first step is to inject 20 μL of NCTC2472 cells into the bone cavity by inserting 23-gauge needle at the intercondylar notch level (Schwei et al. 1999). Then, the distal condyles of the femur are exposed through the incision of the posterior patellar ligament (Schwei et al. 1999). Bone destruction and osteoclastogenesis have been observed 5 days later, causing spontaneous (Kumar et al. 2017). Mouse calcaneus bone cancer pain model: The modeling approach is the same as the model of femoral bone cancer pain in mice, but NCTC2472 cells are injected into calcaneus bone (Mao-Ying et al. 2008). Tibial bone cancer pain model: Rat mammary gland carcinoma cells (MRMT-1) are injected into the tibial bone of rats (Mao-Ying et al. 2008) and pain hypersensitivity and ectopic pain occurred after 10 to 12 days. In addition, Meth A sarcoma cells (50,000 cells) are injected near the sciatic nerve at the gluteal level and can simulate neuropathic intractable cancer pain induced by malignant tumors near the sciatic nerve compressing or infiltration of peripheral nerves (Shimoyama et al. 2002). These models produce symptoms which are common in people suffering from cancer pain, such as enhanced mechanical and thermal sensitivity, enhanced palpation induced pain, and reduced grip force (Gregory et al. 2013).

3.4 Visceral Pain Models

The visceral pain models are used to observe pain behavior by irritating the peritoneum or hollow organs of the pelvis and abdomen. In visceral pain, noxious stimuli include current, mechanical damage, ischemia, and chemical drugs (Ness and Gebhart 1990). The common methods to prepare visceral pain in the abdominal cavity, abdomen, and pelvic cavity are the acetic acid torsion, colorectal expansion, and cystitis models. The acetic acid twisting model is used to study the peritoneal nociceptor and measures the spontaneous pain. To stimulate the visceral and parietal peritoneum by injecting 0.6% acetic acid into the abdominal cavity of the laboratory animal, resulting in large area and long duration of pain. Researchers can observe and record of pain behavior (stretch, curled up, abdominal post; Koster 1959). The model is simple and good repeatability, so it is usually used in the research of the central and peripheral analgesic. But there are some limitations to this model, such as using more animals, poor specificity, and individual difference. Distension of the colon is the most common of the abdominal cavity viscera expansion methods, which has been validated as painful in human subject (Ness et al. 1990). The model is built by inflating the colon and then measuring the electrical activity of the abdominal muscles (Ness and Gebhart 1987). The cystitis model is modeled by injecting noxious agents, such as vascular endothelial growth factor (VEGF), cyclophosphamide, and bacterial infection, into the bladder. Evoked pain behaviors, visceromotor response to distension, or secondary hyperalgesia on the abdomen or paw is assessed (Malykhina et al. 2013; Stemler et al. 2013).

In conclusion, differences in pain outcomes were found in animal models and in humans with experimental pain (King et al. 2009). With a better understanding

of the disease mechanisms in animals using an animal model of a proven clinical disease, one is trying to build a model and multiple outcome measurements should be informed to clinical translation. Then, clinical trials can be more appropriately designed to test a variety of outcomes based on the animal data. In fact, it could prove valuable to enhance translation between basic and clinical research that modeling a battery of outcome measures in animals across the domains proposed through consensus for clinical trials. Therefore, translation in pain research must be two-way by modifying and adapting animal models and outcome measures as more pathology data on a clinical disease is discovered, and translating animal models and outcome measures to appropriate clinical pain conditions and measures. Undoubtedly, new models will continue to be developed as our knowledge of disease pathology advances and more advanced techniques emerge; however, these methods should be evaluated against the criteria and validated against the conditions under which they are intended to model (Gregory et al. 2013).

4 Mechanistic Research on Acupuncture Analgesia

In recent decades, our understanding of how the brain processes acupuncture analgesia has undergone considerable development (Zhao 2008). The nervous system is divided into the CNS and the peripheral nervous system (PNS) (Catala and Kubis 2013). The mechanism of acupuncture analgesia remains a subject of particular interest to researchers, aiming to combine clinical practice with the understanding of pain transmission and the mechanism of acupuncture analgesic.

4.1 The Role of the Peripheral Nervous System in the Acupuncture Analgesia

The PNS is made up of the different nerves arising from the CNS. Acupuncture can block the pain signal conduction fibers in the nerves. The nociceptive response is therefore inhibited, providing a theoretical basis for local acupoints in the treatment of pain. Peripheral nerves are also afferent nerves of acupuncture signals. It is assumed that acupuncture needle is a physical sensory stimulation; the intensity, frequency, duration, and interval of the stimulation directly affect the type of receptor being activated. There is growing evidence that the types of afferent nerve fibers activated by acupuncture are diverse and depends on the different methods of operation of acupuncture and individual differences in acupuncture sensitization (Zhao 2008).

The stimulation current of different parameters at acupuncture point can produce bilateral analgesic effect on human and experimental animals (Han et al. 1983; Kim et al. 2000; Lao et al. 2004). It is widely believed that sustained analgesia can be induced only if the longer pulse duration is used (Romita et al. 1997). There has

been a controversy about which afferent fibers mediate EA analgesia since the 1970 s. Sensory receptors are supplied by afferent nerves of varying sizes, degrees of myelination, and conduction velocities. On this basis, sensory nerves can be simply divided into three main groups (conduction velocity given in brackets): thick diameter myelinated group II or Aβ fibers (>20 m/s), small diameter myelinated group III or Aδ fibers (2.5–20 m/s), and unmyelinated group IV or C fibers (<2.5 m/s) (Schaible and Grubb 1993). The debate is about whether C-type afferents are involved (Zonglian 1979). Electrophysiological and behavioral evidence from animal and human studies demonstrate that acupuncture can induce analgesia in the presence of an electric current that is sufficiently intense to excite Aβ-type afferents (group II) (Chung et al. 1984; Toda et al. 2002). However, the excitement of certain Aδ-type afferents (group III) can induce more analgesic effect (Leung et al. 2005). The early electrophysiological studies have shown that EA activates the entire spectrum of A-type afferents, which can strongly inhibit the pain response of dorsal horn neurons in cats than if only Ab fibers were stimulated (Pomeranz and Cheng 1979). Similarly, it was significantly correlated between the amplitude of Aβ-fibers in the compound action potentials of EA stimulation and the inhibitory degree of the jaw opening reflex induced by noxious stimulation in the rat (Toda et al. 2002). When the EA current intensity partially activates Ad -type afferents (group III), the EA-induced feeling is acceptable in humans and even comfortable for some people.

However, C afferents may play an important role in EA analgesia. Nagy (1982) injected neonatal capsaicin treatment (50 mg/kg) into rats to destroy 90% of unmyelinated fibers, and then used the same treatment to test the effect on EA analgesia in the rat (Zhu et al. 1990). In the capsaicin-treated group, EA analgesia was significantly reduced when compared to the control group. Additionally, researchers found that EA also played a role in analgesia when conduction in Ab- and Ad-type fibers was blocked, which suggests that C-type afferents are involved in EA analgesia (Zhao 2008). However, there are some opposite voices (Pan et al. 1997; Uchida et al. 2003). In normal rats, 45–50% of DRG neurons show TRPV1-immunoreactivity. All of these neurons disappeared from the DRGs after destroying of the C afferent fibers by neonatal capsaicin. Fos expression in the dorsal horn was significantly reduced by the treatment of neonatal capsaicin after injection of formalin into the hindpaw, but after EA to the pads of the hind paw, Fos expression was unaffected by the same treatment, which revealed that EA induces the expression of Fos in dorsal horn neurons via capsaicin-insensitive afferents, presumably Aδ-rather than C afferents. (Pan et al. 1997).

The role of the PNS in the MA analgesia may be different. Acupuncture points in the periphery are mainly deep receptors, and these acupuncture points are divided into five types: rich points of muscle, especially the limbs of the muscle spindle-based; muscle and tendon joints at the acupuncture points, the acupuncture center is Golgi's tendon organ, muscle shuttle around; tendon attachment points seem to ring body-based body; acupuncture point acupuncture sensory receptors are free nerve endings; and joint capsule acupoints receptors are likely to Ruffini body-based. It was initially observed that all types of acupuncture points have their own receptors. An experimental research showed that MA at the Hegu (LI 4) acupoint increased the

pain threshold (Chen-Yu et al. 1973). Blockage of cutaneous branches of the radial nerve innervating the skin at Hegu (LI 4) by procaine cannot alter the acupuncture-induced increase in pain threshold, while after blockade of the muscular nerves, deep branches of the ulnar nerve and the median nerve innervating muscles at Hegu (LI 4), the acupuncture analgesia completely disappeared, which suggests that afferent fibers are activated by muscle.

The types of afferents activated by MA are related to stimulating intensity and duration of manipulation (Zhao 2008). For instance, A-type fibers are mainly activated with gentle stimulation (Zhao 2008). However, when the needles are repeatedly twisted up and down, the deep tissues, especially muscle, are locally injured and proinflammatory mediators (such as histamine, bradykinin, PGE2, 5-HT, and ATP, etc.) are released, directly or indirectly stimulating pain receptors (Boucher et al. 2000; Ringkamp et al. 2013). It can thus be seen that C-type fibers are involved in MA-induced analgesia. Zhu, et al. found that MA-induced analgesia completely disappeared in the rat with capsaicin injected into the bilateral sciatic nerves for the selective blockade of conduction in Aδ- and C-type afferents (Bing et al. 1990; Okada et al. 1996; Zhu et al. 2004). In addition, the acupuncture feeling remains for several hours to even a few days after withdrawal of the acupuncture needles in the clinic, which also revealed that C-type afferents are involved in acupuncture analgesia (Zhao 2008).

The peripheral afferent fibers of acupuncture impulse. More studies have shown that II, III, IV fibers are possibly involved in the acupuncture analgesia. The results of Lv Guowei et al. have shown that the main needle acupuncture is related to electrical activity of crude fibers. The electroacupuncture or hand acupuncture impulse is mainly transmitted through type II fibers and part of type III fibers, and it was found that reducing the activity of fine fibers and/or increasing the activity of crude fibers helps to improve acupuncture's analgesic effect. Chen Longshun et al. also analyzed afferent fibers exposed to acupuncture. They stimulated the somatic nerve pain of the awake rabbits, then observed the mandibular reflex movement and vascular motor response which are indicators of pain response. The gradual increase in stimulus intensity, in turn, controlled the excitement of the "Zusanli (ST 36)" point of the peroneal nerve fiber. The results show that excitement of all kinds of fibers can significantly improve the analgesic effect. Some results proved that fine fibers play a major role in acupuncture analgesia and the analgesic effect of the finer fiber is the better.

These conflicting results may be related to the differences in stimulation parameters used such as two-phase square pulses of variable duration, single-phase pulses, and different frequencies and intensities (Zhao 2008). In short, the peripheral afferent mechanisms of acupuncture analgesia produced by EA and MA are homologous, but there are some differences (Zhao 2008). Moreover, when EA and MA are used at the same time, there is more potent analgesia than when only one is applied (Kim et al. 2000).

4.2 *Key Regions of the Central Nervous System Associated with Acupuncture Analgesia*

Acupuncture analgesia is a multi-channel and multi-level integrated process in the CNS. In fact, acupuncture analgesia may be the manifestation of integrative processes at different levels of the CNS in varying degrees of synthesis between afferent impulses from the pain regions and impulses from acupoints (Zhao 2008). The CNS is composed of the brain, the brainstem, the cerebellum, and the spinal cord (Catala and Kubis 2013). Experiments have shown that all levels of the CNS, from spinal cord to cortex, are involved in the acupuncture analgesic process. Acupuncture can postsynaptically inhibit the posterior horn of the spinal cord. In addition, nociceptive information travels from the spinal cord to the brain in several different pathways (McMahon 2005). These ascending pathways include direct projections of the thalamus (the spinal thalamus bundle), direct projections to homeostatic control regions (spinomedullary and spinobulbar) and projections of the hypothalamus/ventral forebrain (spinohypothalamic) (McMahon 2005). The periaqueductal grey (PAG) and reticular formation are important components of the spinobulbar system. The thalamus, a key structure in pain management, can be projected upwards into multiple regions, which includes the primary and secondary somatosensory cortices, the cingulate cortex, and the anterior insular cortex (Tracey and Dickenson 2012). The subjective experience of pain is highly complex and involves other regions, such as the prefrontal cortex, amygdala, basal ganglia and cerebellum (Tracey and Dickenson 2012). The major modulatory circuits exert bidirectional control over dorsal horn nociceptive transmission which include the rostral ventromedial medulla (RVM) and PAG. This network receives a large amount of direct and indirect input from pain pathways including the amygdala, the anterior insula and the anterior cingulate cortex, thus providing a mechanism for the way in which emotion affect pain perception (Tracey and Dickenson 2012). The RVM has separate descending antinociceptive and nociceptive outputs to the dorsal horn.

4.2.1 The Role of the Spinal Cord in the Acupuncture Analgesia

The spinal cord is the first station of nociceptive information processing and interpretation, in addition to functioning as a center of pain reflex. Dorsal root ganglion neurons (DRGs) are main afferent neurons responsible for transmitting sensory information from the periphery to the CNS. The DRGs are part of the PNS, located in the neural foramen of the vertebrae in close proximity to the CNS. Peripheral nociception was introduced into the spinal cord through the dorsal root, which was then classified and analyzed.

The spinal cord is hypothesized to be the primary level of acupuncture analgesia, and the underlying mechanism may be associated with the specific release of certain neurotransmitters, such as substance P (SP), somatostatin, and 5-HT, as well as the upregulation of glutamate transporters in the spinal cord (Ruan et al. 1996; Qiao et al.

2011; Zeng et al. 2016). Furthermore, opioid peptides may be involved in acupuncture analgesia in the spinal cord to varying degrees (Zyloney et al. 2010). Pharmacological inhibition of ascending nociceptive control at the spinal cord, nucleus accumbens, or supraspinal may prevent acupuncture-induced analgesia (Tobaldini et al. 2014). Recently, some researchers have been working on pathways. Strong EA stimulation is necessary to produce strong analgesic effect but is possibly associated with p38 activation in spinal microglia (Hsu et al. 2015). In addition, EA produces analgesic effect by inhibiting the activation of ERK1/2-CREB-NK-1 pathway and ERK1/2-COX-2 pathway in the dorsal horn of the spinal cord (Fang et al. 2014).

In addition to neurons, microglia and astrocytes, which were activated in the spinal cord dorsal horn (SCDH), are involved in the pathogenesis of chronic pain. Inhibition of the activation of spinal microglia and astrocyte may promote the immediate effects and maintenance of EA analgesia, respectively (Liang et al. 2016).

4.2.2 The Role of the Brain Stem in the Acupuncture Analgesia

The brain stem is the relay station responsible for sorting, discriminating, and synthesizing information related to pain. An important mechanism which underlies acupuncture-induced analgesia involves activating the reticular formation of the brain stem descending pain-inhibitory system. The main part of the system is located in the periaqueductal gray and medulla oblongata nucleus raphe magnus (NRM). NRM is a supraspinal area, mediating a negative feedback circuit modulating pain. Raphe-spinal (R-S) neurons were identified in the NRM. EA can increase the firing rates of the excitatory R-S neurons to inhibit their nociceptive responses. It suggested EA can activate NRM, inducing analgesia via descending inhibition (Liu et al. 1986), and the activity of NRM can be controlled by some higher central structures, such as PAG, caudate nucleus, and accumbens nucleus. The underlying mechanism is associated with a variety of neurotransmitters involved in analgesia, such as 5-HT and opioid peptides (Lee et al. 2001; Zhang et al. 2012). A previous study demonstrated that damage to the locus ceruleus may improve the analgesic efficacy of acupuncture (Kim et al. 2011).

4.2.3 The Role of the Hypothalamus in the Acupuncture Analgesia

The hypothalamus is one of the structures of the descending antinociceptive pathway which is believed to participate in the analgesic mechanism of acupuncture analgesia (Yu and Han 1989; Wang et al. 1990a). The most abundant endorphinergic neurons and long descending projections to the raphe nucleus and periaqueductal gray matter of the mesencephalon. The hypothalamus have been considered to be essential for acupuncture analgesia (Yu and Han 1989; Wang et al. 1990a, b). Some studies showed that EA can increase the expression of proopiomelanocortin mRNA and preproenkephalin (PPE) mRNA in hypothalamus in the rats with third lumbar vertebrae transverse process syndrome, which may contribute to its effect in relieving

pain in the treatment of lumbar muscle strain (Guo et al. 2010). Wu et al. (1999b) had previously found that acupuncture stimulation at the Large Intestine 4 (LI 4) and Zusanli (ST 36) can activate the hypothalamic-limbic system by using functional magnetic resonance imaging (fMRI). Xu et al. (2013) indicated that repeated electroacupuncture at bilateral Zusanli (ST 36) and Yanglingquan (GB 34) has a cumulative analgesic effect and can effectively relieve chronic NP by reshaping the paraventricular synaptic structure of the hypothalamus.

The frequency of needle manipulation may be important for acupuncture analgesia according to the previous observations that the hypothalamus, a nucleus densely aggregated with β-endorphinergic neurons, is central to the analgesic mechanisms of low frequency acupuncture stimulation (Wang et al. 1990a, b). In addition, some results demonstrated that levels of 5′-AMP-activated protein kinase (AMPK) gene expression in the rat hypothalamus determine the individual differences in the sensitivity to EA analgesia. It can explain the phenomenon that the clinical effect of acupuncture analgesia usually necessitates longer stimulation sessions (Han and Terenius 1982) and about 30–40% of the rats were insensitive to EA in an acute thermal pain test and tail flick latency test in animal research (Takeshige et al. 1981; Lee et al. 2002; Sekido et al. 2003; Kim et al. 2007). Thus, the findings provide a clinically useful evidence for the application of acupuncture or EA for analgesia (Kim et al. 2014).

4.2.4 The Role of the Thalamus in the Acupuncture Analgesia

The thalamus has been shown to play an important role in pain and acupuncture analgesia. In the anatomic studies of cat and rat, we found that the nucleus submedius (SM) receives major projections from the trigeminal subnucleus caudalis and the spinal dorsal horn lamina I (Craig and Burton 1981; Ma et al. 1988; Dado and Giesler 1990; Yoshida et al. 1991; Blomqvist et al. 1992). Additionally, a series of studies provided evidence for the hypothesis that the hypothalamus is involved in the regulation of pain (Dostrovsky and Guilbaud 1988; Snow et al. 1992; Kawakita et al. 1993). The SM, ventrolateral orbitalcortex (VLO), and the PAG constitute an important pain modulatory pathway, activation of which also can activate the PAG–brainstem descending inhibitory system and depress nociceptive inputs in the spinal cord and trigeminal nucleus (Tang et al. 2009).

Most neurons in the SM respond to needle acupuncture. In general, the neurons that respond to acupuncture needles have a similar pattern of response to harmful mechanical skin or muscle stimulation. Some neuron responses last 10 min or more after stimulation (Yang and Hatton 1997). Studies have shown that the SM-VLO-PAG pathway plays an important role in the analgesia induced by electroacupuncture on acupoints for exciting small diameter fibers (Aδ and C groups) afferents (Yang et al. 1996; Tang et al. 2009). Endogenous opioids (Yang et al. 2002; Xie et al. 2004; Wang et al. 2006, 2008; Feng et al. 2008), serotonin (Xiao et al. 2005; Huo et al. 2008; Qu and Wang 2008), glutamate (Zhang et al. 1997, 1998), GABA (Jia et al. 2004; Wang et al. 2005; Qu et al. 2006), and their related receptors are involved in SM-

and/or VLO-mediated descending antinociception, and a GABAergic disinhibitory mechanism participates in mediating the antinociception induced by activation of mu-opioid receptors, serotonin 1A receptors, and dopamine D2-like receptors (Tang et al. 2009).

4.2.5 The Role of Caudate Nucleus in the Acupuncture Analgesia

Caudate nucleus is located near the center of the brain, sitting astride the thalamus, which there is a caudate nucleus in each hemisphere of the brain. Individually, they resemble a C-shape structure with a wider "head" at the front, tapering to a "body" and a "tail" (Yeterian and Pandya 1995). The caudate nucleus is an important neural structure in pain modulation and acupuncture analgesia. Caudate nucleus influenced pain modulation through oxytocin. Histological study has revealed that there are oxytocin-containing nervous fibers in the caudate nucleus (Antunes and Zimmerman 1978) which has been shown to act in nociception (Millan 2002; Yang et al. 2008). One study has pointed that oxytocin in the caudate nucleus increases the pain threshold while oxytocin-receptor antagonist decreases the pain threshold (Yang et al. 2011). Pain stimulation also induces the release of oxytocin in the caudate nucleus (Yang et al. 2011). Many bioactive substances including dopamine and acetylcholine, which are involved in pain modulation, show the interaction with oxytocin in the caudate nucleus (Sarnyai et al. 1991).

Through chronic implanted electrode stimulation in 17 patients, the role of the caudate nucleus in acupuncture analgesia was studied to alleviate intractable pain caused by advanced malignant tumors (Chen et al. 1982). The study has confirmed that the caudate nucleus may play a role in acupuncture analgesia and the effect of caudate stimulation is generated by inhibiting the activity of the medial thalamus (Chen et al. 1982). The role of the caudate nucleus in acupuncture analgesia may be associated with neurotransmitters in the caudate nucleus. Acupuncture can increase oxytocin concentration in the caudate nucleus (Yang et al. 2007a, b, 2011). In addition, experiments showed that endogenous opioids in the caudate nucleus are involved in the descending nociception of neurons in the parabronchial nucleus during the acupuncture analgesia regulatory effect.

4.2.6 The Role of the Cerebral Cortex in the Acupuncture Analgesia

The cerebral cortex is the center of higher nervous activity, including consciousness, intelligence, analysis and synthesis, reasoning and judgment. Any signal has to enter the cerebral cortex for consciousness, and pain is no exception. In other words, the cerebral cortex participates in the pain and the analgesic effect of acupuncture. In the cerebral cortex, acupuncture-induced analgesia is not a process of excitation or inhibition, but a complex process of regulation (Newberg et al. 2005; Wang et al. 2008; Yi et al. 2011). Electrophysiological records in experimental animals (Ogawa and Wang 2002) and brain imaging studies in human subjects (Brooks et al. 2005;

Schweinhardt et al. 2006; Henderson et al. 2007) have consistently shown that the insular cortex plays an important role in pain management. The insular cortex receives afferent projections from thalamus nucleus, and it forms reciprocal connections with the amygdala, limbic system, and cortical association areas (Craig et al. 2000; Jasmin et al. 2003; Craig 2014). This cortical and subcortical circuit provides a reliable basis for animals and humans to process disobedient and/or frightening information. Under pathological conditions, they can also lead to long-term emotional pain in these patients, such as illness and pain caused by chronic anxiety and depression (Zhuo 2016).

4.3 Neurotransmitters Involved in Acupuncture Analgesia

Acupuncture analgesia involves many types of transmitters and modulators. In 1974, Han's group (Han et al. 1974) conducted a study which revealed that the pain threshold of recipients was increased when the cerebrospinal fluid of donor rabbits given acupuncture was infused into the cerebral ventricles of recipient rabbits. The results suggest that central chemical mediators may be involved in acupuncture analgesia. Since then, many findings from human and animal studies have demonstrated that acupuncture analgesia is a complex physiological process mediated by various neurotransmitters and neuromodulators (Zhao 2008), including endogenous opioids, adrenalines, serotonin, cholines, GABA, and etc. We have previously commented the impact of acupuncture on the neurotransmitters and neuromodulators (Wen et al. 2010a; b; Liang and Xia 2012). The below contents will briefly review the role of neurotransmitters and neuromodulators in acupuncture analgesia.

4.3.1 The Role of Endogenous Opioids in Acupuncture Analgesia

The Endogenous Opioids

Endogenous opioids coined by the morphing of the two descriptive terms into endorphins, are opioid neuropeptides which are naturally produced in the body that serve a primary function as an agent blocking the perception of pain (Chaudhry and Bhimji 2017). It is well known that the three main groups of opioid peptides, β-endorphin, enkephalins and dynorphins, and their preferable opioid receptors, μ-, δ- and κ-receptors (MOR, DOR, KOR), are widely distributed in peripheral primary afferent terminals and areas of the CNS related to nociception and pain (Zhao 2008).

The function of endorphins can be stated in general terms as well as broken down specifically and observed per each endorphin type. In general, the release of endorphins is understood to be associated with the body's response to pain. In the PNS, the perception of pain relief is produced beta-endorphins bind to opioid receptors (Chaudhry and Bhimji 2017). Opioid receptors are broken down into four primary classes of G protein-coupled receptors: MOR, DOR, KOR, and nociceptin receptors

and the greatest binding potential exists between the beta-endorphins and the mu-receptors (Da Fonseca Pacheco et al. 2014). MOR can be found throughout nerves of the PNS. When beta-endorphin to MOR binding occurs on nerve terminals (happening pre-synaptically or post-synaptically), analgesic effects are realized. The effects are realized as the aforementioned binding results in a triggering of chemical events preventing the release of SP, amongst other tachykinins, which is an instrumental undecapeptide in the conveyance of pain (Chaudhry and Bhimji 2017).

The Presence and Distribution of Opioid Receptors

Opioid receptors are a class of G-protein coupled receptors with 7 transmembrane regions, which consist of a series of small molecules including morphine derivatives and opioid ligands and can also be activated by various peptide types. Classic opioid receptors mainly include MOR, DOR and KOR. Classic opioid receptors are widely distributed in the central nervous system, such as the descending conduction pathway of the brain, brain stem, and spinal dorsal horn, at the same time widely in the spermaduct, alimentary canal, heart and immune system (Peng et al. 2012). Functional heterogeneity of orphanin FQ receptors in the periaqueductal gray matter of rats were revealed by the simulated effect of Ro 646-6198, the orphanin FQ receptor agonist (Liao et al. 2011). The different distribution of opioid receptors indicates that there are different mechanisms in analgesia. The MOR, DOR, and KOR in peripheral tissues are known as peripheral opioid receptors. Opioid receptors in peripheral sensory nerves are finely regulated by inflammation.

The Role of Endogenous Morphine in Acupuncture Analgesia

The role of endogenous opiate peptides in acupuncture analgesia has been studied extensively in China. The results showed that endogenous opiate peptides are correlated with the effect of acupuncture analgesia (Leung 2012).

The effects of EA on the regulation of neurons are involved in opioid receptor. Zeng et al. (2014) verified that EA analgesia effect is mediated through opioid releases in a plantar incision-induced pain model. Du et al. (2015) used bone cancer SD models to explore the possible mechanism of EA against bone cancer pain. 90 healthy female SD rats were randomly divided into a control group (no treatment), a model group (no treatment), EA groups (6 subgroups according to different frequencies; EA at bilateral "Housanli" (ST 36) and "Genduan" (Extra) with 3 different current frequencies, as 2 Hz, 100 Hz and 2 Hz/100 Hz), and a sham EA group (the same as the EA group but without electrical stimulation). The mRNA expressions of MOR, KOR, DOR and prodynorphin (PDYN) in DRG and lumbar spinal cord dorsal horn (SCDH) of L4-L6 of the affected side were detected via PCR. The results indicated that EA against bone-cancer pain may be associated with increasing the mRNA expression in some peripheral opioid receptors and precursors. The studies have directly demonstrated the role of endorphin/opioid receptors in acupuncture analgesia. Some

indirectly revealed the role of endorphin/opioid receptors in acupuncture analgesia. Mayer (2000) clarified the role of endogenous opioid in acupuncture analgesia by confirming that opioid receptor blocker naloxone reversed the acupuncture effect. This result is supported by others studies such as Zhou et al. (2012). They reported that the opioid receptor blocker can decrease the analgesic effect of EA.

Different frequencies of EA can lead to differential release of various analgesic neuropeptides. For example, EA at 2 Hz accelerates the release of enkephalin β-endorphin while EA at 100 Hz selectively increases the release of dynorphin (Leung 2012). Chen and Han (1992) and Wu et al. (1999a, b) reported that 2 Hz EA-induced analgesia is mediated by met-enkephalin via μ and δ receptors; however, the antinociception effect induced by high-frequency (100 Hz) EA is mediated by dynorphin via KOR in the spinal cord of rats. Kim et al. (2004) showed elective KOR antagonist did not work with the low frequency (2 Hz) used in the experiment. Xiang et al. (2014) using rhesus monkey models to provide direct evidence that specific frequencies of EA are mediated by different opioid receptors in the CNS.

The results from these animal studies provide an explanation for the clinical observation that synergistic analgesia can often be obtained if EA is performed using an alternating low (2 Hz) and high (100 Hz) frequency (Leung 2012). Indeed, the role of endogenous opioids in EA analgesia has been well confirmed. Zheng et al. (2008) reported a reduced demand for opioid-like medications in patients with chronic pain after a course of EA.

Although the role of endogenous opioids in acupuncture analgesia has been well established, the precise mechanisms for acupuncture induced endogenous morphine release, opioid receptor expression, and signaling process require more in-depth investigation.

4.3.2 The Role of 5-Hydroxytryptamine in Acupuncture Analgesia

The Synthesis, Presence, and Distribution

Serotonin (5-hydroxytryptamine, 5-HT) is a monoamine neurotransmitter synthesized in the serotonergic neurons. It is widely distributed in animal tissues, such as gastrointestinal mucosa, spleen, platelet, serum, lung, salivary night glands. There is more 5-HT in the CNS. It is mainly distributed in the medial thalamus, the hypothalamus, the brain stem, and the new striatum, especially in the nuclei raphe magnus (NRM), which is a crucial site in the descending pain modulation system (Millan 2002). In addition, there are multiple 5-HT receptor subtypes in the nervous system (Millan 2002). For example, 5-HT_{1A} and 5-HT_{1B} receptors are densely present in neurons of the dorsal horn in the spinal superficial laminae in which primary nociceptive afferent fibers terminate (Hamon and Bourgoin 1999), while 5-HT_{2A} and 5-HT_3 receptors are expressed by primary nociceptive afferent fibers (Hamon et al. 1989; Carlton and Coggeshall 1997).

5-HT synthesis and metabolism are schematically shown in Fig. 1. Under normal conditions, the level of serotonin is dependent on the intake of tryptophan and degra-

Fig. 1 Schematic representation of 5-HT synthesis and degradation pathway. TRP, Trytophan; TPH, trytophan; 5-HTP, 5-hydroxytryptophan; AADC, aromatic-L-amino-acid decarboxylase; 5-HT, hydroxytryptamine; MAO, monoamine oxidase; %-HIAA, 5- hydroxyindole-3-acetic acid

dation by monoamine oxidase (MAO). In the CNS, serotonin is believed to play an important role in the regulation of body temperature, mood, sleep, vomiting, pain, appetite, and more.

The Relation of 5-HT and Morphine in Analgesia

The spinal release of opioids may be driven by a serotonergic in descending pathway and is at least in part elicited by activation of 5-HT3 receptors. In a rat formalin model, Shen et al. (2013) thought the balance between norepinephrine and serotonin transporter inhibition affects the degree of antinociceptive synergy observed between monoamine reuptake inhibitors and morphine. Morphine has a strong analgesic effect on acute pain, but has no effect on NP. Kimura et al. (2014) compared the efficacy of systemic morphine between normal rats and rats with peripheral nerve injury. The results introduced that systemic administration of morphine increases 5-HT levels in the spinal cord, and the increase in 5-HT contributes to morphine-induced analgesia in the normal state but attenuates that in NP through spinal 5-HT_3 receptors. In conclusion, the effect of hydroxytryptamine and morphine on analgesia is a cooperative relationship, which promotes and restricts each other and maintains a dynamic equilibrium relationship.

The Role of 5-HT in Acupuncture Analgesia

Serotonin may also be one of the neurotransmitters for acupuncture analgesia. 5-HT has a dual role in pain. In physiological conditions, the facilitation and inhibitory pathways of 5-HT are in equilibrium, and are regulated by a variety of factors. However, the inhibitory pathways always play a leading role, which depends on the receptor type activated.

Some early studies revealed that EA can increase the central content of 5-HT and its metabolic products, particularly in the NRM and the spinal cord (Cheng and Pomeranz 1979; Han et al. 1979a, b; Ye et al. 1979; Zhu et al. 1997a, b). The p-chlorophenylalanine, which is a 5-HT synthesis inhibitor, can decrease the effect of acupuncture analgesia by blocking 5-HT biosynthesis while pargyline, a monoamine oxidase inhibitor, can increase the effect of acupuncture analgesia (Han and Terenius 1982). Additionally, blockage of 5-HT receptors by cinaserine, cyproheptadine, methysergide, or 5-HT receptor antagonists resulted in acupuncture analgesia (Han et al. 1979a, b; Chang et al. 2004). The results verify that both serotonergic descend-

ing and ascending pathways induced by NRM were related to mediating acupuncture analgesia (Zhao 2008).

A significant amount of data has demonstrated the critical role of 5-HT receptors in the acupuncture analgesia. Zhang et al. (2012) showed that 5-HT_{1A} receptors are involved in the EA inhibition of inflammatory pain. Wang et al. (2014) profiled gene expression in the spinal dorsal horn after application of 2-Hz and 100-Hz EA and found that the levels of mRNAs encoding 5-HT_1 receptors were upregulated in responder rats. In addition, acupuncture can effectively inhibit the mRNA expression of pain-related genes such as 5-HT_{2A} receptor in the spinal cord (Kim et al. 2010). In a study on antagonists of 5-HT receptors, Erthal et al. (2013) injected naloxone (nonselective opioid receptor antagonist), pindolol (nonselective 5-$HT_{1A/B}$ receptor antagonist), ketanserin (selective 5-HT_{2A} receptor antagonist) and ondansetron (selective 5-HT_3 receptor antagonist) into rat models of acute nociception to confirm the effect of Zusanli (ST 36) laser acupuncture analgesia mediated by activation of the opioidergic and serotonergic (5-HT_1 and 5-HT_{2A} receptors) systems. These data suggest that 5-HT_{1A} and 5-HT_{2A} receptor subtypes play important roles in mediating EA analgesia.

It has been determined that 5-HT, which plays a key role in acupuncture analgesia, seems to have two different central 5-HT energy pathways. The descending pathway starts from the middle seam and the transmission of the harmful input at the spinal level. The ascending 5-HT pathway starts in the middle cerebral seam and it can be activated with acupuncture which cause 5-HT to release in the forebrain structure.

4.3.3 The Role of Catecholamine System in Acupuncture Analgesia

The Presence and Distribution of Catecholamine in the Nervous System

Catecholamine (CA) is a monoamine medium, which mainly includes the epinephrine (AE), norepinephrine (NE), dopamine (DA) and their metabolites. CA is not evenly distributed in the CNS, and peripheral nerve contains more. Earlier studies suggested that the analgesic effect of noradrenaline occurs at the level of the spinal cord. However, since then there has been cumulative evidence for noradrenergic modulation at supra-spinal levels, which involves several brain areas (Strobel et al. 2014). Noradrenergic receptors can be found in all supraspinal structures that are involved in pain processing, even though the exact mechanism of action is still not understood (Pertovaara 2013).

The Role of Norepinephrine in Acupuncture Analgesia

NE is known to be one of the main transmitters involved in the descending inhibitory system (Nagakura et al. 2009), and noradrenergic fibers are known to bring about direct inhibition on the many types of spinal cell with which they make synaptic con-

tacts. Martins et al. (2013) indicated that noradrenaline may enhance pain facilitation from the brain during inflammatory pain.

Researchers found that NE plays a different roles in acupuncture analgesia. Most experimental studies with rats have shown that EA-induced analgesia is associated with a decreased level of noradrenaline in the brain (Wang et al. 1994; Zhu et al. 1997b). However, in a gastric ulcer rats model (Sun et al. 2015), the expression of NE in hippocampus in the model group was significantly reduced (both $P < 0.01$) when compared to the blank group, but compared to the model group, the expression of 5-HT and NE in the EA group was increased (both $P < 0.01$). Immunohistochemical staining demonstrated that α2a-ARs are on primary afferents in an inflammatory pain rat model (Zhang et al. 2012). In addition, noradrenaline seems to act differently in the spinal cord depending on the receptor subtypes. One early study revealed that the analgesic effects of EA are blocked by administering the precursor of noradrenaline, whereas it is potentiated by administering intrathecally (Xie et al. 1981). In a study (Kim et al. 2005), the alpha (2)-adrenoceptor (α2-AR) antagonist yohimbine (i.t.) blocked EA analgesia in an NP model, while the α1-AR antagonist prazosin did not. The finding supported the previous reports (Brown and Caulfield 1979; Akasu 1985). These results are in line with our knowledge that, in the spinal dorsal horn, α2-adrenergic receptors suppress nociceptive signaling whereas α1-adrenergic receptors facilitate it (Millan 2002).

The Role of Dopamine in Acupuncture Analgesia

DA is a precursor of NE and an independent medium, so they share many common metabolic pathways. Clinical and human imaging studies suggested DA is disrupted in NP patients, and release of DA in the ventral striatum is normally associated with analgesia. In addition, local injection of a dopamine receptor 2 (D2) agonist, produce analgesia (Sotres-Bayón et al. 2001; Taylor et al. 2003). Furthermore, Parkinson's Disease is sometimes associated with lower pain thresholds that can be recovered with Levo-Dopa treatment.

However, in acupuncture analgesia, dopamine receptor antagonists potentiated EA analgesia (Wang et al. 1997); in other words, DA systems may antagonize the effect of acupuncture analgesia. D1 receptor antagonists upregulated opioid receptors in many brain regions (Zhu et al. 1995). Some results showed that D2 receptor activation may oppose opioid analgesia (King et al. 2001), but in an arthritic pain model, one presented that the D2 antagonist metoclopramide reduced the analgesic effects of EA (Liao et al. 2011). These somewhat conflicting results may be related to differences in the route of drug administration, receptor subtype selectivity, and differences in the experimental pain model.

4.3.4 The Role of Cholinergic System in Acupuncture Analgesia

Acetylcholine (ACh) is the transmitter of cholinergic neurons in the brain. Choline acetyltransferase A and acetyl coenzyme A were used for synthesis. The release ACh stimulates the cholinergic receptors and this interaction is quickly terminated by the local choline esterase, resulting in the hydrolysis of acetylcholine into choline and acetate. Choline acetyltransferase (ChAT) regulates the level of ChA to determine the level of ACh.

Brain cholinergic mechanisms of areas such as hypothalamus, thalamus, locus ceruleus, caudate-putamen complex, and cortex are surely involved in the production of acupuncture analgesia; the central ACh is the essential transmitter or modulator in the analgesic pathway. The results of Wang et al. (2012) revealed that repeated EA can significantly up-regulate acetylcholinesterase (AChE) and vesicular acetylcholine transporter (VAChT) activities and ChAT mRNA and M1R mRNA expressions in the hypothalamus of chronic constrictive injury and ovariectomy + chronic constrictive injury rats, which may contribute to the cumulative analgesic effects of repeated EA and be closely related to the animals' memory ability. The synthesis of ACh, release of ACh, and degradation of cholinergic systems in the caudate are beneficial to acupuncture analgesia, and cholinergic systems in the caudate and 5-HT can have synergy in acupuncture analgesia.

The pathway may be related to the metabolism of ACh in the dorsal horn of the spinal cord and spinal ganglia during the course of EA analgesia, and only when signals produced at the acupoints are delivered to the spinal cord via ACh-containing primary somatosensory nerves can they exert the analgesic and therapeutic effect of acupuncture (Guan et al. 1990).

4.3.5 The Role of Gamma-Aminobutyric Acid in Acupuncture Analgesia

In the past 20 years, GABA has been found to have a special effect on the nervous system, and it has a general and strong inhibitory effect on neurons in the central nervous system. It is thought to be the neurotransmitter that transmits inhibitory impulses in the nervous system. The content of GABA is very different depending on the brain tissue. The concentration of GABA is high in the mammalian brain, while more in the substantia nigra, globus pallidus, the cerebral cortex, cerebellar dentate nuclei content, and less in the white matter (Palacios et al. 1981).

GABA and its receptors are involved in pain and acupuncture analgesia. Three GABA receptor subtypes have been identified: GABAA, GABAB, and GABAC, but it has been known that GABAA and GABAB receptors, present in the spinal cord, mainly contribute to the modulation of pain. Intrathecally injected baclofen (GABAB receptor agonist) has been demonstrated to produce analgesia in animal models of acute and NP (Melcangic and Bowery 1996). Also, GABAA and GABAB receptor agonists have been demonstrated to have antinociceptive effects in a variety of rodent models (Sawynok 1987). Recently, one result (Qiao et al. 2017) indicated

that EA at Xialian (LI 18)/Large Intestine 4 (LI 4)-Neiguan (PC 6) increases pain threshold in rats with incisional neck pain, which is likely related to the upregulation of GABA in the primary sensory neurons of cervical dorsal root ganglia. The other result (Gao et al. 2012) found that both EA of Xialian (LI 18) and Large Intestine 4 (LI 4)-Neiguan (PC 6) can significantly suppress formalin-injection induced pain reactions in the thyroid region, which may be closely associated with its effects in upregulating expression levels of cervico-spinal GABAB R1 mRNA, GABAB R2 mRNA and GABAA R mRNA, and reduce regional inflammatory reactions in the thyroid region.

4.3.6 The Roles of Other Neurotransmitters/Modulators

Substance P

SP is a neuropeptide involved in the transmission of pain which impulses from the peripheral receptors to the CNS. It belongs to the tachykinin neuropeptide family. EA treatment can decrease in SP and increase in beta-endorphin levels to induce analgesia in an S-180 cancer pain model (Lee et al. 2009). Furthermore, Gao et al. (2012) proposed that downregulating of pronociceptive mediators SP in the primary sensory neurons of cervical DRG by EA can increases pain threshold in rats, which may be related to analgesia.

Brain-Derived Neurotrophic Factor

The brain-derived neurotrophic factor (BDNF) is a protein synthesized in the brain, which is widely distributed in the CNS. BDNF is involved in the growth and differentiation of neurons, and it is necessary to maintain normal physiological functions of mature neurons. Some evidence suggested that EA analgesia is related to BDNF. Wang, et al. (2016) suggested BDNF may be closely associated with astrocytes that participate in the process of EA relieving chronic pain. In a clinical trial (Chassot et al. 2015), the result indicated EA analgesia is related to neuroplasticity indexed by the adjusted BDNF and EA modulation of pain and BDNF occurs according to the CNS situation at the moment of its administration.

Further investigation into the interaction among neurotransmitter systems at the cellular and molecular level, particularly under neuropathic states, is of great scientific interest and importance, and may lead to new therapeutic approaches for treating various acute and chronic pain conditions.

5 Conclusion and Perspectives

Acupuncture is an ancient medical technology and is proven as a valid anti-pain modality in clinical and laboratory research in the past several decades. As a common technique of traditional Chinese medicine, it is widely used in clinical practice. The laboratory studies, especially neurobiological research have provided strong evidence for the mechanisms for an association between acupuncture and analgesia which involve both peripheral and central nerve systems, multiple brain regions and various neurotransmitters/neuromodulators. However, the precise understanding of the working mechanisms and optimal acupuncture conditions for the maximal analgesic effect for different pain conditions are important in future research. Currently, acupuncture analgesia is not usually the first choice and can even be neglected in the mainstream medicine. The more quality and in-depth research may build a solid basis for the basic theory and practice guideline of acupuncture analgesia. Its our belief that better understanding the mechanisms and conditions of acupuncture therapy for relieving pain will provide theoretical practical foundations for a better application of acupuncture analgesia in future medicine and greatly reduce the side effects of analgesic drugs.

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Effect of Acupuncture on Parkinson's Disease

Tao Chen, Yanhui Liu, Yidong Deng, Shan Zhang, Si Teng, Benchi Cai and Jiali Su

Abstract Parkinson's disease (PD) is a common progressive neurodegenerative disease in middle-aged and elderly people. The prevalence of PD in people aged more than 65 is 1.7%, posing a serious threat to the health of middle-aged and elderly people. Till now, no effective treatment is available that would slow down or halt PD progression. It is important to find new therapies for such serious neurodegenerative disease. Acupuncture is most commonly used as a complementary therapy in patients with PD. In recent years, the clinical and experimental research progress of acupuncture treatment for Parkinson's disease has been reviewed. It is concluded that acupuncture treatment can significantly improve sports symptoms and even non-motor symptoms in patients with PD, reduce the toxic and side effects of drug treatment, and delay the progression of the disease without significant adverse effects. Acupuncture can be considered as a combination treatment with conventional treatment for patients with PD. This paper reviewed the clinical efficacy and mechanism of acupuncture therapy in Parkinson's disease in recent 10 years and presented a systematic review and meta-analysis of the effects of acupuncture for patients with PD.

Keywords Acupuncture · Neuroprotective mechanism · Dopamine · Parkinson's disease

1 Introduction

Parkinson's disease (PD) is a chronic progressive neurodegenerative disease in the middle-aged and elderly people (Jellinger 2001; Asakawa et al. 2016a, b; Ellis and Fell 2017). An epidemiological survey (Zhang et al. 2005) showed that the prevalence rate of PD in people aged more than 65 was up to 1.7%. PD is caused by the loss of dopaminergic neurons in the substantia nigra and it's featured motor symptoms including distal resting bradykinesia, tremor, rigidity, postural instability,

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gait disturbance, and nonmotor symptoms (Bjorklund and Cenci 2010; Asakawa et al. 2016a, b). The underlying molecular pathogenesis involves multiple pathways and mechanisms: α-synuclein proteostasis, mitochondrial function, oxidative stress, calcium homeostasis, axonal transport and neuroinflammation.

There is no cure for Parkinson's disease, with treatment directed at improving symptoms. With the deepening of research, many new drugs, techniques, and therapies were applied in clinical practice gradually, and a certain clinical effect was obtained. The use of levodopa and other dopaminergic treatments in progressive PD lessens the risks of dyskinesia and motor fluctuation. However, the long-term use of levodopa led to a loss of efficacy and complications such as motor fluctuation and dyskinesia. These complications are observed in 50% of patients after 5 years of levodopa use for PD and in 80% of patients after 10 years of levodopa use.

Acupuncture is most commonly used as a complementary therapy for PD (Asakawa and Xia 2012; Chao and Xia 2015). Acupuncture has been reported to have possible therapeutic effectiveness for PD in clinical trials, as manifested by improvement in clinical symptoms such as tremor and improvements in daily life. Increasing evidence shows that acupuncture can alleviate the symptoms of PD, delay the progression of these symptoms, allow for a decrease in the dosage of antiparkinsonian drugs, and decrease side effects. This paper summarized and analyzed the progression of clinical and experimental studies on acupuncture for treating PD.

2 Parkinson's Disease: A View of Traditional Chinese Medicine

PD is classified as "tremor syndrome," "tremor," "spasm syndrome," "endogenous wind-evil," and "limb tremor" in traditional Chinese medicine. The understanding of PD in traditional Chinese medicine could be traced back to the "Huangdi Neijing Suwen Zhizhen yao dalun Essentials on disease and therapy": "All vertigo and shaking is ascribed to the liver," and "All sudden muscular spasm and rigidity is ascribed to vertigo and shaking." Sun Yikui in the Ming Dynasty first proposed the "Tremor Syndrome" to name such a disease as a manifestation of tremor in the "Pearl in Red Water." He expounded the pathogenesis of "Wood and fire impinging the upper, while the kidney Yin is deficiency, lower is deficiency while upper is excess, excess is the phlegm fire, deficiency is the kidney-Yin deficiency." Until the Qing Dynasty, "Shaking means whose limbs trembling," "the tendons and muscles could not been managed well due to wind," "It is rare in the young people, only a little in the middle aged people, and most in the elder people," and "It is difficult to treat elderly people with deficiency of both Yin and blood" were described in the "Standards of Diagnosis and Treatment." In November 1991, traditional Chinese medicine defined PD as an elderly tremor. PD lesions mainly occur in the brain. Asthenia in superficiality is the basic consensus of Chinese medicine scholars on the pathogenesis of PD in traditional Chinese medicine. Asthenia in superficiality is the key to the onset of

the disease, and deficiency in the liver and kidneys, as well as deficiency in Qi and blood, are the main factors. However, phlegm-heat obstructing the collaterals and Yang hyperactivity causing wind are the manifestations of asthenia in superficiality. If a patient develops PD for a long time, the patient has deficiency and excess at the same time, and the transformation between cold and heat becomes uncertain, leading to cold–heat complex. Therefore, PD is a disease of intermingled deficiency and excess (Gu et al. 2013). From the perspective of the theory of biological evolution "Theory of Use and Disuse," dopamine replacement therapy accelerates the degeneration of brain neurons, thereby accelerating the development of the disease (Su et al. 2013). Therefore, starting from the perspective of "Responsible for their own duties" to promote brain neurons, the neurons should be protected in the treatment of PD. That is, the balance of Yin and Yang in the brain should be regulated, thus promoting the recovery of its function.

Acupuncture treatment is one of the traditional Chinese medicine therapies, which emphasize on the treatment of syndrome differentiation and the whole concept. From the perspective of imbalance in Yin and Yang, Qi and blood disorder, and the balance of viscera function, acupuncture helps the body to achieve a new balance by combining regulation and tonification, thus improving tremor, muscle rigidity, and other motor symptoms of PD. Moreover, acupuncture delays the course of the disease, reducing the dosage of Western medicine and its side effects. Therefore, acupuncture has a unique advantage in treating PD. In recent years, the number of acupuncture studies published by many scholars in Western countries, including the United States, Britain, and Germany, is increasing (Lu et al. 2010; Huang et al. 2011; Pfab et al. 2011; Sung et al. 2004). Evidence-based medicine has provided numerous indications for the efficacy of acupuncture in the treatment of diseases. Acupuncture has been included in the "List of Intangible Cultural Heritage," which was also a recognition of the efficacy of acupuncture in treating diseases (Yu et al. 2011).

3 Meta-Analysis of the Clinical Efficacy of Acupuncture in Treating PD

Databases such as China National Knowledge Infrastructure (CNKI), Wanfang Data, Chinese Science and Technology Periodicals Database (VIP), Chinese Biomedical Literature Database (CBM), PubMed, Cochrane Library, and others were searched for randomized controlled trials (RCTs) related to acupuncture treatment for PD published by the end of May 2017. Quality evaluation and data extraction were conducted according to the risk-of-bias assessment tool provided by the Cochrane collaboration evaluation manual (version 5.1.0). The RevMan 5.3 software was used for the meta-analysis. The overall clinical efficacy rate, scores of each scale, and improvement in motor symptoms of experimental (acupuncture or combined acupuncture and drug therapy) and control groups (anti-PD drug therapy) were compared and analyzed to evaluate the clinical benefit of acupuncture in treating PD.

In all, 12 RCTs met our inclusion criterion, a total of 892 patients, including 468 cases in the experimental group and 424 cases in the control group. Meta-analysis showed favorable results for the experimental group compared with the control group in the overall clinical efficacy rate, the total scales of UPDRS and the modified Webster scale. The experimental group was effective in relieving partial symptoms of PD such as rigidity, postural, gait, bradykinesia compared with the control group, while there was no significant difference in rest tremor. Acupuncture had certain clinical effects on Parkinson disease, it can relieve the clinical symptoms of Parkinson disease to some extent, and postpone the progression of PD, thus improve the quality of life of PD patients. Acupuncture can be recommended as a combination treatment for Parkinson disease.

3.1 Retrieval Strategy and Selection Criteria

According to the international PICOS principle (Bento 2014), retrieval strategy as well as the inclusion and exclusion criteria of studies were formulated.

Retrieval strategy: Databases such as China National Knowledge Infrastructure (CNKI), Wanfang Data, Chinese Science and Technology Periodicals Database (VIP), Chinese Biomedical Literature Database (CBM), PubMed, Cochrane Library, and others were searched for randomized controlled trials (RCTs) related to acupuncture treatment for PD published by the end of May 2017. The retrieval strategy was designed as a combination of the following key words: “acupuncture” or “electroacupuncture”, ”parkinson disease” or “parkinson’s disease”. At the same time, the references cited in the studies were further screened to expand the scope of retrieval.

Inclusion criteria: (1) The subjects met the diagnostic criteria of clinically diagnosed primary Parkinson’s disease. (2) Only acupuncture or acupuncture combined with anti-Parkinson’s disease drugs as the main intervention measures. Acupuncture includes all kinds, such as electroacupuncture, scalp acupuncture, body acupuncture, abdominal acupuncture and acupuncture treatment with special names. (3) The experimental group was treated with acupuncture or acupuncture combined with anti-Parkinson disease drugs, while the control group was treated only with anti-Parkinson disease drugs. (4) Outcome measures included at least one internationally recognized scale for the evaluation of Parkinson’s disease, such as the Unified Parkinson’s Disease rating scale (UPDRS), the modified Webster scale and the Hoehn-Yahrs scale. (5) The study must be a randomized controlled trial.

Exclusion criteria: (1) Non-primary Parkinson’s disease. (2) Acupuncture with other traditional Chinese medicine were used in the experimental group of the study. (3) Non-randomized controlled trial and (4) Republished studies.

3.2 Study Screening, Quality Evaluation and Data Extraction

According to the inclusion and exclusion criteria, the retrieved studies were screened first by reading the title and abstract, and then by reading the full text. According to the evaluation standard of RCT study quality and the criteria for judging the risk bias in the risk-of-bias assessment tool provided by the Cochrane collaboration evaluation manual (Higgins and Green 2011), the methodological quality was evaluated from the following six aspects: random sequence generation, allocation concealment, blinding of participants and personel, incomplete outcome data, selective reporting, and other bias, et al. The results of quality evaluation are classified as low bias risk (A), unknown bias risk (B) and high bias risk (C). The contents of data extraction included: author's name, year of publication, sample size, grouping, intervention, observation or evaluation of clinical effect, results (including the overall clinical efficacy rate, scores of each scale, and improvement in motor symptoms of experimental and control groups). The difference of scores in each scale was represented by the mean (X) and the standard deviation (S). The formula is $X = X_1 - X_2$; $S = \sqrt{S_1^2 + S_2^2 - 2S_1S_2 \times 0.4}$ (X represents the mean of the difference of scores in each scale, X_1 represents the mean of the scores in each scale before treatment, X_2 represents the mean of the scores in each scale after treatment, S represents the standard deviation of the difference of scores in each scale, S_1 represents the standard deviation of the scores in each scale before treatment, S_2 represents the standard deviation of the scores in each scale after treatment). The screening of studies, quality evaluation, and data extraction were completed by two researchers independently. In case of any disagreement, a third researcher was consulted.

3.3 Methods of Data Analysis

The RevMan 5.3 software was used for analysis and quantitative synthesis of extracted data. Odds ratio (OR) and 95% confidence intervals (CI) were adopted in dichotomous data, while mean difference (MD) and 95% CI in continuous data. Statistical heterogeneity was measured by chi-square test and I^2 heterogeneity test. When $P > 0.1$ or $I^2 \leq 50\%$, there was no statistical heterogeneity among the studies, and a fixed effect model was applied. If there had heterogeneity ($P < 0.1$ or $I^2 \geq 50\%$), the fixed effect model was applied after the clinical heterogeneity was eliminated by subgroup analysis, otherwise the random effect model was applied.

3.4 Results of Meta Analysis

The current meta-analysis was to examine the associations between acupuncture and Parkinson's disease. Meta-analysis showed favorable results for the experimental

group compared with the control group in the overall clinical efficacy rate, the total scales of UPDRS and the modified Webster scale.

3.4.1 Results of Retrieval Studies

A total of 1515 related studies were retrieved, and 396 studies were selected by reading headlines and abstracts. After reading the full text, 384 studies that did not conform to the inclusion criteria were excluded. Finally, a total of 12 studies that conformed to the purpose of this study were included (Yuan 2013; Chen et al. 2007; Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016).

3.4.2 Description of Inclusion Studies

A total of 892 patients were enrolled in 12 randomized controlled trials, including 468 cases in the treatment group and 424 cases in the control group. Among them, four articles (Yuan 2013; Wu 2006; Chen et al. 2013; Yang 2009) were dissertation papers, eight articles (Chen et al. 2007; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2016) were periodical papers. All of the twelve articles were Chinese articles, no English articles were included according to the selection criteria. All the enrolled subjects were clinically diagnosed patients with primary PD, and all the studies reported their diagnostic criteria. Interventions included electroacupuncture, scalp acupuncture, body acupuncture, abdominal acupuncture and routine acupuncture therapy. The control methods included acupuncture comparing with anti-PD drug therapy (Yuan 2013; Wu 2006; Yang 2009), combined acupuncture and drug therapy comparing with anti-PD drug therapy (Chen et al. 2007; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2016). Evaluation standard of clinical effect: Five articles (Yuan 2013; Chen et al. 2007; Wang et al. 2003; Chen et al. 2013; Fu et al. 2004) adopted the modified Webster scale, five articles (Wu 2006; Liu and Jiang 2013; Chang et al. 2008; Zhang 2015; Yang 2009) UPDRS, two articles (Suo et al. 2015; Yang 2016) both. The adverse reactions of acupuncture treatment were described in two articles (Yuan 2013; Chen et al. 2013).

3.4.3 Results of Quality Evaluation

The source of subjects, method of random grouping, characteristics and baseline of subjects, interventions and control measures, and statistical methods were clearly described in these studies. Sample sizes ranged from 20 to 100 patients per group, Only one (Chen et al. 2013) articles mentioned the estimation of sample size. Ten articles (Yuan 2013; Chen et al. 2007; Suo et al. 2015; Wang et al. 2003; Chen et al.

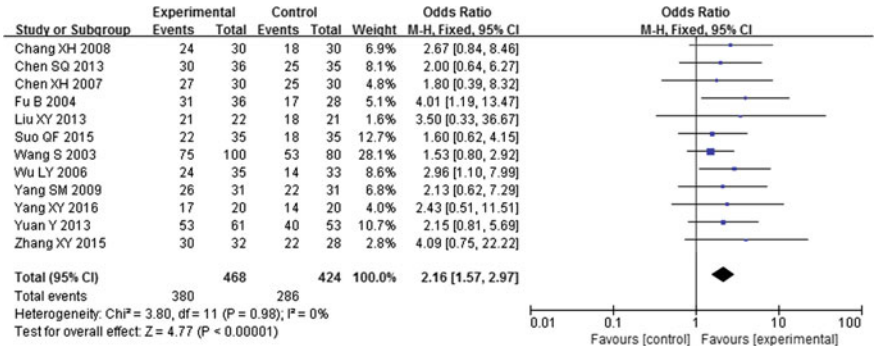

Fig. 1 Forest plot of comparison of overall clinical efficacy rate between the experimental and control groups

2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016) reported the generation of specific random allocation plan. Seven of them (Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Yang 2009, 2016) using random digital table method, two articles (Yuan 2013; Chen et al. 2007) using computer SAS software, one article (Fu et al. 2004) by drawing lots. Two articles (Wu 2006; Liu and Jiang 2013) were grouped according to stratified random method, but the random allocation plan were not specified. One article (Chen et al. 2007) used the closed envelope method to hide the allocation plan, while others didn't report. There was no article reported the use of blind methods. Two articles (Yuan 2013; Chen et al. 2013) mentioned the case of disengagement, but they did not use the intentionality analysis, and they also mentioned that the cases were followed up, and the long-term effect was evaluated. Only two articles (Wu 2006; Liu and Jiang 2013) made a reasonable assessment and analysis of possible confounding factors. Therefore, the quality evaluation of all the enrolled 12 studies (Yuan 2013; Chen et al. 2007; Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016) involved unknown risk bias (B). The authenticity of the results might be biased.

3.4.4 Analysis Results

The overall clinical efficacy rate of acupuncture on PD was reported in all 12 studies (Yuan 2013; Chen et al. 2007; Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016) included, and no statistical heterogeneity was found among the studies ($P = 0.98$, $I^2 = 0\%$). The results of the fixed-effects model showed that the efficacy of the experimental group was obviously superior to that of the control group, and the difference was statistically significant [OR = 2.16, 95% CI (1.57, 2.97), $P < 0.00001$] (Fig. 1).

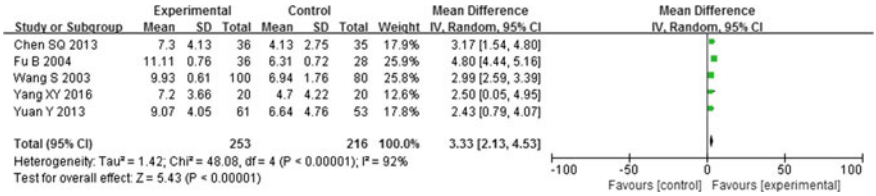

Fig. 2 Forest plot of the comparison of the difference in scores in the improved Webster scale between the experimental and control groups before and after treatment

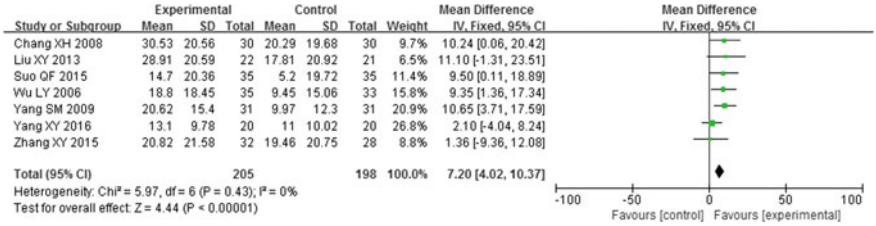

Fig. 3 Forest plot of the comparison of the difference in total scores in UPDRS between the experimental and control groups

The improved Webster scale was adopted in five studies (Yuan 2013; Wang et al. 2003; Chen et al. 2013; Fu et al. 2004; Yang 2016) for evaluation. A meta-analysis was also carried out in these studies for analyzing the difference in scores of the improved Webster scale in patients with PD before and after acupuncture treatment. Statistical heterogeneity was observed among the studies ($P < 0.00001$, $I^2 = 92\%$). The results of the random-effects model showed that the efficacy of the experimental group was superior to that of the control group, and the difference was statistically significant [OR = 3.33, 95% CI (2.13, 4.53), $P < 0.00001$] (Fig. 2).

The unified Parkinson disease rating scale (UPDRS) was adopted in seven studies (Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Chang et al. 2008; Zhang 2015; Yang 2009, 2016) for evaluating efficacy. A meta-analysis was carried out in these studies for the analysis of the difference in total scores of UPDRS in patients with PD before and after acupuncture treatment (Fig. 3). The results showed no statistical heterogeneity among the studies ($P = 0.43$, $I^2 = 0\%$). The results of the fixed-effects model showed that the efficacy of the experimental group was obviously superior to that of the control group, and the difference was statistically significant [OR = 7.20, 95% CI (4.02, 10.37), $P < 0.00001$].

The specific analysis of acupuncture improving the four major motor symptoms in patients with PD was as follows. The improvement in the reduction of bimanual movement was compared in three studies (Yuan 2013; Wang et al. 2003; Fu et al. 2004), and the results showed no statistical heterogeneity among the studies ($P = 0.52$, $I^2 = 0\%$). The fixed-effects model was adopted. The results of the meta-analysis showed that the efficacy of the experimental group was obviously superior to that of the control group, and the difference was statistically significant [OR = 1.80, 95%

CI (1.13, 2.86), $P = 0.01$]. Resting tremor was compared in four studies (Yuan 2013; Wu 2006; Wang et al. 2003; Fu et al. 2004), and the results of the heterogeneity test suggested statistical heterogeneity among the studies ($P = 0.005$, $I^2 = 76\%$). The random-effects model was adopted. The results of the meta-analysis showed no statistical difference in efficacy between the experimental and control groups ($P = 0.22$). The muscle rigidity in patients with PD was compared in four studies (Yuan 2013; Wu 2006; Wang et al. 2003; Fu et al. 2004), and the results showed no substantial statistical heterogeneity among the studies ($P = 0.15$, $I^2 = 44\%$). The fixed-effects model was adopted. The results of the meta-analysis showed that the efficacy of the experimental group was obviously superior to that of the control group, and the difference was statistically significant [OR = 2.32, 95% CI (1.55, 3.48), $P < 0.0001$]. The gait and postural instability in patients with PD were compared in four studies (Yuan 2013; Wu 2006; Wang et al. 2003; Fu et al. 2004), and the results of the heterogeneity test showed no statistical heterogeneity among the studies ($P = 0.94$, $I^2 = 0\%$). The fixed-effects model was adopted. The results of the meta-analysis showed that the efficacy of the experimental group was superior to that of the control group, and the difference was statistically significant [OR = 1.54, 95% CI (1.02, 2.33), $P = 0.04$].

3.4.5 Analysis of Publication Bias

A funnel plot of overall clinical efficacy rate of acupuncture in treating PD was drawn in all the included studies. The results showed that the scattered points in the funnel plot were mainly distributed on the right and central axis of invalid line, indicating a certain degree of publication bias in 12 studies (Yuan 2013; Chen et al. 2007; Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016).

3.4.6 Sensitivity Analysis

After the removal of two studies (Liu and Jiang 2013; Wang et al. 2003) with the maximum and minimum weight out of the twelve studies, sensitivity analysis was carried out in the remainder of the studies. The results showed no statistical heterogeneity among the studies. The fixed-effects model was adopted. The results showed that the odds ratio value fluctuated, but the 95% confidence interval was still in a fixed range. The results of the tests were basically the same, indicating the credibility of the meta-analysis results.

3.4.7 Safety Evaluation

The adverse reactions of acupuncture were described in only two studies (Yuan 2013; Chen et al. 2013), and the manifestations of the first acupuncture treatment included

dizziness, palpitation, sweating, and so on. Patients could continue to participate in the trial after relief from the symptoms without any special treatment. The symptoms were considered as a result of mental tension while receiving acupuncture treatment. No serious adverse reaction was reported.

3.5 Comments

The main pathological changes of PD are the degeneration of substantia nigra-striatum dopaminergic pathway. Significant degeneration of the dopaminergic neurons in substantia nigra (more than 50%) causes a notable reduction of dopamine levels and a hyperfunction of the acetylcholine system in the striatum. The imbalance between acetylcholine and dopamine leads to disturbances in the activity of cortico-basal ganglia-thalamic-cortical loop, resulting in the typical extra-vertebral dyskinesia. In addition, the dopamine levels in the midbrain-marginal system and the midbrain-cortical system are significantly reduced, which also constitutes to a biochemical basis for advanced neurological abnormalities such as cognitive impairment and affective disorders in patients with Parkinson's disease. Recently, many studies were conducted on the efficacy of acupuncture in treating PD, including clinical trials (Aroxa et al. 2017; Fukuda et al. 2016; Doo et al. 2015; Chen et al. 2012a, b, c) and animal experiments (Lu et al. 2017; Jia et al. 2017; Yu et al. 2016; Lu et al. 2012; Wang et al. 2014a, b), indicating that acupuncture could relieve some motor and nonmotor symptoms of PD. This meta-analysis included 12 RCT studies (Yuan 2013; Chen et al. 2007; Wu 2006; Liu and Jiang 2013; Suo et al. 2015; Wang et al. 2003; Chen et al. 2013; Chang et al. 2008; Zhang 2015; Fu et al. 2004; Yang 2009, 2016), which conformed to the purpose of the study, and the evaluation of methodological quality was found to be of grade B. The present study compared and analyzed the clinical efficacy of acupuncture or acupuncture combined with traditional anti-PD drugs in treating PD. After the overall clinical efficacy rate, the difference in the total score of UPDRS before and after acupuncture treatment, the difference in scores of the improved Webster scale, and the improvement in major motor symptoms of PD before and after treatment were analyzed. The results showed that the overall clinical efficacy rate, the improvement in the total score of UPDRS before and after treatment, and the score of the improved Webster scale in the experimental group were superior to those of the control group, indicating that acupuncture treatment could improve partial motor symptoms and nonmotor symptoms in patients with PD. After analyzing the improvement in specific symptoms of PD, the results showed that bradykinesia, muscle rigidity, gait, and posture instability improved significantly following acupuncture treatment. No significant difference was observed in the improvement of resting tremor between acupuncture treatment and Madopar treatment. This might be because acupuncture could only cause the body to produce corresponding pathophysiological changes by indirect acupoint stimulation and microregulate the internal environment of lesion region. However, it could not directly supplement the reduced dopamine to improve transmitter imbalance.

Some scholars also systematically evaluated the clinical efficacy of acupuncture in treating PD. The results of the present study were the same as those of the studies of Yi (Yin et al. 2016), Sook-Hyun Lee (Lee and Lim 2017), and other studies, indicating that acupuncture treatment was effective in improving partial clinical symptoms of PD, which could be used as a supplementary treatment for PD. Moreover, acupuncture treatment had less adverse reactions, was well tolerated, and had a higher safety. Therefore, it was recommended to use it widely in clinical practice. The improvement in motion symptoms of PD after acupuncture treatment was also analyzed in this meta-analysis. The results showed that acupuncture could significantly improve bradykinesia, muscle rigidity, as well as gait and postural instability. However, it caused no obvious improvement in resting tremor. The result guided the selective use of acupuncture as an assisted therapy according to different clinical manifestations.

4 Main Influence of Acupuncture on Parkinson's Disease

Acupuncture is used to treat many medical conditions for 1000 years in China and has gained wider and increasing acceptance within both public and medical profession because it has been a very safe and well-tolerated treatment. In this part, we reviewed main influence of acupuncture on Parkinson's disease.

4.1 Improvement of Life Quality of PD Patients

Although the drugs can improve the motor function of patients with PD, they often produce a series of side reactions, resulting in a large number of complications, affecting the patient's mental status and daily life. The efficacy of acupuncture on patients of PD with depression was assessed by using the Hamilton Depression Rating Scale (HAMD) score and UPDRS before and after treatment. The results showed that the scores of HAMD and UPDRS III decreased after acupuncturing Fengfu and Taichong points on the 14th day after treatment. The effective rate was 80.9% in the treatment group and 28.6% in the control group ($P < 0.05$), suggesting that acupuncture at Fengfuxue and Taichong had a significant effect on PD depression (Lei 2012). Forty-eight subjects who met the inclusion criteria were randomly divided into the acupuncture-drug combination treatment group and the conventional drug treatment group, and scored using the internationally accepted Unified PD Rating Scale (UPDRS). Before treatment, there was no significant difference in mental behavior, mood, daily life, motor function, complications and overall score of UPDRS between the two groups. After treatment, there was a statistically significant decrease in mental behavior, daily life, complications of treatment, and overall scores of UPDRS in the acupuncture treatment group compared with the conventional drug treatment group. They considered that in the treatment of PD patients with mental behavior and mood, daily life,

complications, etc., the combined effect of acupuncture and medicine was superior to ordinary drug therapy (Gu et al. 2013).

4.2 Relief of Movement Dysfunction

Recent report (Chen et al. 2013) used the "skull base seven points" acupuncture method to evaluate the efficacy of Parkinson's disease. The selected cases were randomly divided into acupuncture group and western medicine group. The acupuncture group was treated with acupuncture at the "Skull Base" point on alternate days, and the western medicine group was treated with 250 mg tid of Madopar. A modified Webster score was used to record the symptom changes and evaluate the efficacy. The overall efficacy rate of acupuncture treatment for mild-to-moderate PD patients was 86.89%, while the overall efficacy rate of western medicine group was 75.47%, the difference between the two groups was statistically significant. It is believed that the "Skull Base Seven Points" acupuncture method can improve PD patients' clinical symptoms and its clinical effect is better than that of conventional western medicine. It can improve the limb flexibility of patients with PD, and improve the patient's stiffness, flexion posture and facial appearance. Inflexibility and speech disorders are superior to those of conventional levodopa drugs, especially for face improvement and speech improvement, and their long-term curative effect is better. To observe the clinical efficacy and safety of acupuncture on Parkinson's disease combined with mild cognitive impairment (PD-MCI), Forty-eight patients with PD-MCI were randomly divided into drug group and acupuncture combined with drug group. Both groups were on basic treatment of medopa. By using the Montreal Cognitive Function Scale (MoCA) and the Unified Parkinson's Disease Rating Scale (UPDRS III) to evaluate the two groups before and after treatment, they found that the MoCA scores and the UPDRS III scores improved significantly after treatment in both groups, but there was a significant differences in the MoCA scores and the UPDRS III scores between the two groups. It suggests that the combination of acupuncture and medicine in the treatment of PD-MCI is more effective than simple drug therapy, which can significantly relieve movement disorders and delay the progression of Parkinson's disease (Zhang et al. 2013).

4.3 Effect of Acupuncture on Imaging of PD Patients

A large number of studies had confirmed that the width of the SNc in patients with PD was significantly narrower than that in the normal control group, and the width of SNc was significantly narrowed as PD patients progress. 48 patients with PD were divided into 3 groups according to the Hoehn-Yahr scores and adopted acupuncture treatments for 3 courses. The SNc width was measured before and after treatment in the 3.0T magnetic resonance susceptibility weighted imaging (SWI) axial images.

Results showed that the width of SNc in group III and IV was significantly wider than that before treatment, while the width of SNc before and after acupuncture did not change significantly in the I–II group (Wang et al. 2012). Subsequently, they observed the differences in cerebral activity local consistency (ReHo) before and after acupuncture treatment in PD patients by using resting-state functional magnetic resonance imaging (fMRI). After acupuncture treatment, they found that the ReHo increased in right dorsolateral prefrontal cortex, left posterior cerebellum, right inferior parietal lobe, left anterior wedge anterior, while the ReHo decreased in right inferior temporal gyrus, right auxiliary motor area, bilateral bean nucleus, bilateral thalamus, and left caudate nucleus (Wang et al. 2014a, b).

4.4 Effect of Acupuncture on Electroencephalogram in PD Patients

The frequency of brain electrical activity can reflect the functional status of a certain area of the brain and is an important parameter in brain development and aging. Reduced metabolism of brain cells, slower nerve fiber conduction velocity, and degeneration of neurons may increase the power of the θ and δ bands and reduce the power of α and β bands. Studies (Morita et al. 2009) showed that the power of brain electrical activity in PD patients had increased in the θ and δ bands and decreased in the α and β bands, and this change degree of brain power spectrum was positively correlated with the condition of PD. Quantitative EEG analyses were performed in 45 patients with PD (Chen et al. 2012a, b, c) before and after acupuncture treatment. They found that the relative power values of α and β waves were significantly increased after 30 days' acupuncture, and the relative power values at θ and δ bands were significantly decreased, which showed that acupuncture improved the brain function of patients with PD. The objective evidence for the efficacy of acupuncture on PD was also supported by the observation.

5 Possible Mechanism of Acupuncture in Treating PD

Acupuncture stimulation in Parkinson's disease had generated valuable mechanistic insight and showed that acupuncture treatment was in fact a neuroprotective therapy that increase the release of various neuroprotective agents such as brain-derived neurotrophic factor. In addition, acupuncture therapy slowed cell death process and attenuated oxidative stress to dopaminergic neurons in the substantia nigra. Further, acupuncture therapy modulated neuronal activity of the basal ganglia output structures and so on. In this part, we reviewed possible mechanism of acupuncture in treating PD.

5.1 *Promoting the Proliferation and Differentiation of Neural Stem Cells*

Neural stem cells (NSCs) have the characteristics of self-replicating and multidirectional differentiation, while the typical pathological changes of PD are massive degeneration and loss of dopaminergic neurons in substantia nigra. In the substantia nigra (SN) of a 6-OHDA induced rat model of Parkinson's disease were perfused transforming growth factor α into the forebrain. The results showed rapid proliferation of stem cells in the forebrain, and the rotational behavior of PD rats decreased, indicating the possibilities of proliferation and differentiation of endogenous NSCs in situ (Fallon et al. 2000). A study (Lie et al. 2002) showed that the regenerative potential of NSCs or neural precursor cells existed in the substantia nigra of midbrain, and the potential of differentiation to neurons was inhibited. Therefore, the neurons could not be regenerated during the degeneration of substantia nigra, and instead, glial cell proliferation occurred. Another study adopted the "Shuang Gu Yi Tong" acupuncture treatment and found that the NSCs in the substantia nigra and striatum of PD model rats transformed into neurons, and the number of NSCs on the damaged side of substantia nigra and striatum as well as transformed neurons increased significantly. The results suggested that the "Shuang Gu Yi Tong" acupuncture treatment inhibited the cell proliferation in substantia nigra toward glial scar, but some of the cells might have developed into complementary and alternative neurons with repair function (Wang et al. 2006).

5.2 *Promoting Synaptic Plasticity in Substantia Nigra Pars Compacta*

Some studies (Harris 1999; Ingham et al. 1997; Finkelstein et al. 2000; Calabresi et al. 2000; Berretta et al. 1997) showed that the loss of dopaminergic neurons of PD could not only cause morphological changes in dendrites and dendritic spines but also lead to biochemical changes in the striatum, leading to the inability of the cortical–striatal pathway to undergo two forms of remodeling, including long-term inhibition and long-term potentiation. Electron microscopic examination was adopted in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine dopamine (MPTP)-induced PD model after electroacupuncture at Hegu and Taichong. The results showed that the number density, surface density, and average area of synaptic connections of MPTP-induced PD rat model increased, which might reflect a synaptic compensatory response in the remaining neurons after they were denatured. After 21 times of electroacupuncture treatment, the morphological changes in synapses showed a trend of enhancement, indicating that electroacupuncture had a certain degree of promoting synaptic plasticity in dopamine neurons (Tang et al. 2005).

5.3 *Regulating the Neurotransmitter Level in Basal Ganglia*

Adopting electroacupuncture on head points (Baihui-Temple) in the striatum of 6-OHDA-treated rats, they found that electroacupuncture could increase the expression of tyrosine hydroxylase mRNA and dopamine transporter mRNA in substantia nigra of PD rats and promote the synthesis and reuptake of dopamine (Wang et al. 2009). The protection of electroacupuncture is mediated by excitatory amino acid transporters (EAATs) that have been shown to be neuroprotective. EAAT2 may mediate the electroacupuncture preconditioning-induced neuroprotection (Zhu et al. 2013). Preclinical studies found that acupuncture treatment at GB34 in the MPTP-induced PD model increased the release of dopamine, thereby enhancing the postsynaptic neurotransmission of dopamine and promoting the normalization of the function of basal ganglia (Kim et al. 2011). In MPTP-lesioned rats, which a combination of acupuncture and medicine (Baihui, Fengfu, and Yanglingquan acupoints were adopted), they found that the combination of acupuncture and medicine could increase the levels of decreased dopamine (DA), norepinephrine (NE), and 5-hydroxytryptamine (5-HT) as well as improve the symptoms of PD (Lu et al. 2011). The combination of acupuncture and medicine could reduce the concentration of abnormally increased γ-aminobutyric acid (GABA) and decrease the abnormal expression of FosB (Kim et al. 2014). High-frequency electroacupuncture could reduce GABA and glutamic acid decarboxylase (GAD67) in the substantia nigra of PD model, but it had no effect on the concentrations of GABA and GAD67 in globus pallidus. By regulating the level of neurotransmitters in basal ganglia, the unbalanced neurotransmitters could be restored to normal, thus reducing levodopa-related dyskinesia (Jia et al. 2010; Zhang et al. 2014).

5.4 *Regulating the Neurotrophic Factor in the Substantia Nigra*

The neurotrophic factor is a kind of protein necessary for the development, survival, and differentiation of nerve cells. The nervous system has a wide variety of neurotrophic factors that can promote the regeneration of axons and remyelination, and improve the viability of dopaminergic neurons. Electroacupuncture treatment could enhance the expression of brain-derived neurotrophic factor and its receptor tropomyosin receptor kinase B (TrkB), glial cell-derived neurotrophic factor, as well as its receptor Ret in the substantia nigra of 6-OHDA-induced PD rats, so as to improve the abnormal behavior of PD rats (Huang et al. 2010; Wang et al. 2010a, b, 2015).

5.5 *Activating δ-Opioid Receptor*

Exposure of neurons to opioid immediately before ischemia induces ischemia tolerance, and opioids induce delayed neuropreconditioning (Zhao et al. 2006). Some studies (Zhang et al. 2002, 2006; Ma et al. 2005) showed that a large number of δ-opioid receptors (DORs) were expressed in the striatum and cortex. They were actively involved in the regulation of neuronal survival and had a neuroprotective effect, especially on the cerebral cortex. To explore whether DOR activation could change the aggregation of α-synuclein caused by MPTP injury or hypoxia stress, an experiment was done in HEK 293 cells. It was observed that DOR activation enhanced cyclic AMP response element binding protein (CREB) phosphorylation, prevented mitochondrial membrane potential collapse, and reduced the abnormal aggregation of α-synuclein, thereby alleviating MPP+ damage or hypoxia/ischemia injury (Chen et al. 2014). DOR could reverse the downregulation of the expression of PINK1, weaken the activity of caspase 3, and reduce MPP+ damage or hypoxia/ischemic injury. Nrf2 is a powerful gene activator with antioxidant response element, which could be used to combat oxidative damage by upregulating antioxidant genes (Xu et al. 2016, 2018). The activation of DOR could increase the expression and translocation of Nrf2 protein through the protein kinase C (PKC)-dependent pathway, thus producing the neuroprotective effect (Cao et al. 2015). A study (Tian et al. 2008) discussed the role of DOR in anti-acute cerebral ischemia injury while conducting electroacupuncture treatment. It found that the volume of cerebral infarction decreased, the score of nerve function defect increased, the expression of DOR protein in 60 kD increased, and the expression of 36 kD DOR protein had an increasing trend in the electroacupuncture group, indicating that electroacupuncture might reduce ischemic cerebral infarction and nerve function defect by increasing the expression of DOR. Hypoxia/ischemia injury is a potential cause of PD, and DOR has a neuroprotective effect on hypoxia/ischemia injury. Recently, Delta opioid receptors have been revealed to pose an especially compelling biological function for new neuroprotective therapies (Crowley et al. 2017). The delta enkephalin analogue [D-Ala(2), D-Leu(5)]-enkephalin (DADLE) has been demonstrated to protect against, as well as to reverse methamphetamine-induced loss of dopamine transporters (Borlongan et al. 2000, 2001). Therefore, whether acupuncture activated DOR and thus exerted a neuroprotective effect needs more high-quality studies for further verification.

5.6 *Regulating Oxidative Stress*

Electroacupuncture could upregulate the activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in the substantia nigra of the PD model, increase GSH concentration, downregulate the expression level of malonyldialdehyde (MDA), and reduce the apoptosis of dopaminergic neuron in the substantia nigra (Li et al. 2014). Electroacupuncture (120 Hz, Baihui and Mingmen) com-

bined with a low dose of zinc to treat the PD rat model induced by 6-OHDA. The results showed that the combination of electroacupuncture and low-dose zinc had the synergistic effect of enhancing the activities of SOD, catalase, and GSH-Px in the substantia nigra of PD rat model, increasing GSH concentration, decreasing MDA concentration, and enhancing the expression of tyrosine hydroxylase (TH) in PD rats (Shi et al. 2012). By conducting acupuncture at the Jiaji acupoint in the MPTP-induced PD model, they found that the number of neuronal nitric oxide synthase (nNOS)-positive neurons in the brain of PD model decreased, thus improving the metabolism of free radicals (Wang et al. 2010a, b).

5.7 Improving Mitochondrial Dysfunction

There is accumulating evidence providing a proof of concept that enhancement of mitochondrial oxidative phosphorylation via alternative mitochondrial electron transfer may offer protective action against neurodegenerative diseases (Yang et al. 2017). After electroacupuncture treatment in the PD rat model induced by rotenone injection, they found that the activity of mitochondrial complex I in the electroacupuncture group significantly enhanced and the behavior of PD rat model in the electroacupuncture group significantly improved, indicating that enhancing the activity of mitochondrial complex I and improving the function of mitochondrial electron transfer chain might be one of the underlying mechanisms for acupuncture in treating PD (Wang et al. 2013a). Acupuncture at Baihui and Dazhui could reduce the mitochondrial ultrastructural damage of dopaminergic neurons. Further studies showed that acupuncture at an early stage (day 14) could improve the activity of cerebral mitochondrial complex II. Continuous acupuncture treatment 28 day could inhibit the decrease in the activity of complex IV, while conducting Madopar treatment alone did not significantly improve the activity of cerebral mitochondrial complex. This indicated that acupuncture treatment or acupuncture combined with Madopar could inhibit the activities of some enzyme complexes in the mitochondrial respiratory chain of PD model rats to a certain extent, thereby reducing the energy generation barrier of mitochondrial electron transport chain and improving the function of mitochondria. This might be one of the underlying mechanisms for acupuncture to treat PD and alleviate the side effects of Madopar (Sun et al. 2010, 2011).

5.8 Regulating Abnormal Calcium Homeostasis

Abnormal calcium homeostasis is one of the important factors in the apoptosis of dopaminergic neurons in the substantia nigra of patients with PD. Under normal conditions, intracellular calcium homeostasis is regulated by membrane calcium pump and intracellular calcium pool. If the cells are damaged, the permeability of cell membrane increases and a large number of extracellular calcium ions flow into the

cell. Because of the damage in sarcoplasmic reticulum caused by free radical and membrane phospholipid decomposition, calcium pump inhibition leads to a decrease in calcium intake of sarcoplasmic reticulum and an increase in calcium concentration in the cytoplasm, endangering mitochondrial function and cytoskeletal structure and eventually causing irreversible cell death. Different scalp acupuncture treatment in the rat 6-OHDA model of PD, could improve the activity of Ca^{2+}-ATPase in the substantia nigra of PD rats and intracellular calcium homeostasis. Simultaneously, it could also improve Na^{+}-K^{+}-ATP enzyme, Ca^{2+}-Mg^{2+}-ATP enzyme, and total antioxidant capacity, thereby improving brain energy metabolism, reducing brain injury by free radicals, and alleviating the apoptosis of nerve cells (Bai et al. 2016a). A study (Wang et al. 2001) found that the downregulation of calcium-binding protein D28K reduced the regulation of Ca^{2+} level in cells and the increase in intracellular Ca^{2+} concentration caused cytotoxic effect, resulting in a decrease in neuronal activity or even death. This was an important factor in the imbalance of calcium homeostasis in the dopaminergic neurons of the substantia nigra in patients with PD and PD animal model, and also in cell apoptosis. Further experiments (Bai et al. 2016b) found that acupuncture could increase the expression of calcium-binding protein D28k and exert a neuroprotective effect on dopamine neurons in the PD rat model.

5.9 Increasing the Activity of Ubiquitin–Proteasome

The ubiquitin–proteasome system is the main way of protein degradation in cells. It can maintain internal environment homeostasis by eliminating mutational, damaged, and abnormally folded proteins. A study found that the pathological phenomenon of the decrease in ubiquitin-proteasome activity existed in the substantia nigra of patients with PD. The ubiquitin–proteasome system might have some kind of defect, resulting in protein misfolding, which could not be degraded, as well as abnormal aggregation and deposition in vivo, leading to cytotoxicity. Electroacupuncture (Fengfu and Taichong acupoints) in the rat 6-OHDA model of PD had a protective effect on PD rats and enhanced the function of ubiquitin–proteasome system in substantia nigra, indicating that the mechanism of acupuncture for treating and preventing PD might be related to the ubiquitin–proteasome system. Electroacupuncture (Fengfu and Taichong acupoints) was adopted to treat rotenone-induced PD rats. It showed that the activities of 20s β1, β2, and β5 increased significantly, the number of TH-positive nerve cells increased, and the behavior score of PD rats decreased significantly in the electroacupuncture group compared with the control group. Electroacupuncture enhanced the expression of related molecules in the ubiquitin–proteasome system of the substantia nigra cells of model rats, reduced the abnormal aggregation of α-synuclein, and had a positive effect on the behavioral improvement of PD rats, indicating that improving the function of ubiquitin–proteasome system might be one of the internal mechanisms of acupuncture treatment for PD (Wang et al. 2013a, b, c, d).

5.10 Regulating the Immune System of the Body

Acupuncture (Yang Mausoleum, dance tremor control area) in the rat 6-OHDA model of PD could increased the levels of CD3, CD4, and CD8 in the blood of rats and decreased the concentration of tumor necrosis factor (TNF)-α. The study indicated that the efficacy of acupuncture in treating PD rats might be related to the regulation of the proportion of T-lymphocyte subsets and the improvement in its function. Reducing the concentration of TNF-α in serum might be one of the mechanisms of acupuncture in treating PD (Yao et al. 2009). Electroacupuncture in the rotenone-induced PD rats, could reduce the expression of COX-2 in the inflammatory mediators of PD rats, inhibit phosphorylated p38-MAPK, and reduce the damage to dopaminergic neurons, which might be related to p38-MAPK signaling pathway (Fengfu and Taichong acupoints). Further experiment showed that electroacupuncture could also downregulate the expression of phosphorylated extracellular signal–regulated kinase 1/2 (p-ERK 1/2), TNF-α, and interleukin-1β as well as upregulate the expression of tyrosine hydroxylase in substantia nigra, thereby improving the motor function of PD rats (Wang et al. 2013a, b, c, d, 2014a, b).

5.11 Regulating Brain Metabolism

As much detailed information as possible that is available on various neurodegenerative disorders and their connection with oxidative stress were presented (Chen et al. 2012a, b, c). Studies (Haacke et al. 2005; Zecca et al. 2004) found that the iron level in substantia nigra in patients with PD increased significantly, the ferritin level decreased generally, and Fe^{2+} could catalyze lipid peroxidation under the action of oxygen free radicals, resulting in an increase in the oxidative stress. This, in turn, promoted the degeneration of dopamine neurons, indicating that iron was involved in the pathological changes of PD. The finding suggested that iron metabolism in the central nervous system might be associated with the morbidity of PD. Electroacupuncture treatment could improve neurobehavioral function and brain injury, which were likely connected with regulation of apoptosis-related proteins (Zhu et al. 2017). Head and body acupuncture treatment (Baihui, Shenting, and dance tremor control area for head acupuncture; Fengchi, Hegu, Taichong, and Taixi acupoints for body acupuncture) significantly decreased the iron concentration in globus pallidus and substantia nigra, indicating that acupuncture treatment might promote the absorption of iron in basilar nuclei (Wang et al. 2013a, b, c, d). Electroacupuncture was conducted from the beginning of the day when the 6-OHDA-induced PD model were established (Yanglingquan, Taichong, Xuehai, and Zusanli acupoints were selected). Atomic absorption spectrophotometry was used to determine iron concentration. The results showed that the iron concentration in substantia nigra in the electroacupuncture group was significantly lower than those of the model and sham electroacupuncture groups, indicating that electroacupuncture at certain acu-

points could inhibit the increase in iron concentration in substantia nigra. These suggested that electroacupuncture at some acupoints might have a certain regulatory effect on the metabolism of iron in substantia nigra and an acupoint specificity existed. The rotational behavior of rats improved in this process, which further indicated that the regulatory effect of acupuncture on the iron level in substantia nigra in 6-OHDA-injured rats might be one of the mechanisms underlying its neuroprotective effect (Yu et al. 2011).

5.12 Activating Brain-Related Motor Areas

After acupuncture treatment in patients with PD, electroencephalograph (EEG) power spectrum such as the relative power value of α and β waves significantly increased, and while the relative power of θ and δ bands significantly decreased. This significantly improved the brain function of patients with PD, leading to improved blood circulation to the central nervous system and enhanced brain function (Chen et al. 2012a, b, c). Acupuncture at GB34 could activate the prefrontal cortex and ascending frontal convolution of the brain, thus improving the motor function of patients with PD (Yeo et al. 2014). The resting-state fMRI data of patients with PD before and after six courses of acupuncture treatment using ReHo (consistency of brain local activity) were analysed. A large number of dopaminergic neurons in the impact zone of substantia nigra of patients with PD died, leading to a decrease in dopaminergic afferents in striatal neurons and reduction in cortical-striatal loop function. This might cause an increased compensatory response in the brain activity of other nerve pathways in the extrapyramidal system, for example, substantia nigra–striatum loop and (or) cortex thalamus cerebellar loop. The decrease in ReHo in the local brain suggested a decrease in the consistency of neuronal activity, indicating functional abnormalities in this brain region. The interconnection between neurons was disorganized, and the increase in ReHo was an increased consistency of local neuronal activity, which might be a compensatory response to the occurrence of PD cortical damage. They found that after acupuncture treatment, ReHo increased in the brain region with a decrease in ReHo in the resting-state default network before treatment, while ReHo decreased in the brain region with a higher compensatory response in the resting-state default network before treatment. These different neuroactive regions of the brain might be associated with the improvement in symptoms in patients with PD after acupuncture treatment (Wang et al. 2014a, b).

6 Conclusions and Perspectives

In conclusion, PD is a common and refractory neurodegenerative disease in the middle-aged and elderly people. Drug therapy could only improve the symptoms. Adverse drug reactions related to motor symptoms appeared in long-term drug

therapy. Acupuncture or acupuncture combined with drug therapy could obviously improve the motor symptoms and nonmotor symptoms of patients with PD and delay the progression of the disease without any obvious adverse reactions, showing good prospects for clinical application. Moreover, many studies have provided the basis for the efficacy of acupuncture treatment of PD and its possible mechanism from different aspects. Acupuncture could promote the proliferation and differentiation of NSCs as well as the synaptic plasticity in the impact zone of substantia nigra, regulate the neurotransmitter level in basal ganglia and oxidative stress, improve mitochondrial dysfunction, regulate abnormal calcium homeostasis, increase the activity of ubiquitin–proteasome, regulate immune system and brain metabolism, activate possible mechanisms in brain-related motor area to improve the symptoms of PD, and reduce the side effects of drug therapy. These studies highlighted the internal mechanism of acupuncture for treating PD and provided strong evidence for the feasibility and efficacy of acupuncture for treating PD.

However, the present study had some limitations. The PD animal models and acupuncture methods used in many experiments were different, selected acupuncture points varied, and no unified standard was followed. The frequency and course of acupuncture, as well as the evaluation and indicator of efficacy, were not uniform. Hence, a scientific and rigorous experimental design was urgently needed. Although acupuncture could improve the partial symptoms of PD, further studies were needed to investigate whether it could maximize its efficacy by optimizing acupuncture point, frequency, and therapeutic regimen. Meticulous studies on the development of neurophysiology, pathology, and molecular biology technology, with a rigorous and scientific experimental design, should be conducted to reveal the therapeutic mechanism of acupuncture for PD. The advantages of acupuncture as a Chinese traditional therapy should also be brought into full use so that more patients with PD can benefit from it.

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Aung Vital Energetic Alignment: The Answer to Post-concussion Syndrome and Post-traumatic Stress Disorder

Steven K. H. Aung

Abstract This article will discuss the vital role of body, mind, and spirit in the context of Traditional Chinese Medicine and the treatment of Post-concussion Syndrome (PCS) and Post-traumatic Stress Disorder (PTSD), as proven by practical evidence as a result of Aung Vital Energetic Alignment therapies. It will also discuss the role of the meridian and chakra systems, as well as means for utilizing these systems to improve patients' quality of life in such contexts. In certain difficult cases, when acupuncture is not invoking a response in patients, other treatment modalities should be considered; namely, the treatment modality of Aung Vital Energetic Alignment. In this article, Dr. Aung describes how he discovered the role of treating the body, mind, and spirit as a practitioner and how firsthand experience in treating all aspects of personhood has resulted in his self-discovery of realignment therapies. This chapter discusses alternative treatment modalities for PCS and PTSD using Aung Vital Energetic Alignment acupuncture (i.e. AVEA protocol). It will also discuss natural forms of therapy, such as tree-hugging, which provides natural realignment, as well as the utilization of seven chakra phonation, concentration, meditation and Qi Gong exercises as a means for addressing PCS and PTSD. This chapter will also describe treatment modalities for addressing pediatric and neonatal malalignments via acutouch treatments to ensure the well-being, intelligence and intuitional progression in infants for preventative purposes. Starting from infancy, correctly-aligned pediatric patients will mature influence society as individuals who display optimal intellectual and intuitive health, so as to be a positive and productive force in the universe.

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1 Introduction

In Traditional Chinese Medicine (TCM), human beings are considered tri-part beings, consisting of body, mind, and spirit. Physical aspects of personhood (e.g. organ systems) are intrinsically connected to mental aspects of personhood (e.g. emotional states), which in turn are inseparable from spiritual-energetic aspects. Similar to light bulbs that require unobserved electrical flow for functionality, the circulation of spiritual energy throughout the physical and mental aspects of human beings is an innate, natural phenomenon, though it is often disregarded in western biomedical philosophy.

In a spiritual and energetic sense, health is the alignment of the physical, mental and spiritual bodily components. One can visualize this alignment as the alignment of three parallel lines into a single central axis. When an injury occurs—whether via nature, accident, violence, etc., vital energy alignments are disrupted, along with the physical and mental aspects of an individual's personhood. Though acute conditions are often addressed using Western biomedical modalities, philosophical rejection of the spiritual and energetic aspects of medicine has resulted in the perpetuation of Post-concussion Syndrome (PCS) and Post-traumatic Stress Disorder (PTSD) symptoms of injury that can exist for years on end without resolution. Such perpetuation of vital energy malalignments by the use of incorrect treatment methods is all too commonplace.

Alignment may be metaphorically understood using the illustration of a camera. A camera in focus is optimally functional and able to serve its purpose, much like an individual who is energetically aligned. A loss of focus in a camera, however, is equivalent to the loss of internal balance in human energy and more generally, a loss of health. The body, mind, and spirit are the 'settings' required to keep the human body 'in focus', though the 'settings' may need to be adjusted due to having been disrupted by a variety of causative forces. The adjustment of these 'settings' is the focal point of this chapter, which seeks provide awareness in regards to the unique needs of patients who are non-responsive to Western biomedical, natural and complementary approaches as a result of PCS and PTSD. It is only by gaining an understanding of the nature of vital energetic alignments and the spiritual activities of the body, as seen in TCM philosophy, that an individual can come to terms with effective treatment modalities for such difficult and non-responsive cases. It is my hope that the following recognition of malalignments and treatment protocols for addressing such cases will serve as a foundation for the constant evolution of medical philosophy and the resolution of PCS and PTSD in patients who may consider their situation hopeless.

2 Human Energetic Components in TCM

2.1 Qi, Fluids, and Meridians

In Traditional Chinese Medicine, the human body is a self-regulating energetic system, complete with 6 Zang ('solid') and 6 Fu ('hollow') organs. The Zang organs perform the bulk of bodily functions while the Fu organs are primarily used for storage, excretion, and exchange of energy. The role of vital energy (Qi) flow in the maintenance of health within the human body is mostly ignored in Western biomedical modalities, where all organs are described only by physiological functions. The flow of Qi refers to the circulation of vital energy throughout the *whole* human being—body, mind and spirit.

Each Zang organ is paired with a Fu organ and they function separately in pursuit of a shared objective. As there are 12 organ systems, there are also 12 energy channels known as meridians. The individual meridians are de facto a continuous line of traffic, with Qi circulating cyclically throughout the body without breaks in movement; each organ is designated its own segment of the continuous body meridian (Fig. 1). Meridians are mapped on the skin surface; the meridian specific to an internal organ system may be distant from the organ, which allows for exchange and regulation of energy via the external environment. The Qi moves through the meridians and organs sequentially over the course of a day, much like a train routinely visiting particular landmarks on a predetermined schedule. Each organ is designated an average of 2 h of energy circulation time. Energy peaks at the 1 h mark in each given organ and this sinuosity of energy circulation throughout our daily routine can explain phenomena such as jet lag, as time zone inconsistencies interfere with the diurnal schedule established in our meridians, causing energy imbalances that lead to unease, headaches, nausea, and other related symptoms. Similarly, geographic relocation, as well as the occurrence of events leading to traumatic injury (e.g. accidents, surgeries, etc.), may disrupt Qi circulation in the meridian of an organ system, causing Qi stagnation. The resulting Qi stasis will invoke symptoms of pain, either in the region of the meridian or the region of the organ.

In Traditional Chinese Medicine, pain is perceived as a reliable indicator of blockage or obstruction in the circulation of Qi, blood, or other body fluids. Pain is 'a good sign' that makes us aware of a problem and directs us to its source. This is generally in contrast to Western biomedical philosophies, where the pain is normalized due to invasive, urbanized conditions and often dismissed by the administration of quick-fix drugs, such as painkillers. The main purpose of pain in TCM is to call attention to the site of the blockage and to facilitate its removal from both the meridian and the corresponding organs. The stagnation of Qi in one meridian will affect subsequent meridians and organs and throw the entire meridian system into imbalance. The key to wellness is the maintenance of energy flow at the level of the meridians and organ systems, as it is only through health circulation of Qi that organs can be kept functioning optimally and in tandem. Acupuncture is one viable method for keeping the

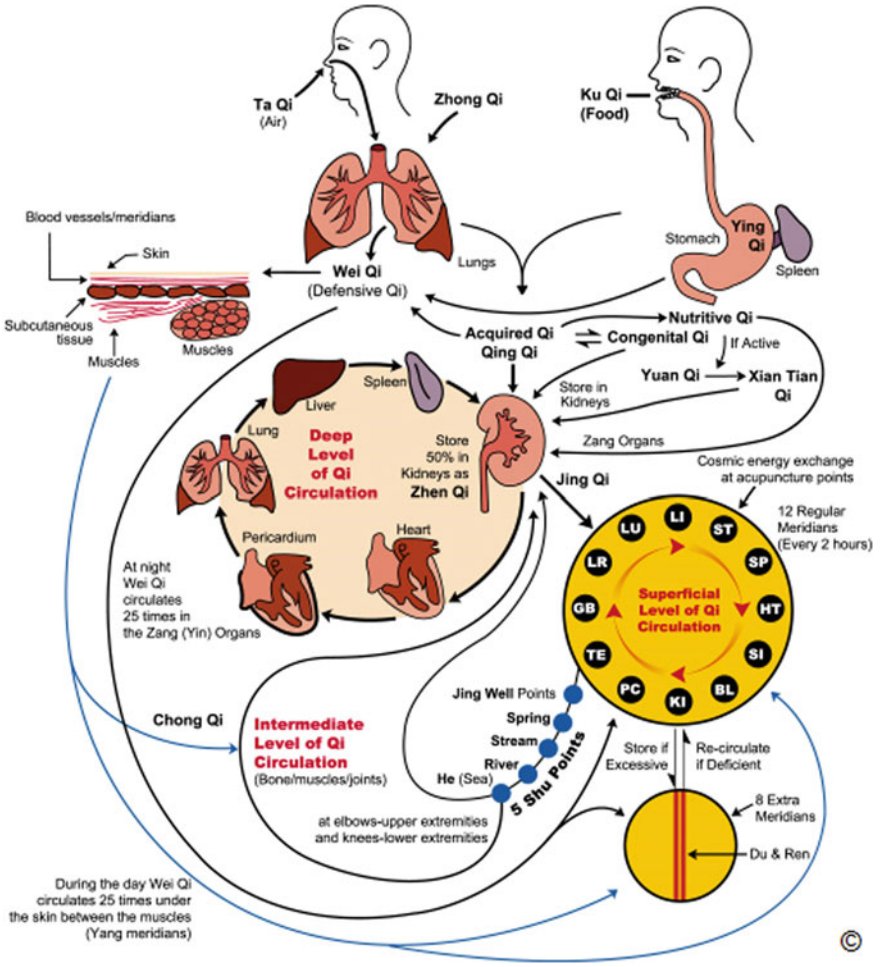


Fig. 1 The circulation of Qi in the meridian system

human body in constant balance, which is accomplished via the manipulation of the flow of energy throughout the meridian system.

Each meridian contains acupuncture points. Some of these points treat acute disorders; others chronic disorders; others are used for tonification (i.e. energy generation) or sedation (i.e. energy reduction), while others still are used for the treatment of specific tissues, the immune system, and exchange and flow of energy, blood, etc. In general, all of these points function to maintain a state of homeostasis. Expectedly, the effects of acupuncture on meridians will also reach the corresponding organ system. Meridians are not only connected to the internal organs; they extend to sensory organs and other bodily tissues, while also wielding influence over mental states.

Table 1 List of organs, meridians, and their connections to the body

Organ	Meridian	Specific tissue	Sensory organ	Mental implications	Spiritual association	Colour
Liver	Liver	Tendon	Eye	Generosity, anger	Inner spirit	Green
Gallbladder	Gallbladder	Tendon	Eye	Courage, indecision	Outer and inner spirit	Dark green
Lung	Lung	Skin	Nose	Decisiveness, sadness	Outer spirit	White
Large intestine	Large intestine	Skin	Nose, sinus	Decisiveness, sadness	Outer spirit	White
Spleen	Spleen	Bulk muscle	Lips	Consideration, worry	Inner spirit	Yellow
Stomach	Stomach	Bulk muscle	Lips, mucosa	Consideration, worry	Inner spirit	Bright yellow
Heart	Heart	Blood	Tongue	Happiness, anxiety	Whole spirit	Pink
Small intestine	Small intestine	Blood, damaged tissue	Tongue	Happiness, anxiety	Outer spirit	Bright red
Pericardium	Pericardium	Blood	Tongue	Happiness, depression	Whole spirit	Purple
Triple energizer	Triple energizer	Blood	Tongue	Generosity, depression	Outer spirit	Purple
Kidney	Kidney	Bone	Ear	Willpower, fear	Inner spirit	Blue
Bladder	Bladder	Bone, teeth	Ear	Willpower, fear	Inner spirit	Navy blue

For example, the Liver meridian is associated with the liver organ, though it opens in the eye (sensory organ) and is connected to tendon tissues throughout the body. The Liver meridian is associated with positive character trait of generosity and the negative emotion of anger, so sedation of the liver via acupuncture can manage anger and secure the inner spirit. Another method for anger management through the utilization of the liver is colour visualization to the acupuncture point using the associated colour, which in this case, is green. Associations between other organs systems and meridians continue in this regard. In the table below, the pairing of individual organs is evident in the similarities between their associated colours, as well as tissues, organs, and mental characteristics (Table 1).

In addition to the 12 regular meridians, a separate subset of meridians known as the 8 Extraordinary Meridians maintains a particularly prominent role in the sustenance of energy balance. Among these, two principal paths travel down the center of the body and act as ‘information super highways’ for the convergence and regulation of Qi with respect to the 12 regular meridians (Bingshan et al. 1993; Khoe 1978).

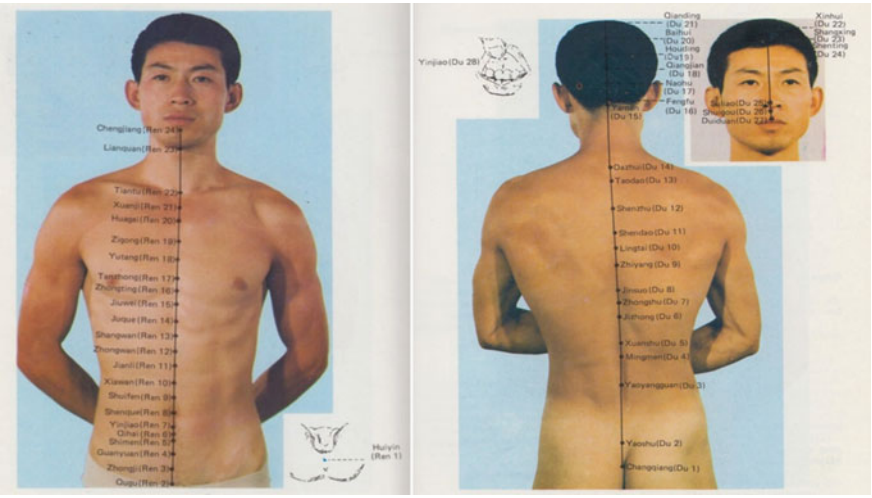


Fig. 2 The conception vessel (anterior) and the governor vessel (posterior)

These paths, designated the CV (Conception Vessel; anterior) and the GV (Governor Vessel; posterior) extra meridians, maintain principal functions in the overall control of the body, mind, and spirit, acting analogously to highways for the distribution of energy throughout the body (Fig. 2). These meridians are superimposed on and inseparable from the chakra system, which reveals their role as highly-relevant to the successful implication of vital energetic alignment procedures. The other 6 Extraordinary Meridians are channels branching off of the central pair in a manner similar to bodily extremities, which serve to store Qi and, when necessary, supplying it to the two main Vessels. The overarching purpose of this subset of meridians is to tonify the meridians and bodily energetic system, concentrating energy at the acupuncture points. There are also meridians specific to certain tissues that are distributed throughout the body, parallel to the 12 regular meridians. All in all, there are 12 musculoskeletal meridians specialized to treat the muscles and 12 cutaneous meridians treat the skin, subcutaneous tissue, and bones and joints.

These four groups of meridians work in conjunction with one another to maintain homeostasis and balance in the body. When a meridian is blocked, the local region is subject to physiological changes such as heat, redness, welts and skin eruptions that reveal the imbalance. If the problem persists to the level of the organs, the symptoms may become systemic. Since unaddressed obstruction in one meridian will prevent Qi from reaching subsequent meridians, organ systems are ultimately affected and latent propagation of rashes and related symptoms will be observed.

In Traditional Chinese Medicine, pathophysiological changes originate in the meridians and reflect the balance of Qi levels (Rasera Zotelli et al. 2017). If not restored, the balance can eventually enter the blood circulation. This transition from Qi to blood circulations, the blood stagnation stage, will incite changes in normal

physiological characteristics such as heart rate, blood pressure, and blood composition, marking the advancement of diseases that can be detected by Western biomedical tests. In this stage, deep vein thrombosis (DVT) may develop and the organs may suffer structural damage. The imbalance may extend to the organs, causing disharmony between the organ systems. Anatomical changes, including tissue damage, will occur, marking the irreversible stage of disease, also considered the pre-cancerous stage. When tissue damage leads to necrosis, the damage incurred by vital organs will become unmanageable and the individual will ultimately die. Therefore, Traditional Chinese Medicine aims to prevent the movement of disease to the blood stagnation stage whenever possible, by meticulously detecting imbalances in Qi and blood. The TCM approach emphasizes routine prevention, balance, and maintenance.

The composition of the human energetic system not only includes Qi and blood, but also bodily fluids, essence, and spirit; all of which contributes to the daily functionality of the body. Bodily fluids serve to rehydrate the subcutaneous spaces, as optimal fluid levels are essential in keeping the body in a balanced osmotic state. Excess fluid can cause phlegm, which can retard body circulation and cause fluid retention. When fluids accumulate in the organ systems and meridians, they can cause swelling and lesions of the organs or the formation of fat deposits and masses along the meridian. Such masses, composed of phlegm, can only be removed by treatment of the stomach meridian, specifically via the acupoints ST 40 and ST 8. Fluid regulation depends on three organ systems: the spleen-stomach system, the lung-large intestine system, and the kidney-bladder system. The spleen and stomach remove water from the subcutaneous tissue, the lungs and large intestine remove water from the Zang and Fu organ systems and the kidney and bladder remove water from their own individual system. When combined, these three systems will contribute to a high success rate in treating fluid retention. It is important to ensure that fluid does not exceed an optimal level in the body.

The fundamental principle of the Traditional Chinese Medicine approach is to balance and harmonize all components of the body. TCM treatment is generally more holistic than modern biomedicine and is a natural request to the body to return to its normal state before progressing into a pathological condition. It is very important to keep an individual's internal state under constant scrutiny, even when he or she appears healthy. Taking care of one's body and remaining vigilant about its internal balance is the key to achieving lasting wellness.

2.2 The Chakra System

An equally important energy system within the human body is the chakra system. Chakras may be best described as 'energy centers' where physical, mental and spiritual energies are synthesized. Also known as the 'human nails' of the body, chakras perform a vital role in perpetuating the maintenance of good health by ensuring that human energy is grounded and harmonized. Comparable to meridians, chakras regulate and maintain the continuous flow of Qi throughout the human body, though

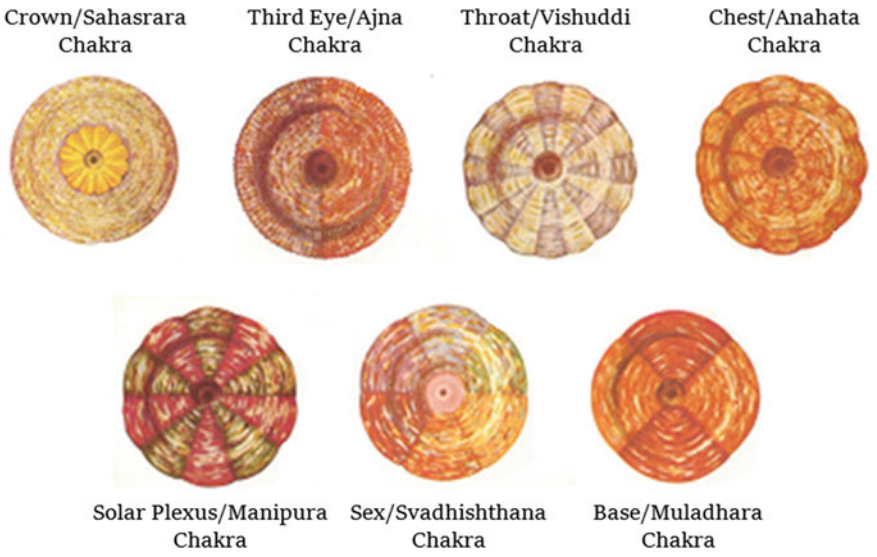


Fig. 3 The seven chakras of traditional ayurvedic and chinese medicine (Leadbeater 1972)

with two additional functions: (a) excess Qi that cannot be retained in the meridian system will naturally accumulate in the chakra system, while (b) the chakra system will also function as a reservoir and energy distribution point whenever the 12 regular meridians are deficient. Analogous to pools of water connected to smaller streams, chakras are superior energy exchange, empowerment, and enrichment centers for vital energy, automatically distributing Qi to meridians from confluent points on chakra bodies. Thus, chakras play a vital role in the maintenance of vital energetic alignment as well as in the enrichment, balancing, and harmonization of the energy system.

Chakras are located along the Conception Vessel (CV) and Governor Vessel (GV) pathways and are inseparable from meridians. Traditional Ayurvedic and Chinese medicine models recognize seven chakras; the Crown/Sahasrara chakra (top of the head; EX HN 1x4; GV 20) and the Base/Muladhara chakra (anus; CV 1; GV 1) constituting the final chakra points along the principal meridian paths with the remaining anterior and posterior chakras located at interior intervals (Fig. 3). In this sense, all chakras are interconnected front to back; top to bottom within the human body.

Chakras exist in perpetual rotary motion, spinning in both clockwise and counterclockwise directions in self-regulation for either tonifying (i.e. energizing) or sedating (i.e. de-energizing) purposes, depending on the physiological requirements of the energy system. The rotation of the chakras is essential for maintaining Qi balance both anteriorly and posteriorly, as well as for enhancing specific bodily functions where it is required. For example, Crown/Sahasrara chakras (EX HN 1x4; GV 20) rotate at 196 rotations per second and primarily operate in the harmonization of the entire human energetic system (Fig. 4). In contrast, Base/Muladhara chakras (CV 1)

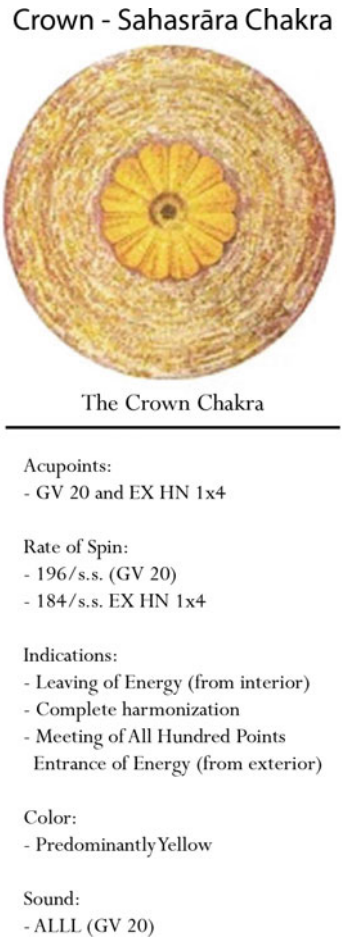


Fig. 4 The crown/sahasrara chakra (EXHN.1x4; GV.20)

rotate 2–4 full cycles per second and operate to produce a grounding effect and the clarification of neural functions.

Chakras are also sensitive to sound waves in a therapeutic sense, as concentrated phonations can inherently act as stimulants to corresponding chakras for self-reparative functions. Each chakra is associated with a specific phonation that can result in self-reparative reactions. Simply by phonating an appropriate sound that corresponds to a particular chakra, whether as self-exercise or via clinical support (Hanser 2016), patients are able to stimulate the realignment of the body (Table 2). Such specific phonations with therapeutic intent will enliven chakras, enabling them to become optimally functional and active when implemented successfully. Therapeutic use of phonation can be accomplished sequentially, moving from the Crown/Sahasrara chakra (EX HN 1x4; GV 20) to the Base/Muladhara chakra (CV 1; GV 1) in subsequent order while employing corresponding sounds,

Table 2 List of acupuncture points, chakras, and responsive sounds

Acupuncture points	Chakra title	Phonation
GV 20/EX HN 1x4	Crown/Sahasrara chakra	Alll…
GV 16/EX HN 3	Third eye/Ajna chakra	Ommm…
CV 22/GV 14	Throat/Vishuddi chakra	Hammm…
CV 17/GV 9	Chest/Anahata chakra	Yammm…
CV 6/GV 4	Solar Plexus/Manipura chakra	Rammm…
CV 4/GV 2	Sex/Svadhishthana chakra	Vammm…
CV 1/GV 1	Base/Muladhara chakra	Lammm…

as well as in reverse order. Regarding the treatment of PCS and PTSD, phonation therapy with chakras can play an important role in the maintenance of vital energetic alignment, as the optimization of the chakra system through regular phonation helps the stabilization process of alignment.

Visualization as a therapeutic modality can also be employed with the chakra system for self-reparation and realignment. Simply visualizing a clockwise-spinning chakra (i.e. tonifying motion) or a counter-clockwise spinning chakra (i.e. sedating) will mentally inform the chakras to produce physiological effects. This self-manipulation of the chakra system through mental activities stimulates energetic responses by the chakras that can aid patients in the process of realignment. Thus, the chakra system maintains a vital role in achieving energetic wellness if properly manipulated through sound and visualization; all of which encourages the stabilization of energetic alignment. In totality, the meridian and chakra systems function to keep the tri-part personhood (i.e. spirit, mind, body) aligned and energetically healthy. In TCM, this alignment is the very definition of health; malalignment, however, due to external, internal and spiritual factors, results in disorder and disease.

3 Etiology and Pathogenesis

Disease and trauma can arise from a variety of causes, which can be classified into four pathogenic groups: external causes, internal causes, subconscious causes, and spiritual causes.

3.1 Externals: Environmental and Traumatic

Pathogenic external forces from the environment include the wind, cold, heat, fire, and accidents, which can push the internal organs into disharmony and imbalance. Wind is typically associated with the liver, though the generation of internal winds can produce tremors, migratory joint pain, and shifting pain between various body areas. Cupping, a sedation technique where cups are applied to the acupuncture points to remove internal wind, is a particularly useful treatment, as is acupuncture for pain management. Acupoints used for the treatment of internal winds are classified as "wind points", which consist of GB 20 (neck wind), GV 20 (crown wind), BL 12 (chest wind), and GB 31 (abdominal wind). There are also peripheral points on the lower and upper extremities, EX LE 36 (x4) and EX UE 28 (x4), respectively.

Cold is associated with the kidney, stagnating the local Qi and introducing blockage. Treatment involves moxibustion, in which heat from burning moxa herbs (harvested from mugwort) can be used to force the cold from the area. The moxibustion is administered to points LU 9, LU 7, LR 3 (x2), and SP 10 (x2). Heat is associated with the heart and the liver and can result in damaged joints and tissues. In Western medicine, it is associated with inflammation. Cupping is once again used as a treatment to extract the heat from the body. For generalized heat, acupoint GV 4 should be cupped. For treating localized heat, LI 11 (x2) is cupped. Cupping of the localized joints will treat the structural damage. Fire is heat in excess, which can cause bleeding and epistasis. Typically, fire originates in the heart and the liver *yang*. Treatment involves bloodletting—a process in which a triangular needle will prick the skin and cause controlled bleeding from the twenty Jing Well points. A single Jing Well point is found on each finger and toe and each point must be pricked for complete treatment; not only for fire but for high heat (i.e., hyperactivity). In the latter case, bloodletting is often coupled with cupping for increased effectiveness. Blood released may appear darker than usual, indicating that heat is rapidly escaping. These pathogenic environmental factors can disrupt vital energetic alignment and perpetuate PCS and PTSD symptoms.

External forces from trauma, such as physical force incurred from a variety of causative factors (e.g., industrial, athletic, or motor vehicle accidents) can also disrupt vital energetic alignment. Industrial and motor vehicle accidents are often compressional in nature, involving the patient being hit by a hard object. Industrial accidents may result in cuts, trauma, lacerations, and compression due to machinery, which typically requires surgical correction. To return to the camera analogy, such traumatic events can cause an energetic shift comparable to the loss of focus in a camera, as an inappropriate increase or decrease in focus will result in blurriness or distortion of the image. The camera can be returned to focus, but only with the proper knowledge. Realignment as a treatment for such traumatic injuries will be discussed in detail later.

3.2 Internal Trauma

Internal forces that can lead to the development of pathological PCS and PTSD states can include phlegm and emotions. Phlegm is associated with Qi stagnation, as previously discussed; the stagnation causes water retention, which accumulates into phlegm when water fails to flow. Phlegm can remain within its local organ/meridian system, but may also extend to other parts of the body. If uncontrolled, structural damage and deformities can occur as a result of excess phlegm. For example, breast cancer is associated with phlegm accumulation in the stomach meridian and stomach cancer is associated with phlegm accumulation and blood stasis in the stomach. Removal of phlegm and redistribution of fluid is the only guaranteed means of early treatment, which can be accomplished via acupuncture at points ST 40, ST 8, SP 9 (x2), LU 9 (x2), and KI 10 (x2).

Emotional pollution can also disrupt vital energetic alignment. As previously discussed, each organ system is affiliated with specific positive and negative emotions (see Table 1). Negative emotions can act as pollutants, which may be minor, but persistent and gradual in their manifestation. For example, unresolved sadness can lead to lung disease and colitis. The slow, continuous onset of negativity can have as much impact as a single, intense outburst of emotion. Excess emotional negativity can strike imbalance in the affiliated organ, which has the potential to permeate other organ systems via the Qi circulation.

3.3 Subconscious Trauma

Related to internal emotions are subconscious thoughts and memories. Memories and facets of knowledge acquired prior to the age of four that are not continually developed are sequestered in an acupuncture "center" at acupoint CV 5; the Subconscious Gate (i.e. Stone Gate). In order to open the Subconscious Gate at this point, acupoint TE 5 must be opened bilaterally (x2), and, if the patient has experienced states of unconsciousness prior to acupuncture (e.g., anesthesia, concussion, fainting, etc.), the opening of PC 6 will also be necessary. These steps will unravel memories stored away, which is critical for uncovering any childhood trauma that may be affecting the subconscious and inadvertently affecting one's vital energetic stability. Once these memories are drawn into consciousness, they are available for permanent deletion from the patient's mind. The removal of subconscious negativity or persistent, repressed trauma will allow for realignment. It is extremely important to respect the patient's privacy; permission to access past memories, despite the patient's own unawareness of these memories, must be obtained. Practitioners should confirm any history of unconsciousness prior to treatment; if PC 6 is ignored under the belief that the patient has no history of unconsciousness, the subconscious will be completely inaccessible and the patient will not respond to treatment.

3.4 Spiritual Trauma

Finally, spiritual trauma can act as a disruptive energetic force in perpetuating malalignment. Spiritual trauma is significantly more serious than physical and mental trauma due to its direct effects on the vital energetic system of the body and responses are more difficult to elicit when spiritual trauma afflicts the vital energetic alignment so closely. Spiritual attachment, contamination, and invasion are all associated with a history of unconsciousness, which is the removal of self-control over an individual's tri-part personhood. Spiritual trauma can be understood through the metaphor of a light bulb. A light bulb (i.e. a human being) is sustained by the constant flow of energy through circuits (i.e. spiritual energy through meridian and chakra systems). The continuous luminosity of a light bulb is analogous to the self-controlled spiritual life of the human being. When trauma events resulting in unconsciousness occurs, it is as if the light bulb is suddenly turned off and on intermittently, resulting in periods of temporary darkness. Similarly, time that an individual spends unconscious or in an altered state is the period most vulnerable to spiritual invasion. Similarly, childbirth is also a period of time where an individual is susceptible to spiritual invasion, as a spiritual entity may gain access to the mother's body via the birthing canal when a physical entity leaves her body (i.e. the baby) in a traumatic event. Spiritual ancestor attachment can also lead to spiritual contamination. Attachments must be severed using acupoints SI 9 (i.e. immediate ancestors) and SI 11 (i.e. distant ancestors) to remove influences that may contaminate. Treatment involves opening the various spiritual gates to release foreign spiritual entities (which will be discussed in greater detail later):

- Inner Gate: PC 6
- Outer Gate: TE 5
- Life Gate: GV 4
- Subconscious Gate: CV 5

The opening of the gates should be followed by the recital of the mantra, *sa-da-ba-wa,* 108 times daily to send the entity from the body with good intentions. After the entity is removed, the acupuncture points GV 9, BL 17, BL 46, and GB 41 should be needled to close the gates once more. The removal, cleansing, and closing of spiritual gates to repair the damage done by spiritual trauma constitute one of the most important, albeit rare means of treatment within TCM.

4 Aung PCS and PTSD Alignment Therapy: A Brief History

In addressing vital energy disruptions and malalignments as a result of PCS and PTSD syndromes, realignment therapies as therapeutic modalities have proven to be clinically effective in aforementioned cases where the flow of Qi remains blocked or stag-

nant for a considerable period of time following a traumatic injury or major surgery. Aung Post-traumatic Stress Disorder and Post-concussion Syndrome Vital Alignment therapy (APVA) represents an application of Qi Gong methods to acupuncture for dealing with malalignment. Qi Gong is often referred to as "acupuncture without needles," and in the case of APVA it is appropriate to view acupuncture in terms of "Qi Gong with needles." This serves to highlight the essential holistic, energetic nature of Traditional Chinese Medicine (TCM). Vital energetic alignment procedures deserve to be better known in Traditional Chinese Medicine and in the discipline of medical acupuncture. I would like to highlight my own discoveries in the formation of these techniques in order to aptly describe the effectiveness of this often-neglected treatment method, before surveying the protocols for the treatment of malalignments using acupuncture.

The treatment method of vital energetic alignment therapy was a self-discovery that occurred while I was practicing sports medicine in 1981. At this time, I was working for players of the local football and hockey teams (i.e. the Edmonton Eskimos and the Edmonton Oilers). The majority of the problems brought to my attention were aches, pains, strains, broken bones, concussions, and fatigue. One of my patients, a football player who had received a concussion from another player, informed me that he had not 'felt' like himself since sustaining the injury. He suffered from constant head and neck pains, fatigue and a general sense that he was not 'feeling' like his old self. Notably, his performance was suffering in a very strange manner: his throwing arm would produce a trajectory contradictory to his aim. I meticulously assessed this patient's central nervous system and pupillary reflexes, concluding that his bodily functions were normal; minus minor impairment of vision.

As I had done numerous times in the past, I attempted to enhance and ground his concentration by treating EX HN 3 with a gentle clockwise twist of the needle (this last step is a routine step I had often provided for all my athletic patients, intending to improve an athlete's movement, coordination, and overall performance in their sport). Following a clockwise turning of the needle, my patient stated that his vision had immediately clarified. Following a reverse of turning of the needle, however, he claimed that his vision had suddenly blurred, while his weight noticeably shifted to one side of his body. I reverted to turning the needle clockwise again and his vision and posture returned to the previous, correct state. Following this procedure, I realized that with the simple turning of the needle, I held the ability to "steer" the direction of energy flow and ultimately manipulate it into an ideally-aligned state. When I tested this procedure with an eye chart, the accuracy of the patient's reading increased gradually with the turning of the needle. Upon lightly tapping the needle three times, the patient described having perfect vision and feeling extremely "straight". As this was an accidental finding, I reviewed the existing literature on post-concussion therapy but failed to find a similar result that had been published.

Instead, I began to develop my own observations into a technique that I could rely on for future treatments. In Chinese literature, acupoint PC 6 was understood to be the opening to the Inner Gate, which was significant for patients with a history of unconsciousness; thus it was implicated for patients with concussions (Aung 2017). I have since treated many Post-concussion Syndrome patients using EX HN 3 and GV

4 for vital energetic alignment, starting at PC 6 (for unconscious patients), with much effectiveness. Following the success of the first 75-100 patients using this technique, I began to document my procedures and protocols, refining and elaborating on the techniques before notifying my colleagues about the importance of implementing this treatment method (My article "The 'pearls' of medical acupuncture: six vital energetic (qi) alignment procedures"). Today, those who have reproduced my procedures around the world have returned remarkably positive reports. Documented recoveries have shown that vital energetic treatment continues to be a very valuable mode of therapy for traumatic and post-traumatic injuries. The following protocols for recognizing and treating malalignments are the results of years of practice and study in the field.

5 Indications of Malalignment in PCS and PTSD Patients

Though many patients may appear to have fully recovered from the initial acute trauma of an event, patients experiencing PCS or PTSD will display signs that their well-being and quality of life are overshadowed by physical disequilibrium, as well as pervasive feelings of mental and spiritual enervation and disembodiment. As has been discussed, the key etiological factor in the equation is the existence of a mild or severe traumatic injury that may have resulted in the temporary loss of consciousness. Major surgery is included as an injury to the body, and in these cases, consciousness has also been lost through the use of anesthesia. Many APVA patients have either been in a motor vehicle accident or suffered a sports injury. Such patients are likely to benefit from APVA, the more specific indications of which are delineated below.

5.1 Symptoms of Malalignment

Physically, the PCS or PTSD patient will show signs of lateralization; notably a tilted head or a deviated walk toward the affected side of the body. The neck and back muscles tend to be tense and stiff on the non-injured side. Pupillary reflex is generally slow, and the eyes are usually dull and blurry. Psychologically, it is often readily apparent that the patient cannot concentrate and is both anxious and depressed. Spiritually, the patient manifests a notable degree of Shen attenuation or emptiness. Shen is the spiritual energetic synthesis of Essence and Qi, and it is active in each of the Yin organs, residing in the Heart (Larre et al. 1986). It is the first thing the physician looks for in carrying out the inspection phase of the comprehensive TCM four-diagnosis. While most visible in the liveliness and sparkle of the eyes, Shen is also seen in the overall demeanor of a person:

> Shen is the capacity of the mind to form ideas and is the desire … to live life. When Shen loses its harmony, the individual's eyes may lackluster and his or her thinking may be muddled. A person so affected may be slow and forgetful, or perhaps suffer from insomnia. Certain Shen disharmonies are marked by unreasonable responses to the environmental, such as incoherent speech (Kaptchuk 1983).

Patients suffering from PCS or PTSD report a variety of symptoms, including chronic fatigue and weakness, inability to concentrate, memory loss, vertigo, tinnitus, diarrhea and headache as well as feelings of sadness, fear, anxiety, irritability, non-groundedness, non-centeredness, disorientation, and disembodiment. These appear to be most pronounced in the early evening.

Neurasthenia or clinical depressions are the most common Western biomedical diagnoses pertaining to the above etiology, signs, and symptoms. PCS and PTSD syndromes are recognized by some family physicians as two of several "new" biopsychosocial disorders such as premenstrual syndrome, chronic fatigue syndrome and temporomandibular joint dysfunction syndrome. The most widely applicable TCM diagnosis is Kidney Qi/Yang Deficiency. This TCM syndrome—when viewed in terms of a PCS or PTSD condition—results from a person becoming frightened or fearful due to the actual or impending impact of powerful external forces, whether in the form of an injury or surgery. Fear and fright have an adverse effect on the Kidney, the source of an individual's sexual and reproductive original vital energy (Yuan Qi). (Xinnong 1987; Bingshan et al. 1993). This, in turn, may generate problems in the Urinary Bladder and other organs/meridians.

6 Management Techniques for Treating PCS and PTSD: Aung PCS and PTSD Vital Alignment Acupuncture

6.1 APVA Procedures

The seven APVA's I have developed over the past thirty-five years of clinical practice constitute the 'pearls' of medical acupuncture. These seven APVA's center around the CV (i.e. Conception Vessel and GV (i.e. Governor Vessel) extraordinary meridians, since these meridians function as streamlined conduits for the convergence and regulation of Qi in relation to the 12 regular meridians. CV controls the circulation of Qi throughout the Yin meridians and GV performs the same function for the Yang meridians. I have found that acupoints located on CV and GV are of value in bringing PCS and PTSD patients back into alignment. Alignment is not merely a 'mechanical' phenomenon, which is why I have chosen to name these APVA procedures after the seven chakras recognized in traditional Ayurvedic and Chinese medicine models. As has been stated, chakras coincide with TCM acupoints. Acupoint EX HN 3, for example, the famous Third Eye of Eastern mysticism, which is the primary point in all the APVA procedures, coincides with the Ajna chakra. It is used in TCM to

balance all spiritual activity within the human body (i.e. Shen) and in Ayurvedic medicine to awaken "one's own divine self … the True Self" (Motoyama 1981).

6.2 Opening the Spiritual Gates

Successful employment of Aung PCS and PTSD Vital Alignment therapy is dependent upon preparatory steps involving the opening of spiritual gates. Gates that coincide with the patient's PCS or PTSD symptoms must be opened prior to proceeding with APVA protocol, as treatment effectiveness can be severely diminished if neglected. The four gates are as follows:

1 *Inner Gate PC 6*—Involves losses of consciousness incurred prior to the traumatic event for which the patient is presently receiving treatment, as well as past periods where the individual's body was not in his or her control. The inner and outer spirits separate and disperse. In an unconscious state, the mind is temporarily incapacitated and the physical and spiritual components of the body both close off all openings and gates to protect the body from invasion from external forces. The body seizes up, muscles and joints becoming very rigid—resembling rigor mortis—and closes all orifices (e.g., eyes, nostrils, mouth, anus, etc.). When treating patients using APVA protocol, the difference between succeeding and failing to elicit a response is the difference between whether the patient has been unconscious at any time in their life. If he or she has been unconscious for any reason (e.g., anesthetics, epilepsy, fainting spells), the Inner Gate PC 6 must be opened prior to attempting regular treatment procedures. It is essential to inquire of all patients as to whether they have been unconscious or not, but it is even more essential to treat all patients displaying PCS and PTSD symptoms with PC 6 so that no opportunity will be missed since many patients who have experienced unconscious episodes cannot recall the experience.
2 *Outer Gate TE 5*—The Outer Gate (TE 5) is the point for emotional ventilation from the inside of the body to the outside of the body. This gate must be opened for proper function of the 12 regular meridians, which are the areas of energy exchange with the external environment.
3 *Subconscious Gate CV 5*—The Subconscious Gate (CV 5) is composed of recollections from before the age of four. Before this age, memory is obscure for the majority of people. Gaining access to the subconscious level and opening the gates can uncover past trauma, the removal of which will restore energy flow and balance in all areas of the body.
4 *Life Gate (Posterior Manipura chakra) GV 4*—The Life Gate, also known as the posterior Manipura (GV 4) provides direct entry into the human consciousness and simultaneously provides the exit channel for the spirit during death. Needling this point can have implications for longevity (e.g., prolonging lifespan by 4–5 days). Opening the Life Gate will revitalize and reunite the inner and outer spirits, which were disturbed from previous states of unconsciousness.

6.3 Clinical Protocol

The APVA clinical protocol encompasses the Crown/Sahasrara (EX HN 1x4; GV 20), Throat/Vishuddhi (CV 22; GV 14), Posterior Manipura (GV 4), Anahata (CV 17; GV 9), Anterior Manipura (CV 6), and Muladhara (CV 1; GV 1) vital energetic alignments. Following the opening of relevant spiritual gates (most notably PC 6), the use of an eight-step protocol, as delineated below, is appropriate after integrated TCM and biomedical diagnostic assessment has found which side of the body remains out of alignment as a result of the previous traumatic injury or surgery. The following protocol is applicable to all vital energetic alignment points with EXHN.3 functioning as the pivot point (Fig. 5):

Step 1. The primary acupoint, EX HN 3, is needled obliquely (45° angle) in the direction of the flow of Qi down the midline of the face on the GV meridian to a depth of 0.5 cun (i.e. measurement of body inches of the patient) utilizing the reinforcing method until De Qi (i.e. arriving of Qi that is noticeable by numbness or tingling sensations) is attained.

Step 2. The secondary acupoint is needled obliquely (45° angle) to a depth of 0.5 cun in the direction of the flow of Qi up the CV (front midline) or GV (back midline) meridians utilizing the reinforcing method until De Qi is attained.

Step 3. The acupuncturist stands to one side of the patient and holds the primary needle with the left hand and the secondary needle with the right hand.

Step 4. The patient is asked to attempt to focus her or his eyes on a small object a short distance (3-5 m) away.

Step 5. The acupuncturist gives both needles a simultaneous ¼ turn (90°) toward the side of the patient's body that is out of alignment.

Step 6. The patient is asked if there is any change in eyesight or vision. The expected response is that the distant object has come into much clearer focus. If this response is not obtained, both needles are given a simultaneous ½ turn (180°) in the opposite direction. When the expected response is obtained, the APVA procedure continues as follows.

Step 7. The primary needle is gently 'forced' in 3 times to reinforce and set ('fix') the correct vital energetic alignment. The same manipulation is performed on the secondary needle.

Step 8. While both needles remain in place, the patient is asked whether he or she feels more 'grounded' or 'embodied'. A positive response is expected, but if the response is negative the entire procedure may be repeated with or without the addition of tertiary acupoints. The needles are retained for 5–10 min.

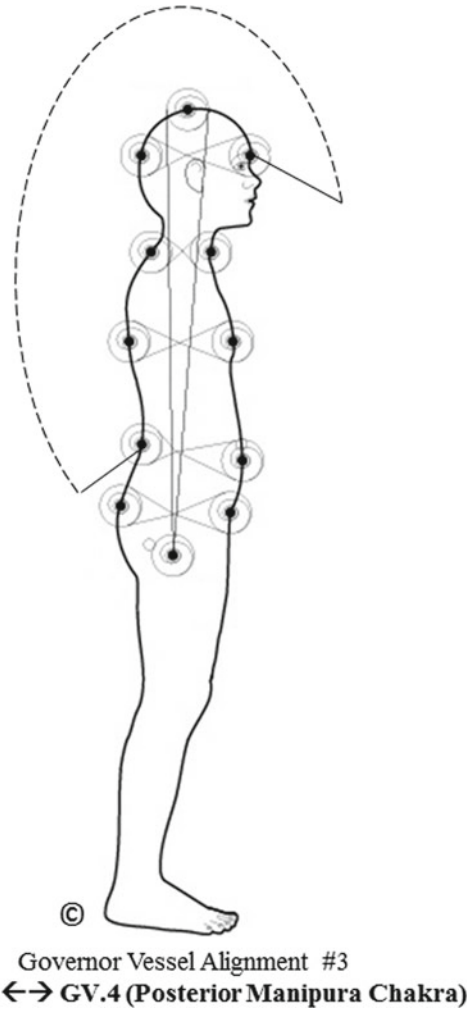
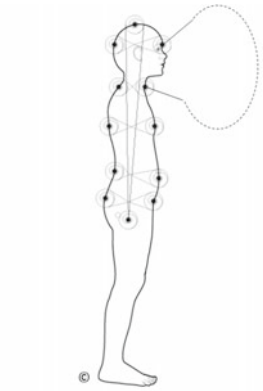


Fig. 5 AVEA protocol illustrated

Protocol for the anterior, posterior and empowering Aung PCS and PTSD Alignments are illustrated as follows; clinical usage is not intended to be an exhaustive list but encompasses the major indications (see also Fig. 6):

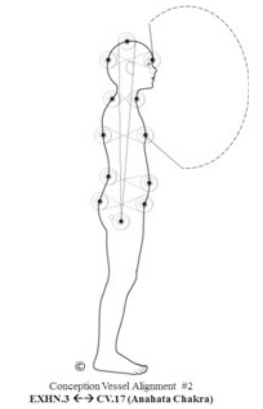


Conception and Governor Vessel Alignment #1
(EX HN 3 - CV 22)

Clinical Use:
- Chronic sinus congestion treatment
- Deviation of nasal septum due to trauma treatment
- Effects of E.E.N.T. surgeries
- Cleft palate treatment
- Harelip and loss of smell treatment
- Effects of face and jaw injury
- TMJ imbalance treatment
- Lateral deviation alignment

Procedure:
- Follow clinical protocol as delineated above, with emphasis on EX HN 3 and CV 22

Remark:
- Located on the interception between the GV and CV channel. Patient's tongue should be touching hard palate during the procedure. Arriving at De Qi is essential

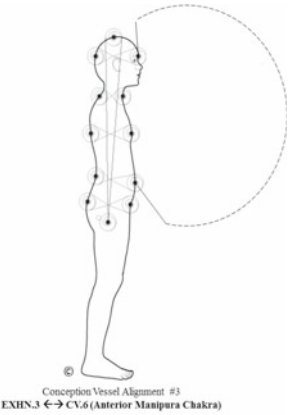


Conception Vessel Alignment #2
(EX HN 3 - CV 17)

Clinical Use:
- Effects of open chest/heart surgery
- Thoracic internal organ injury
- Acute emotional disorder treatment
- Spiritual invasion treatment
- Spinal injury treatment
- Lateral deviation alignment

Procedure:
- Follow clinical protocol as delineated above, with emphasis on EX HN 3 and CV 17

Remark:
- Exercise caution to avoid pneumothorax and pericardium hemorrhage, as well while working with patients who have chest abnormalities, osteoporosis, and kyphosis

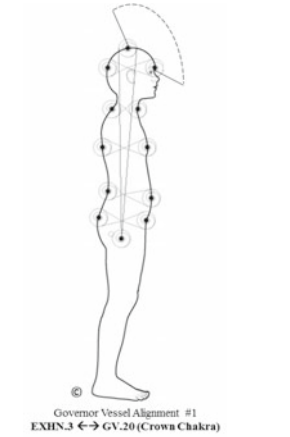


Conception Vessel Alignment #3
(EX HN 3 - CV 6)

Clinical Use:
- Anterior vital energetic alignment
- Effects of open chest/abdominal/pelvic surgery
- Effects of removal of organs from chest, abdomen and pelvic region
- Spinal injury treatment
- Flail chest treatment
- Lateral deviation alignment

Procedure:
- Follow clinical protocol as delineated above, with emphasis on EX HN 3 and CV 6

Remark:
- Exercise caution to avoid internal organ puncture

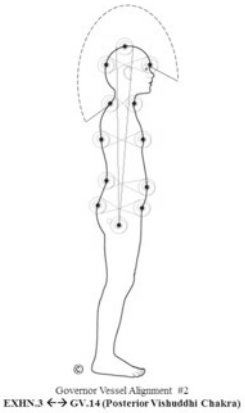


Governor Vessel Alignment #1
(EX HN 3 - GV 20)

Clinical Use:
- Effects of brain surgery
- Improving concentration
- Improving memory
- Invoking deep relaxation
- Frontal head injury treatment
- Lateral deviation alignment

Procedure:
- Follow clinical protocol as delineated above, with emphasis on needle insertion at EX HN 3 and GV 20

Remark:
- Needles should be facing each other for alignment

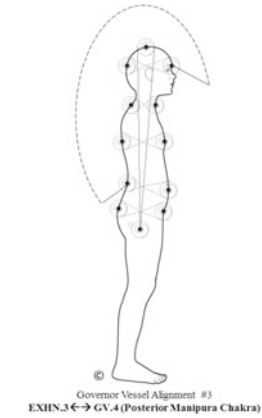


Governor Vessel Alignment #2
(EX HN 3 - GV 14)

Clinical Use:
- Whiplash and motor vehicle accidents treatment
- Neck injury treatment
- Effects of shoulder surgery
- Upper respiratory tract injury treatment
- Effects of upper respiratory tract surgery
- Effects of spinal surgery
- Upper back injury treatment
- Upper limb numbness treatment
- Later deviation alignment

Procedure:
- Follow clinical protocol as delineated above, with emphasis on needle insertion at EX HN 3 and GV 14

Remark:
- Prior to acupuncture, ensure that the patient does not have a history of upper spinal injury, quadriplegia or previous chest surgery.

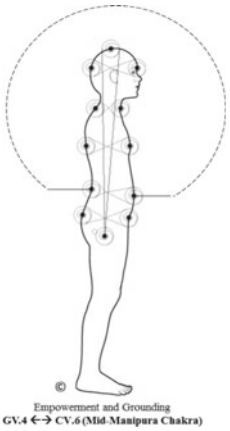


Governor Vessel Alignment #3
(EX HN 3 - GV 4)

Clinical Use:
- Complete vital energetic alignment
- Head, neck and back injury treatment
- Stabilization of chakra system
- Realignment of body, mind, and spirit
- Grounding of the energetic system and all appendages
- Spiritual realignment and reunion
- Lateral deviation alignment
- Raised and compressed deviation alignment

Procedure:
- Follow clinical protocol as delineated above

Remark:
- Ensure that patient is not being treated for a medical emergency
- Avoid spinal injury when puncturing GV 4



Empowerment and Grounding Alignment
(CV 4 - GV 4)

Clinical Use:
- Empowerment of congenital and acquired Qi
- Grounding and stabilization
- Enrichment of abdominal and pelvic energies
- Strengthening of GV and CV channels
- Anterior and posterior deviation alignment

Procedure:
- *EX HN 3 is not involved; protocol is for the direct stimulation of CV 6 and GV 4 for the empowerment of the whole body

Remark:
- *EX HN 3 not utilized
- Alignment used for energetic reinforcement

The follow-up framework I have found to be effective in sustaining vital energetic alignment is APVA treatment once a week for three weeks, then every second week for six weeks and, finally, once a month for three months. Most patients, however, do not need such intensive follow-up and in many cases one or two APVA treatments is all that is required. The protocol often proceeds smoothly, but difficulties may arise during steps 4-6. In the Throat/Vishuddhi (CV 22; GV 14) alignment, for example, the flow of Qi from GV 14 to EX HN 3 may be severely blocked. Having the patient breathe using the Yang methods (In → Out → Hold or In → Out → Hold → Out) helps to resolve this problem.

During the Posterior Manipura (GV.4) alignment, it may be difficult getting Qi to accumulate at GV 4 then flow up the GV meridian. More intense reinforcement with the needle is helpful as well as having patients rub the area around CV 6 with the palm of the hand in a circular clockwise direction. Similarly, with the Base/Muladhara (CV 1; GV 1) alignment, the flow of Qi may get blocked at the 'anal station' and patients should be directed to squeeze their anal sphincter a few times helps to 'pump' Qi up the CV meridian to CV 4. It must be noted that the above difficulties may also be resolved by having the patient learn both the Small Circle and Big Circle (i.e. concentration exercise of Aung Medical Qi Gong) since these fundamental Qi gong breathing and concentration exercises optimize the circulation of Qi throughout the CV and GV meridians. (Aung 1994)

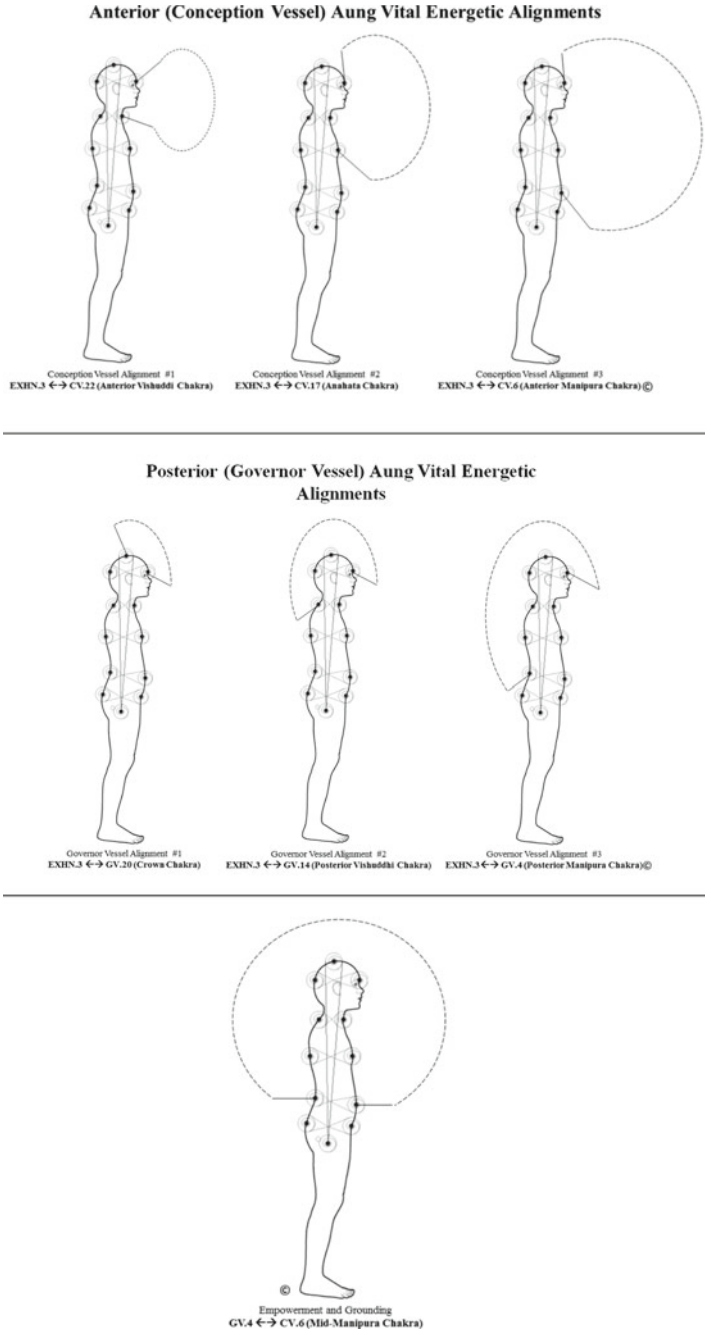


Fig. 6 Seven Aung PCS and PTSD vital alignments

Table 3 APVA procedure and clinical use

APVA Procedure	Clinical Usage
Crown/Sahasrara (GV 20; EX HN 1x4)	Complete harmonization of all organ systems, improved memory, improved concentration
Third Eye/Ajna (EX HN 3)	Improved intuition, improved concentration
Throat/Vishuddhi (CV 22/ GV 14)	Protection from wind invasion of Gallbladder, improved balance, improved endocrine function and metabolism, improved mind-body connection,
Chest/Anahata (CV 17/GV 9)	Improved lung and heart function, increased Qi flow, prevention of uprising stomach heat, emotional stabilization against sadness, anxiety, etc., prevention of a hiatus hernia
Posterior Solar Plexus/Posterior Manipura (GV 4)	Improved kidney, Qi/Yang function, lower back pain relief, decreased neurasthenia, opening of the Life Gate (GV 4)
Anterior Solar Plexus/Anterior Manipura (CV 6)	Qi storage in the middle energizer, bowel stabilization, regulation of bowel peristalsis, opening of the Subconscious Gate (CV 5)
Sex/Svadhishthana (CV 4; GV 2)	Strengthening of the Lower Energizer, improved functionality of the internal genitalia, improved transference functionality of the internal Qi, improved regulation of male/female sexual hormones
Base/Muladhara (CV 1; GV 1)	Strengthening of the Lower Energizer, grounding of the chakra system, improved functionality of the external genitalia, improved digestive function

6.4 Positive Effects of Chakra Manipulation

Each APVA procedure has its own positive result upon the corresponding chakra center (Table 3). The Posterior Manipura (GV 4) alignment is perhaps the most widely applicable, since many PCS and PTSD patients experience some degree of Kidney Qi/Yang Deficiency. An accurate diagnosis will reveal which of the procedures constitutes the optimal treatment of choice in the individual case. However, since there are no deleterious side-effects, any of the seven APVA's can be tried until the most efficacious modality is found.APVA Procedure

6.5 Pearls Within Pearls

The above outlined APVA clinical protocol is effective in most cases, but in the most difficult cases, additional reinforcement of Qi may be necessary. I have developed

two sets of 'pearls within pearls' for this purpose. First, I add SI 3 as a tertiary acupoint for the three GV meridian APVA's (Crown/Sahasrara, Throat/Vishuddhi, and Posterior Manipura) and LU 7 as a tertiary acupoint for the three CV meridian APVA's (Anahata, Manipura, and Muladhara). These points are reinforced contralaterally and, if necessary, bilaterally, in the same direction as the meridian until De Qi is attained. SI 3 is especially useful in APVA because it is the confluent point where the Qi of the GV meridian converges with that of the 12 regular meridians. LU 7 is the confluent point of the CV meridian. Secondly, I may need to utilize two confluent points to prepare the way for the main APVA procedure. These points are PC 6, which is the 'key' to the Inner (Yin) Gate of Qi, and TE 5, which is the 'key' to the Outer (Yang) Gate of Qi. PC.6 is used to open the three CV alignments and TE 5 the three GV alignments. They are reinforced contralaterally or bilaterally in the same direction as the meridian until De Qi is attained. Finally, it must be noted that in a small percentage of cases I have found that APVA procedures simply will not work. These usually involve psychiatric disorders.

6.6 Case Examples

PCS and PTSD patients have typically been referred to me for medical acupuncture by physicians who have done all they can for these difficult cases utilizing Western biomedical therapeutic modalities. Some of my most interesting cases involving APVA methods are outlined below:

6.6.1 Case 1

A 35-year-old male farmer was struck by a car. He lost consciousness for a few minutes and suffered severe whiplash, broken ribs and a fractured hip. He was hospitalized. When his injuries healed he was treated with NSAIDs and physical therapy for a period of seven years. He was referred to me for consultation, his main complaints being chronic neck, hip and back pain, periodic headache and vertigo and a pervasive feeling of non-groundedness. After performing a comprehensive TCM and Western biomedical diagnosis, I accepted the patient as a PCS case. His physical lateralization was so severe that he sometimes could not walk in a straight line. Mentally and spiritually, I observed that he was almost empty of Shen. I decided that the Posterior Manipura (GV 4) alignment would be the most appropriate therapeutic modality. After De Qi was obtained on insertion of the primary needle (EX HN 3), the patient's neck and back muscles began to relax and he reported feeling relieved of tension and discomfort. When De Qi was obtained on insertion of the secondary needle (GV 4), his pupillary reflex became livelier, his eyes began to brighten and he reported feeling joyful. A positive response was obtained during the adjustment proper (steps 4–6 of the APVA clinical protocol), with the patient reporting clearer vision and a feeling that something miraculous was happening to him. Right after

the treatment his wife commented on his improved attitude. The usual follow-up was provided with consistently good results.

6.6.2 Case 2

A 28-year-old male professional football player had a high-speed, forceful head-on collision with another player (they collided helmet to helmet). At the moment of impact he 'saw stars'. Immediately afterward, he suffered a stiff neck, headache, inability to concentrate and focus his eyes and periodic mental disorientation. He was unable to remain in the game. After a day of biomedical testing, NSAIDs, and physical therapy, he was referred to me by the team physician for consultation. I observed that his main problem was the inability to concentrate (asking the same question over and over again). I observed attenuation of Shen, although not as severe as the case of the farmer described above. I performed the Throat/Vishuddhi (CV 22; GV 14) adjustment, which was most successful. On completion of the procedure, the patient reported "I feel like a camera that is back in focus… Finally, I feel myself again." He was able to play professional football the next day.

6.6.3 Case 3

A 35-year-old female had major thoracic surgery. Five years later she was still experiencing chronic fatigue and feelings of disembodiment, for which she was referred to me by her family physician for consultation. A deviated tongue was the most obvious sign of physical imbalance. I perceived her to be almost devoid of Shen. I performed the Anahata alignment. On completion of this APVA, which I judged to be only fairly successful, she reported feeling somewhat more energetic, "more alive." Subsequent Anahata alignments, which included the use of the confluent point LU 7 and the Inner Gate PC 6, slowly helped to enhance her vital energy and strength. Her friends and relatives have noted the improvement in her quality of life over time.

6.6.4 Case 4

A 12-year-old boy banged his head against a doorknob. There was local pain and bruising with hematoma. He was taken to the emergency ward of the hospital, and the examination and tests showed that there was no notable neurological damage. Subsequently, however, he began to experience chronic fatigue as well as periodic vertigo, headache, and inability to concentrate. Comprehensive testing showed his central nervous system to be functioning normally. He received no special biomedical treatment but was referred when the fatigue and vertigo had persisted for over a year. I immediately observed that the boy's pupillary reflex was slow, his pupils were constricted and he was almost devoid of Shen. The Crown/Sahasrara (EX HN 1x4; GV 20) alignment was effective in aligning the patient and PCS/PTSD signs and

symptoms eventually disappeared completely. He is now a normal active child. His mother wanted him to have ongoing APVA treatments, but I explained to her that these were not necessary.

7 Management Techniques for Treating PCS and PTSD: Medical Qi Gong Exercises and Environmental Assistance

The use of Aung vital energetic alignment acupuncture in association with select chakra acupoints has proven itself to be an effective treatment method for PCS and PTSD malalignments as a result of an injury. Aung vital energetic alignment acupuncture may be the most effective treatment method for addressing malalignments, though it is not the only therapy in the armamentarium of natural modalities for malalignment. Any therapeutic modality which aligns the chakra energy system and principal extra meridians can be useful in the treatment of malalignment. One such method that is deserving of greater recognition and popular consideration is the practice of Medical Qi Gong exercises in Taoist tree-hugging.

Qi Gong exercises constitute what is a vital part of the aptly termed 'great treasure house' of Traditional Chinese Medicine. Defined as a key preventative and curative therapy well over 2000 years ago, along with herbal medicine, massage, acupuncture and other TCM therapeutic modalities, Qi Gong exercises can stimulate deep relaxation in patients suffering from malalignment, while certain Qi Gong exercises can even encourage the realignment of vital energies. One such example of a realigning Qi Gong exercise is the ancient practice of tree-hugging. In ancient Chinese history, Shaolin monks and Taoist masters would hug trees ritualistically each morning due to a shared understanding that traditionally hugging trees encouraged the realignment of the chakra energy systems. (Tsung 1983) These individuals found that the simple practice of daily tree-hugging improved one's quality of life, as well as one's digestive system functionality, energy levels, lung functionality and kidney and brain functions. Tree hugging, then, was known to be an effective maintenance modality for optimizing health and alignment.

In my own personal experience, tree-hugging has functioned as a means for the enhancement of life quality in a universal dimension. Taoist and Buddhist medical styles of Qi Gong and tree-hugging emphasize the necessity of cleansing oneself and others of emotional pollution, which refers to negative emotional states such as anger, fear, anxiety, depression, and so on, implicated in the daily stresses of life. Tree-hugging can aid those who are experiencing such negative emotions by extracting stresses and negative emotional states, while also rebalancing an individual's energy system. Thus, tree-hugging can function as a natural therapeutic modality for realignment, along with other natural means (e.g. phonating particular sounds for chakra realignment, standing in the midst of high tide at the beach, engaging in sexual intercourse, etc.).

7.1 Tree Hugging Procedures

While some brave-hearted individuals might prefer to hug a cactus (which provides natural acupuncture as well as realignment), most individuals who attempt to take up tree hugging as a therapeutic modality would prefer to come heart to heart, face to face, trunk to trunk, root to root and leaf to leaf with the tree of his or her own choosing. There is no exact formula for choosing what specific tree to hug, though there are two cautions that patients should first consider:

i. When selecting a tree, an individual should always ask permission of the tree. This automatically grants the seeker permission to participate with the tree in his or her exercise.
ii. Seekers should avoid trees that clearly display traumatic lesions as a result of fire, lightning, accident, etc., as these trees will be malevolent hosts due to a previous injury. Hugging injured, dying or dead tree may transmit negatives effects to the patient.

The following tree-hugging protocol that I have carefully cultivated and developed over the past 35 years may be overseen by practitioners as a therapeutic modality in firsthand dealings with malaligned patients or may be given as instructions to patients for self-exercises. It is enumerated and recommended as follows: (Aung 2000)

1. The patient intuitively selects a tree which feels pleasant and situated in an appropriate location, silently asking the permission of the chosen tree for participation in therapeutic purposes. Straight, strong trees standing near rocks or sources of water that display healthy leaves and bark are amenable for therapeutic purposes.
2. The patient approaches the tree in an erect posture—staying outside the umbrella of the branches—firmly, gently, confidently and compassionately, facing east in the morning, north in the early afternoon, south in the late afternoon and west in the evening (he or she is to assume a horseback riding posture/movement (Fig. 7.)
3. With chest (frontline acupoints and chakras) and palms facing the tree (PC 8 acupoints on both hands), the patient should approach the proximity of the tree to the point of being underneath its branches for the purpose of sensing the vibrant energy of the tree (PC 8 acupoints).
4. The patient should move close to hug the tree, while closing his or her eyes, relaxing the shoulders, slightly bending the knees and turning toes inward (i.e. horseback riding posture).
5. The patient will press what feels to be the center of the trunk of the tree with the Third Eye/Ajna chakra (EX HN 3; GV 16), as well as the Chest/Anahata chakra (CV 17; GV 9), Solar Plexus/Manipura chakra (CV 6; GV 4) and the Sex/Svadhishthana chakra (CV 4; GV 2) (Fig. 8)
6. While pressing the Third Eye against the midline of the tree trunk, the patient is to be smiling both outwardly and inwardly to attain spiritual stability.

Fig. 7 Tree-hugging posture (i.e. Horseback posture) without the reality of a tree

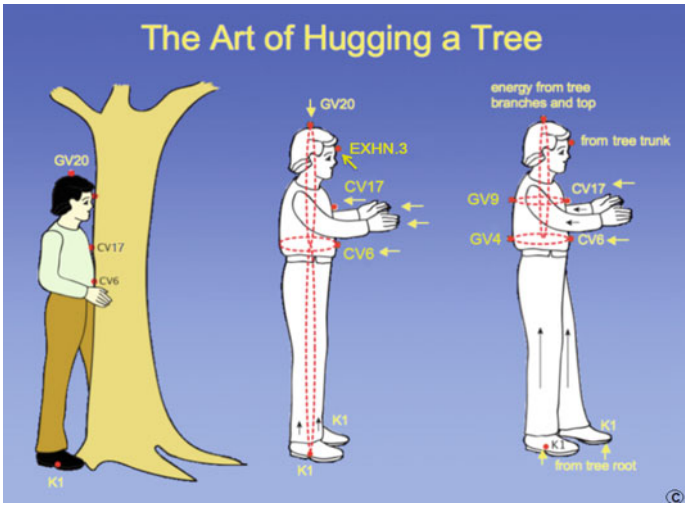


Fig. 8 Energy flow through chakra points during tree-hugging

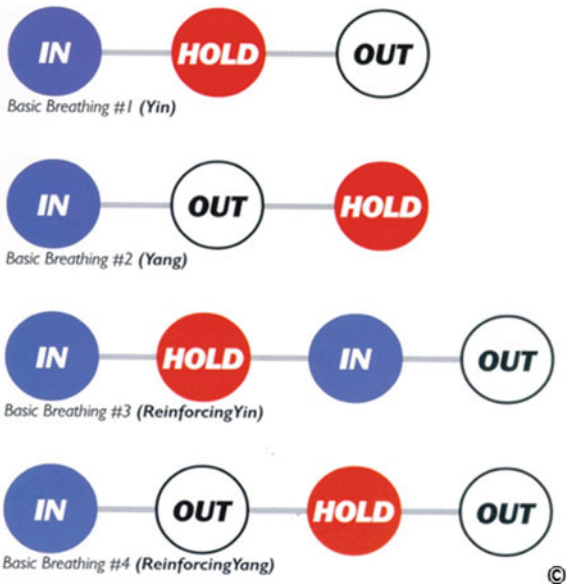


Fig. 9 Aung medical Qi Gong 4 basic breathing exercises

7. If suffering from a Yang condition such as an allergy, asthma, hypertension, headache, fever or any other Yang condition/syndrome as diagnosed by a qualified TCM practitioner, the patient should keep his or her palms flat so that PC.8 is making direct contact with the trunk of the tree. Basic Qi Gong breathing exercises #1 (Yin - inhale, hold the breath, exhale) or #3 (reinforcing Yin - inhale, hold the breath, inhale, exhale) should be utilized (Fig. 9).
8. If suffering from a Yin condition, such as chronic fatigue, diarrhea, poor circulation (cold hands/cold feet), anemia or any Yin condition/syndrome as diagnosed by a qualified TCM practitioner, the patient is to hold the trunk of the tree tight with his or her fingers flexed as much as possible so that his or her knuckles are tight against the trunk of the tree. Basic Qi Gong breathing exercise #2 (Yang - inhale, exhale, hold the breath) or #4 (reinforcing Yang - inhale, exhale, hold the breath, exhale) should be utilized (Fig. 9).
9. In either case—Yin or Yang—the patient will adjust his or her Third Eye and hands until the position feels right and he or she can sense the central Qi of the tree emanating and vibrating from its roots, upward through the trunk and outward toward the branches and leaves—from the earth to the heavens. The tree can be tested whether Yin or Yang by touching the tree using the Omura Bi-Digital O-ring test. (Shinnick 1996) If this reacts positive with the palm of the hand, then it is a Yang tree; if negative, then it is a Yin tree (Fig. 10).
10. The patient will try to maintain this position for several minutes (no exact time specification), according to the energy and the type of sensations or vibrations that he or she may be receiving from the tree (i.e. whether positive or negative).

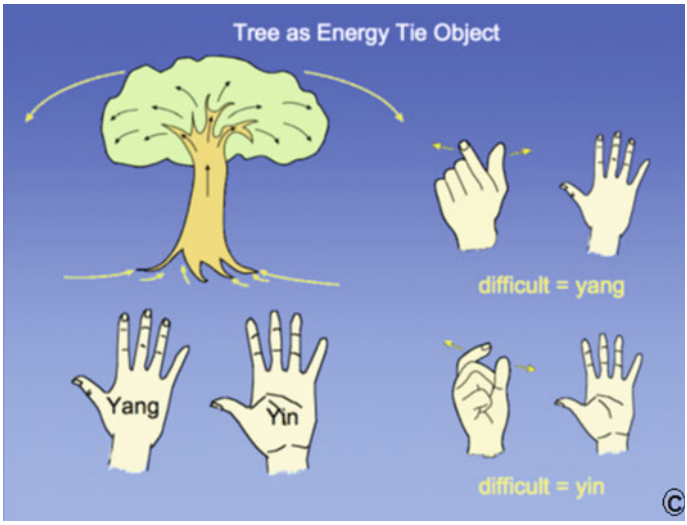


Fig. 10 Testing tree gender (i.e. whether Yin/female or Yang/male) for compatibility

The patient may notice a vibrating, healing sensation or colour flashes emanating from within the tree.

11. Chanting a mantra (such as 'ahrahammm…ahrahammm…ahrahammm…') or phonating Qi Gong chakra or organ sounds may also be appropriate according to the needs, wishes and medical Qi Gong prescription of the patient. (Swami 1994; Aung 2002)
12. To conclude the realignment exercise, the patient will place his or her back midline against the central tree trunk with his or her hands hugging the tree behind (Fig. 11). This realigns the posterior chakras as well as the Governor Vessel meridian (at the superficial level, up the back and top of the head and down to the gums and centre of the front teeth midline, connecting with the Conception Vessel) and Bladder meridian systems (many acupoints of the Urinary Bladder meridian run up and down the back parallel with the Governor Vessel).
13. When finished, the patient should bless and thank the selected tree and all sentient beings within his or her proximity.

This is a suggested systematic, environmental Aung Medical Qi Gong approach for patients suffering from malalignment and PCS/PTSD symptoms.

7.2 Group and Family Tree Hugging Assemblage

Group tree-hugging as a therapy for realignment has proven to be even more effective than individual tree-hugging. The gathering of groups or families to hug trees results

Fig. 11 Realignment of posterior chakras using the back midline for tree-hugging

in a faster and more effective realignment of energy due to the combined energetic forces of friends, family, and colleagues. Group tree-hugging is especially valuable during Qi Gong retreats, guided by a genuine Qi Gong healing master. Such retreat experiences offer seekers the good opportunity to fellowship and appreciate the wonders of Mother Nature, while also providing the group with blessing and opportunity for reconciliation. Large trees are not necessarily more therapeutically effective than small or newly implanted trees, but large and ancient trees which outlive our human lifetimes—sometimes by many centuries—provide the opportunity for groups to hug a tree in unison at the same place and time. When selecting a large tree for a group hug, patients should consider the core of the tree and learn to discern the character via colors, preferably with guidance by Qi Gong instructors. This is accomplished by adjusting the acupoint EX HN 3; gazing at the middle of the tree together with the midline chakras, while hugging the tree with the right hand raised to the level of the mouth and the left lowered to the navel. This movement is followed by adjusting the head in a sideways, back and forth motion for clarification of focus on the core

of the tree. Such movements and direct gaze into the middle of the tree will reveal the colors, core, and character of the tree to the seeker.

7.3 Intimation of Tree Hugging

It may not always be possible for patients to hug a physical tree due to various circumstances beyond an individual's immediate control. In these instances, a patient may seek out what may be termed a different psychic or 'Zen' level—then, at that time and place, meditate and/or visualize his or her own, unique tree for the performing of the following type of exercise session or a variation of it. (Chia 1986) Some may be confined in various situations and unable or unwilling to move from our dwelling space—or otherwise we may be relatively immobile due to various medical conditions—but this need not deter patients from the tree hugging method of realignment. It is a simple, inspiring and energetically-effective protocol. The following instructions are to be encouraged and distributed by practitioners for patients with physical or mental limitations suffering from malalignment:

1. The patient assumes the horseback riding posture:
    i. Feet apart the same distance as the shoulders and turned slightly inward (medial rotation).
    ii. Knees slightly flexed.
    iii. Hands at the sides with the tip of his or her middle finger touching the thigh.
    iv. Chest and shoulders relaxed and spine straight.
    v. Weight to be felt and directed downward to a midway point between both feet.
    vi. Smiling inwardly and outwardly.
    vii. With his or her head tilted slightly forward so that the Crown/Sahasrara chakra (GV 20) which is located on the midline of the vertex 7.0 cun above the posterior hairline on the midpoint of the line connecting the apexes of the auricles, is pointing straight upward to the sky (GV 20).
2. Patient extends his or her arms and hands straight out in them as if embracing the trunk of a tree.
3. Patient rotates his or her wrists inward about 90º with PC.8 facing toward the front midline (CV meridian and associated acupoints and chakras).
4. For females, the right palm PC 8 should be pointing toward the Throat/Vishuddhi chakra (CV 22; GV 14) and the left palm PC 8 should be pointing to the Solar Plexus/Manipura chakra (CV 6; GV 4)
5. For males, the left palm PC 8 should be aimed toward the Throat/Vishuddhi chakra (CV 22; GV 14) and the right palm PC 8 should be aimed toward the Solar Plexus/Manipura chakra (CV 6; GV 4)

6. The patient is to stand as still as possible, in deep relaxation, smiling inwardly and outwardly and maintaining this posture for 5–20 min, breathing as appropriate for his or her medical condition and as prescribed by his or her Qi Gong master.
7. The patient will gently end the posture, relax, thank and bless the tree and all sentient beings.

8 Management Techniques for Treating PCS: Acupressure Therapy (Neo-Natal and Pediatric)

A final section on realignment therapeutic modalities that deserves mention is the use of acupressure therapy in neonatal and pediatric care. Both parents and medical practitioners often do not realize that post-concussion brain injuries can also occur in infants due to violent birth delivery or use of improper techniques (e.g. suction, forced delivery, etc.). These methods can cause damaging effects and the disruption of energetic alignment, as well as post-concussion symptoms at a very young age. Though acupuncture is not to be utilized for patients at such a young age due to heightened discomfort and softness of the cranium, acu-touch (i.e. touching specific acupoints on the child with the middle finger of the parents' hand), will provide realignment for bipolarity.

Parents should be guided to use the middle finger as a means for transmitting realignment. This is accomplished through both the EX HN 3 and GV 4 acupoints being touched by the middle finger of the corresponding parents; mothers touching the acupoints of sons using the right hand (PC 9 touching the child's GV 4) and fathers touching the acupoints of daughters using the left hand (PC 9 touching the child's GV 4) (Fig. 12). This is all to be done with the parent touching the child's forehead (i.e. EX HN 3) with the same appendage (i.e. PC 9) of the other hand. Parents must seek to 'feel' the Qi moving from the direction that is specific to his or her gender into the child (i.e. right to left for the mother; left to right for the father) with good intentions and love. This is the most effective correspondence of gender due to the flow of opposing sexual sensitivities and will improve the response of the child to the treatment. Electromagnetic forces also play an important role during infancy and parents should take precautions to ensure that they are cooperating with the universal laws. In this sense, it would be wise for parents to turn the child's head to face north if located in the northern hemisphere, or to face south if located south of the equator. This is due to the polarity of the universe and will improve the response of the child to the treatment.

Neo-natal and pediatric patients have shown a very fast response to acu-touch treatments due to the youth of meridians and energy system functionality. Acu-touch need not be applied only for the management of PCS symptoms and malalignment, but also as a preventative modality for encouraging wellness in children.

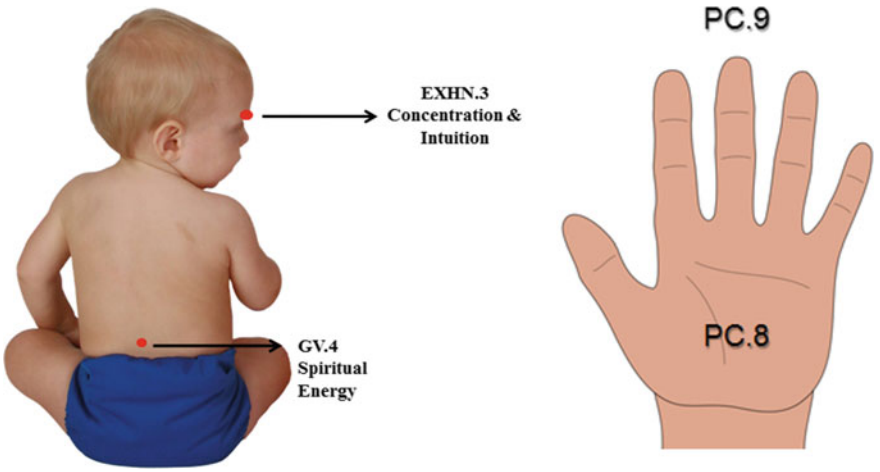


Fig. 12 Acu-touch points for realignment of pediatric patients

9 Pearls from Dr. Aung—Conclusion

After 35 years of practicing TCM and Aung PCS and PTSD Vital Alignment therapeutic modalities, several key 'pearls' of treatment for PCS and PTSD cases have been developed and refined as fundamentals for success in treating non-responsive and difficult patients. As has been seen, treatment for PCS and PTSD syndromes are a body, mind and spirit issue; only a tri-part solution accomplishes fruitful and proven results. The APVA procedures outlined in this chapter are, as the above protocols and case examples illustrate, useful therapeutic modalities to add to the clinical armamentarium of TCM and medical acupuncture. While the procedures are not an acupuncture panacea, they do suggest the viability—and advisability—of a closer and more fruitful relationship between medical acupuncture as a pain management/curative treatment and Qi Gong exercise as a vital energetic reinforcement/preventive measure. This is especially evident with respect to treating and preventing PCS and PTSD. Such a therapeutic relationship can only serve to increase the sense of mutual trust and respect between physicians and their patients. Moreover, it is evident that the working relationship between medical acupuncture and Western biomedicine is a complementary one, which is a definite benefit to patients receiving primary care. Four concluding 'pearls' should be addressed regarding AVEA preparatory procedures:

(a) The importance of opening the Inner Gate PC 6 prior to employing AVEA protocol is paramount, as prior experiences of unconsciousness can significantly reduce the effectiveness of AVEA treatment and deter vital energetic alignment. Practitioners must inquire as to whether or not patients have experienced unconsciousness before administering AVEA treatment, but would be wise to

administer acupuncture for the opening of PC 6, regardless. This is due to the fact that many patients cannot recall past experiences of unconsciousness.

(b) Similarly, the importance of opening the EX HN 3 and GV 4 acupoints prior to employing AVEA protocol cannot be overemphasized. This opening occurs through the needling of SI 3 x2 and LU 7 acupoints; needling LU 7 will automatically open and realign all anterior chakras (i.e. along the conception vessel) and needling SI 3 x2 will accomplish the same purpose for posterior chakras (i.e. along the governor vessel).

(c) Opening up TE 5 (i.e. Outer Gate) is essential for patients suffering from chronic stress and/or emotional contamination prior to engaging in AVEA protocol (e.g. PTSD patients). As chronic stress and PTSD cases have escalated in the West as well as globally (e.g. frequency of PTSD symptoms among active military employees), along with coinciding illnesses and mental debilitation, opening up the Outer Gate will lead to emotional ventilation and return patients to a stable of mental status. Following the opening of the Outer Gate, AVEA protocol must be employed for the patient to return to an optimal physiological state. For addressing spiritual components of emotional contamination and suffering, opening the Subconscious Gate (i.e. CV 5) and the gallbladder (GB 41) will provide spiritual positivity and stabilize positive mental attitudes.

(d) For the full effectiveness of treating PCS and PTSD, the self-manipulation of a sequential chakra phonation exercise will prove very helpful (i.e. phonating from the Crown/Sahasrara chakra through to the Base/Muladhara chakra and back). These simple phonation exercises will ground and align the chakras, returning them to their original state. Aung Medical Qi Gong exercises (e.g. tree hugging) will further reinforce progressive success, while concentration exercises (e.g. Small Circle/Big Circle, Alternating Circle and Figure Eight mental exercises) will strengthen the stability of vital alignment and ensure permanence.

The permanence of patient recovery must be the central goal for all practitioners as we work with our dear patients. Practitioners are responsible to treat and guide these patients towards the goal of wellness, which has been difficult, but not an impossible path for Post-concussion Syndrome and Post-traumatic Stress Disorder patients. Through adherence to these ‘pearls’, practitioners will be equipped with the means to treat what has been previously unanswerable. I am confident that my colleagues and friends who daily experience the difficulties associated with these stubborn lingering illnesses will be happy to witness the positive response of our dear patients, who may now take strides towards optimal well-being and a beautiful, healthy future.

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GV.20—which is near the top of the head when bowing slightly forward in respect to all sentient beings—is one of the most mentally and spiritually stimulating acupoints in TCM

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My article "The 'pearls' of medical acupuncture: six vital energetic (qi) alignment procedures" was accepted and published by *La Revue Française de Médecine Traditionelle Chinoise,* a French scholarly journal on TCM, in 1995. I eventually expanded the treatment for concussion trauma to trauma due to motor vehicle accidents, industrial accidents, and other related injuries, consistently seeing results with the technique

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The PC.8 acupoints are the two major TCM energetic acupoints located near the center of the palms between the 2nd and 3rd metacarpal bones, which function as energy-exchange points. While acupoints are the gates of Qi energy flow and circulation in the TCM system of medicine, chakras are the most powerful sites for the exchange of energy

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Acupuncture in Oncology

E. D'Alessandro

Abstract Acupuncture within an oncology setting carries specific risks and potential benefits that may be attained through needling of soft, mostly superficial tissue. This chapter brings up-to-date clinical and basic research. It is divided in one session where the contra-indications of needling are discussed and few sessions regarding it's use for specific side effects of cancer therapy as well as its probable mechanisms of action. To this point, acupuncture has been studied and applied for management of pain and specific oncologic treatment side-effects, namely post-chemotherapy nausea and vomiting, aromatase-inhibitor related arthralgia, hot flashes secondary to hormonal blockage, oncological fatigue, xerostomia and chemotherapy induced peripheral neuropathy. Clinical research has faced serious difficulties mostly influenced by small sample sizes and mixed protocols regarding different point selection. Nevertheless, a few high quality papers have been able to provide some reassuring evidence of substantial benefits especially within the patients' referred quality of life aspects. Although the mechanisms of action are not completely unveiled yet, this is a promising field for acupuncture research and practice with much interest from the specialised media as well as from the general public.

Keywords Cancer · Oncology · Neoplasm · Nausea · Vomiting · Neuropathy · Aromatase-inhibitor related arthralgia · Hot flashes · Fatigue · Xerostomia · Chemotherapy

Abbreviations

AIs	Aromatase Inhibitors
AIDS	Acquired immunodeficiency syndrome
ANC	Absolute neutrophil count
aPTT	Activated partial thromboplastin time

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BDNF	Brain-Derived Neurotrophic Factor
BMC	Best Medical Care
CIE	Chemotherapy induced emesis
CIPN	Chemotherapy induced peripheral neuropathy
EA	Electroacupuncture
CRF	Cancer Related Fatigue
h	Hours
HFs	Hot Flashes
HPA	Hypothalamic-Pituitary-Adrenal
HRT	Hormone replacement therapy
i.e.	in example
IL	Interleukins
INR	International Normalized Ratio
MFI	Multidimensional Fatigue Inventory
Min	Minutes
PT	Prothrombin
SA	Sham Acupuncture
TA	True Acupuncture
TNF-alpha	Tumor Necrosis Factor alpha
wk	Week

1 Introduction

Acupuncture use within the field of oncology has been experiencing a steady growth in the last decade, shown by recent surveys among cancer patients of great cancer centers around the world and also by the increasing amount of research papers published in the scientific media.

Currently, this is a promising field of research with many published studies in scientific periodicals investigating the possible benefits of this traditional art of healing for cancer patients.

Interesting enough, acupuncture use remains within the realms of complementary medicine and its application serves, as adjunct therapy for optimizing the symptom control in this specific population, a very special group of patients that must endure a constellation of bothersome symptoms, be it from the underlying disease or from its aggressive treatment regimen.

It is not uncommon for patients to visit the cancer center where they are being treated 3–5 times a week in order to be submitted to therapies, medical consultations, medical imaging and blood exams. Usually they comply with every assignment with little room for discussion once the majority of them are terrified with the oncological diagnosis.

To add a complementary therapy may help with the overall well-being but it may also consume otherwise precious down time with family and friends.

Being a complementary therapy implies that the risk-benefit ratio has to be fully accessed on a shared decision basis with the patient. This should happen in order to establish priorities and targets for symptom control as well as to exclude futile procedures that may prevent other more meaningful actions to be taken.

As in every other field of medicine, the patients must be aware of the possible benefits and limitations of acupuncture, they have to understand the amount of time and money that will be invested, the possible adverse events and compare those to the beneficial outcomes that may be reached. The resulting ratio must be of significant importance for the patients.

To clarify the above mentioned, let us analyze two cases that may be seen not so eventually in practice:

56 years old woman who was diagnosed with breast cancer one year ago in a screening mammography. She was submitted to biopsy, neoadjuvant chemotherapy, underwent total mastectomy with axillary lymph node extraction, local radiotherapy and finally was put on hormonal blockage with tamoxifen.

She is now a "cancer survivor", enduring post-mastectomy pain that prevents her to raise her arm higher than her chest and suffers from hot flashes that wake her up 5 times each night soaking wet from perspiration due to the hormonal blockage that is supposed to last at least 5 more years.

She has been trying to regain her upper limb functionality with physiotherapy and occupational therapy but the pain she feels prevents her to advance in the treatments although the pain medicine regimen is optimized. She is also not a candidate to hormonal treatment for the hot flashes and the currently available pharmacotherapies (serotonin re-uptake inhibitors and gabapentin) have not helped her.

This patient would be a great candidate for acupuncture since such pain and hot flashes could be relieved to some extent according to recently published research and she should be referred to a licensed acupuncturist to discuss such possibilities.

Now a second case, a 42 years old man who has a background of drug abuse (namely Ketamine and Ecstasy), suffered an ischemic stroke fifteen years ago without any identifiable cause at the time, which resulted in minor loss of motor strength in the right leg. A few months back, he presented with a deep venous thrombosis in such leg as well as dyspnea, which was first attributed to a possible pulmonary thromboembolism but initial pulmonary images refuted this hypothesis and suggested pneumonia.

Unfortunately, that did not resolve under usual antibiotic therapy and latter was diagnosed as a locally advanced small cell lung cancer with bone metastasis to the lumbar vertebrae. During this investigation he was also diagnosed with acquired immunodeficiency syndrome (AIDS) with low CD4 count and high viral load.

He is now under aggressive chemotherapy treatment, is scheduled to receive local lumbar radiotherapy, and uses enoxaparin for anticoagulation and antiretroviral medication.

Although he suffers from lumbar pain due to the bone metastasis it does subsides with the use of non-steroidal anti-inflammatories. Even if he chooses to search treatment for his pain with acupuncture, once he's had a previous good experience with it, the risk-benefit ratio is poorly acceptable since the possibilities of bleeding, infec-

tions and loss of precious time are far greater than the eventual benefit of reducing the amount of anti-inflammatory drugs that he needs to control his pain.

Exposing the risk-benefit rational in each setting should help attain a shared decision whether or not to undertake the acupuncture treatment, and in order to do so, one must be aware of the current knowledge in the field.

2 Clinical Application

2.1 Contra-Indications and Cautions When Needling a Cancer Patient

Neutropenia

Neutropenia is a condition where the absolute neutrophil count (ANC) drops below 1500 per mm3. This is associated with a higher risk of developing an infection either viral or bacterial, the lower the ANC the greater the risk.

In the oncology setting the neutropenia is usually caused by the chemotherapy, but it can also be due to radiotherapy that impairs the bone marrow production (i.e. radiotherapy to the chest that reaches the sternum bone marrow) or in critical cases where the bone marrow is invaded by metastatic cancer cells.

When due to chemotherapy it is usually transient, its beginning and duration can be predicted according to the drug that is being used so the needling can be postponed.

Mild neutropenia (ANC between 1500 and 1000 per mm3) is still an acceptable scenario for needling but moderate to severe neutropenia (ANC below 1000 per mm3) carries an important risk of spontaneous development of febrile conditions and needling should be refrained once any bruise to the skin might facilitate a local organism to initiate an infection.

Thrombocytopenia

Thrombocytopenia is a condition where the platelets count fall below 150.000 platelets per mm3. Platelets are an important coagulation factor specially when dealing with needle punctures once platelets stop bleeding by binding together to form plugs in blood vessel injuries.

Platelets count below 100.000 per mm3 demands a cautious superficial needling and a 5 min observation after the removal of the needles is advised. Below 50.000 per mm3 the risk of uncontrolled bleeding increases to the point where needling becomes contra-indicated.

Anticoagulation Therapy or Coagulation Disorders

Anticoagulation therapy is not uncommon within the oncology population since it is an important measure to prevent and treat deep vein thrombosis as well as pulmonary thromboembolisms.

Coagulation disorders may be present in cancer patients due to anticoagulation factors produced or even normal coagulation factors impaired by neoplasms products,

usually a coagulation laboratory test that measures prothrombin and activated partial thromboplastin times (PT and aPTT) showing a PT with a International Normalized Ratio (INR) lower than 2.0 and a aPTT faster than 60 s are enough to provide a certain safety for needling.

Warfarin is usually administered in situations where long-term anticoagulation is warranted and the intensity of its action can be measured through PT expressed in terms INR. Cautious superficial needling and a 5 min observation after the removal of the needles is advised in patients receiving warfarin that present with an INR between 1.0 and 2.0. Further alteration of PT may pose a threat of high volume bruise formations and needling should be avoided.

Enoxaparin is very common in practice and other newly available medications like Xarelto are rapidly becoming mainstream practice. These substances also present laboratory tests that can measure its action but they vary from drug to drug, so a very reliable indication of safety for needling is the objective sought with the prescribing of such drugs. A prophylactic prescription regimen is a safe needling situation whereas a treatment prescription regimen (i.e. established deep vein thrombosis or pulmonary thromboembolism) contra-indicates deep needling.

Lymphedema

Patients submitted to lymph node extraction or those presenting lymph node metastasis may develop lymphedema. These situations impair the normal lymph circulation slowing the drainage from limbs and the normal reaction to local infections. Limbs with lymphedema must not be needled and alternative points located elsewhere should be used to prevent local complications. Although a high quality pilot study (Cassileth et al. 2013) suggested that needling limbs with lymphedema is actually safe, this unfortunately has not been replicated so far and is still not considered mainstream practice (Fig. 1).

Tumor Sites and Bone Metastasis

Local needling is dangerous and must be avoided as tumors produce chaotic blood

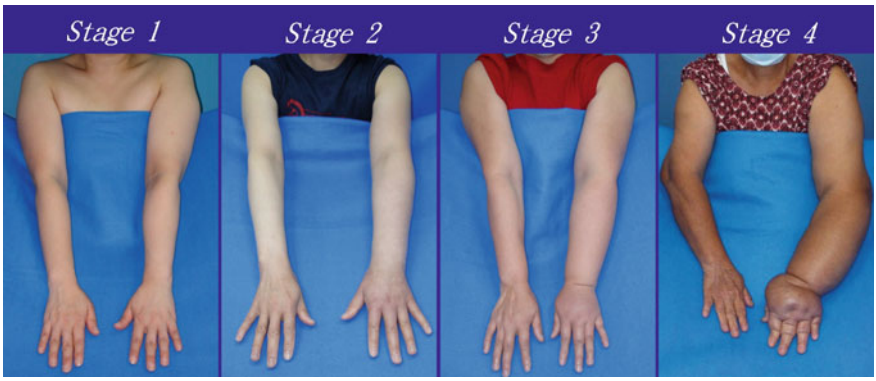

Fig. 1 Clinical stages of upper limb lymphedema—wikimedia images

Table 1 Contra-indications for needling

Neutropenia	Avoid needling with ANC below 1000 per mm3
Thrombocytopenia	Avoid needling with platelets count below 50.000 per mm3
Anticoagulation therapy or coagulation disorders	Avoid needling when patients are under a treatment prescription regimen or with a INR larger than 2.0
Lymphedema	Avoid needling limbs with lymphedema
Tumor sites and bone metastasis	Avoid needling sites with tumor formations
Prosthesis	Avoid needling sites with prosthesis

vessel formations. Bleeding may become uncontrollable and local infections may be difficult to treat.

Bone metastasis, especially to vertebrae may generate instability and local muscles can be tense in order to maintain stability, needling these local muscles may further increase the instability, risk of fractures and even medullar compression and therefore should be avoided.

There is even a possibility of local tumor spread induced by local needling as reported by a Taiwanese team from the Changhua Christian Hospital (Tseng et al. 2011) describing an event of post-acupuncture cutaneous spread of metastatic breast cancer after the puncture of a tender cervical mass that was probably deemed an "Ashi point" but, in reality, was a metastatic mass.

Prosthesis

Some patients present with metallic endoprosthesis due to bone metastasis that was removed or even due to fractures. These locations should not be needled once local infections would be very difficult to treat and could even need surgical intervention for removal of infected material (Table 1).

3 The Use of Acupuncture in Specific Side Effects of Usual Cancer Care

Nausea and Vomiting

Chemotherapy induced emesis (CIE) is one of the most acute distressing side-effects of cancer treatment, it can happen in up to 80% of patients with significant effects on quality of life and possible complications like metabolic derangements, dehydration, nutritional deficiency, esophageal tears and eventually may limit one's tolerance to comply with the chemotherapy regimen (Fernández-Ortega et al. 2012).

Although the use of plural antiemetic medication regimens have been able to reduce the incidence of vomiting, nausea remains as one of the most severe side effects experienced by those undergoing Chemotherapy (Coates et al. 1983).

A few risk factors for CIE have been identified, for example female sex and previous history of motion sickness (de Boer-Dennert et al. 1997), as well as characteristics related to the treatment regimen like dosage and frequency.

The major subtypes of CIE are:

- *Acute:* onset of nausea and vomiting within minutes to hours after administration of chemotherapy and resolving within 24 h
- *Delayed:* occurs 24 h or later after administration of chemotherapy
- *Anticipatory:* occurs before chemotherapy administration; thought to be an indicator of previous poor control of nausea and vomiting
- *Breakthrough/refractory:* nausea and vomiting that occur despite appropriate prophylaxis; requires the use of rescue medications.

Current medication available to control CIE includes ***5-HT$_3$ receptor antagonists*** (i.e. Ondansetron), ***NK$_1$ receptor antagonists*** (i.e. Aprepitant), ***Corticosteroids*** (i.e. Dexamethasone), ***Dopamine receptor antagonists*** (i.e. Metoclopramide) and eventually ***Benzodiazepines***, ***Olanzapine*** and more recently ***Cannabinoids.***

Acupuncture has been deemed useful for nausea and vomiting control for a long time now and in 1998, a National Institutes of Health consensus panel reported acupuncture was effective in controlling postoperative pain and chemotherapy-related nausea and vomiting (NIH Consensus Conference 1998). Despite being far from establishing itself as standard treatment, acupuncture for nausea/vomiting is a safe treatment that can relieve distress and may be an option for patients who do not achieve significant symptom control with medications listed above.

Of notice, **Electroacupuncture for Control of Myeloablative Chemotherapy-Induced Emesis: A Randomized Controlled Trial** (**Shen** 2000) is a high quality study with a low risk of bias that examined the antiemetic effects of electroacupuncture (EA) on breast cancer patients admitted to hospital wards that were receiving myeloablative chemotherapy.

The study consisted of 104 patients divided in 3 groups, all patients received the same triple pharmacological agents for emesis management, which included prochlorperazine, lorazepam and diphenhydramine hydrochloride. These medications were started 1 h prior to chemotherapy and were continued until 48 h after the last chemotherapy infusion. Rescue medications that were available to all patients included additional prochlorperazine, lorazepam, and diphenhydramine, as well as metoclopramide and droperidol.

The EA group (37 patients) received two sessions per day during 5 consecutive days, needles were placed on PC 6 and ST 36 with initial manipulation searching for DeQi, then the electrodes were connected (negative on PC 6 and positive on ST 36), Electrical frequency was delivered over 2–10 Hz, 0.5–0.7 ms duration pulse width, under a variable direct current output with square wave-form balanced alternating polarity of less than 26 mA for 20 min (Figs. 2 and 3).

Fig. 2 PC6

The "placebo" group (33 patients) received minimal needling meaning that the needles were placed subcutaneously and without stimulation near the sites of LU 7 and GB 34, electrodes were connected and the machine would generate the same audiovisual effects but no electrical stimulus during 20 min.

The Medication group (34 patients) only received the medication regimen described above.

The number of emesis episodes per person along the 5 days of intervention was counted and the median was 5 episodes for the EA group, 10 episodes for the Minimal Needling group and 15 episodes for the pharmacotherapy alone group.

Statistical analysis showed that the EA group had significantly fewer emesis episodes than the minimal needling group or the pharmacotherapy alone group. Also, the minimal needling group had significantly fewer emesis episodes than the pharmacotherapy alone group.

This stands as a very strong evidence of acupuncture value in post-chemotherapy nausea and vomiting prevention.

Fig. 3 ST36

4 Probable Mechanisms of Action—Nausea and Vomiting

The consensus points for treating nausea and vomiting are PC 6 and ST 36, although PC 6 neuroanatomical and specific molecular profile correlation to this perceived effect is unclear, some hypothesis have been formulated for the effectiveness of ST 36.

Cheng (2009) postulated that ST 36 needling may elicit a potent somato-autonomic reflex and thus modulate gastric activity once this has been shown by Sato and Schmidt (1987) and Sato (1997) where the stimulation of the muscles in the hindpaw of anaesthetised rats increased gastric vagal efferent nerve activity and increased gastric motility. To further establish this hypothesis, Cheng KJ present us the study (Wang et al. 2007) on the regulation of gastric activity by acupuncture at ST36 where the vagus nerve implication is clear once a bilateral vagotomy essentially abolishes the effect.

Somato-parasympathetic reflex is a possible mechanism of Nausea and Vomiting control effect. Needling would generate the somatic sensory stimulation that is conducted by the muscle afferent fibres to the medullary reflex center, and eventually the efferent parasympathetic nerves that innervate the stomach elicit the gastric response.

Hot Flashes

Hot Flashes (HFs), also referred to as Vasomotor symptoms are a sensation of heat flushing over the body surface, often accompanied by heart palpitations, spontaneous sweating, nausea, dizziness, mood and sleep disturbances. HFs usually happens a few times per day and night but some patients may present as many as hourly episodes lasting from 3 to 20 min. These symptoms may persist for years and can affect work, social activities, concentration, energy levels, and overall quality of life.

HFs are a common complaint among cancer patients specially those that underwent surgical castration and hormone therapy. Although quite frequent, 80% of women receiving Tamoxifen present those symptoms, only about 21% of the patients receive treatment for such ailment.

Despite the exact mechanism being unknown, It has been suggested that HFs due to hormonal changes may be related to a reduced concentration of b-endorphin in the hypothalamus, which leads to a drop in the set point of the thermoregulation center and increased release of calcitonin gene–related peptide, a potent vasodilator.

In general practice the usual care would be hormone replacement therapy but in the context of estrogen receptor–positive cancer this is not advisable and the options are narrowed to antidepressants and gabapentin which may present some relief but may also cause unpleasant side effects as nausea, drowsiness, dizziness, dry mouth, or headache.

Many cancer patients turn to integrative practices to help manage hot flashes and acupuncture is often prescribed.

The most recent systematic review of the use of acupuncture for the management of HFs in cancer patients (Garcia et al. 2015) identified 8 high quality RCTs. All studies showed significant within-group improvement from the baseline to the end of treatment for true acupuncture which is an important finding since spontaneous improvement is not likely once 50% of women with breast cancer report HFs lasting 10 years after menopause. Although the major concern regarding this particular review is the fact that none of the included trials presented a low Risk Of Bias preventing the achievement of definitive conclusions, the analyzed studies present some interesting strategies to treat this particular condition.

Characteristics of Studies Included

Psychological well-being improves in women with breast cancer after treatment with applied relaxation or electro-acupuncture for vasomotor symptom (**Nedstrand et al.** 2006).

Investigators used Electroacupuncture (EA) on a standard set of points for 30 min twice a week for 2 weeks then once a week for 10 more weeks.

EA	BL23 BL32	GV20	BL15	HT7	SP6	SP9	LR3	PC6

Actually EA was performed on BL23 and BL32 with 2 Hz, the other points were only manually stimulated.

The control group was submitted to weekly 60 min applied-relaxation sessions for 12 weeks.

This paper had a small number of subjects (n = 38) and performed a long period of follow-up (6 months) with vasomotor symptoms being recorded daily and mood and psychological well-being scales applied during follow-up visits.

Results showed no significant differences were between groups. Both showed a significant decrease in number of HFs/24 h as well as a significant psychological well-being increase from the baseline in both groups.

This paper suggests that both interventions may be of benefit and further investigations could contribute to develop such strategies.

Two modes of acupuncture as a treatment for hot flushes in men with prostate cancer—a prospective multicenter study with long-term follow-up (Frisk et al. 2009**).**

This paper opted to further investigate the same point selection described in the previous study but this time the comparison was between manual and electroacupuncture, besides the fact that this was a study conducted in men. Two groups were differentiated only regarding the presence or absence of electrostimulation on BL23 and BL32. Sessions happened twice a week for 2 weeks and then once a week for 10 more weeks.

The number of participants was once again small (n = 31) and as an improvement the outcomes also included a HF scale and dosing of Calcitonin gene-related peptide (CGRP) in the subjects 24 h urine samples besides the usual HF diaries.

Results showed that both groups attained significant reductions in number of HFs/24 h (74% for EA and 69% for Manual after 12 wk) as well as in the HF score (78% for EA and 73% for Manual after 12 wk).

Both EA and Manual acupuncture had a persistent significant effect over time maintaining effect up to 9 months after the start of treatment, CGRP urine measures did present a decrease but this was not statistically significant.

Although this paper lacks the presence of a placebo group on a non-treated group the authors claim that previous studies have shown that a placebo pill can contribute to a maximum of 20–30% decrease in the number of HF/24 h and wouldn't last longer than 3 months whereas they saw a greater reduction with a longer period of effect contributing to the notion that the placebo effect wasn't the main ingredient in this study.

Randomized, controlled trial of acupuncture for the treatment of hot flashes in breast cancer patients (Deng et al. 2007**).**

This study applied manual acupuncture on a standard set of points for 20 min twice a week for 4 weeks.

True acupuncture	GV14	GB20	BL13	PC7	HT6	KI7	ST36	SP6	Ear shenmen and sympathetic

The control group was submitted to "Sham Acupuncture" (SA) which consisted of nonpenetrating needles applied a few centimeters from TA points.

Again, the number of participants was restrained (n = 72) and this paper only analysed HF frequency as outcome.

Results showed that although no significant differences between groups were found, TA was associated with 0.8 fewer HFs/24 h than SA at week 6.

This paper raises the hypothesis that the acupuncture effect may have been be amplified had the treatment period been longer.

Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial (Hervik and Mjåland 2009**).**

The authors opted for manual acupuncture on a standard set of points for 20 min, twice a week for 5 weeks then once a week for 5 more weeks.

True acupuncture	CV4	LR3	GB20	LU7	KI3	SP6	PC7	LR8

Control group was submitted to SA with superficial needling in non-acupuncture points.

Outcomes included number of HF/24 h and the Kupperman index a well-validated health score, follow-up was conducted up to 12 weeks.

Results implied a significant decrease in daytime and nighttime HFs in favor of TA (50% daytime and 60% at night) over SA (25% daytime and no reduction at night) the same was seen in the Kupperman Index with the TA group presenting a 44% reduction after treatment and the SA group remaining unchanged. Also the follow-up showed that for the SA group the minimal effects where gradually reversed while the TA group maintained response.

Despite its small sample size (n = 59), this study provides a nice insight into the potential role of acupuncture for HF control in women with breast cancer, the authors suggest that a individualized prescription of points according to TCM diagnostics could provide a greater effect.

Reducing vasomotor symptoms with acupuncture in breast cancer patients treated with adjuvant tamoxifen: a randomized controlled trial (Liljegren et al. 2012**).**

This paper investigated manual acupuncture on a standard set of points for 20 min twice a week for 5 weeks.

Bilaterally	**SP6**	**KI7**		
Unilaterally	LI4	HT6	LR3	ST36

Control group with SA placing nonpenetrating needles on same meridian 1 cm from TA points.

Endpoints included HF frequency scale and circulating levels of estradiol, progesterone, testosterone, prolactin, follicle stimulating hormone (FSH), luteinising hormone (LH) and Sex hormone binding globulin (SHBG) measured before treatment and at 18 wk.

Both groups reported similar reductions in the HF scale but with significant between-group differences in favor of TA only for nighttime HFs. Also, the hormone levels remained unchanged.

Again, despite being the second largest study included in this review, the sample size remains modest (n = 84) and the question whether a more prolonged treatment regimen could provide better results is raised by the authors.

Acupuncture versus venlafaxine for the management of vasomotor symptoms in patients with hormone receptor-positive breast cancer: a randomized controlled trial (Walker et al. 2010**).**

The authors opted to use a tailored approach comprised of manual acupuncture on some core set of points plus points selected according to Traditional Chinese Medicine (TCM) theory, 30 min sessions twice a week for 4 weeks and then 8 weekly sessions.

Core points	BL23	KI3	SP6						
Tailored points	GV14	GV20	GB20	LU9	LR3	ST36	CV6	PC7	HT7

Control group was medicated with Venlafaxine at 37.5 mg taken orally at bedtime for 1 wk followed by 75 mg at bedtime for 11 wk and follow-up was undertaken for 1 year.

Results showed that TA was as effective as venlafaxine and by 2 weeks after treatment, the venlafaxine group experienced significant increases in HFs, whereas HFs in the TA group remained low. The venlafaxine group experienced 18 occurrences of adverse effects (nausea, dry mouth, dizziness, and anxiety), whereas no adverse effects were reported in the TA group.

Albeit small in sample size (n = 50) this paper raises the opportunity to further encourage the use of this complementary treatment in face of the most common adopted pharmacological regimen.

Acupuncture relieves menopausal discomfort in breast cancer patients: A prospective, double blinded, randomized study (Bokmand and Flyger 2013**).**

This paper still remains with a modest sample size (n = 94) but in comparison to the previous studies attains an important improvement for the statistical analysis and investigates manual acupuncture on a standard set of points, with 15–20 min weekly sessions for 5 weeks only.

TA bilaterally	HT6	KI3	SP6	LR3

The control group received SA on bilateral nonacupuncture points with superficial insertion. Also there was a third arm comprised of no acupuncture (Fig. 4).

The primary outcome was deemed “HF distress” on a visual analog scale (VAS) marked as a 0–10 logbook, also, plasma estradiol was measured right before and 30 min after the first treatment as well as at week 5. Follow-up was conducted up to 12 weeks (Fig. 5).

TA group showed better results for HF distress compared to SA or no acupuncture groups is this study. The TA group started to show improvements right after the second acupuncture session, which remained significant until the 12 wk follow-up. The estradiol plasma levels remained unchanged thus eliminating safety issues

Fig. 4 KI 3

Fig. 5 SP 6

regarding the possibility of greater occurrence of breast cancer relapse related to acupuncture.

Conclusions
In light of the current published data and above mentioned strategies of treatment, to this author, seems like the use of a core set of points with Kidney and Qi enhancing properties allied with Heart and Liver harmonization points should be combined with a tailored selection of acupoints according to the patient's most disturbing symptoms (i.e. night sweating, anxiety, mood and sleep disturbances, and so on) in order to provide the best possible acupuncture effect when controlling HFs.

5 Probable Mechanisms of Action—Hot Flashes

A hot flash frequently occurs in menopause and can be exacerbated by premature ovarian failure or estrogen deprivation resulting from cancer therapies.

The flashes in women are probably initiated by a sudden downward shift in the set point for the core body temperature in the thermoregulatory center, which seems to be affected by sex steroids and beta-endorphins.

Vasomotor symptoms have been shown to correlate with the decrease in estrogen production during the menopausal transition and with testosterone decreases after castration therapy in men with prostate cancer.

Also, Serum levels of serotonin are lower in postmenopausal women that associated with the reduced *beta*-endorphin concentrations could increase the release of noradrenaline causing sudden drops in the temperature set point in the hypothalamus eliciting inappropriate heat loss.

Acupuncture possibly modulates serotonin and noradrenalin activity in the central nervous system influencing the thermoregulatory center.

Calcitonin gene-related peptide (CGRP) is a potent vasodilator, and may be a proxy for beta-endorphin activity. Wyon et al. (2000) showed that plasma concentration of CGRP and neuropeptide Y (NPY) increases during a hot flush, and the urine excretion of CGRP seems to be reduced parallel to the reduction of hot flushes after acupuncture treatment.

In conclusion, acupuncture affects the beta-endorphin levels and also affects serotonin and noradrenalin activity in the central nervous system, besides that, a possible direct effect on regulating the release of CGRP could mediate the symptoms control seen in recent trials.

Aromatase Inhibitor Arthralgia
Breast cancer tissue has been shown to produce higher levels of estrogen, which then induces growth of breast cancer cells both in pre and post-menopausal women. Since aromatase plays a major role by catalyzing the final and rate-limiting step in estrogen biosynthesis, aromatase inhibitors (AIs) are used as first-line adjuvant therapy in post-menopausal women with hormone receptor-positive breast cancer.

When compared with Tamoxifen, which is a selective estrogen receptor modulator and unfortunately increases the risk of endometrial cancer and thromboembolism, AIs present with a less severe myriad of adverse events like hot flashes, vaginal dryness and headaches. However, 28–47% of patients receiving AIs experience musculoskeletal disorders and 5–25% of them discontinue therapy due to adverse effects.

To this date the exact etiology of these musculoskeletal symptoms is not well understood and this probably is what prevents an excellent management to be developed. Acupuncture has been shown to effectively increase the rate of musculoskeletal pain control (Vickers et al. 2012) and several trials have tested this treatment modality in breast cancer patients experiencing AIs related arthralgia.

The first systematic review of such trials (Chien et al. 2015) identified 5 high quality studies, 3 of them present favorable effects while the other 2 do not, meta-analysis of the results shows no statistically significant effects when compared with sham acupuncture.

A few points are worth mentioning when analyzing this review, the studies included looked for a possible downregulating effect of acupuncture on the inflammatory status of the participants by measuring pro-inflammatory cytokines like IL and TNF-alpha in blood samples, the exact molecules analyzed as well as the measurement methods were not consistent, also, as noted before, the role of inflammation in this particular entity has not been fully clarified. Moreover, the treatments chosen were also not consistent with point selection varying greatly between studies. Finally, most of the included trials applied questionnaires of self-reported outcomes for end-point measurements. While the used instruments are valid and consistent they would better reflect an accurate measurement if more patients and treatment centers were included since these are inherent subjective.

Characteristics of Studies Included

Acupuncture for treatment of arthralgia secondary to aromatase inhibitor therapy in women with early breast cancer: pilot study (Oh et al. 2013).

This study was a small pilot study with 32 subjects divided in two groups, one where the subjects received real EA and another where they received SA

EA:

Day 1	LI4	LI11	GB34	ST40	LR3	GV20	Shishencong	Baxie
Day 2	GB21	TE5	ST36	SP6	LR3	GV20	Shishencong	Baxie

SA was performed with non-penetrating needles (Streitberger placebo needle) at the actual acupoints and the EA device was set to produce the same audiovisual stimuli as in the EA group but with no actual electrical current.

Patients received sessions 2 days a week for 6 consecutive weeks.

Outcomes were measured with 3 scales, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Brief Pain Inventory Short Form (BPI-SF) and Functional Assessment of Cancer Therapy-General (FACT-G). Also there was a handgrip strength test and serum dosage of C reactive protein and erythrocyte sedimentation rate.

Follow-up was conducted until 12 weeks.

Investigators were unable to identify any significant changes in the markers selected for this study although they do point a "trend" of better outcomes at week 12 for stiffness, physical function and total WOMAC and inflammatory markers at week 6.

A dual-center randomized controlled double blind trial assessing the effect of acupuncture in reducing musculoskeletal symptoms in breast cancer patients taking aromatase inhibitors (Bao et al. 2013**).**

This study utilized yet another set of acupoints:

CV4	CV6	CV12	LI4	PC6	GB34	ST36	KI3	BL65

SA was performed with non-penetrating needles placed away from real acuponits.

This protocol was undertaken once a week for 8 weeks and follow-up was performed for 12 weeks.

Outcome measures were differences in change in Health Assessment Questionnaire Disability Index (HAQ-DI) and pain VAS scores from baseline, also there was an attempt to find valid biomarkers with the measurement of plasmatic concentrations of estrogen, cytokine profile and beta-endorphin.

Again, the number of participants was low (n = 51) with 4 dropouts, remaining 47 for the analysis. Both groups presented improved function but there was no statistical difference between groups.

Estradiol remained indetectable, result consistent with other protocol that investigated acupuncture for hot flashes (Bokmand and Flyger 2013). Interestingly the cytokine profile showed a significant reduction of IL-17 in both groups (IL-17 is a pro-inflammatory cytokine that has been linked to severity of rheumatoid arthritis and psoriasis) raising the hypothesis of clinical improvement through IL-17 modulation.

Pilot study of acupuncture for the treatment of joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients (Crew et al. 2007**) and Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer (Crew et al.** 2010**).**

This protocol opted for a combination of core body acupuncture points combined with core auricular acupuncture points plus a tailored set depending on the most symptomatic joint:

Body	TA5	GB41	GB34	LI4	ST41	KI3
Auricular	Shen men	Kidney	Liver	Upper lung	Sympathetic	
Shoulder	LI15	TA14	SI10			
Wrist	TA4	LI5				
Fingers	TA5	SI3	Baxie	LI3		
Lumbar	GV3	GV8	BL23			
Hip	GB30	GB39				
Knee	SP9	SP10	ST34			

SA consisted of superficial needling in non-acupoint sites

Sessions lasted for 30 min twice weekly over 6 weeks.

Outcome measures included Brief Pain Inventory Short Form (BPI-SF), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Modified Score for the Assessment of Chronic Rheumatoid Affections of the Hands (M-SACRAH) and the Functional Assessment of Cancer Therapy-General (FACT-G) at baseline, 3 and 6 weeks.

This study also had a small sample size (n = 51) with 38 subjects evaluated and results showed improvement in joint pain, stiffness, functional ability and physical well-being in the True Acupuncture group and no significant benefits on the SA group, this poor response to the placebo intervention may have been caused by insufficient blinding of subjects to their treatment assignment once 43% of patients in the SA group correctly guessed that they were on the control group.

A randomised trial of electro-acupuncture for arthralgia related to aromatase inhibitor use (Mao et al. 2014).

On this protocol, the investigators decided to use a tailored set of points depending on the most painful joints and at least four distant points were used to address constitutional symptoms such as depression/anxiety and fatigue. Also, the EA was according to the symptoms with two pairs of electrodes at the needles adjacent to the painful joint with 2 Hz stimulation. Sessions happened twice weekly for 2 weeks, then weekly for 6 more weeks (Table 2).

There were two other control groups, one was a wait list control group (WLC) and a SA group with the sham procedure performed with non-penetrating needles (Streitberger device) at non-acupoints and the EA device would be on a different channel than the ones connected to the needles.

Measures included the Brief Pain Inventory (Mendoza et al. 1999) with the change in pain severity score at week 8 of intervention compared to the baseline between EA and WLC as primary outcome, secondary outcomes included Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Quick Disability of Arm, Shoulder, Hand scale (DASH) and the Physical Performance Test (PPT). Follow-up was completed at 12 weeks.

This study attempted a larger sample size with 159 patients screened for eligibility and 67 actually evaluated.

Results showed that the EA group had a significant greater decrease in the BPI severity score than the WLC at week 8. The EA group also had a statistically significant greater reduction in pain related interference score compared to the WLC group. Compared to baseline, the EA group experienced a 43.1% reduction in pain severity and a 52.6% reduction in pain-related interference at the end of the intervention period, results that remained significant at week 12.

Despite the impressive results, this study failed to find significant differences between EA and SA groups which could be explained by the somewhat small sample size, underpowered to difference between those groups. Also the authors suggest that maybe the follow-up period was to short to adequately find long-term potential separation of effects and complement raising the issue that maybe the non-penetrating needles are not as inert as a placebo procedure should.

Table 2 Points selected

Joint pain location		Acupuncture points				
Shoulder	Jianyu	Jianliao	Jianzhen	Naoshu		
	(LI 15)	(TA 14)	(SI 9)	(SI 10)		
Scapula	Tianzong	Bingfeng	Jianwaishu	Gaohuangshu		
	(SI 11)	(SI 12)	(TA 14)	(BL 43)		
Elbow	Quchi	Chize	Tianjing	Waiguan	Hegu	
	(LI 11)	(LU 5)	(TA 10)	(TA 5)	(LI 4)	
Hand/finger	Houxi	Sanjian	Baxie			
	(SI 3)	(LI 3)	(Extra)			
Hip	Huantiao	Yinmen	Juliao			
	(GB 30)	(BL 37)	(GB 29)			
Knee	Lianqiu	Dubi	Ne Xian	Yanlingquan	Xiangguan	Yinlingquan
	(ST 34)	(ST 35)	(Extra)	(GB 34)	(GB 35)	(SP 9)
Leg	Chengshan	Feiyang				
	(BL 57)	(BL 58)				
Ankle	Jiexi	Shangqui	Quixu	Kunlun	Taixi	
	(ST 41)	(SP 5)	(GB 40)	(BL 60)	(KI 3)	
Foot/toe	Gongsun	Shugu	Bafeng			
	(SP 4)	(BL 65)	(Extra)			
General symptoms						
General aching	Houxi	Shenmai	Dabao	Geshu	Yinlingquan	
	(SI 3)	(BL 62)	(SP 21)	(BL 17)	(SP 9)	
Generalized anxiety	Neiguan	Taixi				
	(PC 6)	(LR 3)				
Generalized fatigue	Sanxinjiao	ZusanLi				
	(SP 6)	(ST 36)				

Modified from (Mao et al. 2014) appendix to suite World Health Organization Nomenclature

6 Probable Mechanisms of Action—Aromatase-Inhibitor Arthralgia

Aromatase-inhibitor Arthralgia pathophysiology is unknown, estrogen deprivation has been temporally associated with this condition (Mao et al. 2011). Possibly, estrogen deprivation would decrease the generation of endogenous opioids, thereby leading to a lowered pain threshold. Mao J. J. then conducted an RCT (Mao et al. 2014)

testing the hypothesis that Electroacupuncture (EA) would be able to restore the normal pain threshold since EA animal research demonstrated its clear physiological effect on the endogenous opioid system. This study revealed a significant effect when compared EA x usual care but failed to find differences between EA and Sham as reported earlier in this chapter.

Another possible mechanism would be the acupuncture effect on modulating the pro-inflammatory cytokines such as IL and TNF-alpha and, as previously mentioned, this was tested by a few investigators with Bao et al. (2013) being able to identify a reduction of IL-17 and a trend toward greater reduction in TNF-alpha ($p = 0.095$). This is very encouraging and future trials should focus on such analysis to reinforce the current evidence.

Cancer Related Fatigue

Fatigue is a subjective sensation of tiredness or even exhaustion that encompasses physical, psychological, emotional and cognitive activities and is not proportional to recent activities neither can be mitigated by adequate rest.

Cancer Related Fatigue is the most prevalent symptom of cancer patients being reported in up to 40% of individuals at diagnosis, 90% of those treated with radiation, and 80% of those under chemotherapy treatment (Hofman et al. 2007). It may start during treatment and increase in a cumulative manner, it may diminish when treatment is halted but some patients refer that it may last for years after cancer treatment is done.

This condition is often underreported, sometimes because patients feel that it is a standard condition of being sick, other times because survivors fear that it can indicate that the disease is relapsing and refrain from mentioning it so that the treatment and screening procedures won't be re-started and also many doctors don't actually investigate its presence since there is not much that can be offered for its treatment.

Nevertheless some treatable comorbidities may contribute to Cancer Related Fatigue (CRF) intensity like anemia, depression, anxiety, decreased ability to ingest food (nausea, vomiting, xerostomia), dyspnea and pain and must be addressed for optimal clinical management.

Treatment possibilities are antidepressants, mild psycho-stimulants, corticosteroids and erythropoietin. Non-pharmacological options includes diverse mind-body therapies and exercise. Although it may sound illogical to spend a fatigued one's energy with exercise, a good body of evidence shows that it actually increases the well-being of patients suffering from cancer related fatigue (Kuchinski et al. 2009).

Acupuncture treatment for this condition has been tested since many patients turn to complementary medicine for symptoms that mainstream medicine can't provide much relief.

A few RCTs have been conducted but once again the results have been mixed, as were the treatment protocols.

Acupuncture for cancer-related fatigue in patients with breast cancer: A pragmatic randomized controlled trial (Molassiotis et al. 2012**)** presents the largest RCT focused on investigating the benefits of acupuncture in CRF to date.

It included 302 individuals with breast cancer randomly assigned to usual care (75) and to acupuncture plus usual care (227) (assignment of 1:3 respectively). This unusual disbalance between group sizes was justified due to a second phase in the study **A randomized, controlled trial of acupuncture self-needling as maintenance therapy for cancer-related fatigue after therapist-delivered acupuncture (Molassiotis et al.** 2013**)** where maintenance was done through self needling and acupressure. Statistical analyses deemed this a feasible design capable of detecting a 2-point change in scores. The primary outcome measure was the difference in general fatigue, as self-reported by patients with the baseline Multidimensional Fatigue Inventory (MFI) at 6 weeks (treatment completion). The MFI is a brief 20-item well-validated scale measuring general fatigue and the dimensions of physical and mental fatigue, activity, and motivation.

The acupuncture procedure per se consisted of weekly sessions of 20 min with manual acupuncture on standard points (LI 4, SP 6, ST 36) plus tailored points according to the acupuncturist's discretion, no manipulation was allowed once the needles were placed. This was a multi-center study and involved 12 different practitioners. The results were significant and showed an impressive magnitude of effect ($P < 0.001$ and -3.11 from baseline score).

The main concern regarding this study was the lack of a placebo group plus the fact that the patients were not blinded to the group allocation. Since the main outcome was patient reported, this lack of concealment generates a high risk of bias jeopardizing the study findings.

There have been two other RCTs that were conducted recently and exhibited relatively high methodological quality.

Acupuncture for the treatment of post-chemotherapy chronic fatigue: A randomized, blinded, sham-controlled trial (Deng et al. 2013**)** compared manual acupuncture in standard points (CV 6, CV 4, KI 3, SP 6, ST 36, LI 11, HT 6 and auricular point "anti-depression") with weekly sessions of 20 min for 6 weeks against Sham acupuncture with placebo needles placed a few millimeters away from true acupuncture points and meridians. The blinding was adequate and the main outcome was measured by the Brief Fatigue Inventory (BFI) (Mendoza et al. 1999). 74 patients were evaluated for the primary end-point (34 in the acupuncture group and 40 in the Sham acupuncture group), follow-up was attempted at 6 months after intervention but there was a huge loss of patients in this phase. Although there was a slight improvement in the questionnaires applied, this was not statistically significant and neither was the difference between groups. The conclusion of this study was that the treatment provided did not alleviate Post-chemotherapy Chronic Fatigue, the authors remark that the study was limited by the number of patients lost to follow-up and also that they cannot exclude the possibility that a more intensive treatment regimen may be more effective.

The effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer: a pilot randomised controlled trial (Smith et al. 2013**)** also attempted a randomized sham-controlled trial using sham acupuncture needles but this was a much smaller study since it was deemed a pilot study with 30 patients, 10 in the acupuncture group, 10 in the sham acupuncture group and 10

on wait list group. The intervention consisted of needling KI 3, KI 27, SP 6, ST 36, CV 4 and CV 6 plus tailored points at the acupuncturist's discretion (maximum of 3 extra points), 20 min sessions with manual stimulation twice during this time, twice weekly session during the first 3 weeks and 3 more weeks with one weekly session (total of 9 sessions in 6 weeks). 3 questionnaires were used to measure the outcomes, one specific to fatigue, the BFI previously mentioned, plus two for general well-being, the Wellbeing questionnaire (W-BQ12) (Bradley 1994) and Measure Yourself Concerns and Wellbeing questionnaire (MYCaW) (Paterson et al. 2007). This feasibility study conclusions were deemed positive but the questionnaires findings only showed significant differences between groups at week 2 for the BFI (with loss of this difference in weeks 4 and 6), and for MYCaW at week 6. Once again, the indication that a more intense acupuncture treatment (i.e. 2 or more times a week) would be of greater effect was implied.

7 Probable Mechanisms of Action—Fatigue

The pathological mechanism of Chronic Fatigue Syndrome is still uncertain, major findings reported in Tang et al. (2015) include cerebral blood flow reduced in some brain regions, ventricular cerebrospinal fluid lactate and corticosteroid alterations combined with enhanced feedback of the hypothalamic-pituitary-adrenal (HPA) axis, as well as brain-derived neurotrophic factor (BDNF), serotonin and brain cytokines system distress.

Although there are various findings, none of them can explain the mechanism and clinical symptoms in this entity as well as in Cancer Related Fatigue and so far no specific mechanism of acupuncture action in this scenario has been minimally suggested.

Xerostomia

Xerostomia or dry mouth is a subjective feeling often associated to insufficient production of saliva to keep the mouth moist. This condition may present a myriad of discomfort encompassing difficult chewing, swallowing, tasting and talking, oral cavity ulcers or cracks, tooth decay, halitosis as well as make it difficult to wear dentures.

Radiation therapy to the head and neck as well as certain types of Chemotherapy, may cause damage to the salivary gland impairing its production of normal saliva. Chemotherapy generates xerostomia by making saliva thicker, which is an often reversible condition months after the treatment stops. Local radiation may destroy salivary glands diminishing it's saliva output, some patients experience a normalization within the first year after radiotherapy but some may present xerostomia as a permanent condition.

Some medications commonly used by cancer patients such as antidepressants, muscle relaxants, diuretics and opioids may contribute to the dry mouth feeling and

plausible alternatives must be considered when treating a patient with a severe case of xerostomia.

Usual management includes saliva substitutes also known as artificial saliva and mouth rinses with hyetellose, hyprolose or carmellose, physical methods to induce saliva production like chewing non-sugary gums, candy or even ice pellets. Medications that increase saliva output as pilocarpine and cevimeline are also an option but these may present some limiting side-effects, mostly systemic anti-cholinergic effects like nausea, dizziness, weakness, bladder dysfunction, rhinitis, headache, flushing, chills, and diaphoresis.

Acupuncture has been used in the management of radiation-induced xerostomia and a few trials have produced encouraging results both in the treatment and prevention of this condition.

Xerostomia Prevention

Randomized controlled trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma (Meng et al. 2012) is a very wise trial testing the use of acupuncture for prevention of xerostomia on patients undergoing radiotherapy compared with usual oral-hygiene care. The patients undergoing the acupuncture intervention (n = 40) were needled 3 times per week during the 7 week radiation period with a six-months follow-up, the points chosen were

Body	CV24	LU7	KI6	LI4
Auricular	Shenmen	Point zero	Salivary gland 2'	Larynx

Except for CV 24 located in the midline, all points were treated bilaterally with the session lasting for 20 min. Subjects in the control group (n = 46) were under standard oral care, with no special education regarding prevention of xerostomia (Fig. 6).

The outcome measures selected were two specific questionnaires regarding Xerostomia and Head and Neck symptoms as well as salivary flow both spontaneous and induced (Fig. 7).

By week 3 of treatment the difference between the study groups began to be significant both on the questionnaires and on the induced salivary flow measurement, this difference reach it's peak by week 7 and remained significant until 6 months after the end of radiotherapy suggesting that acupuncture is a valid resource for radiotherapy induced xerostomia prevention (Fig. 8).

Treatment

Few papers examined the effectiveness of xerostomia treatment with acupuncture, of notice **Functional magnetic resonance imaging (fMRI) changes and saliva production associated with acupuncture at LI-2 acupuncture point: a randomized controlled study (Deng et al.** 2008), have shown that salivary flow can be increased by needling LI 2 in healthy subjects and a recent literature review (Zhuang et al. 2012) identified 3 other studies of high quality methodology that are worth mentioning:

Fig. 6 LI 4

Fig. 7 KI 6

Fig. 8 CV 24 and ear points

Acupuncture treatment of patients with radiation-induced xerostomia (Blom et al. 1996**)** this protocol included 38 subjects with 20 in the experimental group treated with classical acupuncture plus 18 in the control group with superficial acupuncture as placebo and treated patients twice a week for 12 weeks. The points chosen were diverse varying from 5 to 8 local and distal points (ST 3, ST 6, ST 5, GV 20, ST 7, SI 17, LI 18, PC 6, HT 7, ST 36, LR 3, LI 11, LI 10, LI 4, SI 3, SP 8, SP 3, SP 6, KI 7, KI 3, KI 5); 2 to 4 auricular points (Shenmen, Kidney Mouth, Stomach, Gl. Parotis, Sympathetic, Subcortex).

The outcomes were patient reported alleviation of symptoms and improvement in quality of life. Although salivary flow rates increased within group, this study failed to find a statistically significant difference between groups.

Manual acupuncture improved quality of life in cancer patients with radiation-induced xerostomia (Cho et al. 2008**)** this protocol was designed for a shorter period of treatment needling patients twice a week for 3 weeks on 5–8 local and distal points (ST 6, ST 36, LI 4, SP 6) and compared them to a group submitted to sham needling with the Streitberger device. This study had an extremely reduced sample size (n = 12) but questionnaire addressing problems in communicating, eating, sleeping, and daily functions showed positive results for the acupuncture group encouraging further investigations.

Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial (Pfister et al. 2010**)** larger in size (n = 58), also opted for a shorter period of treatment consisted of once a week for 4 weeks with needling on standard distal points (LI 4, SP 6, GV 20) and auricular shenman, plus various customized points and compared this group with a group submitted to "usual care". The main outcome was not the xerostomia but Xerostomia Inventory was the secondary outcome measurement chosen and it showed a significant improvement in the intervention group.

Nevertheless this particular review (Zhuang et al. 2012) considered that the potential bias and great variation between study protocols prevented them to "positively identify the therapeutic effect of acupuncture for radiation-induced xerostomia". They consider that the xerostomia should be analysed as being a yin deficiency syndrome specially stomach and kidney yin according to TCM as well as the radiation pathogenic factor as toxic heat and in being so they suggest the following treatment regimen:

- Local points: ST 4, ST 6, ST 7, CV 23, CV 24;
- Distal points: LI 2, LI 4, LI 11, PC 6, LU 7, ST 36, KI 3, KI 5, KI 6, SP 6, LR 3;
- Auricular points: Shenmen, Point zero, Salivary gland.

8 Probable Mechanisms of Action—Xerostomia

Possible mechanisms of action have been identified in this particular setting, (Deng et al. 2008) fMRI study showed central nervous system imaging changes (activation

of the insula and adjacent operculi) during acupuncture at LI2 with consequent saliva production. Also it is suggested that autonomic changes induced by needle manipulation inducing specific de-qi sensations might be mediated through the central nervous system.

Also the release of neuropeptides that stimulate the salivary glands and increase blood flow like CGRP (afore mentioned) and vasoactive intestinal polypeptide has been shown by Dawidson et al. (1997, 1998) in the saliva of xerostomia patients submitted to acupuncture.

These findings indicate that a central nervous system activation inducing saliva production together with a local increment of vasodilator and salivation stimulator peptides would be a plausible mechanism of Xerostomia mitigation by acupuncture.

Chemotherapy Induced Peripheral Neuropathy

Chemotherapy induced peripheral neuropathy (CIPN) is a common side effect resulting from nerve damage after exposure to certain Chemotherapy agents such as platinum compounds, taxanes, vinca alkaloids and also to newer agents such as bortezomib and thalidomide.

The clinical presentation may consist of a diverse array of symptoms such as persistent loss of feeling perceived as numbness or less ability to sense pressure and temperature, pain that may be constant or intermittent with characteristics of shooting or stabbing pain, burning, tingling or electric-shock like. This may impair manual abilities and increase the odds of stumbling or tripping while walking. Severe cases may present difficult swallowing, constipation, urinary retention and blood pressure changes. Usually the symptoms start farthest away from the head and tend to move closer over time, in most cases the changes will begin in the feet then later on in the hands. Some patients have symptoms that last for a short period of time but the symptoms may also persist for a long time and some patients refer that it never actually goes away.

Trials for prevention of CIPN with Vitamin E, Calcium and magnesium, antidepressants, anti-seizure drugs and glutathione have yield mixed results and more studies are needed to provide any conclusion, strategies like reduced chemotherapy doses, longer periods of infusion and fractioned doses may be tried in order to reduce the risk of CIPN.

Acupuncture has been tested in the treatment of CIPN in various trials with different point combinations in order to address the most bothersome symptoms.

A recent review (Brami et al. 2015) identified 4 recent high quality trials:

Chemotherapy-induced peripheral neuropathy in cancer patients: a four-arm randomized trial on the effectiveness of electroacupuncture (Rostock et al. 2013) compared EA versus hydroelectric bath, daily vitamin B, or daily placebo capsules in 60 patients over a 3 weeks, with additional follow-up at 12 weeks. Points chosen were:

LR3	SP9	GB41	GB34	LI4	LI11	SI3	HT3

EA was applied with 50 Hz during 15 min consisting of a combination of rectangular currents and high amplitude waves. This study had a major fall back due

to baseline symptoms being far less intense than expected and significant changes between groups were not found.

Acupuncture for chemotherapy-induced peripheral neuropathy (CIPN): A pilot study using neurography (Schroeder et al. 2012), compared acupuncture for 10 weeks plus best medical care (BMC) vs. BMC only in patients with various cancer types and chemotherapy regimens. Intervention patients received a standard 10-week treatment on:

ST34	EX-LE 12 (at the tip of the toes)	EX-LE 8 (at the web of the toes)

Needles were inserted bilaterally for 20 min. Nerve conduction studies were used to evaluate possible changes and a ±2 m/s change in sural nerve conduction velocity (NCV) from initial assessments was considered significant. Although small in sample size, five out of six patients treated with acupuncture showed a significant mean NCV improvement after 6 months.

A Pilot Study of Acupuncture in Treating Bortezomib-Induced Peripheral Neuropathy in Patients With Multiple Myeloma (Bao et al. 2014) with 27 multiple myeloma patients with moderate to severe bortezomib-induced peripheral neuropathy were submitted to 10 weeks of manual acupuncture beginning with twice a week for 2 weeks, followed by once a week for four weeks and then once every other

Fig. 9 Bafeng (EX-LE 8)

week for 4 more weeks. The points selected were bilateral ear points (shen men, point zero, and 2 additional auricular acupuncture points where electrodermal signal was detected), bilateral body acupuncture points LI 4, TA 5, LI 11, ST 40, and Ba Feng, the subjects experienced significantly reduced neuropathic pain and improved functions measured by specific questionnaires but cytokines analyses showed no significant changes, nerve conduction velocity studies did provide changes but these were not correlated to the subjective changes perceived by the patients (Fig. 9).

Electroacupuncture for thalidomide/bortezomib-induced peripheral neuropathy in multiple myeloma: a feasibility study (Garcia et al. 2014) demonstrated that EA was safe and possibly effective in treating thalidomide/bortezomib-induced peripheral neuropathy in 19 multiple myeloma patients with significant improvements in questionnaire scores and objective timed function tests such as fall risk, walk, postural stability, button and coin tests. The acupuncture treatment consisted of needling LI 4, SI 3, Baxie 2, Baxie 3, LR 3, SP 6, GB 42, ST 36, Bafeng 2, Bafeng 3, GV 20, CV4, and CV6, electrical stimulation was applied bilaterally as follows: from LI 4 (negative) to SI 3 (positive) and from LR 3 (negative) to GB 42 (positive) at 2–100 Hz for 20 min over a 9-week period of 20 acupuncture sessions at 2–3 times weekly (Fig. 10).

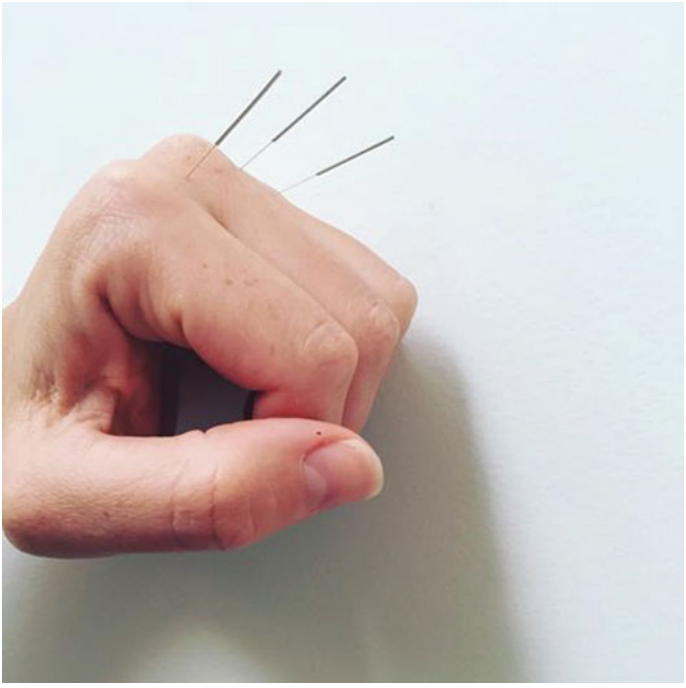

Fig. 10 Baxie

To this point, some high quality trials have yielded positive results in patient reported outcomes and even on neuronal conductions studies, but the accumulated body of evidence is still far from ideal to reach any definitive conclusion.

9 Probable Mechanisms of Action—Chemotherapy Induced Peripheral Neuropathy (CIPN)

The exact pathophysiology of CIPN is unclear. It generally is regarded as a consequence of the disruption of axoplasmic microtubule mediated transport, distal axonal degeneration, mitochondrial damage and direct damage to the sensory nerve cell bodies of the dorsal root ganglia (DRG) as described by Podratz et al. (2012). The DRG neurons seem to lack a vascular barrier, being more exposed to the neurotoxic effects of chemotherapy.

A few experimental models have yielded possible mechanisms through which acupuncture could affect the pain threshold and overall sensibility in CIPN.

Kim et al. (2004) demonstrated that Electroacupuncture (EA) acts through mu and delta but not kappa opioid receptors in mechanical allodynia and Sun et al. (2005) reported that cold allodynia can be reduced in rats treated with EA through the mediation of spinal alfa2-adrenergic receptors. Lau et al. (2008) investigated the role of EA on COX2 in rat spinal cord after spinal nerve ligation showing its action of downregulating COX2 expression. Somers and Clemente (2009) applied EA at the ST 36, which reduced the mechanical allodynia in a neuropathic model and normalized the expression profile of hypothalamic proteins identified as being involved in inflammatory processes, metabolism and signal transduction. Ko et al. (2002) examined such mechanisms of acupuncture in yet another model in rats at the molecular level by cDNA microarray analysis and found an increased expression of 68 genes which in turn could be returned to normal after treatment with EA. Such genes were involved in signal translation, gene expression, and nociceptive pathways. The same study also found a 50% decrease in the expression of the sigma opioid receptor in the neuropathic pain model, which also returned to normal after acupuncture.

The above mentioned findings correlate to the poor clinical response of neuropathic pain to opioids seen in practice, and the analgesic action of acupuncture in neuropathic pain could be that of normalizing the opioid receptor expression while increasing the release of endogenous opioid peptides.

10 Concluding Remarks

Acupuncture use within the oncological patient setting is a very promising therapeutic approach for symptom control especially for cancer survivors that endure lasting sequelae from aggressive treatment and disease.

To this date, high quality acupuncture research has been limited to a few centers of excellence and even though it is difficult to find protocols that have been re-tested in order to increase the level of evidence accumulated so far.

It is important that future research use the published experiences in order to avoid primary mistakes when designing a new trial and take notice of the plausible mechanisms of action so that more specific outcome measurement can be undertaken.

Future perspectives indicate further study in acupuncture regulation of pro-inflammatory cytokines, vasodilator peptides and the correlation between the endogenous opioid system and the serotonin-noradrenalin equilibrium.

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Electrotherapy-An Old Technique for a New Use

Shu-Ming Wang

Abstract Electricity has been integrated into medical practice primary for pain relief since it was first discovered in western medical community. Later, electrical stimulation has been utilized as one of acupuncture treatment interventions. Multiple theories have been proposed as the underlying mechanism of electroanalgesia including the release of neurotransmitters. As electroacupuncture stimulations can be easily replicated in clinical setting, it has found not only providing the analgesic effects but also effective in treating clinical pathological conditions. Recently, electroacupuncture stimulations have been found to provide organ protections from perioperative period to ischemic-reperfusion other major organs protections. Electrotherapy has evolved throughout the history and more beneficial effects been explored.

Keywords Electrotherapy · Medical treatment · Electroanalgesia · Electroacupuncture · Pain and organ protection

1 History

1.1 The Evolution of Electricity for Medical Treatment

Electricity was described as early as 2750 BC in Egyptian papyrus that Nile catfish could stop both the hunter and the hunted at a distance by stunning them into submission (Finger and Piccolino 2011). In their tombstone, catfish was prominent placed in the painting as a symbols of power and this "stunning" power emitted by catfish was also used as a treatment for arthritic pain (Kellaway 1946). Later, Aristotle (the Greek philosopher) also documented the numbing effect of the fish Närke (another fish also able to deliver painful and paralyzing shock), catfish and/or torpedo ray fish that was used to treat headache and gout (Macdonald 1993). In spite of these early

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documentations, electricity was not routinely used to treat medical problems until AD 47 (Largus 1529).

Scribonius Largus, a royal physician for Roman emperor, who witnessed a man's painful gout attack was relief by coming in contact with an electric ray while walking on the breach and lead to the development of electroichthyotherapy (a medical therapy uses live electric ray) to treat various pain conditions (Largus 1529). Through the development of electrostatic machine, the electricity used for medical treatment has changed from the use of live animals (Magendie 1826). Franklinism is the incorporation of static electricity into routine medical treatment (Garratt 1882). Followed by the discovery of pulses of electrical current, Galvanism was used for many medical conditions including destroy human tumor because of its ability to cause necrosis of contacted tissue (Stillings 1975). Later, Faradism has been used successfully in many medical conditions because the intermittent alternative current does not cause direct tissue damage (Stillings 1975).

1.2 The Progression of Electroanesthesia to Electroanalgesia

In early 1847, Fortuné Christophe Ducros first described electrical anesthetic method. Unfortunately, his scientific research work was not published. The use of electricity as local analgesics was brought to light by J.B. Francis, a dentist at Philadelphia who performed 164 tooth extractions using this method in 1858 (Zimmer 2002). Afterward, electrical anesthesia was then used in veterinary medicine (Zimmer 2002). Direct electric current was applied through scalp to induce general anesthesia (electroanesthesia i.e. electricity induced generalized loss of consciousness and sensation) in various animal species in the literature (Zimmer 2002).

A review article by Smith and colleagues listed the advantages of electroanesthesia: a. requires minimum equipment; b. achieves target effect in short duration; c. causes well tolerated physiologic changes; d. resulted in rapid wakening without "drug hangover" after surgery (Smith et al. 1967). The review article also pointed out that electroanesthesia has wide margin of safety and is applicable to virtually all species. However, there are several advantages of electroanesthesia i.e. the amount of current induced anesthesia was determined by trial and error, no standardize waveforms and frequencies, etc. (Smith et al. 1967). Electroanesthesia is best described as "While the best techniques *known* were being employed, they were not good enough, nor well-enough founded on reliable research evidence as being *good* technics." (Smith et al. 1967).

In addition, scientists observed "Fading" which is describing lightening of anesthetic associated with electroanesthesia regardless the electrical current and frequencies used within 5–15 min after induction. In order to deepen the level of anesthesia, additional current was needed (Zouhar et al. 1967). It was thought the impedance of tissue layers between the electrical source and target causes fading of electroanesthesia. Using rhesus monkey, Zouhar and colleagues found fading occurs in every layer of tissue even though less current required when electrodes were placed near

the brain tissue. This observation leads to the hypothesis that the overlying tissues impede the current density arrived the target area (Zouhar et al. 1967). The authors summarized that electrically produced anesthetic states in primates, including human fade within 30 min regardless the electrical pattern employed (Zouhar et al. 1967). Clinically electroanesthesia was successfully employed in the dentistry to reduce pain during the treatment of carious cavities (Nikitina 1972).

In 1977 Smith and colleagues conducted another research, they applied electricity to human volunteers to produce general and local anesthesia (Smith et al. 1977). However, they were not able to induce any general anesthesia in any of the test subjects because of pain. Only one subject experienced local analgesia in the arm and the rest of the subjects experienced muscle spasm and vibration pain. However, when electricity applied to the hand only, all test subjects had a total loss of pain sensation (Smith et al. 1977).

2 History of Electroacupuncture

2.1 The Development of Electroacupuncture

As early as 1800, Sarlandière began to combined electricity and acupuncture. He speculated that "electro-puncture or electrical acupuncture (EA) differs from acupuncture proper in that needle does not play the principal role in the operation, but rather serves as a conductor of electricity from skin into the muscle tissue, or into fibrous tissue and lead to subsiding of pain and the cessation of irritation." (Sarlandière 1825). Sarlandière advocated "All lesions of motion should be treated by Franklinism and all those of sensation should be treated by Galvanism." (Sarlandière 1825). Later in 1816, L.V. J. Bertioz also combination of electricity and oriental needling as the treatment of pain (Berlioz 1816).

2.2 The Scientific Evidence of Analgesia Produced by Electroacupuncture

Whether acupuncture needle insertion and manipulation exerts any analgesic effect was not proven until Professor Ji-Sheng Han at Beijing University performed a series of experimental studies both in volunteers and in animals (Ulett et al. 1998). The results of these studies indicated that manual manipulation of acupuncture needle and different frequencies of stimulations triggered differential release of neuropeptides from the central nervous system i.e. low frequency of EA triggers the release of endomorphine, enkephalin, and ß-endorphin (ß-EP) that act on opioid receptors (μ, δ opioid receptors) to induce synergistic analgesic effects; high frequency EA causes the release of dynorphin which acts on κ opioid receptor (Ulett et al. 1998; Han

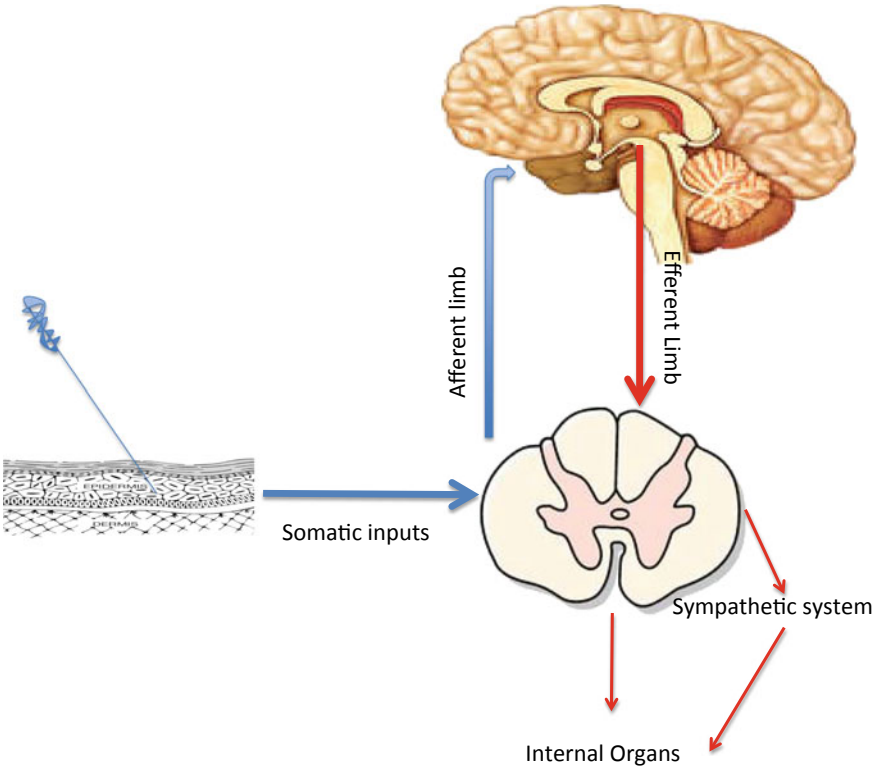

Fig. 1 The schematic illustration of acupuncture stimulations

2003). Lastly, EA's analgesic effect is more profound than that of manual acupuncture stimulation (Han 2003).

It was speculated that there are different mechanisms of acupuncture analgesia western electroanesthesia (Macdonald 1993). Apparently, low frequency and high intensity of EA rises in the pain threshold all over the body after 20–40 min of stimulation and its effect lasts about 90 min (Macdonald 1993). To date, all available scientific data support the neurophysiologic basis of acupuncture analgesia that is peripheral needle insertion and stimulations causing affect signals being propagated ascending along the spinal cord to the midbrain and cerebral cortex and triggering a sequence of inhibitory and excitatory efferent signals (Fig. 1) to minimize pain. Although there may be differences between electrotherapy and electroaupuncture (Table 1), both techniques have currently been used as part of conventional treatment of pain, neuromuscular dysfunction, joint mobility, wound healing, edema, peripheral blood flow, regulate urine and bowel function, etc. (Macdonald 1993; Greathouse 1996). While scientists still debate about the specificity of acupuncture points/ needle in addition to electrotherapy, EA has been investigated as a potential mean for organ protections.

Table 1 The presumptive differences between electroacupuncture and electroanalgesia

	Electroacupuncture	Electroanalgesia
Onset	20–40 min	Rapid onset
Duration	90 min	30 min
Region of analgesia	Generalized	Regional
Analgesia reversal	Naloxone	Not affected by naloxone

3 The Electroacupuncture for Clinical Conditions

3.1 The Correlations Between Ischemia, Ischemia-Reperfusion-Injury, Opioids and EA

Animal studies have shown that the interruption of blood flow, ischemia, to the vital organs causes progressive depletion of ATP and leads to the elevation of intracellular Ca^{2+} level and the production of free radicals. Although immediately restoration of circulation is essential for the dying cells to survival, the reperfusion can cause additional cell/ tissue injury through further accumulation of Ca^{2+} and the release of free radicals and lead to ischemic-reperfusion-injury (IRI). The presence opioids appear to minimize the damage related to IRI (Barry and Zuo 2005). Recent literature also suggests that ischemia and opioids both have cytoprotective effect (Wilderman and Armstead 1996; Mayfiled 1994). Additional studies showed that ischemia and/or hypoxia attenuated IRI of the brain and heart via the opioid receptors (Wilderman and Armstead 1996; Mayfiled 1994; Zhang et al. 2000, 2002). Clinically, IRI after major heart surgery has been one of the risk factors causing prolonged hospital stay and postoperative mortality rate (Moore and Hutchins 1981; Bulkely and Hutchins 1977). Although evidence has supported that ischemic preconditioning is a powerful protective endogenous adaptive response of the myocardium against a prolonged ischemia or traumatic brain injury (Li et al. 1990; Yokobori et al. 2013), the application of ischemic preconditioning may/can be difficult to perform even under controlled (preoperatively) or unexpected situations (accident).

In spite of the limitation of timing and feasibility, opioid pre-conditioning and other forms of interventions such as nitric oxide, inhalation anesthetic agents, propofol, etc. have been considered (Murillo et al. 2011). Multiple animal studies have shown that opioid preconditioning-induced heart protection not only mediates through δ receptors but also involves Gi/o proteins, protein kinase C, ATP-sensitive potassium channels and free radicals (Way et al. 2000, 2001; Law and Loh 1999; Minami and Satoh 1995; Nishizuka 1995; Gross 2004, 2003). Therefore, EA also has been investigated for preconditioning to minimizing the cellular/tissue damage related to IRI.

3.2 The Development of Electroacupuncture in Cardioprotection

3.2.1 Experiment Animal Studies

Using rat model of cardiopulmonary bypass, researchers were able to demonstrate that EA significantly attenuated the elevated ST segment of electrocardiogram, cardiac arrhythmia score, and the ratio of the infarct size/risk zone (Cheng et al.2013). Apparently, the underlying potential mechanism of EA alleviates the pathological changes of cardiac tissue after myocardial ischemia by regulating the protein expression of CLC-2 Cl^-channel and cystic fibrosis transmembrane conductance regulator (Cheng et al. 2013). Furthermore, cardioprotective effect of EA is mediated via inhibition of cardiac ß-adrenoceptors signally pathway, opioid peptides and protein kinase C-dependent pathways (Gao et al. 2006, 2007; Tsou et al. 2004; Zhou et al. 2012)

Lastly, direct electrical or peripheral neural stimulation might also trigger the release of cardioprotective substances into the blood stream (Redington et al. 2012). MicroMRNA (miRNA) is found to play important role in regulating cardiophysiological and pathological process (Wu et al. 2013). A vertebrate-specific family of microRNA precursor miR-214 also serves a sensitive marker for cardiac stresses and controlling Ca^{2+} overload during IR condition. Luo and colleagues (2004)found that acupuncture-serum could decrease Ca^{2+} concentration in cultured rat myocardial cell. Cardiomyocyte Ca^{2+} homeostasis was maintained after EA pretreatment (Gao et al. 2008; Liu et al. 2014). Using culture rat myocardial cells, Liu and colleagues were able to demonstrate that EA pre-conditioning elevates of miR-214 expression leading to cardiac protection (Liu et al. 2014).

3.2.2 Clinical Trials and Applications

Yang and colleague conducted an EA clinical trial in a group of patients undergoing heart valve replacement surgery (Yang et al. 2010). A total of 60 patients were enrolled into the study and they were randomized into one of the two groups (EA and Controlled). The patients in the EA group received EA at bilateral Pericardium 6 (PC6), Lung 7 (Lu 7) and Lung 2 (Lu2) for 30 min for a consecutive 5 days before surgery (Fig. 1). The control group of patients only received standard of care preoperatively. The researchers found that preoperative EA treatment significantly decreases overall serum troponin I release at 6 h, 12 h, and 24 h after reperfusion (removal of aortic crossed clamp). Patients in the EA pretreatment group also had reduced in inotrope score at 12 h, 24 h and 48 h after arrival to the intensive care unit (ICU) and shortened ICU stay. The authors suggested that EA pretreatment will have a palliative action and open a new preventive treatment to alleviate the myocardium injury in adult cardiac surgery (Yang et al. 2010). Wang and Zhang have done extensive studies in determining protective effect of acupuncture on myocardium. According to their

study results that the cardio-protective effect of EA preconditioning is through the following mechanisms: a. regulation of ß-EN, ACTH, cortisol and plasma dopamine level; b. increase HSP70 expression by myocardial cells; c. reducing mitochondrial membrane permeability; and d. inhibiting cell adhesion process (Wang and Zheng 2012). To date, cardioprotection effect resulting from EA-preconditioning not only maintains homeostasis of the body but also regulate circulation to prevent myocardial injury when patients undergoing cardiac surgery. A recent pediatric study performed by Ni and colleagues (2012) showed pediatric patients with congenital heart diseases undergoing open heart surgery who received transcutaneous electrical acupoint stimulation (TEAS) at PC-6 (Pericardium -6) for 30 min have mean cardiac troponin level significantly lower at 8 h ($p = 0.043$), and 24 h ($P = 0.046$) after aortic unclamping as compare with those patients without receiving TEAS. There was also significant lower level of c-reactive protein at 8 h in TEAS group as compare with control group but both c-reactive protein and cytokine level were no differences at 24 h between the two groups. The results of this study suggested that another form of electrotherapy i.e. TEAS may have some beneficial effect in attenuation myocardium injury.

3.3 The Role of Electroacupuncture in Neuroprotection

Electrical stimulation of the central or peripheral nervous system has long been used as part of western medical practice to treat pain, depression and other illnesses such as status epilepsy, Parkinson tremor, eating disorder, etc.

3.3.1 Experimental Animal Studies

Electroacupuncture was found to improved memory impairment related to cerebral infarction significantly and the underlying mechanism was regulating the expression anti-apoptotic gene Bcl-2 and pro- apoptotic Bax gene in hippocampus (Wang et al. 2009). EA at specific frequency and intensity (potentially via the activation of δ opioid receptors) can increase cerebral blood flow and effectively protects the brain from ischemic injury. EA is also found to maintain the integrity of blood-brain barrier, inhibit apoptosis, activate the endocannabinoid system and attenuate glutamate excitotoxicity (Yang et al. 2009; Zhou et al. 1985; Li et al. 2012). Long-term high-frequency EA treatment is effective in preventing the degeneration of dopaminergic neurons and up-regulating BDNF mRNA in the in the substantia nigra (SN) and selective regions of ventral midbrain (Liang et al. 2002). In Summary, EA is found to maintain the integrity of blood brain barrier (BBB), inhibit apoptosis, activate of endocannabinoid system, attenuate glutamate excitotoxicity, up-regulate the level of Brian–derived neurotrophic factor (BDNF). The observed EA- precondition neuroprotection effects are: a. to lessen the degree of inflammations. b. to minimize cerebral impairment caused by free radicals and excitatory amino acids, c. to increase regional cerebral blood flow to remove the release of vascular bioactive substances, and d. to promoting repair and regeneration of the neural tissue.

3.3.2 Clinical Trails and Applications

Although clinical evidence of EA neuroprotection is limited, Hong and colleagues (2009) conducted a randomized controlled trial to determine the effect of EA as a treatment of balance and gait disorder s in patients suffering from Parkinson's disease. The participants were randomly assigned to receive EA or standard of care. Three weeks after treatment (1 treatment/week, duration 30 min.), patients received EA had 31% improvement in balance and 10% increase in gait speed and 5% increase in stride length but those patients in the control group had no improvement at all. Using transcutaneous acupoint stimulation at selected acupoint (Large Intestine 4; Li 4) vs. a mock point at the fourth interosseous muscle area on the left hand in high (HF: 100 Hz) vs. low-frequency (LF: 2 Hz) stimulation by counter-balanced order in the meantime monitoring with 3 D (124 channels) EEG power spectrum mapping and source imaging, Chen and colleagues (2006) were able to demonstrate that the activity of Theta wave significantly decreased ($p = 0.02$), compared with control during high frequency (HF) but not low frequency (LF) at acupoint simulation. A decreased Theta EEG power was prominent at the frontal midline site (FCz, Fz) and contralateral right hemisphere font site (FCC2 h). The observed HF acupoint stimulation effects of Theta EEG were only present during, but not after, stimulation.

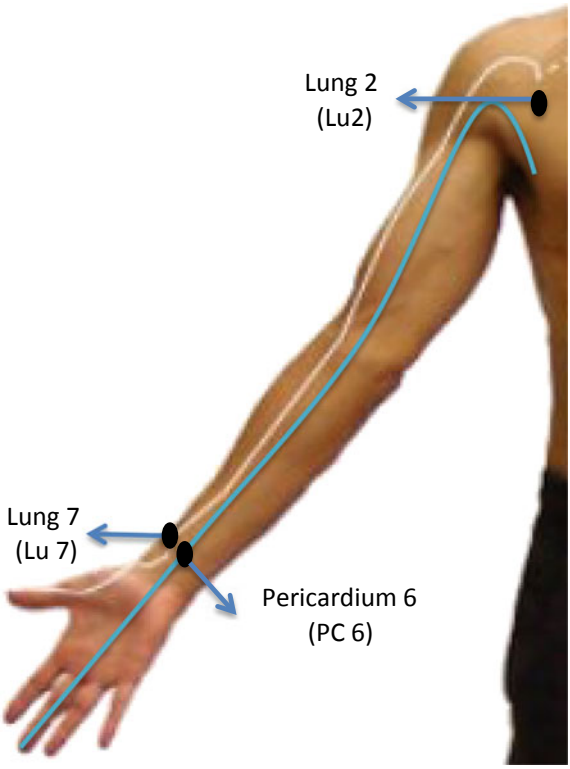

Fig. 2 Acupuncture points for electroacupuncture pre-condition cardiac protection

Although EA preconditioning has been shown to reduce cerebral ischemic injury in animal studies, it is unclear whether EA preconditioning can be useful in clinical setting. Lu and colleagues (2010) performed a randomized controlled trail, enrolling 32 patients undergoing brain tumor resection. Two hours prior to surgery, patients in the EA group received EA stimulations at Governor Vessel 16 (Du 16) and Gallbladder 20 (GB 20) for 20 min (Fig. 2) and those in control group received no intervention. The researchers found that patients in the EA group had significant lower serum level of S100ß and neuron specific enolase (NSE) at the end of treatment and 24 h postoperatively. The researchers suggested that EA preconditioning might have potential protective effects on surgical brain damage (Lu et al. 2010) (Fig. 3).

Zhou and Jia (2008) performed EA at Shenmen (HT7), Zusanli (ST 36), Fenglong (ST 40) and Taixi (KI 3) on 26 patients with Alzheimer under functional Magnetic Resonance Imaging and found areas of brain closely correlated with cognitive func-

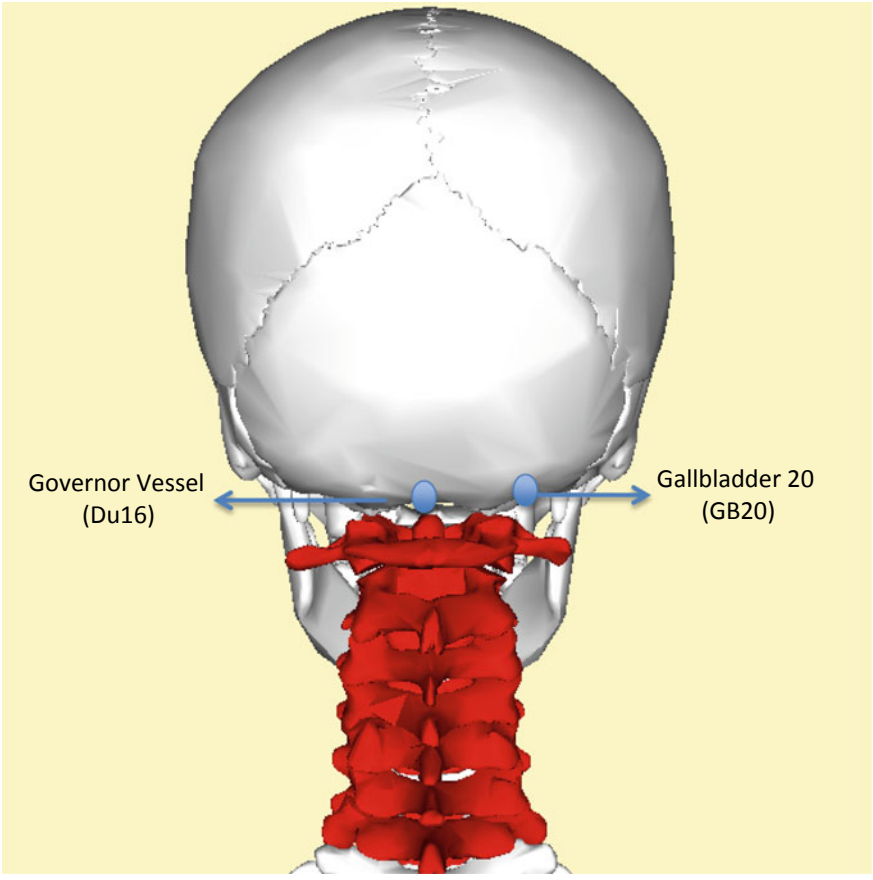

Fig. 3 Acupuncture points for electroacupuncture pre-condition cerebral protection

tion (memory, reason, language, executive, etc.) were activated by EA stimulation. The results of this study provide strong evidence that EA had a potential beneficial effect on Alzheimer patients. Other acupuncture studies without using electrical stimulation also showed that the acupuncture stimulations enhance the activities and connectivity in areas where are important in cognitive functions (Wang et al. 2012; Feng et al. 2012).

4 Summary

Electrotherapy has been part of medical treatment for centuries. Recent development has widened the applications of electrotherapy especially when it combined with acupuncture. Thus far many forms of electrotherapy are used not only for pain treatment but also for protecting vital organs dysfunction. More experimental and clinical studies are needed to determine the underlying mechanisms and clinical efficacy of EA treatments, respectively. Furthermore, recent observation of neurotoxicity/cognitive dysfunction related to exposure of anesthesia may be an important area where clinical electrotherapy research should be conducted to determine whether electrotherapy may improve the neurological outcomes postoperatively in patients with extreme ages required surgery.

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Factors Influencing Acupuncture Research

Martin Wang and Ying Xia

Abstract Acupuncture research has been conducted in western countries for more than 50 years, with both positive and negative results being published. Therefore, some researchers question whether acupuncture is just a placebo effect. We believe that acupuncture signal production, process and outcomes are complex and need careful investigation. Many factors may contribute to the failure of a study and result in a wrong conclusion. In this chapter, we aim to analyze the factors that might influence acupuncture research and outcomes. There are mistakes and errors in current acupuncture research in several aspects, including acupuncture methodology, personal ability of acupuncture, study design, data analysis, and selection of participants. We hope that future acupuncture researchers will pay attention to these factors and avoid mistakes and misunderstandings of acupuncture effects.

Keywords Acupuncture · Placebo effect · Influencing factors · Research design

1 Introduction

Acupuncture has been studied for more than 50 years in western countries with both positive and negative results being published, especially in clinical studies. Most published studies support that acupuncture has a unique healing effect, but there are also a lot of data that do not support this view because the acupuncture healing effect in an acupuncture group is not significantly different from that in a sham acupuncture group. It seems that both sides of the argument insisted their own opinions but are hardly able to point out possible mistakes or errors of the opposite side. Indeed,

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contradicting data are still published up to now (2016) (Fleckenstein et al. 2016; Schiller et al. 2016; Feng et al. 2016).

Acupuncture research is not simple, as some researchers believed. For example, in western medicine, the quality of a new drug in a clinical study is standardized for its purity or concentration. Whether the drug is used in New York or in Vancouver, it is regarded the same in quality. However, clinical acupuncture is a very person-skill dependent therapy. The success of the acupuncture treatment largely depends on the person that performs the acupuncture treatment. It is not as simple as inserting a needle into skin and leaving it for 20 min to expect a healing effect.

Furthermore, in a new drug study in western medicine, the sham tablets or sham pills are relatively easy to prepare. It is difficult for study participants to tell the difference between a true tablet and sham tablet. In acupuncture, it is still questionable what the best and most reliable sham acupuncture group to use is. Sham acupuncture should exert only a placebo effect and no healing effect, but none of the sham acupuncture groups used have ever met this characteristic. Therefore, much more attention is needed in regards to acupuncture research in clinical settings.

We feel that it is necessary to analyze the methodology of the current acupuncture research and indicate potential factor(s) that may contribute to the failure of an acupuncture study that have not been well recognized yet. This chapter will summarize these potential factors that influence the outcomes of acupuncture research. We hope that our summary would be helpful to reduce the errors and mistakes in the acupuncture research and move the acupuncture study forward.

2 Method of Acupuncture

2.1 What Is Acupuncture?

From the research articles published from western countries, it was found that acupuncture researchers had confused electrical acupuncture, finger-press, acupuncture point massage, point injection, ear point press, and etc. all as just “acupuncture”.

All of these therapies belong to traditional Chinese medicine (TCM) and are broadly used in acupuncture clinics. However, each therapy has its own favorite spectrum to fit the scope of the treatment. Mixing all these therapies with acupuncture therapy and attributing their therapeutic outcomes, either success or failure, are not appropriate in terms of the evaluation of acupuncture healing effects. Acupuncture has its own and unique way in clinical practice.

In many past review articles on acupuncture, these various therapies were considered as acupuncture for the review and analysis. For example, they were classed as acupuncture in the review by Colquhoun (2015), Colquhoun and Novella (2013), Furlan et al. (2010) and by Linde et al. (2009a, b).

In the acupuncture review by Liu et al. (2015) the author collected randomly designed articles from 2011 from Science Citation Index Expanded (SCIE), but

excluded those articles published in Chinese journals, or those in which the first author was from China. Using this method, they collected 33 articles from totally 867 articles. Among these, 17 articles are negative and 23 articles are positive regarding the acupuncture efficiency. We found that in these 33 articles, some of the studies used electrical acupuncture, auricular press, auricular acupuncture, or finger press, acupuncture injection or cupping, and acupuncture was actually not the main therapy in these studies. Furthermore, most of these studies only paid attention to the treatment costs, residence days or long-term healing effect. In addition, some authors might make a wrong conclusion for their study results (e.g., an apparently negative result was interpreted and concluded as a positive one (Smith et al. 2011). After exclusion of these articles, we can actually only be able to get 21 "valid" articles in which 7 articles showed negative results and 14 showed positive results.

Azad and John (2013) listed 25 negative articles about acupuncture. Among them, there are 8 articles that used intradermal needling, acupuncture point press, auricular press, or magnetic therapy.

Matthews (2015) collected 55 articles about acupuncture treatment of nausea/vomiting in early stages of pregnancy. From these articles, the author had chosen 27 articles for review. Among which only 2 articles can be regarded as true studies on typical acupuncture and all other studies included in the review were Fresh-ginger press (10 articles), finger-press (5 articles), TENS (1 article), auricular press (1 article), moxibustion (1 article), Vitamin B6 (2 articles) and antiemetic (6 articles).

One current question in acupuncture research is if acupuncture is a placebo effect. It is therefore better to test the effect of acupuncture therapy alone, rather than the cupping, moxibustion, acupressure, point injection, auricular acupuncture, or the combination of them with acupuncture. In this article, we try to separate the healing effect of acupuncture from that by other therapies. This is possibly a better way to test if acupuncture is a placebo effect, or if it has its own specific healing effect.

2.2 Different Acupuncture Systems

There are various forms, styles, and systems of acupuncture. The traditional style of acupuncture chooses acupuncture points according to the theory of Chinese medicine or that of meridians, while some other styles do in different ways.

Furthermore, based on the acupuncture points chosen from the whole body or from just a local part of the body, acupuncture can be separated into two major categories:

Whole body acupuncture that includes those introduced in classical acupuncture textbook, and other personalized acupuncture styles such as Pan's Classical Chinese Acupuncture system (https://doi.org/10.1002/14651858.cd007575.pub4), the Dong Shi Qi Xue style (Dr. Dong's out-meridian acupuncture system Huang 2010; 2002), Ping Heng Zhen Fa (Balancing acupuncture system, Wang 2014a, b; Ding and Ding 2005) Fu Zhen (Fu's transcutaneous acupuncture system), Fu et al. (2006) as well as Japanese acupuncture style.

Local acupuncture that includes scalp acupuncture, ear acupuncture (also known as auricular acupuncture), facial acupuncture, nose acupuncture, tongue acupuncture, wrist/ankle acupuncture, palm acupuncture, abdomen acupuncture, and etc.

We will mostly discuss possible factors that may affect the whole body acupuncture treatment and study, though each of these styles of acupuncture has its own advantage and disadvantage.

2.3 Selection of Acupuncture Points

One of the principles in the selection of acupuncture points is the combination of basic and complementary points.

Basic acupuncture points can be on meridians, such as the ST36 point for disorders in the abdomenal area, PC6 point for disorders of heart beat and nausea, or Hegu (L14) point for disorders in the face and head. In the treatment of disorders in the leg, the basic points are ST36, Snayinjiao (SP6) and Taichong (LIV3) in the Jin-San-Zhen acupuncture system. In the treatment of pain in the knee, the basic point is the Jianzhong point in the Ping-Hen-Zhen-Fa system. Evidently, the basic point can be one or more points. The number of complementary acupuncture points can also be small or large, depending on the disease treated.

There are two ways to choose complementary points: the diagnosis according to TCM basic theory or that according to meridian theory. In acupuncture treatment, the meridian diagnosis is relatively more important.

Generally speaking, acute diseases need lower numbers of basic or complementary acupuncture points, but chronic disease needs higher numbers. For example, in the treatment of menopause, the basic points are Guanyuan (REN4), Qihai (REN6), Zhongyuan (REN12), Shenshu (UB23), L14, ST36, Yingtang (EX2). The diagnosed points (based on TCM diagnosis) would be Taixi (KID3), Ganshu (UB18), Baihui (DU20) for Liver-kidney Yin deficiency, Xinshu (UB15), Tongli (HT5), Zhishi (UB52) for Heart-kidney un-connection syndrome), or Pishu(UB20), Yinlingquan (SP9), Sanyinjiao (SP6) in Spleen-kidney Yang deficiency.

In the treatment of migraine, the meridian diagnosis is mostly used. Some basic points and chosen complementary points together are necessary for better healing results. For example, if the migraine pain is mostly located on the side of the head, acupuncture points on the Shaoyang meridian should be chosen. If the pain expands down to the arm, acupoints on the hand Shaoyang meridian should be used for the treatment. Otherwise, if such pain expands down to the shoulders or also has muscle spasm on calf, acupuncture points on the foot Shaoyang meridian should be chosen.

Most acupuncture studies in western countries have basic acupuncture points but not complementary points, or they use the same basic point and the complementary points for all patients. There should be some healing effects with this method, but they are not as strong those with the selection of acupuncture points that match the need of each individual.

For example, in the treatment of menopause, we must use complementary acupuncture points according to TCM diagnosis. This is a tough task for a doctor with a western medicine background or for someone who is not used to evaluating patients from TCM point of view. For proper treatment of infectious diseases in western medicine, it is important to make a precise diagnosis to identify the infectious source, i.e., bacteria, virus, fungus, or something else. Even in the category of bacterial infection, it is still nescessary to determine if it is due to gram-positive or to gram-negative bacteria. The same is true in TCM. An effective treatment needs a precise TCM diagnosis for each clinic condition, by which suitable acupoint and acupuncture manipulation can be properly selected. Failure to do so may lead to an unsuccessful attempt to true results of the acupuncture research.

For the treatment of hot flashes and night sweats, using only a basic acupuncture point is not enough if symptoms are due to chemotherapy or radiation therapy, the use of estrogen, hysterectomy, or ovariectomy. On the other hand, one PC6 point (or with an ST36 point) might be able to solve the problem in the treatment of a nausea/vomiting, if it is caused by acute gastritis, motion sickness, or anesthesia. However, if nausea/vomiting is due to chemotherapy/radiation therapy, one PC6 point acupuncture usually is not enough to solve the problem. It would be necessary to use a combination of the PC6 with more complementary acupuncture points, or use a different acupuncture point combination.

2.4 Specificity and Universality of Acupuncture Point

The effects of acupuncture points have specificity and universality. The healing effects of an acupuncture point are usually shared more or less by neighbor points as well (Lu 1994). These neighbor points can belong to the same meridian, or to different meridians. For example, the ST36 and Yanglingquan (GB34) points in the Foot Yangming meridian are under and outside of the knee and can be used to treat pain and bloating in the abdomen. The SP9 and Diji (SP8) points in the Foot Spleen meridian are located under and inside the knee and can also be used to treat the stomach pain and bloating.

Acupuncture points also have specificity in healing functions. It is reported that acupuncture on the Shuigou (GV26) point of the rabbit can increase the blood pressure of the rabbit with hemorrhagic shock, whereas acupuncture on the ST36 point cannot (Zhu 2003). Acupuncture on the Suliao (GV25) point can treat severe craniocerebral injury coma (Xu et al. 2014). The wake-up effect of this acupuncture point is stronger than Renzhong (DU26) point. Although these two points are very close to each other and both of them belong to the same meridian (the Du meridian), their healing effects are different in terms of efficacy.

2.5 Acupuncture Sensation

To obtain a reasonable level of healing effects, patients need to feel special sensations on the acupuncture spots. The typical acupuncture sensation is described as a tingling, numb, bloating, pressure, or tired feeling on and around the acupuncture spot. This is the Deqi sensation. It is not the Deqi sensation if the patient feels sharp pain (suggesting that the needle touches blood vessels or bone membrane); or pain as an electric shock (suggesting that the needle touches nerve). So, if the sensation is mostly a painful one, the spot of needling might not be correct.

However, it should be noted that the most important mark for the Deqi is the feeling of the acupuncturist. The acupuncturist should feel a descending, tight, or unsmooth feeling under the needle. If there is a hollow, loose, or slippery feeling under the needle, the Deqi sensation has not been reached yet.

There are three types of acupuncture sensations. The first one is the Deqi sensation. Clinically, inducing such sensation is not difficult in most patients, except for those who are in poor health conditions.

The second kind of acupuncture sensation is along-meridian sensation, where the Deqi feeling passes up or down the meridian to some distance. Whenever there is such along-meridian sensation, the healing effect is usually good (Xie et al. 2014; Along-meridian sensation and clinic efficacy of acupuncture treatment 2011). It is the aim of an acupuncture expert to induce this along-meridian sensation, since it is the key to having marvelous healing effects in acupuncture treatment.

For example, in the treatment of periarthritis of the shoulder, Dazhui (DU14) points are stimulated. After manipulating the needle to induce the Deqi sensation, the needle tip is turned towards the affected shoulder and continues to be manipulated to let the patient feel the Deqi sensation passing towards the affected shoulder. Clinical experience showed that healing effects are better with farther passes of the along-meridian sensation. The ability of an acupuncture expert is reflected, at least, in his or her ability to induce this along-meridian sensation. Due to the higher healing effects with the along-meridian sensation, acupuncture experts do not need to use lots of needles or acupuncture points for the treatment, nor do they need to repeat the treatment many times.

The third kind of acupuncture sensation is far-away acupuncture sensation. This is when upon acupuncture on a point, the patient feels a strange feeling far away in some other part of the body. The feeling can be typical Deqi feeling, or something else. Such far-away acupuncture sensation does not need to manipulate the needle for a long time to happen. People feel these far-away sensations fairly easily. They may belong to a special group of people, whom we call as “meridian-sensitive people”. If such far-away acupuncture sensations happen, the healing effect is usually very good, no matter the experience of the acupuncturist.

We noticed that in a majority of the acupuncture studies, there are indications that the researchers have paid attention to induce such Deqi sensations for the patients. However, it is difficult to tell if these acupuncturists have stimulated out the Deqi sensation every acupuncture point, or only some points. Our doubt comes from the

blinded study design (single or double blind); if we do not know whether the patients receive a real acupuncture treatment, how do we know if the patients feel the Deqi sensation or not? Moreover, we do not know if the Deqi feeling is from the patient's description, or from the feeling of the acupuncturist's feeling (under the needle). Again, we did not find any articles describing attempts to induce the along-meridian sensation during treatment.

Though we believe that the acupuncture sensation is very important for a better healing effect, it is difficult to study since it is hard to standardize the intensity of the feeling (Zhou and Benharash 2014).

There are more data telling that the manipulation of the acupuncture needle is important to get higher healing effects (Hu and Shi 1982; Yuan et al. 2004; Ding et al. 2004; Shen et al. 2005a, b; Wang and Di 2006; Xiong et al. 2006; Zeng et al. 2006; Zhang 2006; Liu et al. 2007; Luo and Wang 2008; Deng 2007; Liu and Zhu 2008; Guo and Shi 2013; Meng et al. 2006; Ni et al. 2011; Shi 2005; Zhao 2003; Wang 2015; Wang and Wu 2006; Zhu 2013; Liu 2013; Zhu and Shi 2008).

2.6 Along-Meridian Acupuncture Sensation

As stated previously, the first kind of acupuncture sensation, Deqi, is not difficult to induce, while the second acupuncture sensation, along-meridian needling sensation, is. The second sensation requires the acupuncturist to focus on the needle handling with various manual skills, such as to insert and to pull the needle with different frequency and speed, and so on. The proficiency of an acupuncturist is defined by the acupuncturist's ability to induce this along-meridian sensation, and if the sensation can pass on to the diseased spot of the body. It is commonly accepted clinically that if such a sensation can reach the diseased spot, the disorder on that spot will be improved much faster (He 2004; Liu et al. 2005; Cheng 1997; Sun 2006; Li et al. 2001).

To induce the along-meridian sensation, an acupuncture master must use different acupuncture manual techniques on different acupuncture points. For example, the needle may be manipulated for different insertion directions or depths. The needle can twist, pull, and push up and down, with various frequencies. These manipulations may last one minute or longer. A variety of special manipulating technique may also be used, such as Slow-inserting technique (Cheng et al. 2004; Huang et al. 2005), Fei-Jing-Zou-Qi technique (Cao et al. 2014), Short-Distance-Following technique (Liu and Jiang 1981; He et al. 1991), Jie-Qi-Tong-Jing technique, (Cheng and Zheng 2001) Needle-Detaining technique (Cheng et al. 2015), Yi-Teng-Zhu-Tong technique (Zhang et al. 2014), the Both-Hand-Manipulation technique (Lou 1998), and many more.

When considering acupuncture anesthesia, most clinic observations showed that if the along-meridian sensation reaches the area of the surgical operation, the effect of the acupuncture anesthesia is better (Lin et al. 1999). However, this effect is not related to the types of the surgical operations.

The patch of the along-meridian sensation mostly follows that of a meridian, though there could be differences among persons, and meridians, but not follows the long axis of muscle, blood vessels, or nerves (Xie et al. 2014). Patients may feel bloating or numbness. Some may feel water flowing, ant crumbing, or cold or warm sensations. This sensation passes slower than that of a nerve signal. The width of the patch is variable among people. Most of the path is as broad as a band, not a line, which can be narrow or broad. The depth of the along-meridian sensation varies from person to person. The direction of the sensation is mostly the same as that of a meridian. Depending on the acupoint stimulated, the direction of the feeling goes either single direction or also to opposite directions. The sensation can be stopped by external interference, such as pressing the skin with a finger between the needle and the sensation spot. The along-meridian sensation can also induce internal organ reactions, such as changes in heart beat and intestine movement. The presence of the along-meridian sensation supports the meridian theory, but its nature still needs in-depth investigations.

A study on 97 students with Myopia (Yang et al. 2003) showed that the intensity of the along-meridian sensation tends to increase with the increase in stimulation. The younger students have stronger sensations than older students. A pure numbness feeling from the along-meridian sensation is better than a mixed feeling of numbness, tingling, bloating, or sore. With another needle on a far end of the same meridian, this sensation is easier to induce than with only the needle on the tested acupoint.

The along-meridian acupuncture sensation is correlated with patient body constitution and nationality. It was found that a patient in a diseased condition is less prone to feel the along-meridian sensation, than someone in a healthy condition with the similar physical attributes (You and You 2002). However, the reverse is true when the patient is stimulated with Hot-moxibustion-sensitive stimulation (Xie and Cheng 2015).

The incidence of the along-meridian sensation in Chinese is reported as12–24% (Cooperation study groups on along-meridian phenomenon 1979), 4% in Japanese (Wang and Wang 1984), 81.8% in Mozambique (Li 1982), and 30% in Guinea (Zhang 1984).

In clinical observation, we found that the healing effect of acupuncture was usually good when the skin around the inserted needle showed pink color. This observation suggests that the healing effect may be partially related to the body constitution of the patients. We also noticed that for patients using steroid medications in Chinese herbal therapy, including steroid injection into an acupuncture point or a trigger point, the healing reaction to the herbal therapy is relatively poor.

In practice, acupuncturists try to use multiple acupuncture needles to enhance the chance for such sensation and therefore increase the healing effect. Some acupuncturists may use different methods to induce such acupuncture sensation and maintain a high healing effect. For example, they may use “Reverse-horse needle technique”, “Paralleling-needle technique”, and “Needling-in-circle technique.”

We may also use electrical acupuncture or warm-needle acupuncture (to warm up the needle by a burning moxi cone) (He et al. 2014), electrical-warm needle, or hot needle (burn or heat the needle on fire, then inserted into the acupuncture point

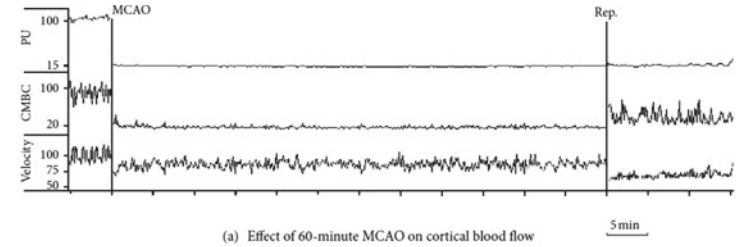
very quickly and pulling out very quickly too). Someone may use Needle-detaining technique (Cheng et al. 2015), or Yang-Ci technique, or insert several needles around a painful spot or a diseased spot of the body. If the healing effect is still not so satisfied, we may increase the acupuncture frequency and times, by doing acupuncture every day, or even twice a day.

Since the sensitivity to along-meridian acupuncture sensation is different among study participants, this could be one of the factors affecting the healing effect of acupuncture among studies.

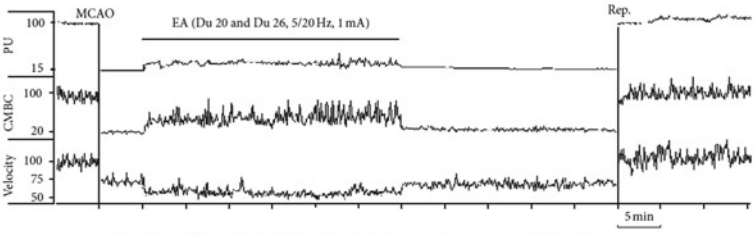
2.7 Proper Selection of Acupuncture Points

Proper selection of acupoints is extremely important for acupuncture efficacy. Here we mean two issues: proper acupoints for different diseases or clinical conditions and accurate insertion of needles to the acupoint(s).

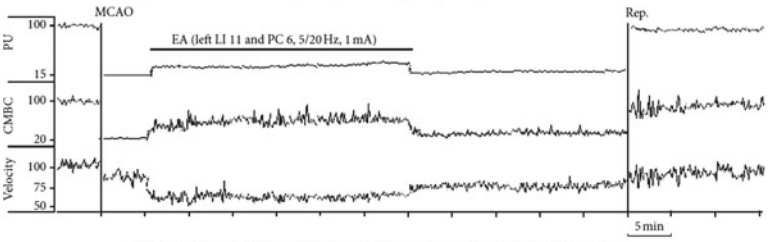
In a study on the effect of electroacupuncture (EA) on cerebral blood flow in the stroke model (MCAO), (Zhang et al. 2013) we found that EA-induced changes in cerebral blood flow varied with different acupoints (Fig. 1). Using a laser-doppler perfusion monitor, we monitored the real-time changes in cerebral blood flow in all experimental groups. Firstly, we tested if brief stimulation of these acupoints alters the blood flow in the ischemic rats ($n \geq 6$, repeated ≥ 6 times for each pair of acupoints). EA with 5/20 Hz sparse-dense current at 1.0 mA was delivered to the acupoints in a manner of 5 min stimulation/5 min cessation. When a nylon suture was successfully inserted into the appropriate place of right middle cerebral artery (MCAO), the blood perfusion (PU) of the monitored cortex decreased immediately from average 100 ± 20 PU to 15 ± 2 PU, that is, a ~85% drop in blood supply with a decrease in CMBC by ~80% and relatively slight deceleration of blood cell velocity by ~25% ($P < 0.05$) (Fig. 1). EA stimulation at Baihui (Du20) and Renzhong (Du26) immediately induced a significant increase in blood flow. This increase in blood perfusion was synchronous to EA. Among the changes in blood flow, EA induced a 2-fold increase in PU (from ~15 to ~32% of the base level before MCAO, $P < 0.01$) with a 3-fold increase in CMBC (from ~20 to ~65% of the base level, $P < 0.01$) and a slight decrease in the Velocity (from ~75 to ~50% of the base-value, $P < 0.05$). Similarly, EA at left Quchi (LI11) and Neiguan (PC6) also significantly increased the blood flow immediately after the onset of EA. During the EA stimulation, PU increased almost 2 folds (from ~15 to ~29% of the base-value, $P < 0.01$) with a significant 3-fold increase in CMBC (from ~20 to ~60% of the base level ($P < 0.01$), and a slight decrease in the Velocity (from ~75 to ~50% of the base level, $P < 0.05$). In sharp contrast, EA at right Quchi (LI11) and Neiguan (PC6) or left Sanyinjiao (SP6) and Yanglingquan (GB34) did not induce any significant changes in blood flow despite the use of same EA parameters. Our data strongly suggest the importance of proper selection of acupoints in the outcomes of acupuncture (Schiller et al. 2016).



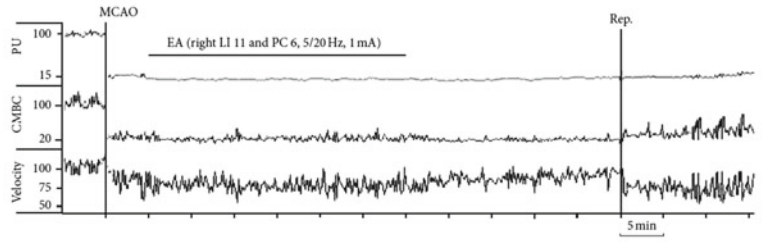
(a) Effect of 60-minute MCAO on cortical blood flow



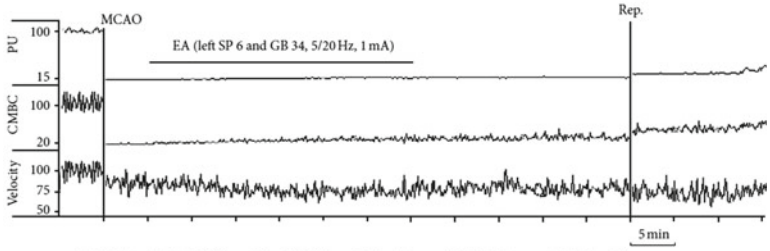
(b) Effect of EA at "Baihui" (Du 20) and "Shuigou" (Du 26) on cortical blood flow



(c) Effect of EA at left "Quchi" (LI 11) and "Neiguan" (PC 6) on cortical blood flow



(d) Effect of EA at right "Quchi" (LI 11) and "Neiguan" (PC 6) on cortical blood flow



(e) Effect of EA at left "Sanyinjiao" (SP 6) and "Yanglingquan" (GB 34) on cortical blood flow

◀**Fig. 1** Representative trace recordings of the blood flow. Blood perfusion (PU), concentration of moving blood cells (CMBC), and Velocity of blood cells (Velocity) were measured in the ischemic rats by a laser Doppler perfusion monitor system. **a** Effect of MCAO-60 min on CBF during ischemia and reperfusion in the Ischemia group. **b** Effect of EA at acupoints Baihui (DU20) and Renzhong (DU26) on CBF. **c** Effect of EA at left Quchi (LI11) and Neiguan (PC6) on CBF. **d** Effect of EA at acupoints right Quchi (LI11) and Neiguan (PC6) on CBF. **e** Effect of EA at acupoints left Sanyinjiao (SP6) and Yanglingquan (GB34) on CBF. Note that the PU and CMBC decreased immediately after the right middle cerebral artery was occluded by a nylon suture. The blood flow was kept at a low level with fluctuant waves during the entire MCAO duration. After onset of reperfusion, PU and CMBC increased while the velocity further decreased. EA at right Quchi (LI11) and Neiguan (PC6) acupoints induced no significant change in the CBF during or after MCAO. EA at left Sanyinjiao (SP6) and Yanglingquan (GB34) acupoints induced no significant change in the CBF during the early stages of MCAO, but slightly increased the CMBC after a 10−15 min period of EA. EA stimulation at acupoints Baihui (Du20) and Renzhong (Du26) or left Quchi (LI11) and Neiguan (PC6) induced an isochronous increase in PU and CMBC with a decrease in velocity. After reperfusion, PU, CMBC, and Velocity all increased rapidly and reached the baseline values Cited from Zhou et al. (2013)

On the other hand, the needle must be inserted into the correct spot of the acupuncture point for a high healing effect (Zhang et al. 2013; Cheng and Kang 2007; Wan et al. 2014). When the needle is in the right spot, it would be easier to induce the acupuncture sensation. The farther the distance from the acupuncture point, the less the intensity of the acupuncture sensation will be (Yang 2008).

In acupuncture studies that involve sham acupuncture group, the needles are usually inserted several millimeters away from true points (inserted sham group). Theoretically, the insertion of needles as such may have some level of healing effect. This is one of the reasons why some researchers give up the inserted sham group and turn to more "proper," non-inserted sham techniques. However, we do not believe that simply inserting needles into sham spots induces any noticeable healing effect, especially if the insertions are shallow and not manipulated to induce acupuncture sensation. This is because there is no sufficient data suggesting that the inserted sham group may yield higher healing effect than non-inserted sham group (see below).

2.8 Size of Acupuncture Point

The effective surface area of an acupuncture point describes two things. First, it describes the size of the skin area, within which an inserted acupuncture needle could exercise a healing effect. Second, it describes the size under the skin area, within which an inserted acupuncture needle can also exercise a healing effect.

Generally, it is believed that the healing effect would be highest if the acupuncture needle is inserted into the acupuncture point. If it is inserted into the surrounding areas, the healing effect would not be as strong, and decreases with increasing distance from the acupuncture point. Most acupuncture points are zones or areas of significant size, though some acupuncture points may be small.

In the clinic, if the location of an acupuncture point is not correctly chosen, the overall healing effect of the acupuncture treatment could be compensated by choosing more acupuncture points, electrical acupuncture, or moxi acupuncture to increase the stimulation to the points. We may also insert the needle vertically into the skin first, and then insert the needle obliquely in different directions under the skin. This means that even if the point chosen to insert the needle is not the exact acupuncture point, moving the needle under the skin can still stimulate the effective area of the acupuncture point to induce a healing effect.

2.9 Nourishing or Depleting Technique of Acupuncture Manipulation

The way of manipulation of the acupuncture needle is important to induce a higher healing effect (Li 2014). The needle is handled by the acupuncturist to control the speed to insert the needle, the direction of the needle, the ways to pull or push the needle, and to bend or to scrape the needle. Different ways of needle manipulation have different impacts to the body function, yielding a so-called nourishing or a depleting effect to the body Qi (the Qi can be understood as body energy Zhang and Lin 2004; Cui et al. 2010).

Studies on human (Zheng 1995) and animal (Zheng et al. 1996) showed that different methods of the nourishing or depleting technique in acupuncture treatment can differentially influence body functions. It was further found that the overall effect of the nourishing or depleting technique depends on the body condition too. The body condition, i.e., healthy or sick, is also important for the final effect of the acupuncture technique (Ding et al. 2004; Gao 2002). If a patient is in a weak condition, both the nourishing technique and the depleting technique could produce a nourishing to the body, though the nourishing technique induces a higher nourishing effect than the depleting technique. If a patient is an overwhelming condition (TCM concept), both the nourishing and the depleting technique could induce a depleting effect, but the depleting technique induces more depleting effect than the nourishing technique (Sun and Meng 1994; Sun and Yao 1995).

Paying more attention to the nourishing or depleting technique would yield higher healing effect than otherwise (Li 2014; Liu 2013; He et al. 2007), and yield even higher healing effects than those of electrical acupuncture (Xie and Wen 2013; Zhang 2010). If we insert the needle into the acupuncture point, pull or insert the needle to induce the Deqi sensation, and then stop the handling of the needle further, then there will be a healing effect. However, this method of acupuncture can only exercise a low level of healing effect.

2.10 Depth of Acupuncture Needle Under Skin

In acupuncture treatment, different acupuncture points require different depths of needle. In area with more muscle mass, the needle needs a deeper insertion; in areas with less muscle mass, the insertion needs to be shallow. This suggests that even shallow insertions of needles can also have healing effect.

Furthermore, even for a given acupuncture point, different depths of needle stimulation may induce different healing effects. For example, in Dr. Dong's out-meridian acupuncture system, stimulating the Ren Shi, Tian Shi and Di Shi points at 0.5 in. treats asthma; at 1 in., it treats heart failure. For Di Zong point, shallow stimulations at 1 in. treat mild diseases, while deeper stimulations at 2 in. treat severe diseases. When the Ren Zong, Tian Zong and Di Zong points are stimulated at 0.8 in., it treats the common cold; at 1 in., it treats upper arm pain; at 1.2 in., it treats diseases of the liver, spleen, and gallbladder.

Based on the literature, it is difficult to tell if the acupuncture needles were in proper depths, since the Deqi sensation was always reported to have occurred.

2.11 Length of Acupuncture Treatment for Each Session

The Chinese style of acupuncture requires the continuous manipulation of the needle after the Deqi sensation in order to get as much as possible of the along-meridian sensation. If such along-meridian sensation cannot be induced, we may need to leave the needle in longer, use electrical acupuncture, or use warm-needle acupuncture to increase the stimulating dose.

The time to manipulate the needle might be several seconds, one minute (Ding et al. 2004; Liu and Zhu 2008; Meng et al. 2006; Shen et al. 2005; Wang and Wu 2006; Li et al. 2015), two minutes (Cheng et al. 2015; Wang 1983), 1−3 min (Yang 2011), or 3−5 min (Sun 2006; Wang et al. 2003).

It was found (Lin et al. 2012) that in the treatment of post-stroke syndrome, after getting the Deqi sensation, continuous manipulation of the needles for 30 s induces a better efficacy than the immediate ending of manipulation after "Deqi".

One unclear question about acupuncture in western countries is how long the acupunctures manipulate the needles during the treatment. Do they stop the needle manipulation right after the patients feel the Deqi sensation, or do they continue the manipulation after the induction of the Deqi sensation?

In our previous studies, we found that appropriate length of continuous EA stimulation gained better outcomes in terms of brain protection against cerebral ischemia in the rat model of right middle cerebral artery occlusion (MCAO) (Guo et al. 2010). EA starting at 5 min after the onset of MCAO induced a marked protection against cerebral ischemia, leading to a significant reduction of infarct volume, neurological deficits, and death rate (Wang et al. 2009). Interestingly, increased periods of the stimulation from 5 to 30 min increased EA protection as shown in Fig. 2. In the group

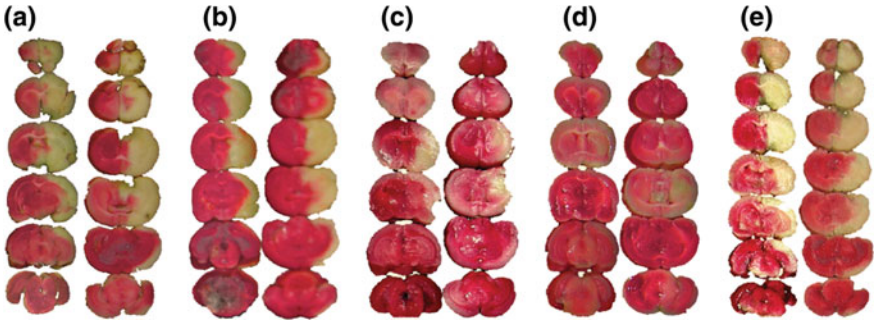


Fig. 2 EA-induced changes in cerebral infarct size in a time-dependent manner. The brain slices were subjected to TTC staining and the ischemic infarct volume was quantified by a computerized image system. The slices on the right of each column show the backside of the left slices. Note that the infarct region (pale-white portion) was mainly located in the striatum and the frontoparietal cortex in the right hemisphere. The MCAO-induced infarction **a** was significantly reduced by EA at Baihui (DU20) and Renzhong (DU26) acupoints for 5 min (**b**), 15 min (**c**), and 30 min (**d**). In contrast, EA for 45 min (**e**) enabled no protection against the cerebral infarction. Cited from Wang et al. (2009)

of MCAO plus EA for 5 min (EA-5 min, $n = 18$), except for 2 rats that died at 5 and 15 h after the onset of reperfusion (11%, 2/18, $P < 0.01$ versus Ischemia), the degree of average neurological deficits in the living ischemic rats was slightly improved ($n = 16$, $P < 0.05$ versus Ischemia). The infarct volume was slightly reduced (25.6% + 5.3%, $n = 12$, $P < 0.05$ versus Ischemia). In the group of MCAO plus EA for 15 min (EA-15 min, $n = 16$), only one rat died at ~3 h after the onset of reperfusion (6%, 1/16, $P < 0.01$ versus Ischemia), with a greater improvement in average neurological deficits ($n = 15$, $P < 0.01$ versus Ischemia) along with a significant reduction in infarct volume (15.4% ± 4.2%, $n = 12$, $P < 0.01$ versus Ischemia). In the group of MCAO plus EA for 30 min (EA-30 min, $n = 30$), the neurological deficits were greatly attenuated ($n = 28$, $P < 0.01$ versus Ischemia) and a significant decrease in death rate (7%, 2/30, $P < 0.01$ versus Ischemia) was noted. The infarct volume was reduced by 85% (4.9% ± 1.2%, $n = 12$, $P < 0.01$ versus Ischemia). In comparison to the groups of EA for 5 min and EA for 15 min, EA for 30 min induced more beneficial effects in all aspects including neurological deficits, ischemic infarct and death rate. These results suggest that the EA protection is dependent on an appropriate duration of EA duration (Wang et al. 2009).

However, the EA protection was not further enhanced by a longer duration of EA stimulation. In contrast, an "over-length" stimulation of EA exacerbated ischemic injury. We assigned a few rats to a new group with MCAO plus EA for 45 min (EA-45 min, $n = 30$). To our surprise, EA for 45 min significantly increased the mortality in this group of ischemic rats. More than half of the animals in this group (60%, 18/30) died within 0.5−10 h after the onset of reperfusion. All of the dying rats manifested symptoms such as convulsions, tumbling, piloerection, and perspiration (wet feathers) and other abnormalities. When compared the Ischemia group, the

death rate increased by 3 folds (60%, 18 out of 30, $P < 0.01$ versus Ischemia) in this group. Although the remaining 12 living rats survived for 24 h after the reperfusion, they suffered from severe neurological deficits and were even worse than the group with only Ischemia. In terms of the infarct volume, EA for 45 min did not reduce the infarct volume at all (34.3% ± 2.4%, $n = 12$, $P > 0.05$ versus Ischemia) (Fig. 2e). These results suggest that an increased duration, beyond "appropriate" period, for EA stimulation may exacerbate the ischemic insult, instead of conferring any protection. (Wang et al. 2009)

Interestingly, Wang et al. (2009) also observed a similar phenomenon in their studies on EA-induced hypoalgesia in healthy volunteers. The subjects were randomized to receive different durations (0, 20, 30, or 40 min) of asynchronous EA stimulations and then subjected to the test of hypoalgesia using a human experimental cold thermal pain threshold model. They found that 30 min of asynchronous EA stimulation resulted in the most significant hypoalgesic effect compared with 0, 20, or 40 min stimulations. Therefore, it seems that a 30 min period is the most optimal duration for EA-induced analgesia and brain protection against ischemic injury. In fact, most acupuncturists in China apply acupuncture or EA on patients for 20−30 min each time.

2.12 Retention Time

Retention time is one of the ways to enhance the stimulation of acupuncture treatment, by keeping the needle in place for the period after the Deqi sensation.

Liu et al. (1999) treated 30 cases of primary dysmenorrhea. The pain reduction started from 10 min after acupuncture. The painless period prolonged with the stay of the needle remained in the spot. The healing effect of acupuncture to stop the pain with 30 min retention time is better than that with 20 min retention.

He et al. (1999) treated post-stroke syndrome. He found that retention time of 60 min or 30 min is better than that of 20 min.

Acupuncturists in China have done a lot of studies on the relationship between retention time and the healing effect. The overall results showed that the proper length of retention time is related to the type of the disease treated.

(1) Post-stroke syndrome: retention of 60 min is better than 40 and 20 min (He et al. 2005a).
(2) Acute cerebral infarction: 12 h is better than 15 min (Fang and Yu 1996).
(3) Cervical vertigo: 60 min is better than 45 min or 30 min (He and Ma 2013).
(4) Trigeminal Neuralgia: 1.5−3 h is better than 30 min (Huang 1999).
(5) Intractable facial pain: 60−90 min is better than 30 min (Cai 1996).
(6) Primary dysmenorrhea: 30 min is better than 20 min (Liu et al. 2014).
(7) Acute ankle sprain: 20−40 min is better than 5 min or 60 min (Xu and Cheng 2001).
(8) Chronic ankle sprain: 60 min is better than 5−40 min (He and Ma 2013)

(9) Prolapse of lumbar intervertebral disc: 45 min is better than 15−30 min (Hou et al. 2015).
(10) Intractable hiccup: 60 min is better than 30 min (Bao et al. 2003).
(11) Vertebral basilar artery insufficiency vertigo: 4 h is better than 30 min (Dong and Xing 2013).

For these diseases, it seems that longer times of retention yield a better effect than shorter times. Each disease has its own proper retention time for the highest healing effect. However, for some diseases, shorter retention times seem to work better than longer retention times.

(1) Simple facial nerve palsy: 10 min is better than 40 min (Yu 2004); 20 min is better than 10 min or 40 min (Zhang et al. 1991).
(2) Trigeminal Neuralgia (by electrical acupuncture): 20−30 min works better than 2−3 h (Lin 2002), 10 min is better than 30 min (Su and Cui 2011).
(3) Acute fever diseases: Without retention, the reduction effect of fever has already reached 59.6% (Wei 1999).

It is difficult to measure a unique proper retention time for all types of diseases. For a given disease, once the method of the acupuncture treatment is changed, the proper retention time would also change. For example, in the treatment of trigeminal neuralgia, with ordinary manual acupuncture, a retention of 1.5−3 h is better than 30 min (He et al. 2005), but with electrical acupuncture, a retention of 10−30 min is more effective (Bao et al. 2003; Dong and Xing 2013). Therefore, for the acupuncture treatment of a given disorder, it is needed to check the literature for available data on the proper retention time to use.

In most articles published in China and other countries, the needles were left on the spot for 30 min. Some needles were left in for 20 min. In most of the articles reported from western countries, the needle was also left for 20−30 min. However, acupuncturists in the UK did not leave the needle for a retention time after manipulating the needle to reach a Deqi sensation (Ecevit et al. 2011; White et al. 2000). Generally speaking, if the needle does not remain in place for some time, the stimulation intensity must be made? stronger by other means (see below).

2.13 Intensity of Acupuncture Stimulation

Similar to most medical therapies, acupuncture treatment needs a proper dose of stimulation. For different kinds of diseases or clinical conditions, it is important to stimulate proper numbers of acupuncture points, induce the Deqi sensation, manipulate the needles for a proper length of time, leave the needle for a suitable time in the acupuncture points, and repeat the treatment for proper treatment frequencies.

Indeed, we have found that stimulation intensity at acupoints critically matters acupuncture outcomes (Qing et al. 2015). In our studies on cerebral blood flow in the stroke model (MCAO), we examined the effects of EA intensity on the blood

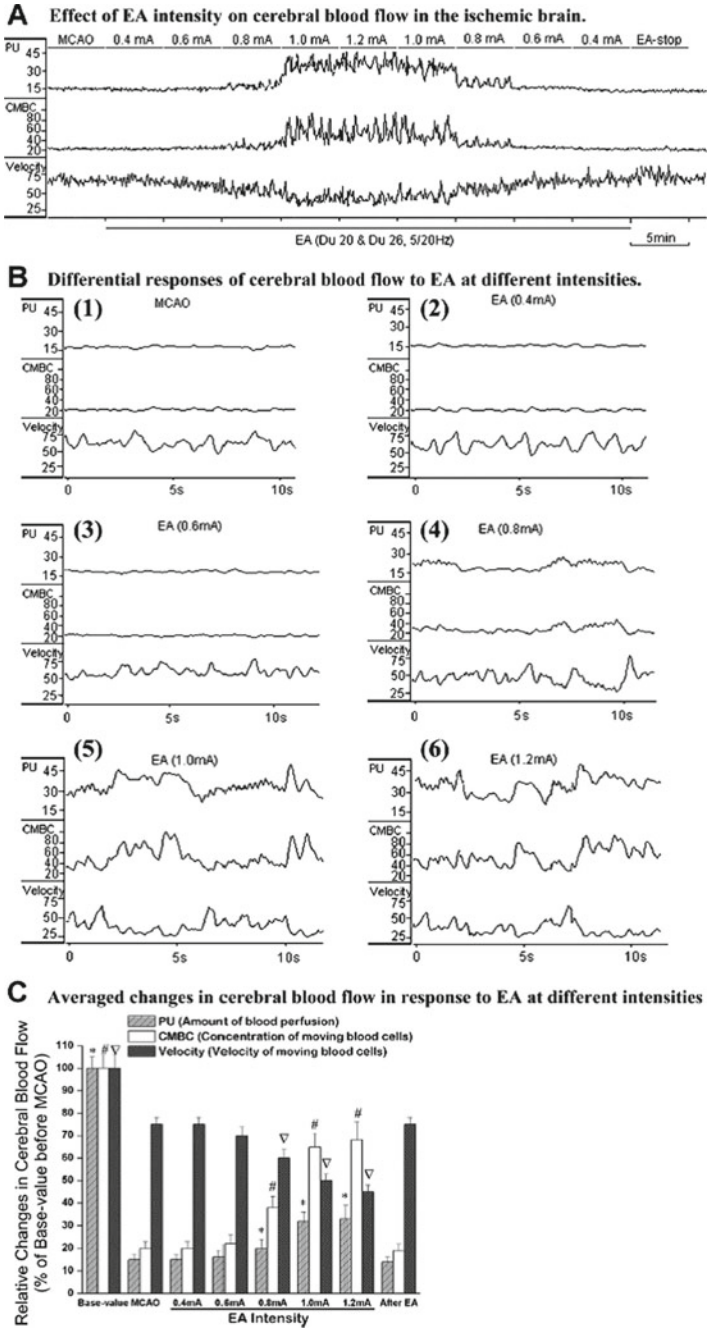
flow (Fig. 3) and found that an intensity of <0.6 mA with 5/20 Hz did not induce any significant change in the blood flow. When the intensity was enhanced from 0.6 to 0.8 mA, there was a significant increase in the blood flow with EA. The blood flow further increased when the intensity was enhanced to 1.0 mA. As shown in Fig. 3c, PU (perfusion units, an index of blood flow value) during EA were more than 100% higher than that during the non-EA period ($P < 0.05$). However, the intensity at 1.2 mA failed to boost a further increase in the blood flow (Fig. 3). The EA-induced increase in the blood flow was isochronous to the current impulse in response to EA stimulation and disappeared immediately after discontinuing EA (Qing et al. 2015). These data suggest that EA induces a temporal increase in the blood flow, with an intensity between 1.0 and 1.2 mA being the optimal range (Qing et al. 2015).

As stated above, however, stimulation intensity is differentially required for different disease/conditions. In certain conditions, mild intensity is optimal for acupuncture treatment. Sometime, only one or two acupoints are needed for the treatment, such as for acute pain, or nausea from motion sickness. In these cases, it is needed to pay more attention to a proper stimulation dose. The use of trigger point acupuncture, catgut embedding therapy, or acupuncture injection therapy are just some examples where stronger and long-lasting stimulations should be given due to small numbers of acupuncture points in the treatment. Since acupuncture treatment for nausea and vomit is a common practice in acupuncture clinics, we take it as a typical example to specially discuss this issue below.

2.13.1 Nausea and Vomiting After Surgical Operation

To stop post-operative nausea and vomit, the acupuncturists in western countries commonly used a single acupuncture point named Neiguan (PC6). The way of stimulation of the point can be acupuncture needle (Streitberger et al. 2004; Gamermanna et al. 2015; Rusy et al. 2002; Al-Sadi et al. 1997; Kotani et al. 2001; Weightman et al. 1987; Liodden et al. 2015; Korinenko et al. 2009; Wani et al. 2015; Yentis and Vashisht 1998; Alizadeh et al. 2014; Sharma et al. 2007) point injection (Irnich et al. 2001), point massage, (Agarwal et al. 2000; Agarwal et al. 2002; Alkaissi et al. 1999; Alkaissi et al. 2002; Allen et al. 1994; Barsoum et al. 1990; Duggal et al. 1998; Ferrara-Love et al. 1996; Gieron et al. 1993; Harmon et al. 1999; Harmon et al. 2000; Ho et al. 1989; Klein et al. 2004; Lewis et al. 1991; Samad et al. 2003; Schultz et al. 2003; Turgut et al. 2007), acupuncture plus point pressure (Shenkman et al. 1999; Norheim et al. 2010), electrical stimulation, (El-Deeb and Ahmady 2011; Gan et al. 2004) Transcutaneous electrical nerve stimulation (TENS), (Frey et al. 2009; Habib 2006) laser (Schlager et al. 1998), or dermal needle (Weightman et al. 1987).

Some studies reported positive (Gamermanna et al. 2015; Kotani et al. 2001; Weightman et al. 1987; Liodden et al. 2015), whereas others reported negative results (Rusy et al. 2002; Al-Sadi et al. 1997) of the effect of acupuncture as compared with their sham groups. This controversy also existed when comparing the effect of acupuncture group with that of no-treatment groups. For example, acupuncture worked better for reducing the incidence of nausea/vomit in some studies, (Wani


A
Effect of EA intensity on cerebral blood flow in the ischemic brain.
MCAO
0.4 mA
0.6 mA
0.8 mA
1.0 mA
1.2 mA
1.0 mA
0.8 mA
0.6 mA
0.4 mA
EA-stop
PU
CMBC
Velocity
EA (Du 20 & Du 26, 5/20Hz)
5min
B
Differential responses of cerebral blood flow to EA at different intensities.
(1) MCAO
(2) EA (0.4mA)
(3) EA (0.6mA)
(4) EA (0.8mA)
(5) EA (1.0mA)
(6) EA (1.2mA)
0
5s
10s
C
Averaged changes in cerebral blood flow in response to EA at different intensities
PU (Amount of blood perfusion)
CMBC (Concentration of moving blood cells)
Velocity (Velocity of moving blood cells)
Relative Changes in Cerebral Blood Flow (% of Base-value before MCAO)
Base-value
MCAO
0.4mA
0.6mA
0.8mA
1.0mA
1.2mA
After EA
EA Intensity

◀**Fig. 3** The EA-induced changes in the blood flow varied with EA intensity. PU: perfusion units. CMBC: concentration of the moving blood cells. Velocity: velocity of blood cells. A: comparative view of changes in cerebral blood flow. B: changes in the blood flow in response to EA at different intensities. C: statistical summary of the changes in the blood flow in response to EA stimuli. *P < 0.01, MCAO versus MCAO plus EA (PU). #P < 0.01, MCAO versus MCAO plus EA (CMBC). ΔP < 0.01, MCAO versus MCAO plus EA (Velocity). The frequency of EA was 5/20 Hz. Note that EA at < 0.6 mA could induce an isochronous increase in PU and CMBC with a decrease in Velocity. Within the ranges of 0.6−1.0 mA, the EA-induced increase in the blood flow was proportional to the increase in the EA intensity. Cited from Zhou et al. (2011)

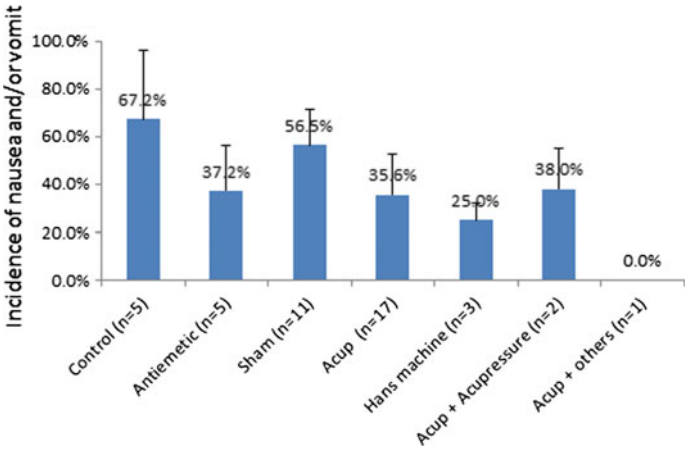


Fig. 4 Incidence of postoperative nausea after treatment with various remedies (data from western countries). n = experiment groups. Data not include articles that use grade scale for healing effects (Mean ± SD)

et al. 2015; Agarwal et al. 2000) but not so in other studies (Korinenko et al. 2009). However, the effect of electrical acupuncture seems always better than that of a sham group (Gan et al. 2004; Frey et al. 2009). More than one acupuncture point of acupuncture treatment seems better than a single point (Sharma and Goswami 2007).

After pooling all the data together, it can be seen that without treatment, the incidence of nausea/vomiting after operation is 67.2%. Sham acupuncture can only reduce it down to 56.5%, antiemetic drugs can reduce it to 37.2%, acupuncture can reduce it to 35.6%, and TENS can reduce it to 25% (Fig. 4).

To treat the post-operative nausea/vomiting, acupuncturists in China also choose the PC6 point (Fig. 5), but they mostly use point injection (Zhao et al. 2013; Liu et al. 2015; Zhu et al. 2010; Lu 2010; Chen et al. 2014; Wang and Kain 2002; Zhu et al. 2010) TENS (Yu et al. 2012; Zhou et al. 2014; Jin et al. 2013; Wang et al. 2010), or combine acupuncture with antiemetics (Li and Wu 2015; Cheng et al. 2015; Huang et al. 2013). It is not common to use ordinary acupuncture. (Lu et al. 2013; Lu 2011; Ouyang et al. 2009; Tang and Cheng 2015) Studies comparing acupuncture to sham acupuncture are rare.

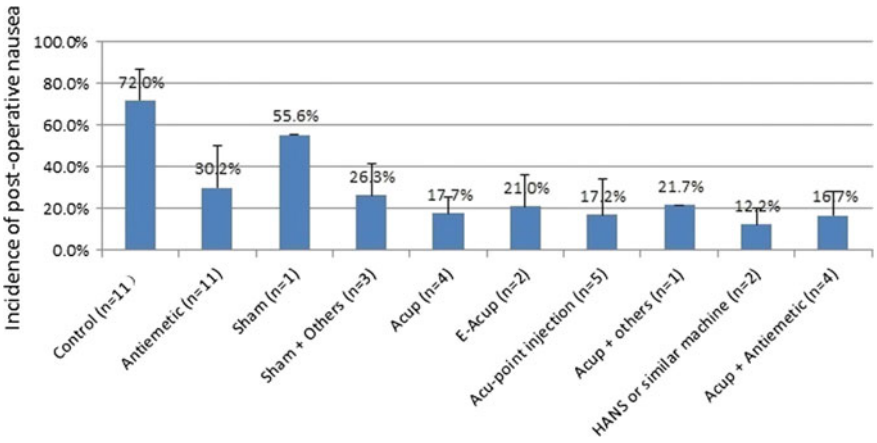


Fig. 5 Incidence of post-operative nausea after treated by various methods (data from China). n = experiment groups. Sham + others: Sham acupuncture plus Ondansetron, or vitamin B1 injection into either acupuncture points or into non-acupuncture points. Acupuncture + others: acupuncture plus acupressure (Mean ± SD)

Figure 5 shows that without treatment, the incidence of nausea/vomiting after a surgery could be as much as 73%, similar to that summarized in the western group. Antiemetic medicine can reduce the incidence down to 30.2%, and acupuncture reduces it to 17.7%. Other forms of acupuncture (including electrical acupuncture, TENS, joint injection) had the same effect as ordinary acupuncture. The combination of acupuncture with antiemetics did not further reduce the incidence.

Comparing Figs. 4 and 5, it can be seen that the incidence of post-operative nausea/vomiting in Fig. 1 both western Chinese groups are similar in the non-treatment group and in the antiemetic group. Acupuncturists in China have successfully reduced the incidence of postoperative nausea/vomiting to less than 20%, while the acupuncturists in western countries can only reduce it to about 35.6%.

Data in Figs. 4 and 5 suggest that, for the treatment of post-operative nausea/vomiting, the ordinary acupuncture for only one session using a single point worked to reduce the incidence. This is consistent with the reviews by Lee and Fan (2009), Bao (2011), Stoicea et al. (2015).

Even so, for the four acupuncture studies in China, one used acupuncture from the start to the end of anesthesia, while another used more than three rounds of acupuncture. This might explain the more reduction in the incidence of post-operative nausea in China compared to the western country group. It appears that even when using single point acupuncture, acupuncturists in China tend to have stronger stimulations of acupuncture points than those of acupuncturists in western countries.

Possibly because acupuncture works well to reduce the incidence of postoperative nausea/vomiting, acupuncturists in western countries have tried to simplify acupuncture into acupressure on the same points. However, acupressure is not the same as acupuncture. It is not as reliable as acupuncture by a professional acupuncturist,

especially if the acupressure is performed by patients themselves at home. So, it is no wonder that the healing effect of acupressure in the treatment of post-operative nausea/vomiting could be repeatedly reported as either positive or negative.

2.13.2 Nausea/Vomiting After Chemotherapy or Radiation Therapy

For the treatment of nausea/vomit after chemotherapy or radiation therapy, acupuncturists in the western countries also use point-pressure (Molassiotis et al. 2007; Dibble et al. 2000; Dundee and Yang 1990; Dibble et al. 2007; Gardani et al. 2007; Genç and Tan 2015), auricular needle (Yeh et al. 2012), electrical acupuncture (Choo et al. 2006; McKeon et al. 2015), TENS (Roscoe et al. 2002), acupuncture plus antiemetics (Aglietti et al. 1990; Gottschling et al. 2008; Streitberger et al. 2003), electrical acupuncture plus antiemetics (Shen et al. 2000), acupuncture alone (no sham group) (Tas et al. 2014; Nystrom et al. 2008; Kasymjanova et al. 2013; Reindl et al. 2006; Rithirangsriroj et al. 2015), acupuncture plus point-pressure (Melchart et al. 2006). Only the studies by Enblom et al. (2011, 2012) compared acupuncture to sham acupuncture. These two publications, however, seem to be the same article.

As for the acupuncture treatment of post-operative nausea/vomiting, the acupuncturists in western countries also used single PC6 point for treatment of nausea/vomiting due to the chemotherapy and radiation therapy. Indeed, most articles reported using this single acupuncture point for the treatment. The acupuncture was performed twice a week, (Roscoe et al. 2002; Shen et al. 2000; Rithirangsriroj et al. 2015) once to twice per week, (Reindl et al. 2006) or three times per week, (Kasymjanova et al. 2013; Enblom et al. 2012; Liu et al. 2011) Only one paper stated the use of acupuncture every day for five days (Tas et al. 2014). In the views of acupuncturists in China, the stimulation dose is not enough to induce a reasonable healing effect due to the low treatment frequency.

Acupuncturists in China tend to use multiple acupuncture points, such as the ST36 (ST36) or Yongquan (K11) points for treatment, and rarely use a single point. They also tend to use point injection, (Liu et al. 2011; Chen 2007; Tao et al. 2000; Tong 2007; Hu 2003; You et al. 2009) electrical acupuncture (Fu et al. 2006; Yang et al. 2009), TENS (Zhang et al. 2014), or acupuncture plus auricular pressing plus antiemetic (Sima and Wang 2009). No matter the type, all suggest that acupuncturists in China apply higher doses of simulation to the acupuncture point for the treatment, compared to those in western countries.

Stimulation by point injection and electrical acupuncture are usually stronger stimulation therapies, but for the treatment of nausea/vomiting due to chemotherapy or radiation therapy, higher treatment frequencies and more treatment sessions are required.

2.13.3 Nausea/Vomiting During Early Stage of Pregnancy

Matthews (2015) reviewed 27 articles on the treatment of early stages of pregnancy. Among the 27 articles, 2 articles are acupuncture studies. The other studies are using Fresh-ginger press (10 articles), finger-press (5 articles), TENS (1 article), auricular press (1 article), moxibustion (1 article), Vitamin B6 (2 articles) and antiemetic (6 articles). The stimulations by the fresh-ginger press, finger-press, auricular press, moxibustion, are not stronger than the acupuncture stimulation.

Between the two articles on acupuncture, one is from Knight et al. (2001). The authors used multiple acupoints, twice a week for two weeks, then once a week for another two weeks. The authors reported no difference in reducing the nausea/vomiting rate between real acupuncture and sham acupuncture.

The second article is by Smith et al. (2002), which used acupuncture in the same frequencies as above. The author reported that the healing effect of using multiple acupoints worked better than a single point (PC6 point), and much better than the sham group and the no-treatment group.

These two studies used typical western style acupuncture: twice a week, for less than 10 sessions. These methods of acupuncture work for some, but not for others (see below).

Acupuncturists in China tend to use multiple acupoints. More importantly, they perform acupuncture every day (Jiang 2014; Song 2012; Mao 2012; Wang and Chui 2002; Xie 2013; Xie 2014; Yan et al. 2012; Cheng 2001) and reported much higher success rates. However, it is hard to tell if such higher healing effects are better than a sham acupuncture, since most clinical studies in China do not design a sham group for a control.

Using a single point (e.g., PC6) may be effective enough for the treatment of post-operative nausea/vomiting, but not enough for that from early stages of pregnancy, or from chemotherapy or radiation therapy. The post-operative nausea/vomiting is due to side effects of anesthesia medications. After several hours, blood concentration of the medication reduces (usually within 24 h), and nausea/vomiting will therefore subside. So, one-time acupuncture with single acupoint might be good enough to stop the nausea/vomiting. However, nausea/vomiting during pregnancy is due to the disorder of hormones in the body that could last several weeks or months. The nausea/vomiting during chemotherapy and radiation therapy is due to the side effects of the highly toxic therapies. The chemotherapy must be used several days in a row, and repeated continuously. Radiation therapy is one occasion, but the toxic materials from damaged and dead cells need several days to excrete out of the body, and cause nausea/vomiting. Therefore a one-time acupuncture with single point stimulation for 20 to 30 min is not effective in treating nausea/vomiting in early stages of pregnancy and in chemotherapy and radiation therapy.

2.14 Frequency of Acupuncture Treatment

Acupuncture frequency and schedules are different in various clinics. For example, it may be performed 1−2 times per week for 2 weeks, and then once a week for the following weeks. It may also be performed as once a day for 5 days and after a 2-day break, it continues for five more sessions. In the former case, the first two weeks is regarded as the first treatment course, and in the later, the first 7 days is regarded as the first treatment course.

The healing effect of acupuncture is not only determined by the stimulation dose of each session, but also by the frequency of the acupuncture treatment and the total number of sessions.

2.14.1 Acupuncture Stimulation Dose: Treatment Frequency in the First Session

We have tried to compare the acupuncture treatment frequency and the total number of treatment sessions in western countries and in China (Wang 2016). The data of western countries come from the review of Colquhoun (2015), Colquhoun and Novella (2013), Wang and Kain (2013), Furlan et al. (2010) Linde et al. (2009a, b), Madsen (2009), Vickers (2012), Azad and John (2013), Moffet (2009). The Chinese data from the reviews of Furlan et al. (2010), the journal of Shang Hai Acupuncture and Moxibustion (January 2015−August 2015), and other sources (Cheng and Kang 2007; Yao 2015; Wan 2015; Song et al. 2012; Song and Chen 2013; Huang et al. 2010; Li 2010; Ai et al. 2011; Huang et al. 2010; Cheng et al. 2009; Yang 2013; Shi et al. 2012; Chang et al. 2011; Zhang and Dong 2013; He 2013; Liu 2013; Lin 2013; Wang 2014; Tian and Yin 2006; Fang 2014; Zou 2014; Guo et al. 2014; Han 2014; Huang and Zhou 2014; Lu and Yao 2014; Yu and Zhang 2016; Xu et al. 2014; Wang and Liu 2015; Xie 2001; Dou 2015; Wang et al. 2013; Wu 2013; Li 2013; Jia 2013; Yang 2015; Hou et al. 2014; Zhan 2014; Shen 2013; Zhao 2014; Liu 2011; Liu and Xu 2003; Wei 2013; Zu et al. 2013; Wu 2011; Cong et al. 2015; Shi and Li 2006; Sun et al. 2003; Sun and Tao 2015; Yang et al. 2014; Yu et al. 2015; Bao et al. 2015; Li and Yu 2002; Pan 2014; Wang 2014; Liu et al. 2004; Shen et al. 2003; Sun et al. 2010; Jin et al. 2008, 2007; He et al. 2005; Shi et al. 2011, 2015; Zhou et al. 2006; Jiao and Xiao 2015; Xia et al. 2008; Er et al. 2015; Li et al. 2009; Dong et al. 2010; Guo and Liu 2005; Ma et al. 2011; Song and Xiao 2013; Wang and Yin 2005; Tang 2004; Zhang 2012; Cai and Long 2004; Ding 2007; Bao and Cao 2008; Wang and Xie 2006; Liu 2005; Dong 2001; Gao 2014; Fu et al. 2007; Kang and Li 2006; Yang and Lan 2004; Lu 2013; Liu 2000; Zhang 2005; Fan and Yang 2006; Chen et al. 2003; Wei et al. 2012).

When comparing the schedules of acupuncture treatment in the first treatment course, it is found that about 77.4% of acupuncture treatments in the published papers in China are 5−6 sessions a week, while also about 90% of the acupuncture treatment reported in western journals are once or twice a week (Fig. 6). This means

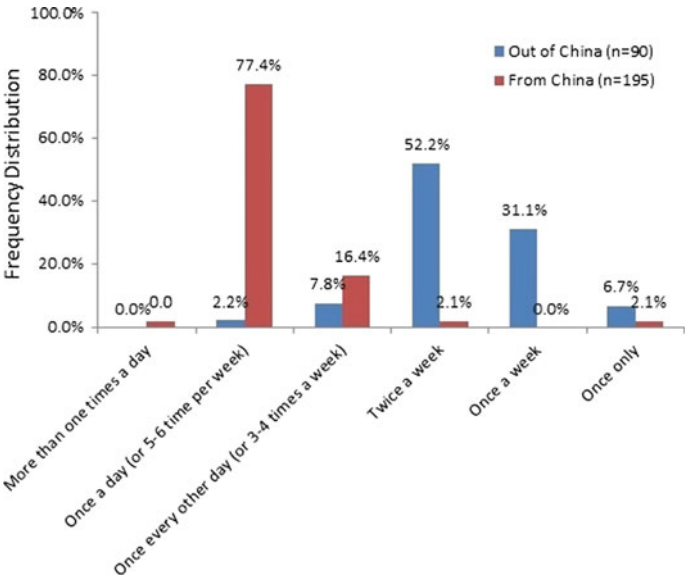


Fig. 6 Acupuncture frequency in the first week of treatment in or out of China. n = number of published articles. Note: Duplicated articles have been deleted. Articles indicating the acupuncture treatment such as "10 times over 3 months" is hard to interpret, so they are not included in the summary

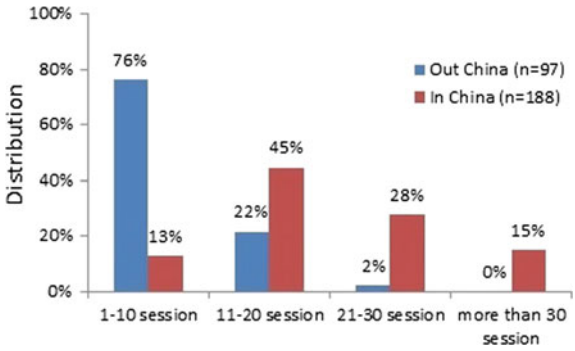


Fig. 7 Total number of acupuncture treatment in or out of China. n = number of published articles

that in the first 7−10 days, Chinese acupuncturists performed acupuncture treatment nearly every day to their patients, while the western acupuncturists leave their patients at home to wait for next acupuncture treatment several days later.

Figure 7 shows that most (76%) of the acupuncture treatment in the western groups are within 10 sessions, while most treatments (88%) in China are between 11 and 20 or more sessions.

Chinese acupuncturists use such concentrated acupuncture schedules, not only in acupuncture research, but also in practical acupuncture clinical treatments. Only when the disease is not severe, or when the patient has difficulty financially, or when

the acupuncture is used together with other therapies, would the Chinese acupuncturists use a less concentrated schedule of acupuncture, such as once every 2 or 3 days.

2.14.2 Average Daily Dose and Total Course Dose

There is a simple way to calculate the acupuncture dose. If the acupuncture is performed twice a week for two weeks and then once a week for two weeks, the average daily dose of the stimulation in the first two weeks (the first treatment course) is 4/14 = 0.28 and that in the second course is 2/14 = 0.14. The course dose of the first course is 0.28 × 4 = 1.12, and that in the second course is 0.14 × 2 = 0.28. The total course dose from the first and the second courses will be therefore 1.12 + 0.28 = 1.40.

Based on the published studies, it seems that acupuncturists in China performed acupuncture in different ways than those in western countries. The major difference is that the former used much higher average daily doses of acupuncture stimulation over the first course, as well as in total.

For further comparisons in the treatment schedules between western countries and China, we compared the average daily dose and total course dose. This is because the acupuncture treatment is usually performed through scheduled courses in China. Each course could be between 7 and 10 days or between 7 and 10 sessions. The next course will be started if there has not been progression from previous courses.

It was found that the average daily dose values for the three western groups are around 0.26 and for Chinese groups, 0.80 (Fig. 8). The total course doses for western groups are about 2.4, while it is about 18−20 for Chinese groups (Fig. 9). Evidently, the average daily stimulation dose and the total course dose are much higher in China than those in western countries.

2.14.3 Acupuncture Efficiency Comparison

We have also tried to compare the healing effects of acupuncture on non-specific lower back/neck pain and migraine/tension headache between the acupuncturists in China and those in western countries, by using the above data sources.

For non-specific lower back and neck pain, the healing effect of the acupuncture groups is higher in Chinese groups than in the western groups (50.8% vs. 37.2%) (Figs. 10 and 11).

For migraine and tension headache, the healing effect of acupuncture groups in China is also much better than in western groups (42.7% vs. 28.0%) (Fig. 12).

All the data above suggest that there might be some relationship between a higher average daily stimulation dose and the total course dose of acupuncture, and the higher healing effect of acupuncture treatment in China.

In the clinic, for the treatment of acute diseases or disorders, such as acute neck pain, acute low back pain, acute ankle sprain, and etc., it can be said that acupuncture

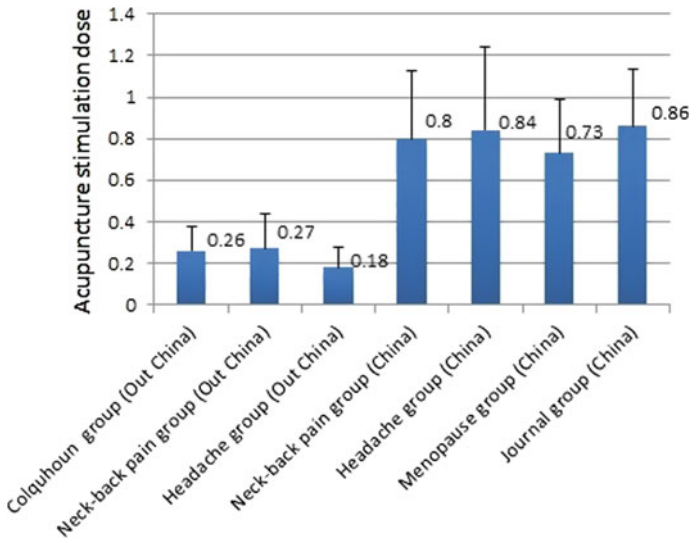


Fig. 8 Average daily stimulation dose of acupuncture in and out of China

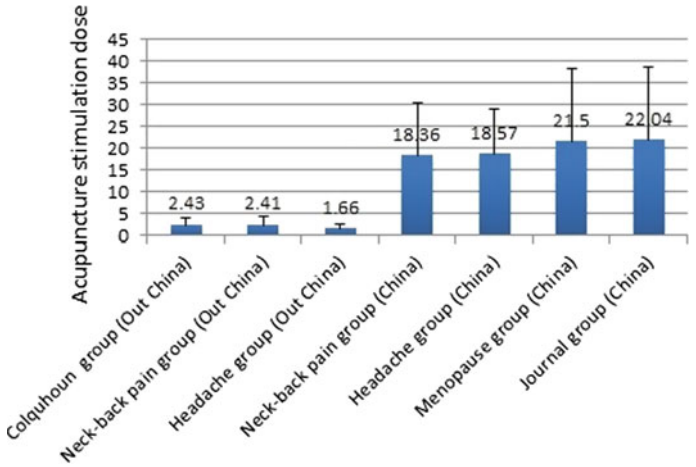


Fig. 9 Total stimulation dose of acupuncture in and out of China

one to two times can stop the pain dramatically, and even reduce the pain level down to zero.

However, for a better therapeutic effect of chronic diseases, such as chronic shoulder pain, chronic low back pain, chronic sciatic pain, chronic migraine, chronic knee pain, and etc., a concentrated treatment schedule, in addition to repeated treatment, is needed, e.g., acupuncture for once a day for many sessions. Generally, when repeating the treatment as such for about 3−5 times, the pain level can be reduced to 20−30%

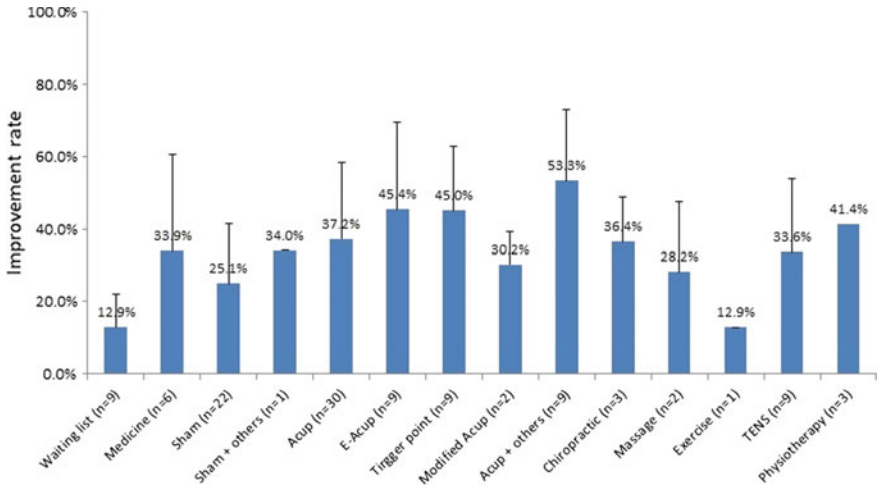


Fig. 10 Improvement rate of neck and low back pain by various modalities (Data from Furlan D review, western group)

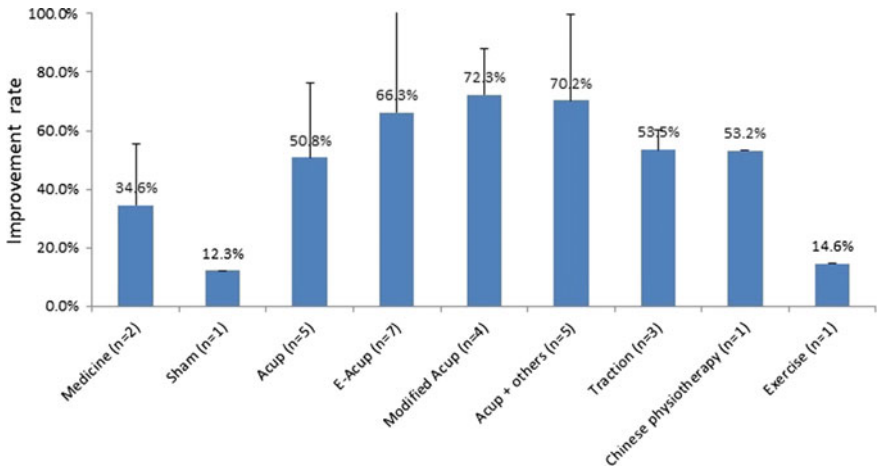


Fig. 11 Improvement rate of neck and low back pain by various modalities (Data from China)

of the initial pain level. After that, the treatment can be shifted to once every two to three days, until the pain subsides completely. After that, a maintenance course (acupuncture once per week for 3−4 weeks) is still necessary. An improvement of a chronic disease is not impossible through acupuncture using this treatment schedule. In the treatment of musculoskeletal pain, for example, the patients can gain a satisfactory efficacy so that they no longer need physical exercise or ice patch use on the painful spot at all. Since the pain can be reduced within 7−10 days, the patients

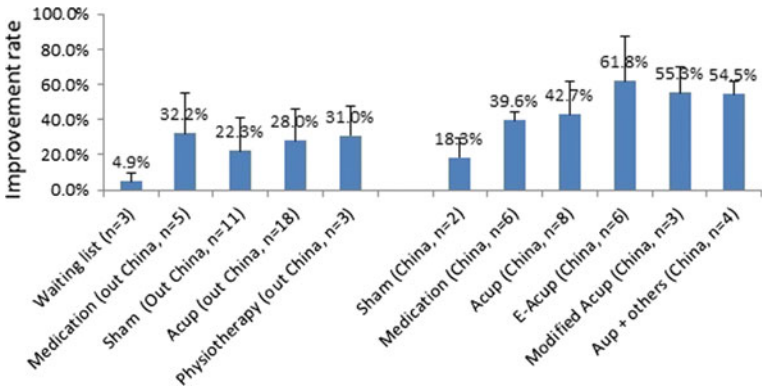


Fig. 12 Migraine and tension headache pain reduction in and out of China. n = number of published articles

usually stop the use of painkiller and have no need to visit their family doctors for the same problem.

Streitberger et al. (2003) treated nausea after chemotherapy on breast cancer patients. They performed acupuncture once a day for two days. The nausea rate in the acupuncture group and the sham group is 61% and 64%, respectively, with no significant differences. Shen (2000) also performed acupuncture on breast cancer patients after chemotherapy. The acupuncture, together with electrical stimulation, was performed on the patients once a day for 5 days. The number of the days with nausea was only 5 days in the acupuncture group, comparing to 10 days in the sham group and 15 days in the no-treatment group.

Meng et al. (2012) reported that when treating cancer patients with acupuncture three times a week for 6 weeks, the incidence of dry mouth in acupuncture group a month after stopping treatment is 25%, while that in the sham group is 90%, suggesting that high treatment frequency can yield dramatically prevent effects of dry mouth in cancer patient after chemotherapy.

In the treatment of hot flashes, Vincent (2007) used acupuncture once every two weeks for 5 weeks. The incidence of hot flash in the acupuncture group and the sham group has no significant difference. However, Huang (2006) also treated hot flash with acupuncture, but twice a week for two weeks, then once a week for the following 5 weeks. After 7 weeks of such treatment, hot flashes were reduced significantly in the acupuncture group compared to the sham group.

In the treatment of chronic low back pain, Ceccherelli et al. (2003) used acupuncture, five sessions per week for a pain reduction rate of 68.7%. When the acupuncture was performed 10 times a week, the pain reduction rate was 86.7%.

Acupuncturists in China have conducted more studies on the influence of treatment frequency on the healing effect of acupuncture treatment.

Qi et al. (2004) suspected the possible relationship between the low treatment frequency and the low healing effect of acupuncture treatment in western countries.

They treated 33 cases of stroke patients with acupuncture five times a week (first treatment group), 32 cases twice a week (second treatment group), and another 30 cases with conventional western medicine (medicine group), all for three weeks. After three months, they found that the Barthel scale reduced by 70.5% in the first treatment group, 31.5% in the second treatment group, and only 26.1% in the medicine group.

Li et al. (2015) treated 30 cases of slight cognitive disorder with acupuncture. They found that acupuncture once a day, 5 days a week for 3 weeks, yielded better results than that of 3 times a week for 5 weeks.

Xu et al. (2006) tested how acupuncture treatment once a day (treatment group A, 32 cases) or twice a day (treatment group B, 35 cases) would influence the healing effect of acupuncture treatment on functional recovery (using fugl-Meyer scale and ADL scale) of the arms or legs of post-stroke patients. They found that after two courses, treatment group B showed more improved functional recovery than treatment group A. They summarized that twice a day of acupuncture works better than once a day of acupuncture in these patients.

When using acupuncture for quitting smoking, acupuncture should be every day for 7−10 days. This method can reduce cigarette smoking from more than 20 cigarettes per day down to 0−1 per day. Acupuncture once a week for 7−10 weeks has no effect on the amount of daily cigarette smoking. Therefore when checking published studies on quitting smoking through acupuncture, the poor result may be due to a low treatment frequency.

There are data (Bian and Zhang 2003) showing that the half-life period of acupuncture treatment is 3−6 h. So, to increase the stimulating dose of acupuncture, one must increase the acupuncture session frequency. This opinion is supported by Xing et al. (1993) The author found that to treat post-stroke syndrome, acupuncture three times per day works better than once a day. For the same type of disease, Jiao (2008) reported that acupuncture twice a day with a retention time of 30 min works better than that of once a day with a retention time of 6 h. This suggests that frequency of acupuncture treatment is more important than the length of retention time.

Zhang (2014) believed that acupuncture treatment needs an interval between each session. For some acute diseases, such as acute laryngopharyngitis, acute conjunctivitis, or acute appendicitis, acupuncture can be performed twice to three times per day. For chronic diseases, it can be performed once a day, with 7-days as a healing course and a 2−3 day break between each course. The author noticed that in the treatment of some chronic diseases, such as post-stroke hemiplegia and facial paralysis, the healing effect usually is not apparent during the treatment, but it is if there is an interval between the healing courses.

Yuan et al. (2009) compared the healing effect of acupuncture twice a week for five weeks to that of five times a week for two weeks. There was no difference found between the 2-session group and the 5-session group. However, they used moxibustion and cupping together with the acupuncture. It was a comprehensive treatment, not acupuncture alone. This suggests that with the combination of other therapies, similar to a real clinic situation, the acupuncture treatment can be performed twice a week. However, the healing effect in the 5-session group is better than the 2-session group in the treatment of severe cases. Moreover, the healing effect in the 2-session

group has no improvement in the following weeks, but the treatment in the 5-session group may have further improvement if treatment was continued. This possible means that after five weeks, the healing effect in the 5-session group might be better than that of the 2-session group.

Current data show that different diseases need different treatment frequencies. Even for a given disease, the interval of acupuncture sessions might also be different between the acute and chronic phases of the diseases (Xu et al. 2006; Bian and Zhang 2003; Xing et al. 1993; Lin et al. 2013; Yu and Sheng 2015; Hu et al. 1995; Cai 2003). It has been reported that for the treatment of chronic fatigue after stroke (Lin et al. 2013), cervical spondylopathy (Wu et al. 2010). peripheral facial paralysis (Yang 2013), Bell's palsy (Cheng et al. 2009), three times a week of acupuncture (or once every other day) achieves the highest healing effect. Increasing the treatment frequency to once a day does not further increase the healing effect. However, these data still recommend three times of acupuncture sessions per week for the treatment. It is very rare for Chinese acupuncturists to perform acupuncture only once a week.

2.14.4 Healing Effect in High Frequency Treatment

Now a new question arises whether a placebo effect in a sham acupuncture group might be also higher with a higher treatment frequency of acupuncture.

It is not easy to answer this question with current data. Currently, it is hard to find an acupuncture study in western groups that perform acupuncture as 5−6 times per week for 10−20 sessions. On the other hand, acupuncture studies in China normally do not involve a sham group.

There are 27 articles on this topic (Cheng and Kang 2007; Dibble et al. 2000; Li and Yu 2002; Xu and Zhang 2015; Alfredo et al. 2012; Fukuda et al. 2015; Cheing et al. 2002; Hagstroem et al. 2009; Lazovic et al. 2014; Mollasadeghi et al. 2013; Warke et al. 2006; Li et al. 2012; Foroughipour et al. 2014; Zizic et al. 1995; Yeung et al. 2011; Zhan et al. 2015; Yu et al. 2001; Fan et al. 2005; Hollisaz 2006; Yeung et al. 2009; Zhang et al. 2013; Yao et al. 2012; Wang et al. 2015; Guo 2014). Among these articles, 15 were from western countries, and 12 from China. For a better analysis and reliable conclusion, we excluded the following studies: the studies is a thesis work of Ph.d. or master students; studies on animal or on healthy person; studies used grade parameters as a mark for healing effect; studies used continuous parameter as mark but the parameter is increased at the end of the study, and the studies that used acupuncture and other therapies at the same time (Liu 2013; Lu et al. 2009; Liao et al. 2015).

Figure 13 showed that with acupuncture or electroacupuncture for three sessions per week (middle frequency schedule) or five or six sessions per week (high frequency schedule), the healing effect of the sham group is only 17–20%. The healing effect of the inserted and the non-inserted sham groups (see below) were the same. For the inserted sham group, one article was from a western country, one from Taiwan, one from Hong Kong, and 6 from mainland China. For the non-inserted sham group, two articles were from western countries, three from Hong Kong, and three from mainland

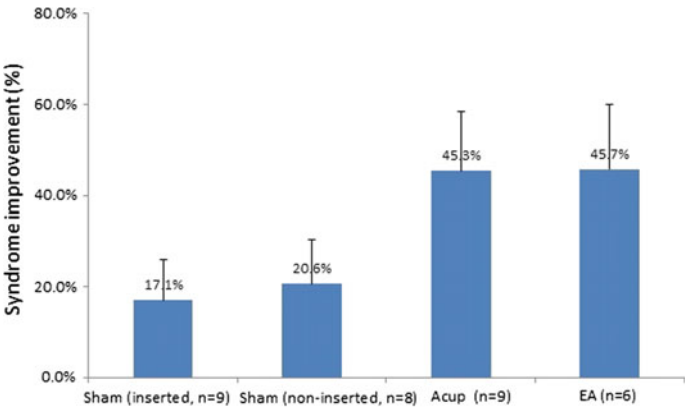


Fig. 13 Healing effect in Acupuncture and Electrical acupuncture, sham acupuncture groups with middle and high treatment frequency. n = number of published articles. EA: electroacupuncture

China. With the same treatment schedules, the healing effect of both the acupuncture group and the electrical acupuncture group reached 45%, which is much higher than both the sham groups. Clearly, with higher treatment frequency, the healing effect of the acupuncture groups was significantly higher than that of the sham groups.

It was also found that for the healing effect of TENS or laser at the middle or high treatment frequencies (Fig. 14), the healing effect of either the TENS or laser treatment seems less than that with higher treatment frequencies (5−6 sessions per week). (44.1% vs. 56.3%). Again, the healing effect of the sham TENS or the sham laser groups remained at low levels, i.e., 13−18%. There are major differences between the TENS or laser group, and sham groups. In these studies, all of the sham groups were non-inserted sham groups and the needles were not connected with either electric or laser energy. Among these studies 7 articles were from western countries, 2 from Hong Kong, and another 2 from the Mainland of China.

These data strongly suggest that the healing effect of acupuncture, electrical acupuncture, TENS or laser treatment is higher with higher treatment frequencies, while that of sham groups (inserted or not inserted sham group) remained low. This also suggests that the higher frequency of treatment schedules may not have enhanced the placebo effect in sham groups.

2.15 Proper Time to Start Acupuncture Treatment

When to start acupuncture treatment is a practical question. Generally speaking, for the treatment of chronic diseases, acupuncture can be started anytime. However, for paroxysmal diseases, such as paroxysmal hemicrania, or for periodic diseases, such as lower abdomenal pain before menstruation, the time to start acupuncture is a

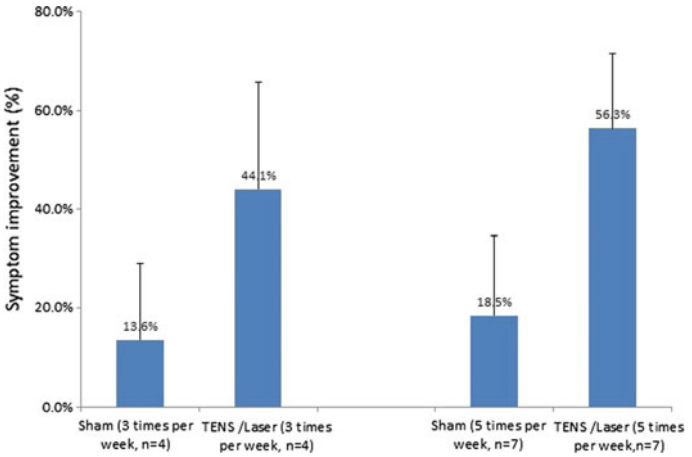


Fig. 14 Treatment by TENS or laser at three sessions per week or five sessions per week. n = number of published articles

question that needs to be discussed. For the treatment of these diseases, we normally start the acupuncture 2−3 days before the onset of diseases (once a day), rather than start the acupuncture after the onset.

For example, in the treatment of dysmenorrhea, acupuncture can be applied for 3 days before the menstruation, once a day for three to four days, or until the pain completely disappears. Usually it needs only 1−2 days or 4 days in a rare case before the pain subside. After that, acupuncture can be performed once or twice a week until the next period. This is one treatment course. This treatment plan can be repeated for 2−3 months. The level of the pain can be dramatically reduced or even disappear completely. The studies by Ma et al. (2013), Du et al. (2012), Cai (2012) support this schedule. This treatment plan is also suitable for the treatment of infertility, where the acupuncture should be started 3 days before ovulation day.

Zhang and Song (1994) reported their methods of treating acute stages of cerebral infarction plus cognitive dysfunction. They found that acupuncture started within 7 days of the infarction (20 cases) works better than acupuncture started after 7−30 days of the infarction (20 cases).

Acupuncturists in China have had many studies on the treatment of cerebral infarction (Zhang et al. 2013; Wang et al. 2009; Qing et al. 2015; Fan et al. 2005; Li and Huang 2001; Liu et al. 2010; Wang and Cai 2015; Liu et al. 2015; Zhang et al. 1998; Xu 2015; Qian et al. 2015; Hu et al. 2013). Indeed, acupuncture works in both acute and chronic phases of stroke. For the treatment of acute cerebral infarction or cerebral hemorrhage, the healing effect is the highest if acupuncture started within 72 h of onset (Du et al. 2012). In our laboratory studies with experimental stroke models, we also found that electroacupuncture is effective to induce neuroprotection against ischemic brain infarction (Fig. 15) and reduce neural defects and the EA-induced neuroprotection is better when applying before and immediately after the onset of

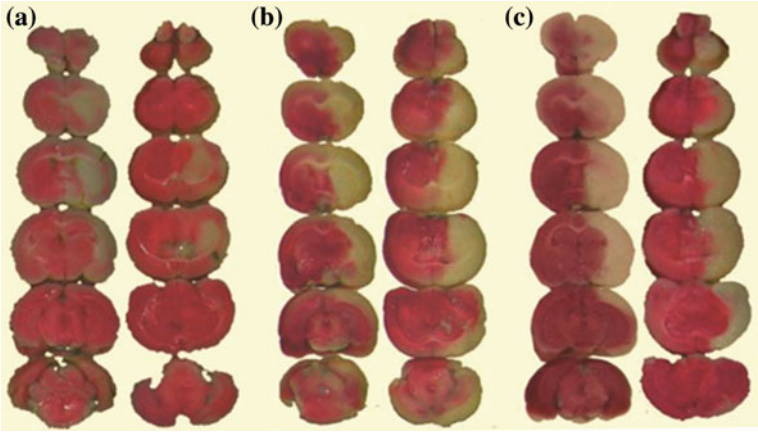


Fig. 15 Effect of electroacupuncture on ischemic infarction. Electroacupuncture was applied at different acupoints starting at 5 min after the onset of cerebral ischemia (MCAO). **a** Stimulation at contralateral QuChi (LI11) and NeiGuan (PC6). **b** Stimulation at ipsilateral QuChi (LI11) and NeiGuan (PC6). **c** Stimulation at contralateral SanYinJiao (SP6) and YangLingQuan (GB34). Note that the stimulation of suitable acupoints (contralateral QuChi and NeiGuan) greatly reduced ischemic brain infarction. Cited from Zhou et al. (2013)

ischemic stress (Zhang et al. 2013; Wang et al. 2009; Zhou et al. 2011; Zhou 2013; Xia 2015). Clearly, timing/applying windows is a determining factor for the healing effect of acupuncture.

2.16 Evaluation of Long Term Healing Effect

How long the healing effect of acupuncture treatment can last is one of the topics in many acupuncture studies in western countries. However, there is little reliable information in the literature to demonstrate the long term healing effect, i.e., from the beginning to the end (symptom relief and/or disappearance).

Most researchers counted the change of the post-treatment healing effect after several sessions of acupuncture treatment. For example, patients were given acupuncture treatment for 2, 3 or 6 months. The treatment stops and then observe the healing effect is observed for one year (Zhang 2014; Avis et al. 2016; Hervik and Mjåland 2009). The researchers measured the healing effect for all the patients as a group. It can be expected that in the group, the symptoms of some patients were possibly much improved, but the symptoms for other patients were not much improved yet. Some researchers even tested the cure rate of open wounds after only one time of acupuncture treatment (Saarto et al. 2010). It is too optimistic for acupuncture to have only a one-time treatment.

Bokmand and Flyger (2013) treated dysmenorrhea with acupuncture for 3 months. The time period of pain period was reduced from 53.8 to 31.5 h. In this particular study, although the pain level is still severe, the authors ended the acupuncture treatment to observe the long term healing effects after acupuncture treatment. The acupuncturists in China usually pursue no or minimal pain as their therapeutic goal.

Sánchez-Araujo and Puchi (2011) tested if acupuncture prevents relapses of recurrent otitis in dogs. The dogs were given acupuncture treatments once every three days, for a total 4 times (without manipulation of needles). They observed the recurrent rate from this treatment schedule. The success rate would be low if the otitis was not improved dramatically after the end of the acupuncture treatment.

Acupuncture is not a miracle cure. If the symptom has not been reduced to zero or to a very mild level, the chance for the relapse is very high, especially if the factors that caused the symptom were not removed or eliminated completely. For example, for knee pain due to prolonged bending of the knee from an occupation (such as in professions that repair floors), the long term healing effect is poor, even if acupuncture reduced the knee pain to zero. This is because patient continues the daily stress on the knees after acupuncture treatment.

Acupuncturists should also ask clients to change their life style or work style that cause these diseases to eliminate the factors that cause them. This is how the disease can be really "cured". Otherwise, there is no other cure for knee pain for these patients. Therefore, it is meaningless to evaluate long term healing effects of acupuncture when the symptom has not been reduced to very low level and the patients are unable to eliminate factors that cause the symptoms.

2.17 Complementary Treatment

When treating many kinds of diseases, patients are asked to take a break from heavy labor or stressful work. Especially for the treatment of painful diseases, patients need to reduce or stop physical exercise, and not use ice on painful locations. This is to reduce the chance of causing more damage to the tissue. Pain is a signal of the body that something needs to be changed, rather than continued. However, in many articles, it is not mentioned whether the researchers asked patients to stop physical activity and the use of ice, which are both very common in physical therapy and in chiropractic treatments.

It is very common for clients to continue exercise and the use of ice on painful spots if we do not emphasize not to. Long term or frequent use of ice can reduce blood circulation on the affected area and cause accumulation of metabolic waste material in the tissue, and slow down the repair of the painful spot. Therefore, Chinese medicine mostly recommends the use of a hot/warm patch. The only condition in which an ice patch is used is for sprains (on knees or ankles, for instance). In this case, the ice patch would only be applied once, for no more than 20 min.

2.18 *Suitable and Non-suitable Diseases for Acupuncture Treatment*

Acupuncture may work for some diseases, but not for all diseases. For example, acupuncture may not work well for fibromyalgia. A survey (Du et al. 2007) showed that among total 3576 studies on the disease of muscle-bone and connective tissue, there were only 13 studies related to the treatment of fibromyalgia, which is only 0.4% of all of the 3576 publications. The low numbers of the literatures in some way also reflects the poor healing efficacy of the acupuncture on the treatment of fibromyalgia. This is true that in China, a negative study cannot be easily published. Acupuncturists in China are seeking for more effective ways of acupuncture treatment.

To meet the needs of acupuncture clinics and research, WHO held a meeting in Milan in 1996, where 64 kinds of diseases/disorders were proposed as the suitable categories for acupuncture treatment (http://www.wfas.org.cn/who/files/2008). The meeting stated:

(1) Diseases that are claimed as suitable to acupuncture treatment, supported by randomization studies:

Alcoholism, allergic nasitis, competitive syndrome, facial paralysis, cholecystalgia, asthma, heart neurosis, cervical spondylosis, chronic pain in motor system, depression, quit drugs, dysmenorrhea, headache, hemiplegic paralysis or other post-stroke syndromes, herpes zoster, hypertension, primary hypotension, impotency, induction, insomnia, hypoleucocytosis, low back pain, migraine, reaction of pregnancy, nausea or vomiting, periarthritis of shoulder, post-operative pain, premenstrual tension, nerve root pain syndrome, renal colic, arthritis pauperum, sprain or strain, dysfunction of mandibular joint, tension headache, quit smoking, trigeminal neuralgia, and urinary stones.

(2) Diseases that are claimed to be suitable for the acupuncture treatment by studies with sufficient numbers of participants, but no randomized study design:

Acute paristhmitis, acute pharyngolaryngitis, back pain, ascariasis of biliary tract, chronic pharyngitis, malposition, infantile enuresis, tennis elbow, gallstones, irritable bowel syndrome, Ménière's disease, myofascitis, children myopia, simple obesity, pain after amygdalectomy, chronic dementia, sciatica.

(3) Diseases suitable for acupuncture treatment by repeated clinic studies for a faster healing effect than conventional medicine, or there is some experimental evidence:

Constipation, hypogalactia, diarrhea, infertility, bathygastry, hiccup, urinary incontinence, painless labor, retention of urine, nasosinusitis.

According to a survey (Huang et al. 2013) in 2013 of acupuncturists in the Jiangsu province of China, the most suitable diseases for acupuncture treatment are:

Facial paralysis, stroke, low back pain, headache, neck pain, stiffness of shoulder, insomnia, stomach pain, herpes zoster, and various knee pains.

Other data (Yang et al. 2014) suggest that the suitable diseases for acupuncture treatment are:

(1) Digestive diseases: hiccups, stomach pain, diarrhea, constipation, nausea, intestinal pseudo-obstruction and hemorrhoids.

(2) Skin diseases: acne, urticaria chronica, neurodermitis. Most possible effective diseases: chloasma, corn, cutaneous pruritus. Possibly effective: pelada, eczema, psoriasis, leucoderma, bedsore.

(3) Psychiatric and behavior disorder: dementia, abstinence syndrome, mental retardation, obsession, dyssomnia, gastrointestinal neurosis, depression, alcoholism, and globus hystericus.

The category of dominant diseases for acupuncture treatment is not unchanged. Along with the efforts of acupuncturists in China, the category and the suitable spectrum for acupuncture treatment are growing. On the other side, if an acupuncturist gets just only hundreds of hours of acupuncture training and practices acupuncture according to what they learned from a textbook and only practice acupuncture on two to three patients per day, the acupuncturist may not be able to treat these diseases well, even if the acupuncturist has practiced for more than ten years. This is especially true if he/she has never treated the disease before. In this point, the so-called dominant diseases for other acupuncturists may not be the dominant disease for this given acupuncturist. Therefore, a good conceptual knowledge of acupuncture may not be sufficient to render one to become an acupuncture expert. Practice to gain sufficient experience is critical for an acupuncture expert. This is also true for a successful clinical study on acupuncture treatment.

3 Sham Acupuncture Group

The susceptibility to a hint (placebo) is largely variable. The responder rate (the percentage of people who received more than 50% of symptom reduction) can be 31–45% (Peciña et al. 2015). It can be expected that the higher the responder rate is in acupuncture study (especially in sham group), the higher the healing effect of the sham group (e.g. the higher placebo effect in the sham group) would be. From the literature, the healing effect in inserted sham groups is from 2.6 to 59.1%, and that in non-inserted sham groups is from −3.8 to 55.6%, suggesting that the responder rate among studies is indeed largely variable.

We have tried to see how the level of the healing effect in a sham group relates to the final result (support or deny) acupuncture's specific healing effect. We collected data from the reviews by Colquhoun and Novella (2013), Colquhoun and Steven (2015), Linde (2009a, b), Melchart et al. (2005), Haake et al. (2007), Witt et al. (2005), and Cherkin et al. (2009). We found that (Fig. 16) when the healing effect from a sham group is more than 31, 75% of articles showed negative results. On the other hand, if the healing effect of a sham group is less than 31, 69.2% articles showed positive results sup porting the specific healing effect of acupuncture. Evidently, the level of the healing effect in a sham group strongly affects the result of an acupuncture study.

The sham groups can be classified into two major categories: inserted (Smith et al. 2011; Shen et al. 2000; Wyon et al. 2004), and non-inserted (Park et al. 1999; Streit-

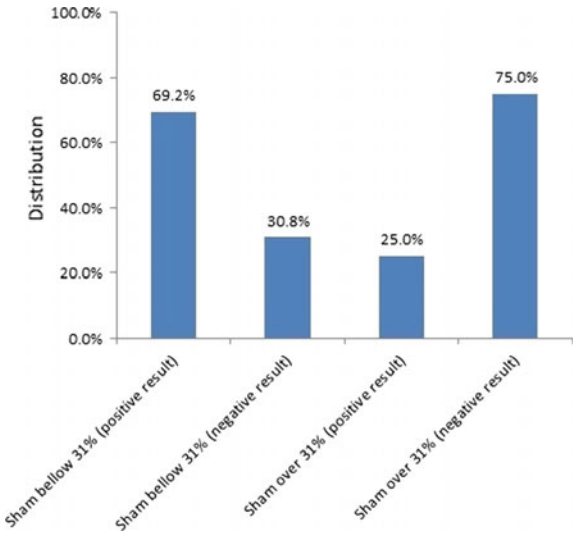


Fig. 16 Distribution of positive or negative results about acupuncture healing effects separating the distribution with sham effectiveness as 31%

berger and Kleinhenz 1998; Takakura et al. 2014; Zhang et al. 2015; Takayama et al. 2015). Inserted means an acupuncture needle is inserted into either acupuncture point (in shallow or in deep), or in a spot that normally does not belong to an acupuncture point (non-point). Non-inserted means a blunt needle is used on acupuncture point or on a non-point without pene the needle into the skin. Alternatively, non-inserted could mean the blunted needle is connected to an electric machine but no electricity is conducted (White et al. 2004; Vas et al. 2006), or the acupuncture point was touched by a laser probe, but no laser is emited (Irnich et al. 2001).

We have tried to compare the placebo effect from the inserted and non-inserted sham groups, using the data from review papers of Colquhoun and Novella (2013), Furlan et al. (2010), Linde et al. (2009a, b), Madsen (2009), Vickers (2012), Azad and John (2013), Moffet (2009), and other sources (Qing et al. 2015; Cheng et al. 2009a, b; Xu and Zhang 2015; Alfredo et al. 2012; Fukuda et al. 2015; Cheing et al. 2002; Hagstroem et al. 2009; Mollasadeghi et al. 2013; Warke et al. 2006; Deng et al. 2008; Bennell et al. 2005; Cheing et al. 2003; Cheing and Hui-Chan 1999; Hawamdeh et al. 2015; Al Rashoud et al. 2014; DeSantana JM et al. 2008; Fleckenstein et al. 2009; Hopwood et al. 2008).

It was found that the sham groups showed around the same average effect level, regardless of insertion. The placebo effect of the inserted sham group was $23.0 \pm 14.7\%$ (32 published articles) and that of non-inserted sham was $22.9 \pm 16.7\%$ (35 published articles).

Yeung et al. (2011) compared the healing effect of inserted sham and non-inserted sham in the treatment of insomnia. The treatment is three times a week for a total of three weeks. The effect of non-inserted sham is 12.8% and that of inserted sham is 24.8%. The difference is very small, and both are at low levels. This result suggests that inserting a needle on a non-point without handling the needle to cause

acupuncture sensations may induce some level of healing effect, but the effect is very limited. The difference in the healing effect between the inserted and non-inserted sham groups may not be detectable with a pool of further studies for review.

This result suggests that the types of sham methods are not the major reason to cause the variation in the healing effects in a sham group, but that of original responder rate might be. It also suggests that perhaps the insignificant difference in healing effect between the acupuncture group and the sham group is not due to the use of an inserted sham group, but to a poor healing effect in the acupuncture group.

The variation in a population's susceptibility to a hint stimulation (placebo stimulation), e.g., the response rate in a population, is a reality. Such variation in the response rate to a hint is a background noise to all medical clinical studies, not only to acupuncture research. Since a clinical study aims to determine if acupuncture has a specific healing effect, the placebo effect in the study should be eliminated.

Currently, many acupuncture studies include a sham group and an acupuncture group. The specific healing effect of acupuncture group was determined as the difference between the total healing effect in the acupuncture group and the sham groups. This way may not be sensitive enough to detect a specific healing effect of acupuncture group. This is because the healing effect level of the sham group (the placebo effect) is largely variable among people due to personal susceptibility, and there are too many factors that can affect the level of the placebo effect in a sham group.

We may recommend eliminating the placebo effect in a clinical study by involving a wash-up phase: giving all the participants a sham treatment for some time, before starting the real treatment phase. This eliminates participants who had their symptoms reduced by more than 30% (instead of 50%). The disadvantage of this is that it will need higher numbers of participants initially, but the advantage is that it should be able to increase the chance (sensitivity) to detect the specific healing effect of acupuncture in real acupuncture groups.

Alternatively, we may recommend using the Chinese high treatment frequency, e.g. to have acupuncture once a day for 5 to 6 days per week, and for a total of 20 to 30 sessions (depending on the type of disease). As we have introduced before, upon such a treatment schedule, the healing effect of the acupuncture group tend to be higher, while that of sham group remained the same. With this high treatment schedule, it appears that there is no need to have the pre-wash up phase to eliminate the susceptible people out of the study.

4 The Ability of an Acupuncturist

Unlike pharmaceutical research in western medicine, which does not involve doctor's personal skill, any study involving personal skill, such as acupuncture, massage, chiropractic, physiotherapy (if it is manual therapy), as well as a surgery, needs to choose the highest level of practitioners to conduct the relevant part of the study.

In the review of the acupuncture studies in western countries, the impression was that anyone may act as an "acupuncturist" in the study. Some physiotherapists, chi-

ropractic, or physicians can receive an acupuncture license after taking acupuncture training courses. For example, a physician could have an acupuncture certificate after 140 h of training, and would be allowed to participate in an acupuncture study (Linde et al. 2009a, b; Haake et al. 2007; Witt et al. 2005; Brinkhaus et al. 2006; Diener et al. 2006; Endres et al. 2007; Witt et al. 2006). Sometimes, even newly graduated students can participate in the research (Joos et al. 2006; McKee et al. 2013).

Those practitioners may feel very confident to participate in an acupuncture study. They might think that they are qualified to do so if they choose the same acupuncture point(s) used by other researchers in other studies. They might believe that the outcome of the study is to the credit of the acupuncture per se, and the success or failure of the study has nothing to do with their own personal skill However, the personal skill of acupuncture performance could greatly affect the outcome.

The ability of acupuncturists in China who participate in acupuncture studies is ensured by their published articles. Their articles would not be accepted for publication if their studies cannot improve the healing effect of current acupuncture techniques, or if their work does not allow a better understanding of acupuncture mechanisms, or any other aspect of acupuncture. However, any study on acupuncture can be published in western countries if the study meets the need of some basic requirements for the publication, such as randomization, blindness, a sham group, a waiting group, over 20–30 patients in each group, and statistical analysis of the data.

The ability of an acupuncturist is not determined by the years of that person's acupuncture license, or where the person received acupuncture training. These should not be the absolute parameters that dictate the skill of an acupuncturist. We believe that if we do not pay attention to the actual skills of an acupuncturist, no acupuncture studies, no matter the design, would ensure to reach the truth.

White et al. (2012) studied acupuncture for the treatment of osteoarthritic pain. The study involved three acupuncturists. The healing effects of the three practitioners are 37, 17, and 62%. Though it was explained by the author that the highest healing effect by the third acupuncturist might be due to his impression by patients as more professional and more like an expert, it cannot exclude that his personal skill in acupuncture might be the highest. No matter what could be the reason, the huge difference in healing effects by the three acupuncturists will affect the data analysis for sure. It is possible that to compare the healing effect by the third acupuncturist with sham acupuncture, it would show a statistically significant difference (such as 63% vs. 28.4%, or 63% vs. 39.2%, as shown in the authors' paper), rather than no difference as reported.

Forbes et al. (2005) reported in their acupuncture study that when Acupuncturist A treated 12 patients with IBS, 50% patients had the symptom level reduced by 4. Acupuncturist B treated 15 IBS patients, and 33.3% of patients had the symptom level reduced by 4. The authors might combine the data from the two acupuncturists together. Their conclusion on the study may be questionable.

Another example is from the report of Deng et al. (2007) for the treatment of hot flashes with acupuncture. During the study, the acupuncturist was changed and the reduction curve of the hot flashes reversed up. They had acupuncture twice a week

for 4 weeks. The hot flashes reduced by about 30–35%, similar to that in the sham group. So, healing clearly depends on the acupuncturist.

If the personal skills among several acupuncture operators are so different, how can we trust the study involving 67 physiotherapists, (Foster et al. 2007) 122 physicians (Brinkhaus et al. 2006), or 320–340 physicians? (Peciña et al. 2015; Scharf et al. 2006).

Fregni et al. (2010) pointed out that in an international placebo symposium working group, "a great number of interventions used in PRM depend on the technician's or clinician's skills such as the application of acupuncture, injections, and nerve blocks. Therefore, controlling for these interventions becomes difficult with this important source of variability. This makes it even more difficult to design an appropriate placebo in these situations. To control for skills and levels of experience, it would be necessary to conduct multicentric studies with various levels of skills and experiences and perform multivariate analyses to adjust for these variables. In this scenario, a large number of patients would be necessary, increasing the difficulties to conduct such studies."

Hawk et al. (2005) reposted their chiropractic study on chronic pelvic pain. The study involved 3 clinic locations. After 6 weeks of chiropractic treatment, the pain level reduced by 59.1, 26.9, 84.6%, in the three locations, respectively, with an average of 56.6%, while the reduction rate in the sham group is 68.5%. The healing effect of the treatment group is even less than that of the sham group. The practitioners in the 3 clinic locations were reported to have 20, 10, and 12 respective years of clinic experience. Having no alternative, the author had to admit that "The technical and personnel resources required to achieve adequate standardization of procedures at multiple sites may make a placebo-controlled trial unfeasible, given our current lack of knowledge about the active agent in manual chiropractic procedures. It might be more efficient to reverse the traditional order of experimentation used for pharmaceuticals, which begins with safety, proceeds to efficacy and finally to effectiveness. Because chiropractic—a CAM profession using manual methods for more than 100 years—can scarcely be considered in the same category as a newly developed medication, it might be reasonable to first investigate effectiveness. If chiropractic care that is provided by experienced chiropractors who are allowed to use their best clinical judgment of how to apply the procedures is documented in such studies to improve patient outcomes compared to standard medical care alone, more in-depth and controlled studies would then be warranted to identify specific aspects of that *gestalt* of care that are most responsible for the outcomes or if there are certain subpopulations of patients who benefit most from them."

To reduce variations in acupuncture studies in personal clinic skills, we recommend a selection process for the candidates of acupuncturists.

Basic selection: the acupuncturist should have a comprehensive healing effect for most of the diseases in his/her clinic, as high as 75% (within one to two months). The comprehensive therapies include the use of acupuncture, cupping, moxibustion, bleeding therapy or whatever commonly used therapies in his/her acupuncture clinic. It should not be difficult to find such acupuncturists.

Specific selection: the acupuncturist should have at least 75% of the average healing effect (as published data from China, for example) for the disease/symptom to be studied. Moreover, only the acupuncture therapy, not other therapies, such as cupping or moxibustion, is used in a pilot study. The average healing effect of acupuncture is different for different disease/symptom. For example, if an average healing effect for non-specific lower back pain in China is average of 55%, the healing effect of the candidate acupuncturist in the western countries for the same types of pain should be more than 41% ($55\% \times 75\% = 41\%$). If the candidate acupuncturist cannot reach such level in acupuncture treatment, he/she should not be regarded as "qualified" acupuncturist in an acupuncture study.

The reason for the comprehensive basic selection is that if the acupuncturist cannot reach such levels of comprehensive healing effects with their own natural and practical ways of acupuncture treatment, it would be impossible for them to create a positive result in a western style of acupuncture study in which only acupuncture is allowed, while moxibustion, cupping, or any other kind of therapies, are not. There is no point in creating significant amounts of negative data through untrustworthy ways of studies.

The reason for the special selection is that even if the acupuncturist passes the basic selection, it still does not guarantee that the acupuncturist is able to treat the disease to be studied. For example, if an acupuncturist never treated coma patients (due to stroke), it would be hard to believe that the acupuncturist can treat such patients in a study. The specific selection allows the study to use an acupuncturist that has experience with the specific disease to be treated.

If there is no acupuncturist that can pass the specific selection, it means that the conditions for an acupuncture study are not met. The study should not be started, similar to how a surgeon should not perform a craniotomy without anesthesia.

5 Suggestions for Acupuncture Studies

Evidently, the study of acupuncture is more complex and difficult than a drug clinical study. For a drug, its concentration or content can be easily standardized. The same tablet can be used at the same time to thousands of participants. Even sham pills or sham tablets can be produced in the exact same shape, color, and same size as the true pills or tablets. It is hard for participants to recognize the difference between taking a true or sham pill.

However in acupuncture studies, the effect of acupuncture treatments can be affected by improper selection and number of the acupuncture points, insufficient stimulation doses in each session, poor treatment frequency, not enough numbers of treatment sessions, and more. It is also hard to standardize the personal skill in acupuncture treatment among practitioners, even if the same acupuncture treatment procedures are requested to be followed since the stimulation of acupuncture in each session is also hardly the same for the same acupuncturist. The sham acupuncture process is also hard to standardize as blind to the participants. Additionally, the sham

acupuncture procedure (inserted or not), may have enhanced placebo effects compared to sham pills (Thomas et al. 1991). All of these factors make the acupuncture studies easy to fail.

Based on our discussion above, we recommend acupuncture studies to pay attention to the following:

5.1 Wash-Out Phase

There should be a wash-out phase.

Give all patients a sham treatment for 3–4 weeks with the same treatment frequency as in the true study phase. It is better to have the sham acupuncture once a day, 5 days per week, for 3–4 week (Knipschild et al. 1991; Pablos-Méndez et al. 1998; Dutile et al. 2014; Ramsay 1997; Trial Designs 2013; Lembo et al. 2009). After the sham period, exclude the patients who had symptoms reduced by more than 30%. These patients are excluded from the latter study because they belong to placebo-sensitive patients and they are not good candidates to test the healing effect of any therapy (inducing new drugs, surgery, chiropractic, or physiotherapy, etc.).

Patients that did not have more than a 30% reduction in their symptoms can be treated with true or sham acupuncture in study phase (acupuncture phase).

5.2 No-Treatment Group

Depending on the aim of the study, this group may be omitted.

If the primary aim is to test whether the acupuncture group is better than a sham group, the no-treatment group can be omitted. However, if the aim is to know exactly how much of an effect of a placebo has in a sham group, the no-treatment group must be included. This is because the healing effect in a sham group is not only contributed by a possible placebo effect but also contributed by some other factors, such as natural turn-over, regression-to-normal. These latter two factors are the main reasons for the healing effect measured in a non-treatment group. The healing effect in a sham group, if any, cannot be credited to the placebo effect directly without exclusion as these latter effects.

5.3 Sham Group

The difference between true acupuncture and sham groups should be that there is acupuncture stimulation in the former but not at all in the latter. The acupuncture group be treated the same as one in a clinical environment, without the use of moxibustion, cupping, or other remedies.

Current data strongly suggest that the failure of acupuncture study is due to the poor healing effect in the acupuncture group, rather than the types of sham groups used. Therefore either inserted or non-inserted sham groups can be used under the condition that the acupuncture and the sham acupuncture are performed in higher treatment frequency, such as once a day, 5 days per week, for more than 20 sessions. The schedule can be variable depending on the disease to study. For example, for the treatment of post-operation nausea, the total number of treatment session may not need such high.

The advantage of the insert sham group (shallowly inserted needle on non-points or other-points) over non-inserted sham groups is that the procedure mimics the true acupuncture procedure. Even patients with previous experience in acupuncture can hardly tell if they are receiving a sham treatment, so there is no need to find acupuncture naive participants, or the need to blind the patient vigorously.

5.4 Acupuncture Group

This group only uses acupuncture, without moxibustion, cupping, bleeding therapy, massage, or Tuina. If the primary aim of the study is to test whether acupuncture works for a given kind of disease, the acupuncturist is allowed to select the basic acupoints or special acupoints, the number of the acupoints during each session, the frequency of the treatment, and length of each session. If the primary aim is to test whether one or more specific acupoints or specific acupuncture technique works for a given kind of disease, the above parameters should, of course, be fixed.

The acupuncture should be performed once a day, 5-6 days per week, for a total of 20–30 days (referring to the method used by acupuncturists in China). Allow the acupuncturists to keep the same way of communication with the patients as in an actual acupuncture clinic (Witt et al. 2006).

One of the characteristics of Chinese medicine (acupuncture or herbal therapy) is individual treatment (Jindal 2008). Traditional Chinese medicine regards patients individually. This is quite opposite to western medicine, which tends to standardize everything to all patients. Failure of many acupuncture studies may be due to a western medicine approach, by not allowing the change of a treatment plan based on each patient's condition. This could also be one of the reasons for a high fall-off rate in acupuncture studies in western countries. For example, if a patient cannot tolerate 10 needles each time, or cannot tolerate the intensity of the needle stimulation, but the acupuncturists insist to perform acupuncture treatment as for all the patients in the study group, the patient may escape from the study.

The stimulation of acupuncture in each session is also very important, but it is hard to standardize the stimulation dose to each session and among acupuncturists. We recommend using electrical acupuncture, or even better, the warm acupuncture, to standardize the intensity of stimulation from session to session and among large numbers of acupuncturists (especially in large scale acupuncture studies).

6 Conclusions and Perspectives

From our clinical experience and bench research, we believe that there are many factors that affect the outcome of acupuncture, whereas these factors are not well recognized by clinical and research community in the western countries. In fact, there is no standard protocol up to now for all acupuncturists to follow in the same way. The personal skill of acupuncturists greatly affects the outcomes of acupuncture. Therefore, clinical acupuncture study is easy to fail due to the disturbance by one or more influencing factors.

We recommend the acupuncturists in western countries to carefully check the methodology of acupuncture in China and use compatible methods in their practice and research since acupuncture origins from China with many acupuncture studies being done there. It is important to well consider all influencing factors, improve the design of research, make informative measurements with advanced approaches and adopt appropriate statistical analysis for reliable conclusions without bias (Asakawa and Xia 2012). It is our belief that significant improvements in the design and methodology of clinical acupuncture will eventually lead to better and more reliable outcomes.

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