



Review Article

The meridian system and mechanism of acupuncture: A comparative review. Part 3: Mechanisms of acupuncture therapies

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Abstract

The human body is a hierarchical organism containing many levels of mutually interacting oscillatory systems. From the viewpoint of traditional Chinese medicine, health is a state of harmony emergent from the interactions of these systems and disease is a state of discord. Hence, human diseases are considered as disturbed functions rather than changed structures. Indeed, the change from normal to abnormal structure may be beneficent rather than maleficent. For example, when one kidney becomes twice the normal size following the destruction of the other kidney, it is good and not bad for us because we might be dead otherwise. Therefore, in Part 3 of this three-part series, emphasis is mainly laid on the acupuncture mechanisms of treating disturbed physiological functions rather than disordered structures. At first, the basic tenets of conventional neuroscience and cardiology are reevaluated so that clear understanding of how nervous and cardiovascular systems work together can be obtained. Then, the general principles of diagnosis and treatment in traditional Chinese medicine from the integrative perspective of complex dynamic systems are proposed. Finally, mechanisms of acupuncture therapies for treating 14 different categories of disorders will be elucidated via the magneto-electric inductive effects of the meridian system.

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Keywords: chaotic wave theory of fractal continuum; complex dynamic systems; magneto-electric induction; mechanisms of acupuncture therapies; meridian system

Introduction

In Part 1 [1], it was mentioned that a report concerning the clinical practice of acupuncture on more than 100 indications had been published by WHO Consultation on Acupuncture [2]. The indications in that report covered a wide range of physiological disorders. They could be roughly divided into the following 14 different types of malfunction: pain, infection, neurological disorders, respiratory disorders, digestive disorders, blood disorders, urogenital disorders, gynecological and obstetric disorders, cardiovascular disorders, psychiatric disorders and mental disturbances, pediatric disorders, disorders of the sense organs, skin diseases, and cancers. To date, most of the proposed mechanisms have not been able to explain how acupuncture might work for all of the

forementioned disorders [3–18]. Recently, a so-called *chaotic wave theory of fractal continuum* has been proposed to characterize the essence of meridian system and elucidate the mechanism of acupuncture analgesia in Parts 1 and 2, respectively [1,19]. The advantages of this proposed theory in elucidating acupuncture analgesia are that it can explain: (1) both acute and chronic pain relief via impedance matching and mismatching; (2) both local and distant acupuncture effects via neurovascular wave propagation; and (3) why sometimes invasive sham controls might have analgesic effects via fractal continuum of the meridian system.

In this final part, in order to explain why acupuncture is so effective in treating the aforementioned 14 various types of physiological disorders or malfunctions, basic tenets in conventional neuroscience and cardiology are first reevaluated. The goal is to obtain a clear understanding of how nervous and cardiovascular systems work together in the human body. Without such understanding, one can hardly decipher why

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acupuncture can be so effective in treating so many different disorders. Then, the general principles of diagnosis and treatment in traditional Chinese medicine (TCM) from the integrative or holistic perspective of complex dynamic systems instead of the reductionist viewpoint will be proposed. Based on these principles, mechanisms of acupuncture therapies for 14 different categories of disorders will be elucidated via the magneto-electric inductive effects of the meridian system. Finally, the conclusion of this review series will be given.

Reevaluation of the basic tenets in neuroscience and cardiology

First, let us recall the three basic tenets in conventional neuroscience. The first is the concept of inhibition; the second is the neuron doctrine; and the third is the leaky cable theory of nerve conduction proposed by Hodgkin and Huxley [20–27]. These three tenets are actually intertwined. Let us consider the concept of inhibition first. It began with the tetanic excitation of vagus nerve that caused the standstill of a frog's heart in 1845 by the Weber brothers [20]. Based on this result, the vagus nerve was believed to have an inhibitory nature on the intrinsic nerves of heart. Opponents of this viewpoint contended that the inhibition was due to overstimulation and exhaustion of these nerve fibers. Hence, it was nothing but an artifact. In spite of strong opposition, Valentin still adopted a similar idea in micturition [20,21]. In the same vein, the volitional elbow flexion was also believed to display reciprocal innervations of antagonistic skeletal muscles [22]. Thus, the idea of inhibition was extended from autonomic to somatic nerves altogether. In the elbow flexion case, Renshaw cells were thought to be the motor interneuron that was responsible for the reciprocal inhibition [23]. However, the real functional roles of this cell in motor control and behavior were still uncertain as could be seen from a quote from a recent review paper [28]:

‘Although Renshaw cells participate in a relatively “simple” local recurrent inhibitory circuit, and much is known about their physiology and morphology, it is humbling to recognize that there is as yet no definitive functional hypothesis regarding their contributions to motor control and behavior... It has been difficult to directly test these and related hypotheses because of the lack of experimental tools to selectively antagonize/delete/knockout Renshaw cells or monitor their behavior in freely moving non-anaesthetized animals.’

Nevertheless, efforts to pursue the idea of inhibition to subcellular levels continued. In 1892, the idea of synaptic chemical transmission in the autonomic ganglia of mammals was proposed by Langley [20]. Sherrington, Eccles and their colleagues then studied the endplate potentials in muscles and the synaptic potentials in nerve cells to conclude that both presynaptic and postsynaptic inhibitory permeability changes were required to account for inhibition [22,23]. Nowadays, the synaptic excitatory and inhibitory concepts have been extensively permeated and even extended to the higher functions of human brain, such as memory and learning. It is noteworthy

that Lashley was against the theory of neural synaptic connections as the basis of learning at the outset [29]. Hebb, however, tried to save this synaptic viewpoint by incorporating a time factor into his theory [30]. As a matter of fact, the main drawbacks of proposing synaptic plasticity in learning and memory with time factor incorporated were twofold. First of all, the time scale of inhibition with regard to synaptic plasticity was in terms of tens of milliseconds in laboratory experiments. To use results of such a short time span to explain higher functions of learning and memory of a much longer time span would not be very convincing. Secondly, the experiments performed in laboratories would usually require repetitive and stronger stimuli to produce inhibitory responses, while weaker stimuli often resulted in excitations [31]. Hence, it would be legitimate to ask if the superimposed inhibitory hyperpolarization was actually derived from overstimulation and exhaustion of these synapses. This important issue in basic neuroscience can be easily resolved if direct proofs of inhibitory response concerning synaptic plasticity in memory or learning of the freely moving nonanesthetized animals or humans can be provided.

Actually, the doctrine of inhibition and reciprocal inhibition has never been observed either in experimental studies of voiding and storage of urine in normal Wistar rats, or elbow flexion and forearm pronation in freely moving normal humans [32–35]. On the contrary, only the synergic and cooperative innervations have been observed instead. From the viewpoint of chaotic wave theory of fractal continuum, the “excitatory” and “inhibitory” effects of nerve signals are nothing but the in-phase and out-of-phase superposition of nerve signals in the reticular neurovascular network. For example, if all of the afferent or efferent nerve signals are in-phase, then the resultant signal will be constructively superposed and “excitatory” effect will be exhibited. By contrast, if the waves of nerve signals are out-of-phase, however, then the resultant signals will be destructively superposed and an inhibitory effect will be exhibited. As to the intensity of inhibition, it will depend on the degrees of phase difference. If the phase difference is 180° , for example, then the two wave signals will be completely annihilated. There is absolutely no need to invoke and devise special neural structures to perform such functions.

Let us consider the neuron doctrine next. This was proposed by Waldeyer-Hartz at first in 1891, and later coupled with the law of dynamic polarization by van Gehuchten and Cajal [24,25]. An earlier rival reticular theory was proposed by Golgi who simply could not agree with the law of dynamic polarization in the neuron doctrine and the cerebral modular organization of functions [26]. However, he was not able to provide enough functional evidence to defend his reticular theory at that time. As time goes by, however, it is now clear that the reductionist viewpoint of neuron doctrine is not flawless. Many important concepts, such as fused neurons, gap junctions, serial synapses, and trophic independence of neurons, can already challenge the neuron doctrine [36]. Moreover, our experimental results in acupuncture have indicated that the neuron doctrine is either infeasible or unable to

explain the fast and global responses of acupuncture effects in the brain [19,37–42]. The number of neurons in the brain is in the order of tens of billions. Each cortical neuron will integrate information from hundreds of nearby cells and tens of thousands of synapses. As a result, the brain becomes a very complex network of neurons and synapses according to neuron doctrine. In conventional neuroscience, however, the neuron-to-neuron communication is mainly accomplished through synaptic neurotransmitters. The time needed for those transmitters to be released and up taken will be in the order of tens of milliseconds. In order to explain the synchronized oscillations of electroencephalograms (EEGs) during or after acupuncture in the whole brain, the neuron doctrine is powerless. For example, on one hand, any tentative parallel model of synaptic transmission to describe the synchronization of neurons will definitely make surface EEGs look like noise instead of synchronized rhythms. By contrast, any tentative serial model of synaptic transmission will take days instead of seconds to achieve synchronized oscillations [39–42]. More importantly, there is a huge gap right now between reductionist neuroscience taught in medical schools and neurology encountered in clinical hospitals. For example, numerous electron microscope studies have failed to implicate synaptic changes in either neuroses or psychoses [43]. In manic or endogenous depression, so far, electron microscope has revealed no structural changes or abnormalities in brain synapses [44]. In order to explain these neuroses and psychoses accurately, we have to examine the next basic tenet in neuroscience.

The third basic tenet of neuroscience is the leaky cable theory of nerve conduction by Hodgkin and Huxley [27]. They used the voltage clamp method to maintain constant voltage longitudinally inside a perfused squid giant axon with axoplasm removed. As a result, the replaced ions inside this axon could not go downstream longitudinally, but had to move across the membrane instead. Consequently, ionic channels and pumps in the membrane of squid giant axon had to be devised to account for the generation of action potentials [27]. In their proposed model, action potentials were generated as a result of sodium, potassium, and other ionic channels that would open and close due to electrical or chemical changes in an axon's intracellular and extracellular environment. The membrane currents that fluctuated according to the opening and closing of ionic channels were mainly contributed by the concentration gradients, membrane conductance, and membrane capacitance. The techniques developed were also adopted to study the mechanism of cardiac rhythmogenesis. However, the number of ionic channels of a typical cell is at least of the order 10^3 of each different type. Hence, the mathematical modeling of ionic channels for physiological systems containing billions of cells is a daunting task. The reductionist model has also suffered from many other drawbacks too. For example, the experimentally observed discontinuous phase-resetting function could hardly be accounted for by models formulated as differential equations [45]. Furthermore, the sodium–potassium pump and other membrane pumps in the ionic theory of action potential could suffer from

insufficient energies to operate [46]. The most serious drawback of the model of Hodgkin and Huxley is that their nerves are capacitive, resistive, and conductive only, but never inductive [27]. According to the transmission line theory of communication, their nerves can never be impedance matched under any circumstances. An obvious problem is that the afferent nerve signals will always be partially reflected back due to mismatch of impedances and they will interfere with the incoming nerve signals. This serious drawback would certainly hamper our proper sensory functions including hearing and vision. Apparently, this is not the case in our daily lives. Many researchers have tried to resolve these serious drawbacks in their theories. For example, an adsorption-and-induction hypothesis was conjectured that the action potential was actually due to the result of transient variation of the surface adsorption potentials on one or both sides of the membrane [46]. Consequently, continual energy expenditure in describing the resting potential was not needed. However, it is fair to say that more experimental tests of the propagation of electric polarizations along the excitable membranes are required to verify this hypothesis.

A more plausible theory of nerve conduction, based on the magneto-electric effects of myelin and neurofilaments, has been proposed recently [1,19]. This theory can also be used in clinical practice to explain the neurological problems with demyelization that have been frequently observed in more than 70% of the neurodegenerative diseases. In addition, this theory can also be used to study the pathogenesis in Alzheimer's disease, which has been attributed to neurofibrillar entanglement. Consequently, both the neurophysiology *in vivo* and neurology in clinical practice can be consistently elucidated under this proposed theory.

As for cardiology, some of its basic concepts will also need reevaluation. For example, in Chang [42], *hypertension* has been indicated as a misnomer and it is actually the blood flow and its distribution in the human bodies that are important. Notice that pressure is defined as force/unit area and it is not a robust parameter when used in cardiology. This is because, first of all, the term *blood pressure* depends also on the cross-sectional areas of blood vessels. Yet, the diameters of blood vessels vary continuously and sometimes discontinuously from main arteries to small arteries and to capillaries. Hence, blood pressure is a constantly changing function of space and time even when the pumping force of the heart is kept relatively constant. Secondly, it is the *relative pressures* or pressure gradients that are important [47,48]. The absolute pressures are meaningless and using a cuff to get the absolute systolic or diastolic pressure will induce a very large amount of error in the blood pressure readings [47]. We have to say that the diagnosis of *hypertension* in cardiology has been very unreliable and questionable.

In TCM, there is no such term as *blood pressure*. It is the smoothness of blood flow in various blood vessels that is important [42]. In other words, the blood pressure problem in modern cardiology has always been treated as a blood distribution problem in TCM. For example, the blood in our body should be distributed more to the digestive tract after meals,

more to peripheral limbs during physical exercise, and more to the brain during mental exercise [42]. Hence, after meals, one should avoid studying or performing strenuous physical exercise immediately so that blood can go to the digestive system for digestive purpose. In the same vein, during mental exercises, one would prefer to be alone in a quiet place so that proper neurovascular flow to the brain can be provided.

So far we have seen that the temporal changes of: (1) radial arterial blood flow with its local impedance; (2) heart rate variability and autonomic nervous system (ANS) of the circulatory system, and (3) EEGs of the central nervous system can be simultaneously obtained after acupuncture at Neiguan [19,37]. Hence, by needling at meridians, it is feasible to redistribute the blood flow in the body via activating somatic innervations, ANS, and central nervous system. Furthermore, the impedance changes of meridians can implicate one or several of the following short-term and long-term consequences: (1) change of the peripheral blood flow speed to induce sweating and reduce high fever; (2) activation of the defense system in blood to protect the body from attacks of bacteria and poisons; and (3) increase of blood circulation motility to improve sluggish body functions.

To sum up the major differences between the viewpoints of modern medicine and TCM in dealing with neural and cardiovascular systems, we have arrived at the following conclusions: (1) the former school of thought views them as two separate physiological systems, while the latter views them as a unified one with two mutually interacting subsystems; (2) the former school of thought treats them as compositions of microscopic cells and molecules that are responsible for disordered structures, while the latter treats them as compositions of macroscopic rhythmic generators that are responsible for emergent functions; and (3) the former school of thought believes that excitatory and inhibitory functions in the neural network have to come from excitatory and inhibitory transmitters or neurons, while the latter believes that excitatory or inhibitory function in the neural network simply comes from in-phase or out-of-phase superposition of nerve signals. With these differences in mind, we are now ready to propose the following.

General principles of diagnosis and treatment in TCM

It is well known that the human body is a hierarchical organism consisting of many levels of mutually interacting physiological systems. In Part 2 of this review series, we saw that the effects of acupuncture on human body are also hierarchical in terms of time [19]. Namely, the magneto-electric effect is the fastest for it takes only tens of seconds to produce significant neurovascular changes of the whole body [37,38]. Then, it is followed by the secondary biochemical changes about tens of minutes after acupuncture. Finally, the tertiary endocrinal changes will be exhibited only days or weeks later. Hence, the human body is hierarchical not only in structure and function, but also in space and time.

In order to diagnose and treat diseases of such a complex hierarchical system, the conventional reductionist viewpoint has to be replaced by holistic or integrative perspective

emphasizing the collective behavior of rhythmic interactions and their emergent properties. The first step to achieve that goal is to collect both the external and internal information of patients. Four basic techniques for obtaining such information are as follows: (1) visual inspection of the patient's external demeanor and bodily motions; (2) auscultatory and olfactory examinations of the patient's voice, odor, and scents; (3) direct dialogue with the patients concerning their internal feelings of pain, appetite, insomnia, living habits, etc.; and (4) involved palpation of the patient's peripheral arterial pulses that contain the information of heart and other internal visceral organs. After collecting the physiological and psychological information with regard to the symptoms or syndrome of the patient, the TCM physicians have to come up with a diagnosis of the diseased states. Integrative yet terse descriptions, such as *Deficient Qi*, *Excessive Qi*, *Deficient Blood*, *Excessive Blood*, etc., have been devised to describe the states of the patient. However, due to lack of modern recording devices, most of the collected physiological and psychological information could not be quantified and analyzed so as to support their integrative descriptions. As a result, these integrative descriptions have been treated as unscientific and could not be justified from a modern medicinal viewpoint. Fortunately, recent advances in modern recording devices and mathematical machinery have enabled us to start recording some of the physiological data and interpreting them in terms of integrative descriptions.

To illustrate, let us use human elbow flexion as an example [32]. The muscles in the upper arm, including short head of the biceps brachii (BBSH), long head of the biceps brachii, brachialis, lateral head of the triceps, and long head of the triceps, are used to study the collective behavior of rhythmic interactions. At first, an electrogoniometer (SG110, Biometrics Ltd., Goleta, CA, USA) is taped on the lateral sides of the forearm and upper arm to measure the flexion angle. The surface electromyograms (EMGs) of the aforementioned muscles are collected and digitized by an MP150 system (Biopac Inc. USA). In Fig. 1, the surface EMGs, temporal fractal dimensions (FDs), spectrograms, and flexion angles of a volitional flexion cycle for a normal subject are illustrated. All of the surfaces EMGs are depicted in black and temporal FDs in color codes. For example, in Fig. 1A, the black surface EMG activity belongs to BBSH and the dark blue patterns (with FDs around 1.2–1.3) within the range of 2–3.5 seconds correspond to the normal flexion of BBSH. Then, the light blue patterns (with FDs around 1.4–1.5) around the range of 3.5–6 seconds correspond to an isometric contraction of the holding position. Finally, the medium blue patterns around the range of 6–7.5 seconds correspond to the period of putting down the forearm smoothly by gravity. The spectral frequencies of BBSH are illustrated in Fig. 1G. The three high peak values are located around 24 Hz, 27 Hz, and 34 Hz, respectively. Similarly, the surface EMG activities, FDs, and spectrograms of the long head of the biceps brachii, brachialis, lateral head of the triceps, and long head of the triceps are represented in Fig. 1B–E and H–K, respectively. During volitional flexion, FDs of these five groups of muscles have all been changed to <1.5 in this period. This result can be seen

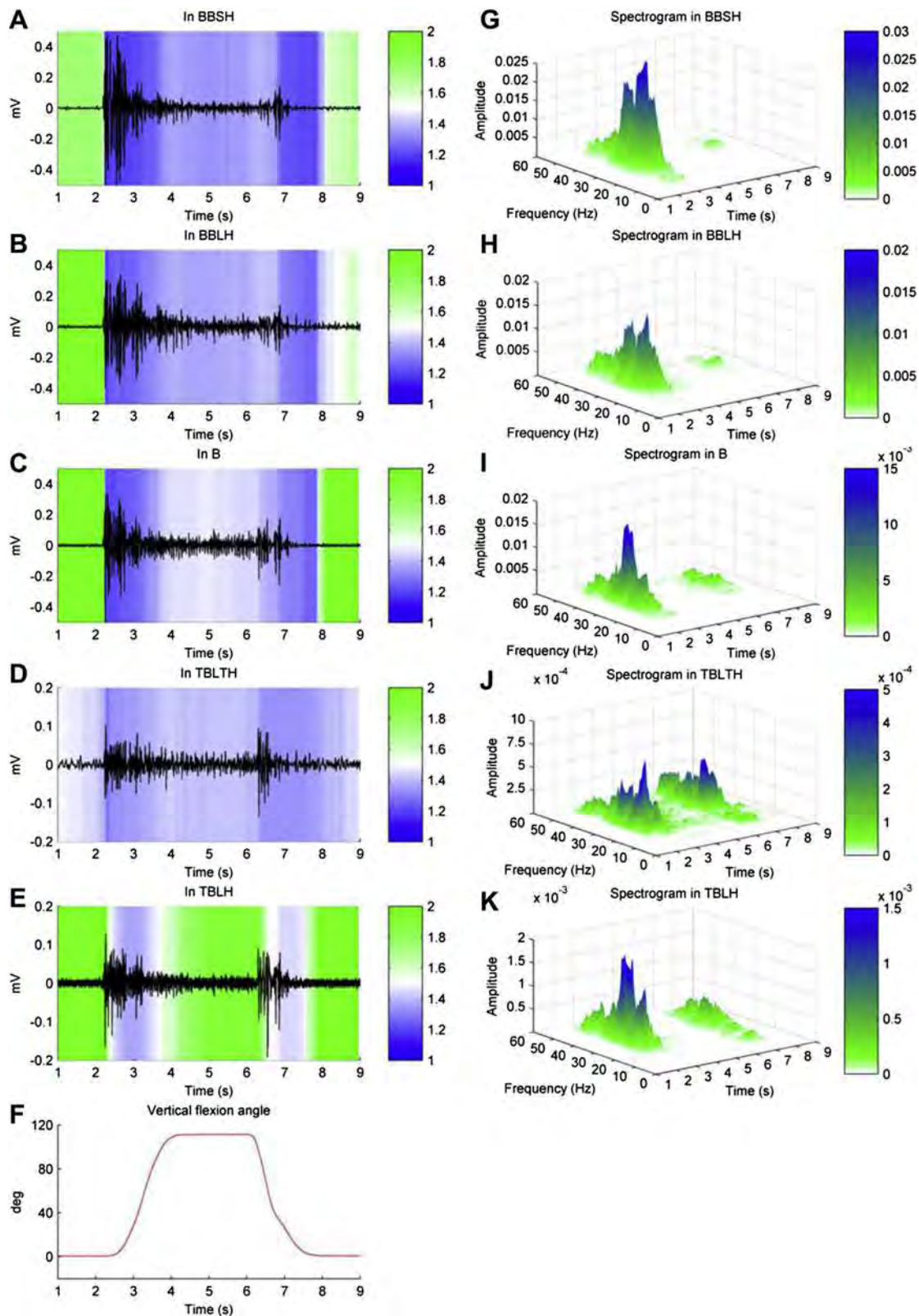


Fig. 1. Surface electromyogram activities, temporal FDs, and spectrograms of five brachial muscles in a right upper arm during one exemplary flexion cycle. The activities of surface electromyograms are in dark color and temporal FDs in color codes for muscles of the (A) short head of the biceps brachii (BBSH), (B) long head of the biceps brachii (BBLH), (C) brachialis (B), (D) lateral head of the triceps (TBLTH), and (E) long head of the triceps (TBLH), respectively. The corresponding spectrograms for these muscles are presented from (G) to (K), respectively. The elbow flexion angle in vertical axis from electrogoniometer is presented in (F). From *Synergic co-activation of muscles in elbow flexion with fractional Brownian motion* [32]. Copyright 2008 Chinese Physiological Society. Reprinted with permission.

from Fig. 1A–E as the color codes have changed from green or light blue colors to blue ones. Moreover, within the range of 2–3.5 seconds, all these five groups of brachial muscles are synchronized in frequencies around the three peaks of 24 Hz, 27 Hz, and 34 Hz.

In contrast, similar surface EMGs, temporal FDs, spectrograms, and flexion angles of the flexion cycle for a volunteer who has been passively flexed are illustrated in Fig. 2. Here, all of the spectral amplitudes in the muscle EMGs are small and no prominent frequencies can be found during the whole flexion process. Moreover, FDs have not exhibited change of color codes from green to blue as in the normal volitional flexion. By comparing Figs. 1 and 2, the elbow condition in Fig. 2 will be diagnosed and labeled holistically as *Deficient Qi*. Here, *Qi* is referred to the collective behavior of neuromuscular activities characterized quantitatively by FDs and rhythms of these muscles, and *Deficient* is indicative of: (1) the collectively weak and incoherent intensities of all EMGs as indicated by their FDs; and (2) the loss of overall synchronizations in rhythms. In this way, the ancient holistic notion of a diseased state *Deficient Qi* can now be characterized quantitatively. Henceforth, some of the holistic descriptions of diagnostics in TCM can be placed on a scientific footing and quantitative characterizations via modern techniques can be performed in the future. One has to keep in mind, however, that indispensable psychological information and mental states gathered by the TCM diagnostics are still very difficult to quantify as yet.

One important advantage in using such integrative descriptions in TCM is that the countermeasures or strategies of treatment can be laid down immediately after the diagnostics is completed. Depending on the diseased states of patients, doctors can use one or several of the following eight countermeasures in their herbal remedies or acupuncture treatment: (1) to induce sweating so that bacteria or poisons can be expelled and high fever alleviated; (2) to induce vomiting via activating the ANS so that poisons or indigestible stuff in the stomach can be expelled; (3) to induce purging so that poisonous stuff in the abdomen can be expelled; (4) to activate the defense system so that bacteria can be expelled; (5) to induce motility so that the sluggish body functions can be improved; (6) to remove congestion, or full or partial blockage of internal organs via adjusting meridian system so that normal states can be resumed; (7) to tonify the human body due to depletion of energy or exhaustion; and (8) to harmonize the discord so that the normal physiological and psychological states can be restored. The last treatment strategy is so general that it is actually up to the doctor to decide what treatment steps should be taken. This is perhaps one of the reasons for TCM being considered not only as a science but also as an art. Based on the aforementioned principles of treatment, let us try to elucidate why acupuncture, sometimes with just one needle, can heal so many different disorders.

Mechanisms of acupuncture therapies

The clinical practice of acupuncture endorsed by WHO Consultation on Acupuncture contains a list of 14 different

types of disorders [1]. Basically, we will follow the order of that list to explain why acupuncture can be so efficacious.

Pain

The mechanism of acupuncture analgesia was reviewed in Part 2 [19]. As indicated in that paper, according to TCM, the root cause of pain is stagnation, full or partial blockade of the normal neurovascular flows in regions of human body. The flows can be stagnant or blocked at the levels of skin, muscle, joints, head, face, throat, chest, or viscera, and especially after surgery. Consequently, impedances of neurovascular bundles in those regions are deviated from their normal values. Pain relief or analgesia can be achieved by acupuncture through adjusting the impedances of the meridian system, which is connected internally with viscera and externally with limbs and sensory organs. Initially, the injury current around the acupoint is produced, then the magneto-electric inductive effects along the meridian system will be triggered, and via the impedance matching/mismatching with pain source/brain, finally the analgesia/pain relief can be obtained [19]. As to the specific treatment of each different kind of pain, the voluminous corpus of TCM can provide clinical practitioners with a complete and clear picture of where, when and how the needles should be inserted. These technical details will be briefly covered when different disorders are discussed in the following sections.

Infections

Several exemplary cases will be discussed here. The first one is acute bacillary dysentery, which is an acute inflammation of the colon characterized by diarrhea, and pus and blood in the liquid stools. Generally, it is agreed that large and small ulcers scattered along the length of the colon are responsible for the pain, pus, and blood in the stools. Here, the term ulcer is referred to the superficial lesion of the skin or mucous membrane due to inflammation nearby. Although the reasons for causing inflammation are varied, but the following four signs have been considered distinctive of inflammation, i.e., redness, swelling, heat, and pain. The first sign of redness is due to the excess of blood. Swelling arises partly from the over-distention of the blood vessels and partly from effusions from them. The heat is in part due to the increased flow speed of the blood. Finally, the pain is due to the stagnation, congestion, full or partial blockade of the normal neurovascular flows. As to the treatment by acupuncture, it has been reported to be effective for treating acute bacillary dysentery without any side effects [49–51]. The acupuncture mechanism of curing this infection can be attributed to the restoration of normal gastrointestinal neurovascular flow by adjusting the impedances of a closely correlated meridian. For example, acupuncture at Zusanli (ST 36) can change the impedances of anterior tibial neurovascular bundle, which includes anterior tibial artery, anterior tibial vein, and the deep peroneal nerve. This meridian is highly correlated to the neurovascular bundles of gastrointestinal tract. By decreasing the local

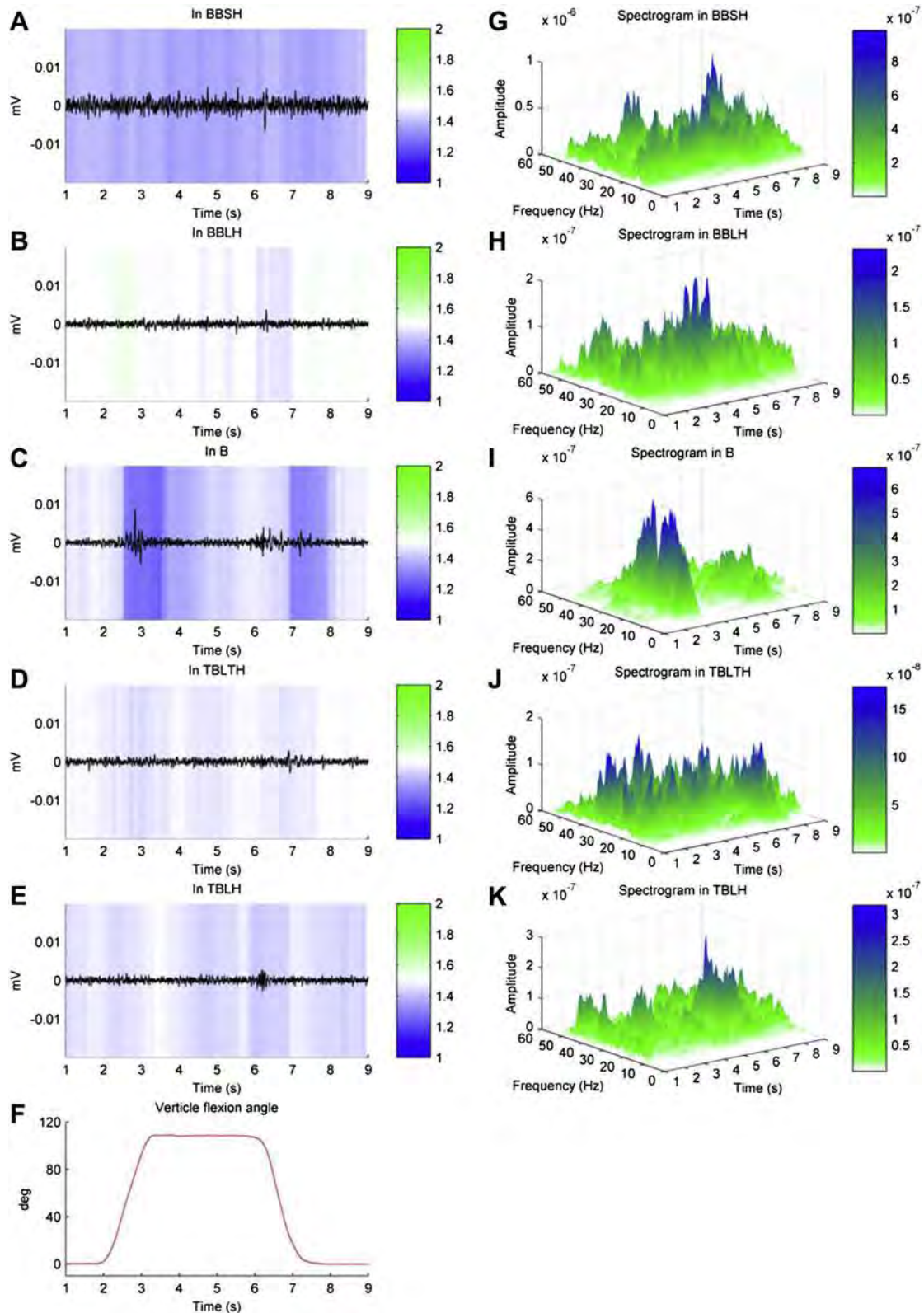


Fig. 2. Surface electromyogram activities, temporal FDs, and spectrograms of the same five different brachial muscles when passively flexed. The activities of surface electromyograms are in dark color and temporal FDs in color codes for muscles of the (A) short head of the biceps brachii (BBSH), (B) long head of the biceps brachii (BBLH), (C) brachialis (B), (D) lateral head of the triceps (TBLTH), and (E) long head of the triceps (TBLH), respectively. The corresponding spectrograms for these muscles are presented from (G) to (K), respectively. The elbow flexion angle in vertical axis from electrogoniometer is presented in (F). From *Synergic co-activation of muscles in elbow flexion with fractional Brownian motion* [32]. Copyright 2008 Chinese Physiological Society. Reprinted with permission.

impedance of anterior tibial neurovascular bundle via acupuncture at ST 36, the excess of blood in the congested or stagnated region of inflammation will rush to the lower limbs or the peripherals that now have lower impedance values. Consequently, two upshots will result: (1) the four signs of redness, swelling, heat, and pain in the colon can be alleviated for there is no more excess of blood, no over-distention of the blood vessels, and no blockade of the neural flows in that region of inflammation; and (2) the relevant bacteria, if they exist, will be mostly carried away from the infected area to peripherals and then be either expelled outside of the body by the nonspecific immune system of tears and secretion of body fluids, or be destroyed by specific immunity of lymphocytes and white blood cells in the circulatory system over a period of time.

It is educational to compare acupuncture with the treatment of modern medicine. The first requisite for healing, in modern medicine, is complete destruction of bacteria. The second step is then the removal of dead fragments of tissue and bacteria by macrophages. Only after these two steps are complete can healing commence. Under this philosophy, acute bacillary dysentery is usually treated by conventional drugs such as norfloxacin, or furazolidone. However, both of them can cause serious side effects [52,53]. For example, joint and tendon problems have been associated with norfloxacin since 1983 [54]. In 1989 Jeandel et al commented on arthritis being induced by norfloxacin [55], which has also been associated with severe and even fatal liver diseases. Furazolidone, by contrast, has the side effects of tremors, convulsions, peripheral neuritis, gastrointestinal disturbances, and depression of spermatogenesis.

A second exemplary case is pertussis or whooping cough. Infected children are liable to suffer from complications such as bronchopneumonia and convulsions. This infection, according to modern medicine, is caused by the bacterium *Bordetella pertussis*. The bacteria can invade the lining of the throat, windpipe, and airways. As a result, the secretion of mucus will be increased and become thick and sticky. The antibiotic erythromycin is usually used to eradicate the bacteria. Erythromycin, however, has serious side effects including arrhythmia and allergic reactions. It has also been linked to an increased probability of psychotic reaction.

Acupuncture at Baxie (EX: E 9), however, has been shown to be useful in treating pertussis by relieving cough and promoting a cure [56]. The mechanism of acupuncture in this treatment is very similar to that of bacillary dysentery. One possible explanation for the efficacy of acupuncture is that the secretion of thick and sticky mucus from the lining of the throat and airways is not too much different from the pus of the colon membrane due to acute inflammation, even though the locations and bacteria may be different from the perspective of modern medicine. The only difference from the holistic perspective of acupuncture treatment is perhaps in where, when, and how the needles should be placed. For example, Hegu (LI 4) can be used for pertussis and Zhusanli (ST 36) for bacillary dysentery due to the essence and properties of meridian system.

The third exemplary case is the hepatitis B virus [57]. Hepatitis is usually used to signify inflammation of the liver, but it is not the inflammation in the sense of pertussis or acute bacillary dysentery that exudates are formed. Instead, the reaction to irritation in the case of the liver is necrosis of the hepatic cells. Necrosis is partly due to reduced blood flow in that part of liver. Acupuncture has been proved effective in strengthening the body resistance to eliminate pathogenic factors in the treatment of asymptomatic hepatitis B virus carriers [57]. One possible explanation is that acupuncture in the right meridian at the right time can help promote the vascular flow to the liver. Furthermore, the relevant virus, if existed in liver, can be carried away from the infected area and be expelled out of the body by the aforementioned specific or nonspecific immune system. As a result, necrosis can be avoided.

Neurological disorders

The nervous system is intricate and its disorders are varied. Acupuncture can be helpful in treating many neurological disorders. Recall that neuralgia was dealt with in Part 2. Let us consider here the treatment of stroke in neurological disorders at first. A number of controlled clinical evaluations have been undertaken. For example, acupuncture treatment of hemiplegia due to cerebral infarction has given better results than conventional medication [58–63] and physiotherapy [64,65] in stroke patients. Acupuncture also has beneficial effects when it is used as a complement to rehabilitation [66–68]. To explain why acupuncture at relevant meridians can be beneficial before and after stroke, recall that acupuncture can regulate and redistribute the blood flow in the body [19,37,42]. For example, acupuncture in the right meridian can decrease the blood flow to the peripheral limbs and internal viscera, so the blood flow to the brain can be increased to avoid stroke due to the conservation of total blood volume in the body. By the same token, acupuncture in the right meridian can increase the blood flow to the peripheral limbs and internal viscera, so the blood flow to the brain can be decreased to avoid hemorrhage. As a possible site of needling, acupuncture at Hegu (LI 4) or Zhusanli (ST 36) for example, can adjust the peripheral blood flow and redistribute the right amount of blood to the brain via special needling techniques.

Peripheral nervous malfunctions can also be treated with acupuncture. For example, it has been reported in randomized controlled trials that acupuncture can be helpful in Bell's palsy [69,70]. The causes of Bell's palsy could be due to stroke in the brain or just a result of inflammation in the facial nerve itself. Hence, one possible reason that acupuncture at Hegu (LI 4) may work so well is that it can improve the blood circulatory conditions to the malfunctioned nerve and remove the nervous conduction blockage via adjusting the meridian system.

Respiratory disorders

Allergic rhinitis is one indication in respiratory disorders that can be effectively treated by acupuncture. In controlled

studies, acupuncture has been shown to be more effective than antihistamine [71–75]. This disorder is characterized by edema, vasodilatation of the nasal mucous membrane, and obstruction. These symptoms have to do with nasal neurovascular flows. It will come as no surprise for us to learn that acupuncture can adjust and regulate the neurovascular flows in the nasal region. In addition, the lack of side effects is another distinct advantage of acupuncture in treating this condition.

The acute symptoms of tonsillitis can also be effectively relieved with acupuncture [76]. Tonsillitis is the acute inflammation of tonsils. The inflamed tonsils are usually edematous and hyperemic. There may be, sometimes, purulent exudates from the membrane. Acupuncture can be helpful via the adjustment of neurovascular flow around tonsils so that sore throat and pain on swallowing can be alleviated.

Controlled trials in treating bronchial asthma with acupuncture have also been reported as effective [77]. Actually, acupuncture brings about modest improvement in objective parameters, but with significant subjective improvement in bronchial asthma [78]. Acupuncture may also provide symptomatic improvement in the late stages of bronchial asthma, where there are complications of disabling breathlessness due to impaired lung function [79]. Acupuncture can be helpful via the adjustment of the ANS and neurovascular flow around the walls of the bronchi so that strong contractions of the smooth muscle layer of the airways can be relaxed.

Digestive disorders

Peptic ulcer, acute and chronic gastritis, and gastric spasm can cause epigastric pain. Acupuncture provides satisfactory relief of epigastric pain as shown in randomized controlled trials [80–83]. Because of acupuncture analgesic effect, it can be used in colonoscopy. It has also been reported that the effect of acupuncture can be used to relieve pain and discomfort during the examination [84,85]. The mechanisms of acupuncture analgesia for all of the aforementioned disorders can be attributed to impedance changes of ANS and vascular flows around the walls of the viscera and intestines so that pain relief can be achieved.

Nausea and vomiting are also common symptoms of digestive or more generalized disorders that might be related to chemotherapy, for example. In these conditions, acupuncture at Neiguan (PC 6) has a specific antiemetic effect. A recent systematic review of trials using acupuncture for antiemetic effects has supported its efficacy [86]. Since vomiting is the forceful expulsion of stomach contents, it will need strong neuromuscular contractions. Acupuncture can be helpful for antiemetic effect via regulation of the ANS around the walls of the stomach so that contractions of its muscle layers can be alleviated.

Acupuncture has also shown good analgesic and antispasmodic effects on the biliary tract and, as indicated previously, can be recommended for treatment of biliary colic [87–90]. In the treatment of biliary colic due to gallstones, for example, acupuncture is not only effective for relieving the colicky pain, but is also useful for expelling the stones. The acupuncture

mechanisms of expelling the stones and relieving of colicky pain can be attributed to dilation of the biliary tract and the impedance changes of the ANS.

Blood disorders

Among various blood disorders, leukopenia is also suitable for acupuncture treatment. This disorder concerns a very low number of neutrophils in the blood with a number of causes. In controlled studies, acupuncture has been shown to be very effective in the treatment of leukopenia due to chemotherapy [91] or benzene intoxication [92,93]. Even though we are ignorant as to its precise causes sometimes, the symptoms of it are anemia, weakness, enlargement of internal viscera, and a marked tendency to hemorrhage. The mechanism of acupuncture in treating leukopenia and similar types of blood disorders can be attributed to: (1) adjusting the vascular flows so as to expel toxic wastes and chemicals from the body; (2) improving blood circulation so as to promote the sluggish body functions; or (3) regulating the impedance of vascular blood flow to avoid hemorrhage.

Urogenital disorders

Urinary retention due to functional disorders can be treated with acupuncture. In addition, for *postpartum* urinary retention, successful micturition can be achieved immediately after acupuncture treatment [94]. A randomized controlled trial on traumatic retention of urine has also been reported [95]. In that report, the efficacy of acupuncture is superior to that of intramuscular injection of neostigmine bromide. The acupuncture mechanism of facilitating micturition has to do with activating the pudental and pelvic nerves so that the synergy of detrusor and external urethral sphincter can be achieved. For details of this holistic or integrative perspective of micturition mechanism, refer to Chang et al [34,96,97].

Acupuncture has also been reported to be useful for expelling urinary stones [98]. The acupuncture mechanism of expelling the urinary stones will be similar to the case of gallstones in digestive disorders. Here, the acupuncture mechanism of expelling the urinary stones can be attributed to dilation of the ureter via modifying its neurovascular impedances.

Acupuncture is also helpful in patients with chronic prostatitis. It has been shown to be superior to oral sulfamethoxazole in relieving symptoms and improving sexual function [99]. In women, it has been shown that acupuncture can lower urethral pressure and relieve urethral syndrome [100,101]. Acupuncture has also been successfully used as a prophylaxis against recurrent lower urinary tract infections [102]. Urinary tract infections are also common during pregnancy because the enlarging uterus will press against the ureters and slow down the urine flow. When the ureters are pressed and urine flow is slow, complete voiding may not be possible and the chance of infection will be increased. The acupuncture mechanism of fighting against infection can be attributed to dilation of the ureter via modifying its neurovascular impedances so that

normal urine flow can be restored and the infectious agents can be flushed out of the urinary tract.

Gynecological and obstetric disorders

Acupuncture is helpful to patients with premenstrual syndrome. In a controlled study, the majority of patients gained relief and no recurrence in the 6-month follow-up [103]. In addition, primary dysmenorrhea is another major indication in the field of gynecological disorders that acupuncture can be very helpful. The beneficial effect was reported in controlled trials [104,105]. The mechanism of acupuncture in pain relief has been covered in Part 2 [19]. In this particular case, pain is mainly derived from strong contractions of the uterus that happen when blood supply to the endometrium is reduced. Acupuncture can restore the normal neurovascular flow and motility of the uterus via impedance change of the ANS so that the pain can be alleviated.

In the medical documents and ancient books of TCM, stimulation of certain acupoints in pregnant women may cause miscarriage due to strong contractions of ANS in the uterus. However, such an action is useful if induction of labor is desired in prolonged pregnancy [106–108].

Acupuncture has also been used in the treatment of female infertility due to inflammatory obstruction of the fallopian tubes [109]. In addition, acupuncture has also been reported to be effective in the treatment of female anovulation and anovular infertility [110–112]. However, according to our studies, the magneto-electric inductive effect of acupuncture is primary, the biochemical effect is secondary, and endocrinal effect is tertiary. So, it may require days, weeks, or even months of acupuncture treatments to regulate abnormal functions of the hypothalamic–pituitary–ovarian axis. It is fair to say that in order to achieve a much better result in normalizing the secretion of certain hormones, such as gonadotropin-releasing hormone, luteinizing hormone, and estradiol, more frequent and long-lasting acupuncture treatments than those in the aforementioned research reports are recommended.

Acupuncture stimulates milk secretion after childbirth. It has also been observed that acupuncture elevates the blood prolactin level in women with deficient milk secretion after childbirth [113]. The clinical use of acupuncture to promote lactation has also been demonstrated in a randomized controlled study [114]. The mechanism of acupuncture in promoting milk secretion can be explained as follows. Notice, at first, that the breast resembles the uterine endometrium in many respects. After delivery, the blood supply to the breast should then be increased and the production of milk from the blood that flows through the breast should be abundant. In case the blood supply to breast is reduced, acupuncture can promote and restore the normal neurovascular flow and motility to the breast so that milk secretion can be increased.

Cardiovascular disorders

Acupuncture is very useful in treating primary hypotension [115] and essential hypertension [116,117]. As indicated by

Chang [19,42] and the reevaluation section of this paper, blood pressure problem should be treated as a blood distribution one. The mechanisms of acupuncture in treating hypotension and hypertension are that needling in the right meridian at the right time can change the impedances of neurovascular bundles so that blood flow can be regulated. As a result, either: (1) more blood will be supplied to the areas of ischemia or regions of infraction through collateral circulation of the body; or (2) less blood will be supplied to an aneurysm so that it will not result in hemorrhage. This type of bidirectional effects of acupuncture has been indicated in Part 2 [19] and can be explained via the impedance diagrams of Part 1 [1]. In addition, acupuncture is often effective and has no side effects.

In angina pectoris, acupuncture has also been shown to be effective [118,119]. Acupuncture has not only improved the working capacity of the heart in patient with angina pectoris but also activated autoregulatory cardiovascular mechanisms in healthy persons [119]. The mechanism of acupuncture can be attributed to more blood being supplied to the coronary arteries through collateral circulation of the heart via impedance change of correlated meridians.

Psychiatric disorders and mental disturbances

Acupuncture has been used in psychiatric disorders, such as depressive neurosis and depression following stroke in controlled studies [120–124]. There have been reports that, in controlled trials of schizophrenia treatment, acupuncture might have a better effect than chlorpromazine [124,125]. Acupuncture has also been reported to be useful for treating alcohol recidivism [126]. Patients in the treatment group also have had fewer drinking episodes and admissions to a detoxification center [126–128]. Basically, acupuncture has fewer side-effects than the drug treatment.

In order to explain why acupuncture may help psychiatric disorders and mental disturbances, we have to realize that all medical treatments to some extent are *psychosomatic*. From the holistic perspective of TCM, psyche and soma are inseparable. For example, in Part 2 of this review series, we saw that the low and very low frequency ranges of heart rate variability in the ANS are highly correlated with the α and δ bands in EEGs. When a person is out of mental harmony with his environment, such as of the stresses of his life are too hard to be borne, he may feel ill as if certain organs are diseased. Conversely, it is fitting to conjecture that if the somatic conditions of a mentally disturbed person can be improved via acupuncture, then the symptoms of psychiatric disorders may be alleviated. Certainly, this conjecture will need more studies to confirm in the future.

Pediatric disorders

Acupuncture is useful in treating diarrhea in infants and young children [129,130]. In a controlled clinical trial, convulsions have been stopped just 2 minutes after needling [131]. In addition, the acupuncture treatment for pertussis could hasten the cure as well as relieving the cough [56]. The acupuncture

mechanism for treating these pediatric disorders can be referred to earlier sections concerning infectious diseases.

Tourette's syndrome is a disorder that has complex motor and vocal tics. There are two controlled studies indicating that acupuncture may be helpful in the treatment of this syndrome in children [132,133]. Both motor and vocal tics have to do with the malfunctions of the central and peripheral nervous systems. The complicated mechanism of acupuncture in treating this syndrome may need the combination of: (1) the mechanism in treating peripheral nervous malfunctions in the section of neurological disorders; and (2) treating the psychiatric disorder and mental disturbances.

Disorders of the sense organs

Deaf–mute children were once extensively treated with acupuncture in China, but no controlled studies have been reported. A recent randomized controlled clinical trial on sudden-onset deafness in adults has favored acupuncture treatment [134]. Clearly, more controlled studies have to be conducted.

Acupuncture has been shown to be effective in unexplained otalgia in a placebo-controlled trial [135]. It is also helpful in the treatment of simple epistaxis unassociated with generalized or local disease. One report of a randomized controlled clinical trial is available. This report indicates that auricular acupuncture provides a more satisfactory effect than conventional hemostatic medication [136]. The mechanism of acupuncture can be attributed to the impedance change of neurovascular flow to cure otalgia and epistaxis.

Skin diseases

In a randomized controlled clinical trial on chloasma, acupuncture has had a significantly better effect than vitamins C and E [137]. Acupuncture is known to have an antipruritic effect. This has been shown experimentally in volunteers, suggesting that acupuncture could be used in clinical conditions associated with pruritus [138]. Acupuncture with dermal needles (7-star or plum-blossom needles) has traditionally been used in the treatment of neurodermatitis, but confirmation of its effect in a controlled clinical trial was only recently reported [139]. Acupuncture has also been reported to have therapeutic effect for the treatment of acne vulgaris [140,141].

Although the reasons for causing pruritus and dermatitis are varied, but the signs of redness, swelling, and itching have all been observed. The redness and swelling arise from abnormal blood flow and over-distention of the blood vessels. The itching is due to the induced neural response. The acupuncture mechanism of curing the skin disorders can be attributed to the restoration of normal neurovascular flow by adjusting the impedances of meridian system as in the aforementioned inflammation disorders.

Cancers

It has been reported that acupuncture can relieve cancer pain [142]. For radiotherapy and chemotherapy, acupuncture

can lessen the adverse reactions in the digestive and nervous systems [143]. As to the cancer *per se*, there are four standard treatments for cancer in modern medicine: surgery, chemotherapy, radiation therapy, and immunotherapy. Alternative cancer treatments via acupuncture and herbal remedies of TCM are not FDA-approved so they cannot be administered in the USA and many other countries.

The efficacy of acupuncture in the treatment of prostate cancer has been reported in China. However, it is imperative to allow countries conduct more controlled studies to verify if acupuncture indeed has uses in treating cancers. Based on our earlier discussions concerning the mechanisms of acupuncture in various therapies, we have reasons to be optimistic about the active roles that acupuncture and TCM can play in cancer treatments. First of all, it is well known that a locally growing cancer has to have the ability to trigger the growth of new blood vessels in the first place. With the growth of capillaries, the cancer can then grow and spread into the body tissues around it. Since acupuncture can regulate vascular flow via impedance change and if we can reduce blood flow to the site of cancer, the growth of this cancer will be very much limited and constrained. Secondly, a malignant tumor can shed cells into venous circulation. Even though the probability of a single circulating tumor cell will become a metastatic nodule is less than 10^{-6} [144], there is still a possibility that the tumor cell will adhere to the vascular endothelium. Acupuncture can change the impedance of neurovascular flow so that either: (1) the tumor cells will be expelled from the body via sweating and urination; (2) the tumor cells will die as a result of trauma within arterial and venous circulation; or (3) the tumor cells will be destroyed by specific immunity of lymphocytes and white blood cells in the circulatory system. Consequently, the metastasis will not develop.

Conclusion

Acupuncture, as a unique technique of treatment in TCM, has been effectively used in clinical practice for more than 2500 years. For centuries, clinical practitioners have been wondering what the essence of the meridian system is, and how the acupuncture might work in analgesia and various therapies. So far, we have critically reviewed various proposals that have tried to answer one or both of these two questions in this three-part review series. All of these proposed theories have been based on either holistic TCM or a reductionist modern medical system. It is noteworthy that all medical systems have been and will continue to be culture-bound. This is because medicine is not only science, but also art and philosophy. It is called an art because it is so delicate and is practiced on the complex human body. Furthermore, during medical treatments, moral principles that apply values and judgments to the practice of medicine will have to be constantly involved. Needless to say, the medical ethics and philosophy toward life and death are culture-bound and they cannot be separated from medical science.

In this review series, we have tried to put the natural philosophy, physiology, pathology, diagnosis, and treatment of

holistic TCM on a scientific footing so that our descendants are willing to study the precious and voluminous traditional Chinese medical and philosophical corpus in earnest in the future. Even though this review series has been entirely concentrated on acupuncture, it is sincerely hoped that this holistic approach of TCM can be appreciated by the whole medical community worldwide so as to help our patients in a compassionate way.

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