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Review Article

The meridian system and mechanism of acupuncture—A comparative review. Part 2: Mechanism of acupuncture analgesia

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Abstract

In traditional Chinese medicine (TCM), pain is never merely a sign of discomfort. It is usually an integral part of a particular disease or physiological malfunction. Thus pain should not be treated in isolation since it will disappear as soon as its cause is identified and removed. Hence, in this Part 2 of a three-part series, initially, clinical pathologies in modern medicine and TCM are compared. Then, the pain pathophysiologies of these two schools of thought are reviewed. In addition, certain unique features of acupuncture effects that any valid mechanism must account for are outlined. Finally, various mechanisms of acupuncture analgesia are reviewed. One plausible mechanism based on the meridian system of Part 1, i.e., the chaotic wave theory of fractal continuum in terms of the neurovascular network, is also proposed. It contends that the injury current due to acupuncture at an acupoint will trigger electromagnetic inductive effects so that the impedances of correlated neurovascular bundles are drastically changed. Two consequent scenarios are possible. (1) If the impedance of the meridian hugely mismatches with that of the brain after acupuncture, then the traveling wave of pain signal will be largely reflected back and only partially transmitted to the brain, hence pain relief can be achieved. (2) If the impedance of the meridian entirely matches that of the pain source after acupuncture, then the pain source would appear to be nonexistent to the brain, hence analgesia can be achieved. The former mechanism can be used to explain the relief for chronic pain and the latter one for acute pain. It is believed that the proposed mechanisms via match or mismatch of the impedances can explain how the acupuncture works not only in the treatment of pain, but also in various other therapies of Part 3.

Keywords: acupuncture analgesia; acute pain relief; chaotic wave theory; chronic pain relief; fractal continuum; mechanism of acupuncture analgesia; meridian system; traditional Chinese medicine

Introduction

Joseph Needham, by comparing China and the West, insightfully concluded that the Chinese physical world view involves waves instead of atoms, and continuum instead of discontinuity [1,2]. As a result, interactions in modern physics and medicine need the collision of atoms and molecules, while the Chinese view is more of a field or wave approach. He then pointed out that "the conception of wave motion … seems sometimes to have acted in an inhibitory way upon the advance of scientific knowledge." On the contrary, the Chinese physical world view has been proven recently to be much closer to reality than its modern Western counterpart [3–13]. In Part 1 of this series of reviews, for example, a chaotic wave theory of fractal continuum was proposed to characterize the essence of the ancient meridian system as a complex network of neurovascular bundles and their smaller branches [14]. This complex network is connected to internal viscera, peripheral limbs and sensory organs. Anatomically, it is a continuum with a self-similar fractal structure. Physiologically, it interacts with the internal viscera, peripheral limbs and sensory organs via the chaotic waves of blood flow and nerve innervations.

In this article, Part 2 of a three-part series, various mechanisms of acupuncture analgesia are reviewed first, while those of acupuncture therapies will be reserved for Part 3, as pain is the most common reason for people to use traditional Chinese medicine (TCM). However, it is worth mentioning that pain is

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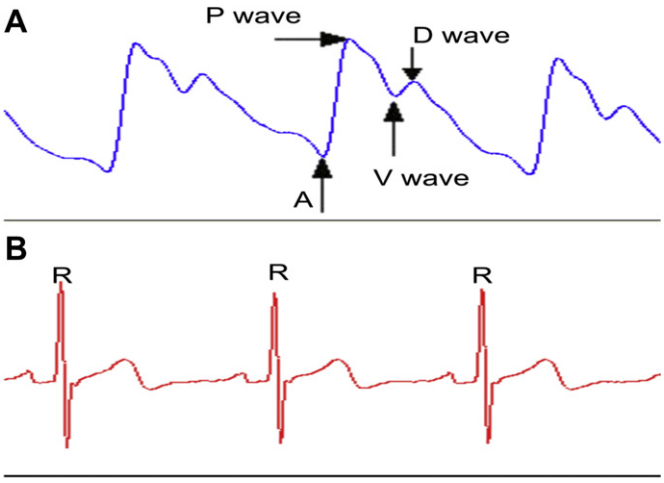

Fig. 1. Radial arterial pulse wave and ECG wave. (A) The typical pulse wave marked with A, P, V, D. Where A stands for a base point, P the percussion wave, V the valley, and D the dicrotic wave. (B) The ECG and its R peak. From "Hypertension: A comparative review based on fractal wave theory of continuum," by S Chang, 2011, Adapt Med, 3, p. 91–8. Copyright 2011, The Society of Adaptive Science in Taiwan. Reprinted with permission. ECG = electrocardiogram.

usually an integral part of disease or physiological malfunction. Thus pain should not be treated in isolation, as it will disappear as soon as its cause is identified and removed. Furthermore, pain *per se* is inherently a feeling that is very subjective and an objective standard in assessment is usually very difficult. Up to now, there have been several primitive pain scales available to assess pain. A very popular one, the visual analog scale (VAS), is basically a 10-cm line with one end being labeled "no pain" and the other end "worst pain imaginable." The patient marks the line at the point that can describe his/her subjective pain intensity. The length of the line is usually measured and recorded in millimeters. As to the interpretation of the marked results, it is the responsibility of the clinician and researcher to take it with a pinch of salt for the nonlinearity of the scale and subjectivity of the patient. In Part 1, we observed a case of misinterpretation that bred misunderstanding. That case was not alone. For example, a review of pain treatment with acupuncture, published in the January 2009 issue of the British Medical Journal, concluded "a small analgesic effect of acupuncture was found, which seems to lack clinical relevance and cannot be clearly distinguished from bias" [15]. The clinical conditions in that paper included knee osteoarthritis, tension-type headache, migraine, low back pain, fibromyalgia, abdominal scar pain, postoperative pain, and procedural pain during colonoscopy. The duration of those treatments varied from 1 day to 12 weeks. As stated by the authors in that paper, a small difference was found between acupuncture and placebo acupuncture with standardized mean difference corresponding to 4 mm on a 100-mm VAS. In addition, a moderate difference of 10 mm was found between placebo acupuncture and no acupuncture. Hence, based on their methodology, a difference corresponding to 14 mm on a 100-mm VAS had already been found between acupuncture and no acupuncture. Their result was obtained under data contamination. For if one examines closely Figs. 1 and 2 of their paper, one will see that the group of acupuncture is more favorable than that of placebo

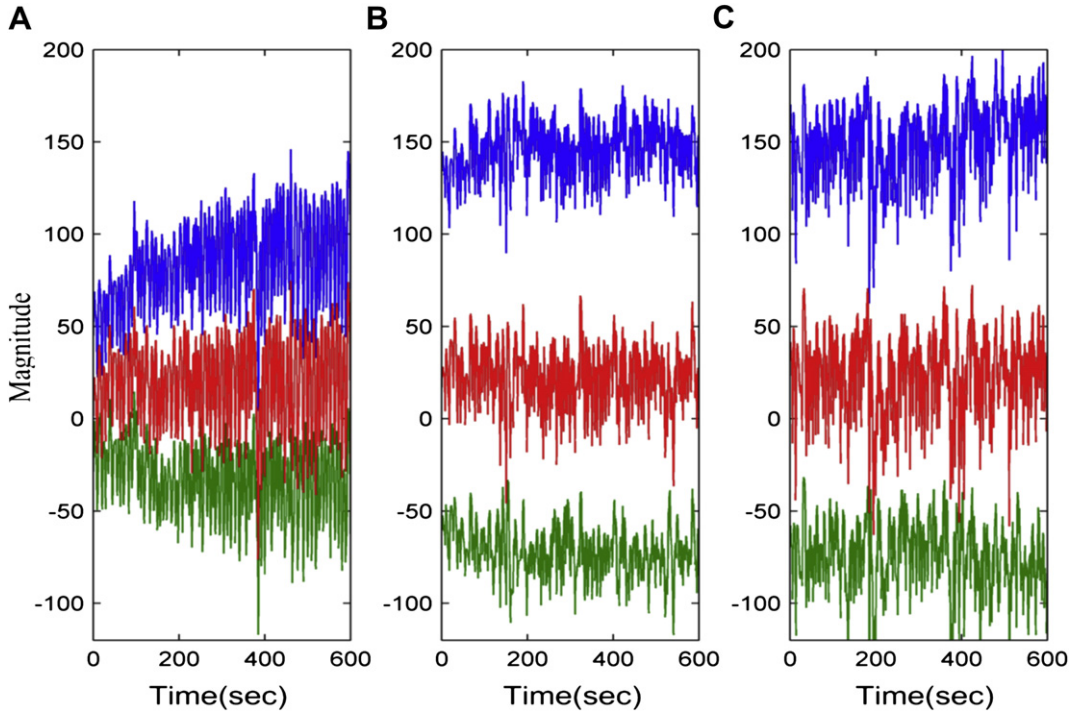

Fig. 2. The increase in magnitudes of the radial arterial pulse: amplitudes of base point A coded in green, dicrotic notch V in red, percussion wave P in blue, (A) before, (B) during, and (C) after manual acupuncture at PC 6. From "Hypertension: A comparative review based on fractal wave theory of continuum," by S Chang, 2011, Adapt Med, 3, p. 91–8. Copyright 2011, The Society of Adaptive Science in Taiwan. Reprinted with permission.

acupuncture in Fig. 1, and placebo acupuncture is more favorable than no acupuncture in Fig. 2 [15]. Out of the 13 trials of acupuncture involving 3025 patients with pain, seven of them were incoherent in the sense that they either violated the synthetic result of Fig. 1 or that of Fig. 2. We have to exclude those inconsistent trials which favor no acupuncture in Fig. 2 and placebo acupuncture in Fig. 1 in the final calculations of standardized mean difference. Consequently, only six of the 13 trials should be eligible and kept for final data analysis. A recalculation of the VAS values of these six trials will yield a standardized mean difference corresponding to 6 mm on a 100-mm VAS between acupuncture and placebo acupuncture, and 14 mm between placebo acupuncture and no acupuncture. As a result, a difference corresponding to 20 mm can be obtained between acupuncture and no acupuncture. This value indicates that acupuncture, compared with no acupuncture, can indeed provide significant pain relief on average. Unfortunately, the investigators failed to point out the efficacy of acupuncture analgesia due to misinterpretation of the data set.

Therefore, it is imperative in this Part 2 to elucidate the mechanism of acupuncture analgesia so that misinterpretation and misunderstanding can be avoided. Hopefully, acupuncture can be adopted to help our patients worldwide in the future. First, however, it is essential to understand the different viewpoints of clinical pathologies in modern medicine and TCM. Then, the pathophysiology of pain will be comparatively reviewed. Next, certain unique features of acupuncture effects that any valid theory of acupuncture mechanism must account for will be outlined. After these unique features are outlined, various mechanisms of acupuncture analgesia will be comparatively reviewed and examined. Finally, the conclusion of this Part 2 will be presented.

Clinical pathologies in modern medicine and TCM

Francis Bacon once laid down that “to know truly is to know through causes”. Any physician will have to seek and determine causes of diseases, for only when the cause is deduced can treatment be rational. The etiologies and clinical pathologies of modern medicine and TCM do have something in common. For example, trauma and parenteral injections of toxic substances can cause disease in both schools of thought. Poverty, malnutrition, and overcrowding can favor the development of tuberculosis even though it is not clear how these contributory etiologic factors increase the risk of developing a disease. In this review article, however, emphasis will be placed more on the differences of pathological viewpoints between TCM and modern medicine.

In modern medicine, clinical pathology is usually divided into three main specialties: anatomic pathology, microbiology, and chemical pathology. Firstly, in anatomic pathology, the influence of Virchow was so strong that the appearances and structures under the microscope of the tissues and cells were more important than their functions. Consequently, this pathological viewpoint has dominated Western mainstream medicine for more than a century. For instance, a young man may die from the terrible convulsions of strychnine poisoning, yet the pathologist will find no structural change or lesion to which he can point as the cause of death. On the other hand, an old lady in perfect health may be found at autopsy to have a tuberculosis lesion of the lung and chronic disease of the heart valves which have been compensated for by cardiac hypertrophy [16]. Are we to consider such a lady in a state of health or of disease? So long as there is harmony of functions, even though the price of that harmony is the structural alterations in compensation, the lady should be regarded as in a state of health. This is indeed true in TCM; but to the pathologists or doctors of modern medicine, the lesions in the organs have to be interpreted as evidence of diseases or even the possibilities of malignant tumors sometimes. One has to distinguish clearly that clinical medicine is concerned with disturbances of function as manifested by the symptoms of the patient, while anatomical pathology is concerned with changes in structure. It should be kept in mind that disease is not a state at the instant of biopsy; it is rather a process ever changing in its manifestations, a process may end in recovery or in death depending on our approach. One of the benefits of this dynamic or functional approach in TCM is that many expensive and unnecessary diagnostic procedures or biopsies can be avoided. Healthcare costs can be drastically reduced if our focus is on function rather than on structure.

Secondly, the medical microbiologist of modern medicine is often responsible for identifying bacteria and viruses isolated from patients with infectious diseases. He/she will then assess the susceptibility of the patients to antibiotics and consult his/her medical colleagues in internal medicine regarding the dosage needed. However, in TCM, the medical doctors are not interested in identifying the species of viruses or fungi and killing them inside the bodies of their patients. It is because the antibiotics may hurt and kill their patients before the viruses. Instead, it is much safer and more efficient to just expel them outside the bodies of their patients without having to kill them.

Thirdly, in chemical pathology, an important question to ask is whether the causes of diseases could be due to disturbances of atomic, molecular, or chemical origin. For example, could diseases be due to deficiency in atoms or ions such as iodine inducing goiter, in human organs? From the viewpoint of modern medicine, the answer will be at least 90% affirmative. From the viewpoint of TCM, however, not all simple goiters could be caused by a lack of iodine in water or food. The simple reason is that it would be very difficult to explain sporadic cases on this basis. Moreover, atoms, ions, and synthetic chemical molecules usually have no optical activities so that human bodies cannot digest them, and these molecules may even block or inhibit regular physiological functions. Man-made molecules can hardly rehabilitate the normal functions of human beings. In the case of simple goiters, thyroid secretion may be deficient or absent due to complicated reasons, and an overgrowth of the supportive tissues is meant to compensate. So, the ancient Chinese doctors in TCM treated patients with simple goiters by using acupuncture to

adjust the activity of the autonomic nervous system (ANS). Alternatively, they would use the whole thyroid gland of animals such as sheep or pigs to restore normal secretion of thyroid due to the fact that the components in animal glands have optical activities and can be digested by humans. This holistic viewpoint can be made rigorous via the notion of topological conjugacy in mathematical dynamical systems. Results were successful and have had no side effects for more than 2000 years. Hence, in the context of TCM, health can be recovered via restoring normal physiological rhythms by acupuncture or administering natural products of plants or animals that have optical activities. From the viewpoint of TCM, hence, diseases can never be due to minor structural changes, or the excess or deficiency of certain ions or chemical molecules. It is, therefore, worth studying whether too much iodized salt can actually cause thyroid carcinoma in the future.

Pathophysiologies of pain in modern medicine and TCM

As to the definition of pain, The International Association for the Study of Pain defines it as "an unpleasant sensory and emotional experience which we primarily associate with tissue damage or describe in terms of such damage, or both". This definition primarily associates pain with tissue damage. It is also currently widely accepted in modern medicine that pain syndromes can be roughly divided into three categories: nociceptive, neuropathic, and psychogenic. The first category, nociceptive pain, is due to the activation of the nociceptive system by tissue injury or noxious stimuli. In this theory, specific receptors are responsible for noxious stimuli. For example, capsaicin was believed to activate C-fiber nociceptors. However, the number and size of the receptive fields served by this C-fiber are not yet known. Furthermore, the relationships between different types of nociceptors and disease states are still rudimentary. In the second category, neuropathic pain is caused by direct injury or malfunction of the peripheral or central nervous system (CNS). These malfunctions may be caused by trans-section, infiltration, or metabolic injury of the neural cell body. For peripherally generated neuropathic pain, including that generated by the ANS, understanding of its mechanism is only rudimentary. As to the centrally generated pain syndromes, information about the processes is very sketchy. Finally, psychogenic pain is an exceedingly complex kind of pain. For example, persistent nociceptive or neuropathic pain may even induce disturbances in depression or anxiety. However, it is fair to say that the mechanism of psychogenic pain is so far uncertain in modern medicine.

However, in TCM, pain need not be due to tissue damage, such as phantom limb pain for there is no more tissue there, and tissue damage may not cause pain, such as acupuncture analgesia, for it can achieve pain relief. Furthermore, there is no need to have a dedicated nociceptive system in conducting pain signals. The meridian system or neurovascular network *per se* can conduct and transmit nerve signals irrespective of whether it is pain or not. To the clinicians of TCM, pain is mainly due to the stagnation, full or partial blockade of the normal neurovascular flows which may or may not result from tissue damage in human bodies. If the flow is blocked at the skin level, bruising or swelling of the tissue is observed. Blockage at the flesh level can produce stiff, sore muscles. Stagnation in the joints will produce arthritis pain. Internal neurovascular blockages or abnormal flows can produce many symptoms and kinds of pain, including headaches, sore throat, chest pain, stomach pain, and menstrual pain. If the stagnation or blockade of the neurovascular flow in that part of the body is removed, then the pain syndrome will also disappear. In terms of the chaotic wave theory of fractal continuum proposed in Part 1, pain, i.e., the stagnation or blockade of the neurovascular flow can be characterized by its abnormal impedances. For example, phantom limb pain is derived from the amputation modifying the original neurovascular flow and changing the limb impedance to a different value. If this value cannot be adjusted and matched with that of the remaining part of the body after a certain amount of time, the amputated limb will act as a source of pain or discomfort. However, if its impedance can be once more matched with the rest of the body, the pain will go away.

Unique features of acupuncture effects

Before proposing any valid theory of acupuncture mechanism, important acupuncture effects must be heeded and taken into consideration. According to the spatial and temporal changes of arterial blood flow, heart rate variability (HRV), and electro-encephalogram (EEG) of acupuncture at Neiguan (PC 6) in the neighborhood of the median neurovascular bundle [17,18], certain unique features of acupuncture effects have been observed and will be summarized here. Fig. 1A was an exemplary arterial pulse wave. In the acupuncture experiments of Chang et al [17], arterial pulses were recorded by a strain gauge under compression mode over the radial artery. This strain gauge will respond to a time-varying compression from the arterial wall. Usually, the compression is related to the blood volume in the artery and its local impedance. For example, the reading of the percussion wave, denoted by P, of the radial artery in Fig. 1A is indicative of a maximal blood volume at a particular time. The dicrotic notch or valley V in the pulse wave corresponds roughly to mean blood pressure in standard physiology textbooks [19,20]. As time moves on, the curve goes downward until it reaches the base point A in Fig. 1A. This point is proportional to its local impedance [7,17,18]. It is worth mentioning that pulse-taking by experienced TCM physicians can be interpreted as performing similar functions of compressive strain gauge sensors. In terms of modern scientific language, the physicians are trying to precisely feel the volume and impedances of the local blood flow with their fingers. From these data, they try to infer or predict what has gone wrong in the viscera of patients. This is certainly a tough inverse problem in sphygmology and needs more studies in the future.

In the research by Chang et al [17], electrocardiograms (ECGs) were also recorded to analyze the HRV, which was

related to the activity of the ANS. A typical ECG diagram is provided in Fig. 1B. For example, the ANS can influence the R-R intervals of the ECG [21] and it is also related to pain [22]. Furthermore, the ANS can also alter the degrees of vasoconstriction in the blood vessels of visceral organs and limbs in our body [19,20]. As to the frequency domain analysis of HRV, it is generally divided into three ranges. The first is called the very low frequency range (VLF: 0.00−0.04 Hz), the second is the low frequency range (LF: 0.04−0.15 Hz), and the third, the high frequency range (HF: 0.15−0.40 Hz) [21]. They are believed to reflect the activities of the ANS [21]. Figs. 2 and 3 illustrate two exemplary sequences of pulse waves before, during, and after manual acupuncture at PC 6. Fig. 4 illustrates exemplary time-frequency analyses of HRV before, during, and after manual acupuncture at PC 6. The spectra exhibited changes in the ANS due to acupuncture stimulation. In particular, spectral frequencies in the LF range almost disappeared after acupuncture at PC 6. In addition, the frequencies became more concentrated and synchronized in the VLF range during and after acupuncture; even though the powers as indicated by the color intensities were about the same. Hence, it is noteworthy that the ANS was perturbed seconds after acupuncture at PC 6. Unfortunately, the parameters proposed by Akselrod et al [21] were not definitive enough to distinguish sympathetic from parasympathetic activities as has been indicated in other studies [7,10,17].

To record simultaneous changes in the CNS, the field electric potentials of 12-channel EEGs were also taken by Chang et al [18]. The spatial and temporal colored images under manual acupuncture at PC 6 are shown in Figs. 5 and 6 using the EEGLAB program (Swartz Center for Computational Neuroscience (SCCN), Version 6) [18]. In Fig. 5, the spatial distributions of signal power for all 12 channels before and after acupuncture are shown. In addition to the spatial changes, the EEGLAB program was also used to plot the temporal changes of the 12 channels, as shown in Fig. 6. Notice that the peaks in the α band for all 12 channels were erratic before the acupuncture, but were almost all synchronized during and after manual acupuncture. The frequencies of 12 channels were quite varied with a mean value of 8.300 Hz and a standard deviation 0.176 Hz in the α band before manual acupuncture. During acupuncture, the frequencies of 12 channels were almost all synchronized at 8.202 Hz, with a rather smaller standard deviation of 0.081 Hz. Finally, after the manual acupuncture, the frequencies were all synchronized at 8.008 Hz, with a very small standard deviation of 2.03^{-7} Hz.

Combining the results of the ANS and CNS, as indicated in Figs. 2−6, the rhythmic changes occurred almost instantly in a spatial-temporal fashion. The ANS activities of the heart were exhibited in the δ band ($\sim$0.2 Hz) and α band (8 $\sim$ 12 Hz) of the CNS, as indicated from the EEGs. The lower frequency band may have to do with the parasympathetic system and the higher α band with the sympathetic system [7−10,17,18]. Another important point provided by this experiment was that both the synchronization of central EEGs and peripheral blood pressure changes with associated HRV were exhibited almost instantly, roughly about 15−30 seconds after acupuncture at PC 6. Figs. 2−6 have indicated such a drastic rhythmic change within a very short time span. The experimental results have thus indicated that the afferent somatosensory input near the median neurovascular bundle of the wrist can initiate neural responses of the heart and the whole brain, not just the somatosensory cortex alone. It is

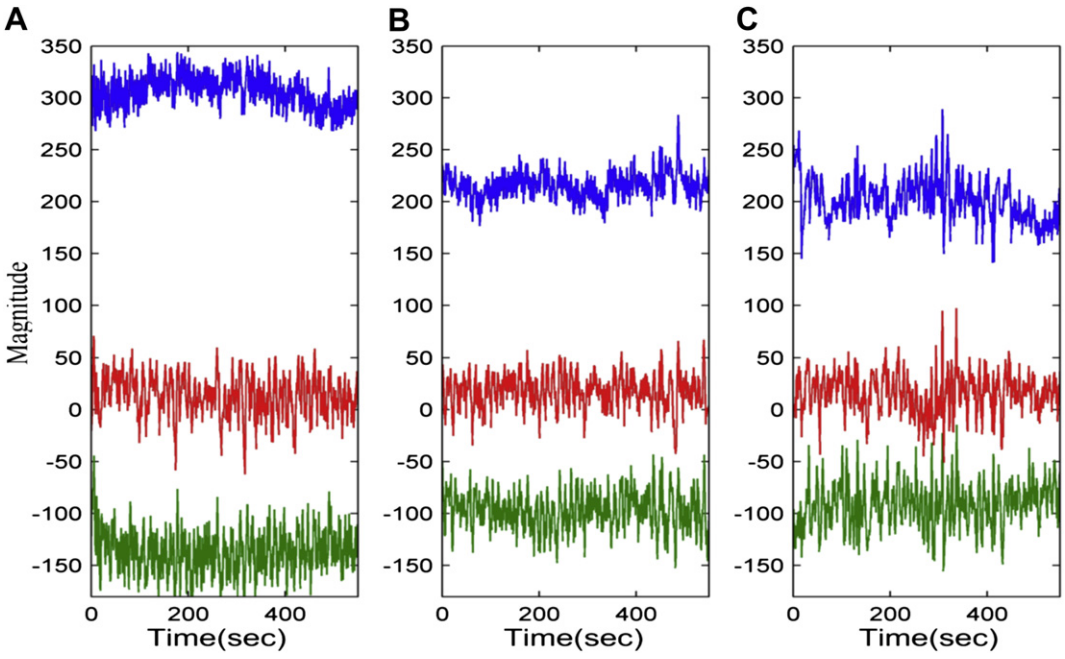

Fig. 3. The decrease in magnitudes of the radial arterial pulse: amplitudes of base point A coded in green, dicrotic notch V in red, percussion wave P in blue (A) before, (B) during, and (C) after manual acupuncture at PC 6. From "Hypertension: A comparative review based on fractal wave theory of continuum," by S Chang, 2011, Adapt Med, 3, p. 91−8. Copyright 2011, The Society of Adaptive Science in Taiwan. Reprinted with permission.

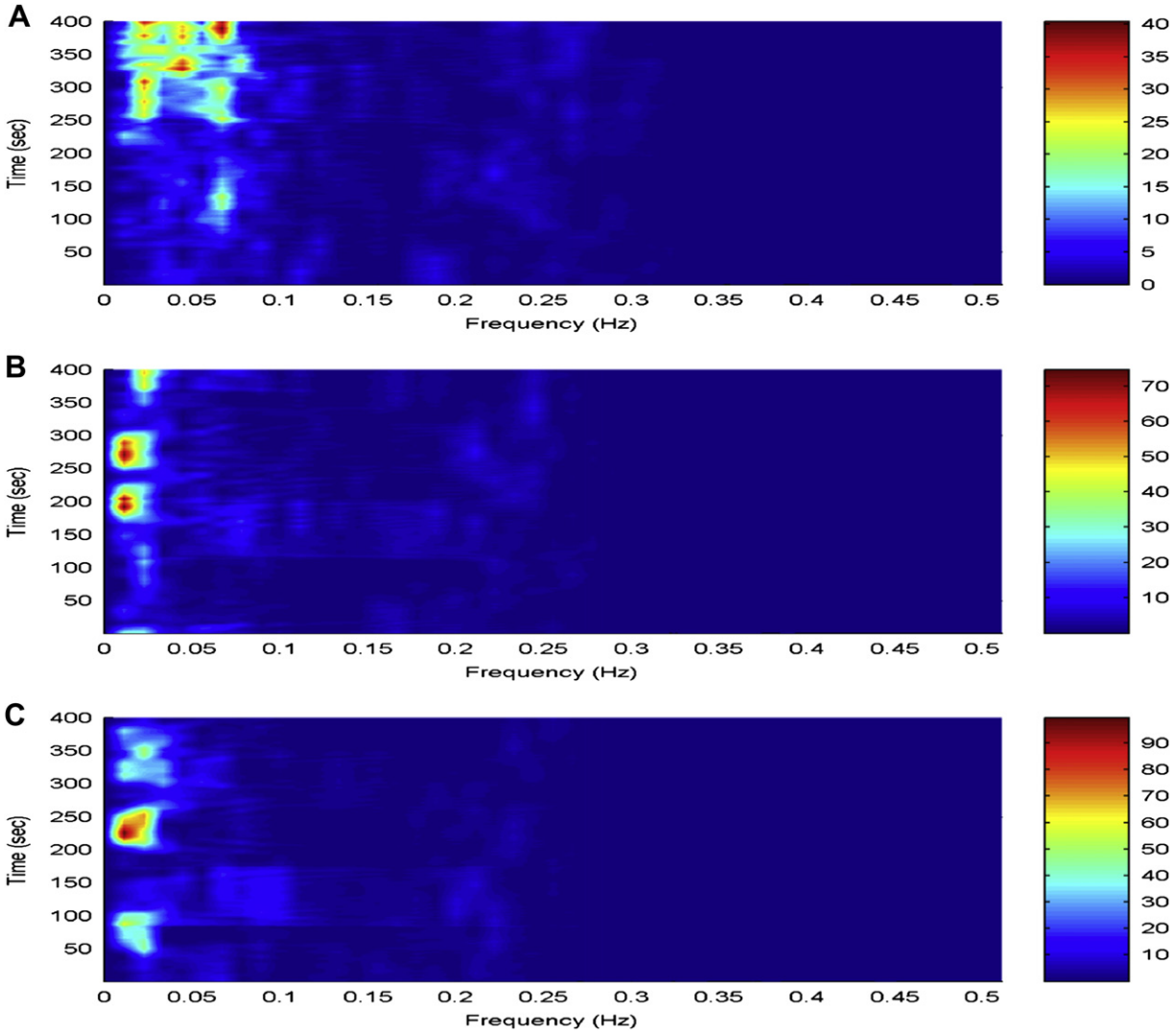

Fig. 4. The time-frequency analysis of HRV for the experiment in Fig. 7: (A) before, (B) during, and (C) after manual acupuncture at Neiguan. HRV = heart rate variability. From "Hypertension: A comparative review based on fractal wave theory of continuum," by S Chang, 2011, Adapt Med, 3, p. 91–8. Copyright 2011, The Society of Adaptive Science in Taiwan. Reprinted with permission.

fitting and proper to conjecture that the brain is more likely to be holographic rather than modularly organized.

In summary, in the peripheral systems, experimental results have indicated that the volume of blood flow could either increase or decrease after manual acupuncture at PC 6 in terms of seconds, and HRV related to the ANS also changed during and after manual acupuncture. In particular, the frequencies became more concentrated and synchronized in the VLF range during and after acupuncture [17]. As to the changes that occurred in the CNS, the intensities of signal power for all 12 channels changed after acupuncture, and all channels were synchronized during and after acupuncture in the α band. In conclusion, these central and peripheral changes all happened almost instantly within less than 30 seconds. As a result, these fast responses of acupuncture can hardly be explained in terms of biochemical or endocrinal origins, which would require tens of minutes, hours or even days to occur. Therefore, the unique features of acupuncture can be briefly characterized as: (1) bidirectional effects, for example, possible increase or decrease of blood flow; (2) synchronization of EEGs of the whole brain and ANS of the peripherals via HRV; and (3) fast responses of the aforementioned effects in terms of tens of seconds. It is imperative to keep in mind that any plausible mechanism of acupuncture will have to take these features into account.

Mechanism of acupuncture analgesia

Over the past few decades, many different mechanisms have been proposed to explain how acupuncture might work in analgesia. In the following section, different schools of thought are reviewed.

Gate control theory

A gate control theory of pain was proposed by Melzack and Wall in 1965. It was thought to be the best model to explain

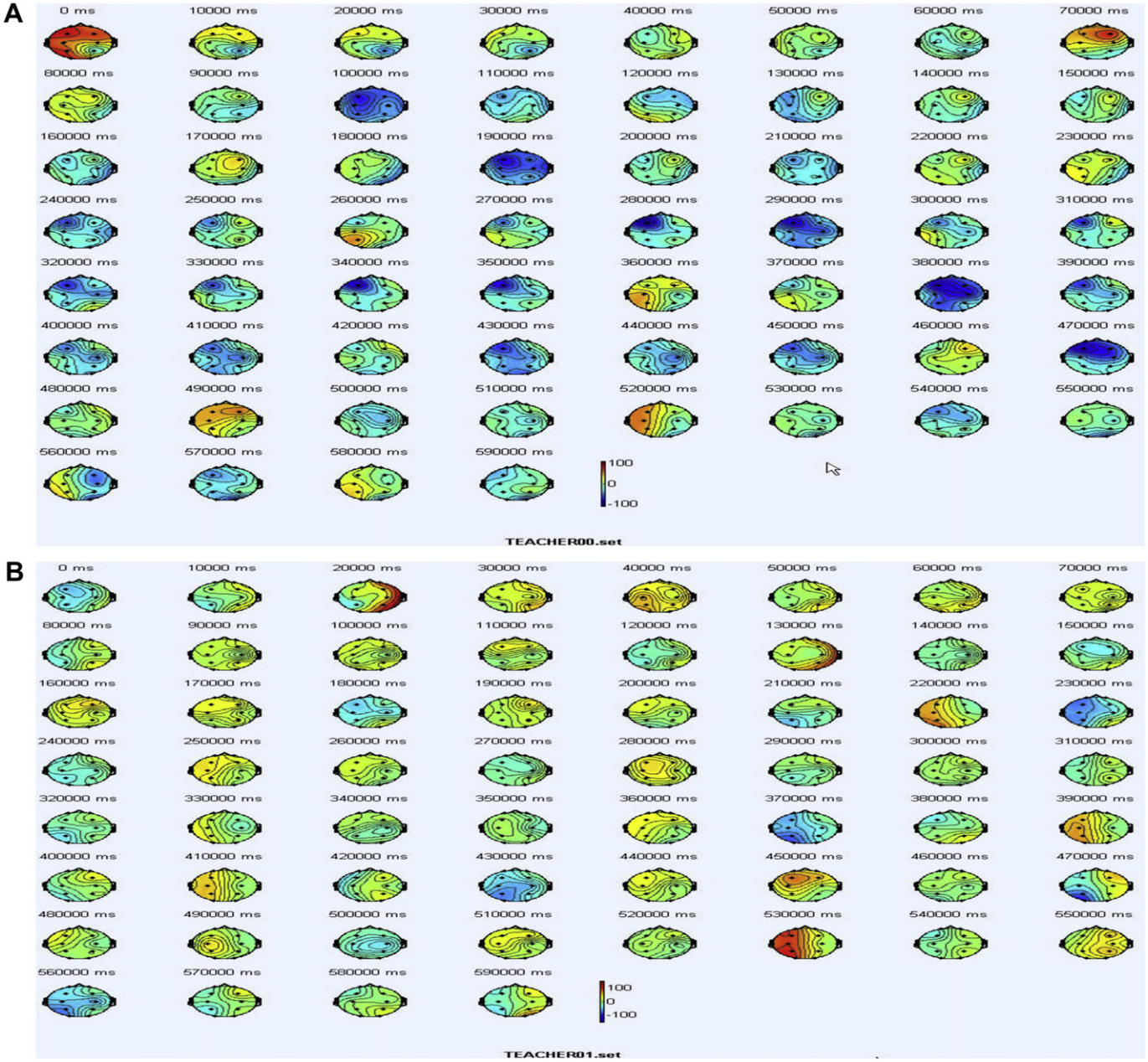

Fig. 5. Spatial powers of the 12-channel EEG for the experiment in Fig. 7: (A) before and (B) during acupuncture. The graph is similar after acupuncture and is omitted here. (A) The average power was relatively lower before acupuncture at PC 6 (as coded in blue). (B) The average power was relatively higher after acupuncture (as coded in yellow). From "Physiological rhythms, dynamical disease, and acupuncture," by S Chang, 2010, Chin J Physiol, 53, p. 72–90. Copyright 2010 Chinese Physiological Society. Reprinted with permission.

the mechanism of pain relief from acupuncture [23]. This theory contended that there were specific nerve fibers that would transmit pain to the spinal cord, while other nerve fibers inhibited the transmission of pain. Both groups of fibers met at the substantia gelatinous in the spinal cord. This special area actually controlled the integration of pain and pain inhibitory stimuli. Pain would be perceived only if the pain input exceeded the inhibition of pain. The first and foremost problem with gate control theory is that it can not explain the full spectrum of acupuncture effects. In addition, this theory cannot explain the prolonged pain relief. More importantly, the concept of nerve inhibition in neuroscience is still a continuing case of controversy [24], which will be fully discussed in Part 3 of this review series.

Neurochemical factors

It is well-known that the perception of pain has definitely to do with the nerves and brain. Hence, since the 1970s, elucidating the mechanism of acupuncture analgesia has also been focused on the secretion of a range of biochemicals or neurotransmitters. For example, small and large ions and

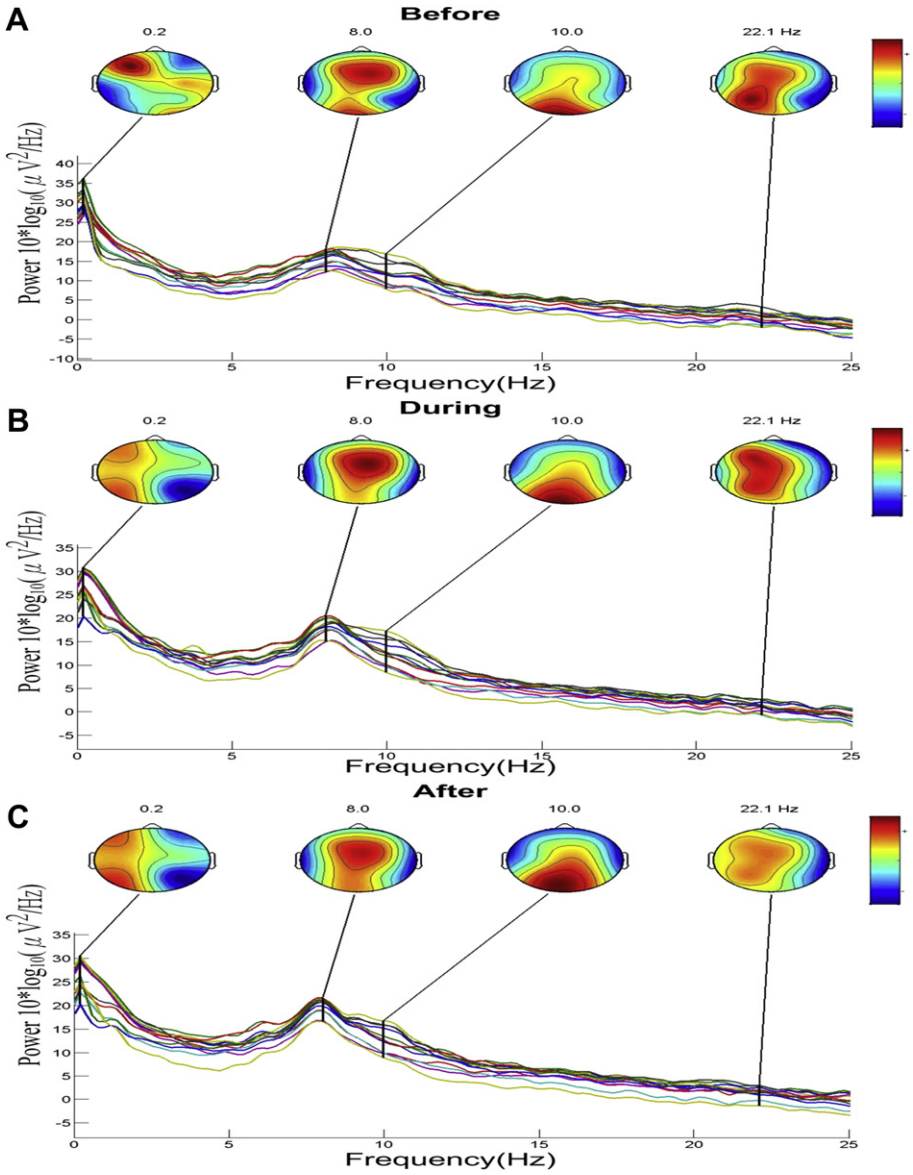

Fig. 6. The plots of the 12-channel brain maps and temporal spectra for the same experiment via EEGLAB software. In the α band, brain waves are synchronized during and after acupuncture. From "Physiological rhythms, dynamical disease, and acupuncture," by S Chang, 2010, Chin J Physiol, 53, p. 72–90. Copyright 2010 Chinese Physiological Society. Reprinted with permission.

molecules, such as adenosine, opioid peptides, cholecystokinin octapeptide, 5-hydroxytryptamine, noradrenalin, glutamate, γ-amino-butyric acid, substance P, calcium ions, angiotensin II, somatostatin, arginine vasopressin and dopamine, have all been considered as possible candidates [25–37]. It is illustrative and should be enough to review the exemplary case of opioid peptides in the brain as a possible biochemical or neurophysiologic mechanism of acupuncture analgesia.

In the early 1970s, studies by Ji-Sheng Han's research group using the infusion of the cerebrospinal fluid of acupunctured rabbits into the cerebral ventricles of recipient rabbits revealed that the pain threshold of recipients could be increased [38]. As a result, they believed that the involvement of central chemical mediators in acupuncture analgesia was necessary. For example, one important class of transmitters and mediators was the opioid peptides. Many researchers thought that the endogenous opioid peptides played a pivotal role in central antinociception [38,39]. Frequency-dependent electro-acupuncture analgesia was also believed to be mediated by different opioid receptor subtypes [39,40]. For example, electro-acupuncture at a low frequency of 2 Hz would facilitate the release of enkephalin, but not dynorphin, while a high frequency of 100 Hz would stimulate the release of dynorphin but not enkephalin in rats [39]. Similar findings were also confirmed in humans [40]. These electromagnetic-dependent results, however, have actually indicated that the primary reason and root cause for acupuncture effects are bioelectromagnetic in character, while the biochemical factors are secondary. In addition to the aforementioned frequency relationship between electro-acupuncture and brain

neurotransmitters, different intensities of electro-acupuncture also influences different brain nuclei in expressing opioid receptors. For example, the microinjection of naloxone into the thalamic nucleus submedius blocked high- but not low-intensity electro-acupuncture analgesia, whereas converse results were observed when naloxone was injected into the anterior pretectal nucleus in the rats [41]. These experimental results, again, clearly suggested that bioelectromagnetism is the primary cause and the opioid receptors or other biochemicals can only be the effects and appear to be secondary. Furthermore, as indicated in the experimental method sections of these papers, the biochemical and neurophysiologic after-effects usually took more than 10 minutes to be observed [26,38]. Hence, using biochemical factors or neurotransmitters in explaining acupuncture analgesia is not conformable to the fast responses of acupuncture effects in terms of tens of seconds on one hand. On the other hand, it cannot be used to explain the mechanisms by which acupuncture cures many other different physiological malfunctions either. It is further compounded by the fact that the levels of these biochemicals are actually varying as functions of time. Therefore, it is not reliable to use elevated or decreased levels of biochemicals as the main causes of acupuncture analgesia. Incidentally, some researchers have recently proposed that the opioid peptide secretions were due to mechanical acoustic shear wave activation and calcium signaling [42]. The reason why such a mechanistic model was contended was that they believed needle rotation was required to reduce pain sensitivity. As a matter of fact, in clinical practice, a needle insertion of proper depth without any rotation can still reduce pain sensitivity. That is to say, the mechanism of acupuncture analgesia should have nothing to do with the rotation of needles.

Neuroimaging in analgesia

Recently, neuroimaging studies, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), have also been used to indicate that multiple cortical, subcortical, limbic, and brainstem areas have been activated or deactivated and must have something to do with acupuncture analgesia. These results should not be surprising if only the primary and secondary somatosensory cortices were activated. Yet, surprisingly enough, the anterior and posterior insula, and the prefrontal cortex (PFC) were also recruited, according to a recent report [43]. Hence, the brain is more likely to be hologramic rather than modularly organized. Another chief concern in the brain imaging approach is its reproducibility and reliability [44]. Consequently, the results of fMRI studies on acupuncture analgesia can hardly lead to any major breakthroughs.

Injury current and match/mismatch of impedances in the meridian system

Before proposing this mechanism of acupuncture analgesia, let us recall two important facts of biophysics at the outset. Firstly, according to Cole [45], there was experimental evidence showing that a current flowed across the myelin internode. This important result was contrary to the saltatory conduction of nerves that flow was restricted only to the Ranvier nodes. Consequently, the existence of a solenoidal current flowing within the myelin sheath is not only a possibility, but also a necessity. A myelinated neural circuit AA was used to illustrate the solenoidal current in the myelin [14]. In an animal or human without afferent or efferent stimulation, the background solenoidal current would generate a very weak magnetic field within the axons. The magnetic flux would then induce a basic “nerve tone”, or a ready state, of the neurofibrils in the axon so as to be able to transmit either the afferent sensory information or efferent motor signals later. It was mentioned in Part 1 that the situation was very analogous to the way iron filings would align in a conformable way with the magnetic field caused by a solenoidal current. If any mechanical, thermal, chemical, electrical, or magnetic stimulus is produced in the neighborhood of a myelinated nerve, the local external potential around that nerve will be perturbed and the solenoidal current will be changed. As a result, the magnetic field inside axons or “nerve tone” will also be perturbed. The upshot is that the peripheral changes due to external stimuli can be quickly detected by the CNS and ANS, just like the alignment shape changes of iron filings would reflect the information contained in the variable solenoidal current. It is certainly true that different intensities and types of external stimuli will produce different degrees and feelings of effect in the brain. For example, if the stimulus is tissue injury rather than a gentle touch stimulating a nerve ending, the former will definitely produce a much stronger response than the latter in the brain.

Secondly, as a result of injury, the resistance and capacitive reactance of a frog sciatic nerve can both change [45]. The ratio of capacitive reactance percentage change to that of resistance is roughly 15:1. In order to keep the action potential from distortion, the ratio of inductive reactance percentage change to that of conductance must be of the same ratio from transmission line theory. Hence, the inductive and capacitive impedance changes play very important roles in acupuncture. Similar experiments have also been carried out in cats [45]. Hence, it is a reasonable conjecture that if the nearby potential of a neurovascular bundle is perturbed or injury current is produced due to acupuncture, then the impedances of the bundle will be changed. These two facts of biophysics are referred to as the electromagnetic inductive effects triggered by injury current.

To present the mechanism of acupuncture in pain relief and analgesia via the chaotic wave theory of fractal continuum, let us assume the pain source generator has an impedance Z_g [14]. Without loss of generality, the brain can be modeled as a load with impedance Z_3. Without any treatment, the afferent pain signal will transmit as a traveling wave from the pain source to the brain and be felt by the patient. However, if the manual acupuncture is administered at an acupoint of the relevant meridian with impedance value Z_2, the local injury current will trigger the aforementioned electromagnetic inductive effects so that the impedance Z_2 will be drastically changed.

There are two possible scenarios. Firstly, if the impedance of Z_2, as a function of space-time and frequency, was changed in such a way that its value would hugely mismatch with Z_3 after acupuncture, the afferent pain traveling wave would then be largely reflected back and only a small portion of it could reach the brain due to a well-known fact in the transmission line theory of communication. Consequently, pain relief could be achieved. Second, if the impedance of Z_2 was changed in such a way that its value would match with Z_g after acupuncture, the pain source would then have the same impedance as that of the meridian. Hence, the pain source would appear to be part of the meridian and nonexistent to the brain, consequently acupuncture analgesia could be achieved. The former mechanism can usually be used to explain relief from chronic pain. It is because, in the chronic pain case, the pain source may have existed for a long time and its associated impedance value has already deviated very much from its normal value. As a result, it is rather easier to mismatch the meridian impedance value with that of the brain so as to partially block the pain signal and obtain pain relief. However, in the case of acute pain, the pain source may have existed only for a short amount of time and its impedance value be only slightly deviated from its normal value. In this case, it is rather easy to change the impedance of its relevant meridian so as to match it with that of the pain source. Since both of them have the same impedances after acupuncture, the brain will not be able to tell the difference between the two and recognize the existence of the pain source. As a result, the acupuncture analgesia can be achieved rather easily for acute pain.

As to the efficacy of pain relief and analgesia, it will certainly depend on where and how one administers the acupuncture. In clinical practice, it may take only a few seconds to obtain analgesia for acute pain, and yet multiple sessions are necessary to obtain a cumulative effect for the treatment of chronic pain. One advantage of this proposed mechanism of acupuncture analgesia is that both acute and chronic pain reliefs can be unified under the same mechanism of impedance matching/mismatching.

In addition, it is often pointed out that the sites of acupoints used by acupuncturists in TCM for analgesia can be either local or distant to the pain locations. Sometimes both methods can work almost equally well in tens of seconds. This fact is extremely difficult for the biochemical approach to explain why the local release of histamine [34] or adenosine [26] can have a distant effect in such a short amount of time. However, for this proposed mechanism, the impedance change can indeed modify the traveling wave of the neurovascular network both locally and globally in a short amount of time. Consequently, both local and distant acupuncture effects can be explained under the same principle of wave or field approach. This is another advantage of the chaotic wave approach.

Finally, it should be pointed out that the meridian system of the neurovascular network is a fractal continuum and its impedances are functions of space-time and frequencies. In invasive sham control or placebo acupuncture, the sham position is always located in the proximity of some neurovascular branches of the fractal network. If the injury current is strong enough, it will certainly change the impedances of near-by meridians and achieve some analgesic effects. By the same token, the invasive sham control will not produce any significant effect if its intensity of stimulation is either too weak or is decayed to an insignificant level when it reaches the relevant meridian.

Conclusion

In this article, I have reviewed various mechanisms of acupuncture analgesia. A recently proposed chaotic wave theory of fractal continuum has been invoked to explain the mechanism of acupuncture analgesia in this review. I have claimed that the injury current due to acupuncture at acupoints of relevant meridians will trigger electromagnetic inductive effects in the fractal continuum of the neurovascular network. As a result, the impedances of meridians or neurovascular bundles can be drastically changed. Due to the match/mismatch of impedances with pain source/brain, analgesia and pain relief can be achieved. The advantages of this proposed mechanism of analgesia from acupuncture are at least threefold: (1) it can explain both acute and chronic pain reliefs under the same principle; (2) both local and distant acupuncture effects can be unified under the same mechanism; and, (3) it can explain why sometimes the invasive sham control may have analgesic effects. It is also believed that the proposed mechanism can explain how acupuncture works in various other therapies, as will be covered in Part 3.

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