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What is the Acupoint? A Preliminary Review of Acupoints

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Abstract

Background. According to traditional Chinese medicine (TCM) theory, acupoints are specifically chosen sites of acupuncture manipulation, and also the basis for studying the mechanism of acupuncture. Stimulating different acupoints on the body surface could provide various therapeutic benefits. However, what is the acupoint? This question is not clear.

Review Summary. We focuse on examining the function of acupoints from different perspectives, including the local and the systemic effects of stimulating acupoints. For example, acupoints may release certain substances or incur some changes, which could adjust the function of organs, maintain homeostasis. Furthermore, the therapeutic effects of verum acupoints versus sham acupoints were discussed. However, due to insufficience in evidence and in current methodologies, research into mechanisms of acupuncture is still incomplete.

Conclusion. This review might explain, to some extent, what an acupoint is. Further research into the identity of acupoints is warranted, and multidisciplinary methods using novel technologies may yield significant advances over existing knowledge.

Key Words. Acupoints; Acupuncture; Local Effects; Systemic Effects; Review

Introduction

Acupuncture is an important part of Traditional Chinese Medicine (TCM), has a history over 2000 years [1]. Due to its efficacy and safe application [2–6], acupuncture has been used widely as a treatment for pain disorders in western countries, including migraine [7,8], low back pain [9], and so on. In addition, along with the dissemination of acupuncture, other traditional medical systems have appeared, including Japanese Meridian Therapy, French Energetic Acupuncture, Korean Constitutional Acupuncture, and Lemington 5 Element Acupuncture [10]. These therapies were influenced by TCM at the origin but developed uniquely in adaptation to its circumstance and culture with distinct features [11]. According to classical acupuncture theory, it is believed that the disorder of visceral conditions and organs is reflected at specific points, either on the skin surface or underneath, which are generally called acupoints [10,12]. The concept of acupoints derived from *Huangdi's Canon of Medicine (Huangdi Neijing)* and *The Great Compendium of Acupuncture and Moxibustion,* which are believed to be the foundations of acupuncture [13]. Stimulating at the acupoints modulates the physiology of the body [1],

such as lowering blood pressure [14], preventing arrhythmic recurrences [15], relieve functional dyspepsia (FD) symptoms, and improving life quality [16]. Therefore, determining the function of acupoints will help to clarify the mechanism of acupuncture treatment on disease and provide the basis for clinical research. With respect to acupoints, recent studies have examined structure, function, and characteristics of acupoints, especially the existence of acupoint specificity [17]. They seemingly have searched for distinct features that acupoints might differ from the surrounding tissues or structures. However, due to the limited research, the existence and function of acupoints is a matter of controversy. At present, there is no persuasive evidence for the existence of acupoints [18]. For example, their location or number and the evidence from histological studies for acupoints are unconvincing [19]. This review focuses on the function of acupoints from different perspectives, which might explain what an acupoint.

The Local Effects When Stimulating Acupoints

The Possible Structure Under the Local of Acupoints

Acupoints could accept a variety of forms of stimulation, such as the mechanical stimulation of the needle, the thermal and Chinese medical stimulation of moxibustion, the electrical current stimulation of electroacupuncture (EA), and the radiated stimulation of laser acupuncture [20–23], which play the important role in the acupuncture treatment of diseases. Early morphological structure studies were analyzed from the perspective of the anatomical structure, which reported that the nervous system [24,25], blood vessels [26], or muscle [27] may have a closely relationship with acupoints. Accumulation of microvessels was shown at the acupoints *Zhongji (RN3)* and *ST36*, whereas the surrounding tissues didn't show these characteristics [28]. Histological investigations have revealed that acupoints have a number of elements such as a high density of nerve endings, A- and C-afferent fibers [29–31] and higher concentration of neural and vascular elements, especially mast cells [32], which could perceive stimulation. Zhang et al. [20] found that acupoints may increase the degranulation of mast cells, and the density of mast cells from the *ST36* of rats was higher than a nearby sham point. Meanwhile, moxibustion may also activate degranulation of mast cells at the *Ximen* (*PC4*) [21], *Tianshu* (*ST25*) [33] of different disease rat model. Langevin found 80% correspondence between the sites of acupoints and the location of intermuscular or intramuscular connective tissues in postmortem tissue sections [34]. During acupuncture, connective tissue, elastic, and collagen fibers entwined around the needle under the local of acupoints to produce a characteristic needling sensation, which was described as "*Deqi*" [35]. However, in the fascia network approach, someone also arrived at the conclusion that there is no structural difference between a traditional acupoint and a sham point, as fascia connective tissue is everywhere in the body. Despite considerable efforts to understand the anatomy and physiology of acupoints, there remains controversy with the anatomic sites related to acupoints. It has not yet been confirmed that whether the so-called morphological structure characteristics of acupoints reflect the acupoints accurately. The difference between a traditional acupoint and other points is in the intensity of response rather than structural components, a difference in degree rather than all or none [36].

The Electrical Properties Under the Local of Acupoints

Under pathological circumstance, acupoint is the important reflex point of body lesions. In healthy persons, electrical skin resistance at acupoints was significantly lower than the nearby nonacupoints [37]. Using an electrical circuit model, Silberstein [38] observed a 10^3 reduction in electrical skin resistance at acupoints. A systematic review concluded that 5 out of 9 point studies showed positive association between acupoints and lower electrical resistance [39]. Furthermore, a single-blinded study showed that skin electrical resistance at acupoints either lower or higher compared with the surrounding area in healthy humans [40]. However, in asthma condition, skin resistance at acupoints *Lieque* (*LU7*) and *Taiyuan* (*LU9*) was significantly higher than healthy subjects [41]. According to the phenomenon of the low skin resistance in healthy states and the high skin resistance in disease conditions, the skin resistance has been used as a means to localize [42] and analyze acupoints for diagnostic purposes [41,43]. However, several studies revealed that the phenomenon of acupoints' low skin resistance did not exist on acupoints compared with the nearby control points for healthy persons [44,45]. In addition to the skin resistance, other electrical properties at acupoints were also discussed. For example, unilateral manual stimulation of acupoints *LU7* and *Zhaohai* (*KD6*) triggers the increase of skin potential amplitude than no acupuncture group [46]; volt-ampere (V-A) characteristic of acupoints has the characteristics of both nonlinear and inertia, and changes obviously in the patients of heart disease or stomach diseases [47]; the skin dielectric property of *PC4* is different from surrounding nonacupuncture sites in the 50–61 GHz range [48]; the electrical conductance of most acupoints on Heart Meridian were decreased after EA stimulation in 10 healthy volunteers [49] and varied with pathogenesis [50,51]. However, a recent review showed that the electrical properties of acupoints were in a condition of imbalance even they have the same name on the affected meridians located symmetrically on bilateral sides of the body [52]. Therefore, whether acupoints are truly associated with electrical characteristics remains controversial and should be systematically studied. From a technical standpoint, the present commercial electrodiagnostic devices are inadequate, and different methods are likely needed to appropriately assess the electrical characteristics of acupoints [53].

The Biomolecules Under the Local of Acupoints

When stimulating acupoints, the local of acupoints may release biomolecules to exert the role of analgesia or

neuromodulation. Preliminary research suggested that adenosine were effective biomolecules of acupuncture information generated locally at acupoint [54]. One animal experiment indicated that adenosine was released during acupuncture at *ST36* in acupuncture-mediated antinociception [55]. Further research in human subjects also supported above opinion [56]. Several experiments [57–60] suggested that nitric oxide levels near or at the acupoints were higher than nonacupoints or nonmeridian control areas. Meanwhile, the cyclic guanosine monophosphate concentrations [57,58] or norepinephrine (NE) concentration and NE turnover rate [59] were also higher. A recent study [61] indicated the higher partial oxygen pressure levels in the acupoints (*ST36, Shangjuxu* (*ST37*)*, Zhongting* (*CV16*), and *Shanzhong* (*CV17*)) of rabbits than the nonacupoints (1 cm apart from the acupoints). Three of the four acupoints also showed significantly higher concentrations of calcium (Ca), iron (Fe), copper (Cu), and zinc (Zn) elements than the surrounding tissue [62].

The Acupoint Sensitization

In recent years, Chen and coworkers [63] put forward the concept of "acupoint sensitization" considering that it is a changing and dynamic site rather than in a stable state for the size and function of the acupoint. That is to say, under pathological circumstance, some acupoints appeared the change of temperature (heat-sensitization) or pain threshold (pain-sensitization). One study showed that the temperature of several points (*CV17, LR14, KI21, CV6, CV4*) persisted at a high level in hyperplasia of mammary glands patients compared with healthy women [64]. Further research was conducted, which they have observed a "heat-sensitization" phenomenon in a large proportion of patients receiving suspended moxibustion treatment. Patients become thermally sensitized to moxibustion stimulation at certain locations on the body, which indicated by sensations of strong warmth or heat penetrating into the body (heat penetration), warmth spreading around the stimulation site (heat expansion), warmth conducting in certain directions and reaching some body regions or even internal organs remote from stimulation sites (heat transmission), or other nonthermal sensations such as aching, heaviness, pressure, and so forth [65]. Pain-sensitive points are also called the *Ashi* points in many Chinese ancient medical books. *Ashi* points were put forward by Chinese physician Sun Ssu-Mo who inserted needles at points of pain in *Valuable Prescriptions for Emergencies* (*Qianjin Yao Fang*) [66]. It is defined as*"Where there is pain, there is a transport point,"* that is, the area where you feel tenderness or pain by finger palpation [67]. In a modern context, changes in pain sensitivity are assessed mostly by measuring the pressure pain threshold. Different diseases have different pain-sensitive points. The pain-sensitive points of patients were located in the abdominal and back region of stomach meridia in gastric ulcer or gastritis [68], while the pain-sensitive points at *sanyinjiao* (*SP6*) in premenstrual syndrome [69]. Researchers have used animal models to explore mechanisms of pain sensitization. It is found that acupoints may be sensitized by visceral noxious stimuli and the sensitive degree of acupoints changed according to malfunction of internal organs [63,70]. Myofascial trigger points (MTrPs) were proposed as a mechanism to explain musculoskeletal pain [12,71,72], and they may resemble acupoints in location and function. Because both types of points have consistent anatomic locations, 99.5% of classical acupoints do have pain indications correspondence with MTrPs [73]. MTrPs are defined as hyperirritable tender spots in discrete taut bands of skeletal muscle or fascia that produce local tenderness and referred pain [72]. Recent studies, applying ultrasound imaging techniques and a microdialysis system, show that MTrPs are distinct from adjacent soft tissue and exhibit a unique biochemical profile of substances associated with pain and inflammation [74,75]. However, the concept of acupoints is clearly broader than MTrPs; MTrPs are much better match to the *Ashi* points for pain [76]. Thus, MTrPs and acupoints are conceptually impossible to equate completely [77]. It is also of note that dry needling is a technique that refers to the insertion of thin monofilament needles into an MTrP to treat myofascial pain [78]. Although the needles are used, the therapy is based on the Western medicine, which is different from acupuncture in theory [66].

The Systemic Effects When Stimulating Acupoints

The Adjustment of Viscus and Organs Function

Acupoints are thought to be the specific points reflecting visceral conditions as well as regulating the function of internal organs [12] and regarded as an important link in the relationship between meridians and viscera [79]. Clinical observations and principal research on acupuncture focused on the adjustment of *zang-fu* organs and have shown that the adjustment by acupuncture relied largely on the neuroendocrine-immune network, which also provides new evidence for the acupuncture effective components in different organs [54]. For example, the results of gene expression profiles in asthmatic rats indicated that the genesis and regulation of the hormone and immune response were involved in acupuncture treatment for asthma [80].

A morphological study was experimented to investigate the neural pathways of stomach and *ST 36* using neuroanatomical tracers. It demonstated that labeled neurons were observed in nucleus tractus solitarius and spinal cord, when neuroanatomical tracers were injected into the *ST 36* in rats, and that there is a specific connection and relationship between the *ST 36* and central nervous system (CNS) neurons [81]. In addition, it was found that EA at *ST36* improved gastric dysrhythmia, alleviated stress-induced visceral pain and accelerated gastric emptying, which were most likely mediated by opioid pathways in the periphery and neurotransmitters pathways in the central [12,82,83]. After EA at *Neiguan* (*PC6*), the functional parameters of the heart related to cardiac function increased significantly [84]. EA at the *Yinlingquan* (*SP9*) and *Ququan* (*LR8*) acupoints could

increase the blood flow in the spleen and liver, respectively, whereas the sham EA did not increase these parameters [85].

The Maintenance of Homeostasis

It is well known that the basic concepts of TCM are derived from ancient Chinese natural philosophy [86]. TCM presumes that there are two opposing and complementary forces that coexist in nature: *Yin* and *Yang*. These two forces interact to regulate the flow of "vital energy," known as *Qi*. When a person is in "good health," *Yin* and *Yang* are in balance, and the flow of *Qi* is smooth and regular. When *Yin* and *Yang* become "unbalanced," there are disturbances in *Qi*, which lead to illness and disease. The ancient Chinese believed that *Qi* flows through a network of channels called meridians and collaterals, which bring *Qi* from the internal organs to the skin surface. Along these meridians, there are acupoints that can be stimulated to correct the imbalance, restore the body to normal health [5] and promote the blood flow (*blood*) [79,87–90]. Therefore, acupoints are also defined as the particular parts of the body surface for infusing or diffusing "Qi" and *blood* of viscera and meridian, the body lesions reflex points as well as the important stimulus points for acupuncture. However, no convincing evidence shows the existence of novel structures or substance serving as the foundations of meridians and collaterals or *Qi*, although related studies have been performed [91–93]. From the traditional Chinese perspective, these concepts are not based on anatomical, physiological, or biochemical evidence, and thus cannot form the basis of a mechanistic understanding of acupuncture [5]. Given that acupuncture has been used for provide various therapeutic benefits, it is conceivable that meridians and collaterals or *Qi* might be functional, not anatomical. The relationship between the traditional theory and the modern understanding involves in a complex summation of multiple physiological functions, including the nervous, circulatory, endocrine, and immune systems [24].

Acupuncture likely has an effect on homeostasis by the somato-autonomic reflex [94]. According to TCM, the theory of "Acupuncture is believed to restore the balance of Yin and Yang" may be also translated into the Western medicine terminology that "Acupuncture modulates the imbalance between the sympathetic and parasympathetic activity" [18,95]. Acupuncture stimulates the somatic afferent nerves of the skin and muscles under the acupoints. Then, the somatic sensory information from the body is carried to the cortex area of the brain. Somatic sensory fibers also project to the various nuclei at the brain stem and hypothalamus [95]. Experimental and clinical studies suggest that afferent input in somatic sensory fibres has a significant effect on autonomic functions [94]. Via somato-autonomic reflex, acupuncture modulates various biomechanical responses of autonomic activities [95], such as heart rate variability [96], blood pressure [14], and gastric emptying [97]. The role of somato-sympathetic reflex has been studied in the acupuncture regulation of cardiovascular function [98] and improvement of metabolic dysfunction with polycystic ovary syndrome [99]. The role of somato-parasympathetic reflex has been studied in the acupuncture regulation of gastrointestinal peristalsis [100]. Moreover, acupoints have a bidirectional regulation effect (the idea that an intervention pushes the patient toward a homeostatic state rather than having a unidirectional effect that may help or harm). For example, acupuncture not only lowers blood pressure, but also modulates low blood pressure in patients and animal models [14,101–103]. Acupuncture can increase enterogastric peristalsis for constipation symptom [100,104] while also has anti-diarrhea effect [105]. In addition, acupuncture at the same point also has the bidirectional regulation effect. Acupuncture at Bahui (GV20) has been shown to be effective in treating both hypertension and hypotension [106]. Siguan (a combination of LI4 and LR3 bilateral meridian points) is one of the most important acupoints to treat multiple gastrointestinal symptoms including constipation and diarrhea [107]. Despite the fact that the opposite regulatory effect of acupoints has been used for treating specific symptoms and/or diseases, it is not fully understood how the effect at acupoints works.

In contemporary, the acupuncture-induced analgesic effect has been widely used to alleviate diverse types of pain in both Asian and Western countries. During the last decades, our understanding of how to play an analgesia role of acupuncture has undergone considerable development. Western theories are primarily based on the presumption that acupuncture induces signals in afferent nerves that modulate spinal signal transmission and pain perception in the brain [5]. Moreover, acupuncture activates some brain areas that contribute to descending inhibitory modulation [108,109] and deactivates multiple limbic areas that contribute to modulating pain emotion [110]. It is suggested that acupuncture is capable of modulating central homeostasis to produce analgesia, supporting the notion that acupuncture regulates the balance of *Yin* and *Yang* [24]. The neural mechanisms underlying acupuncture analgesia include that the activation of afferent nociceptive nerve fibers, the spinal and complex brain neural pathways, and various signal molecules [5,24]. Therefore, acupuncture analgesia is essentially a manifestation of integrative processes at different levels of the CNS between afferent impulses from the pain regions and impulses from acupoints [24]. Moreover, three regulating systems, nervous, endocrine and immune, are involved in maintenance of homeostasis [111,112]. For example, acupuncture could regulate the brain-gut axis [113,114], activate the hypothalamus-pituitary-adrenal axis [115], and downregulate the hypothalamopituitary-gonadal axis [116].

Besides aforementioned mechanisms, the redox homeostasis modulation of acupuncture was also discussed by researchers. Oxidative stress is a normal phenomenon in the body. Under normal conditions, the physiological intracellular levels of reactive oxygen species (ROS) are maintained at low levels by various enzyme

systems participating in the redox homeostasis [117]. Oxidative stress can also be viewed as an imbalance between the pro-oxidants and antioxidants [118], which is associated with disruption of redox circuitry or macromolecular damage and can be quantified in humans as the redox state of plasma glutathione/oxidized glutathione (GSH/GSSG) [119,120]. Oxidative stress has been implicated in the etiology and/or progression of numerous pathologies such as cardiovascular diseases, inflammation, and cancer [118]. Recent studies showed that acupuncture could attenuate oxidative stress and damage [121], inhibit the production of ROS [122], reduce the ratio of GSH/GSSG [123], increase the redox effector factor (Ref-1) expression [124], and so on. Taken together, acupuncture modulates the redox homeostasis through regulating the imbalance between the pro-oxidants and antioxidants.

It is important that the acupoint has its own specific function to maintain the homeostasis, while the manipulation of acupuncture also play a significant role to this effect. In TCM theory, acupunture treatment evoked acupuncture feeling ''*Deqi*'' associated with the efficiency of acupuncture. Acupuncturists usually rotate or twist the needle up and down to get the *Deqi* feeling [24]. Numerous neuroimaging and physiological mechanism studies of *Deqi* have been discussed by the domestic and foreign researchers [125]. It is believed that *Deqi* is not only the needling sensation, but also the perception of changes of *Qi* flowing of the patient elicited by needling on acupoints [93]. Therefore, the efficiency of acupuncture and the mechanism of maintaining the homeostasis by acupoints may due to the *Deqi*.

Verum Acupoints and Sham Acupoints

Several acupuncture randomized clinical trials (RCTs) have found that acupuncture at verum acupoints was superior to acupuncture at sham acupoints. A German randomized acupuncture trial for chronic shoulder pain reported that acupuncture at verum acupoints significantly improved shoulder mobility than sham acupoints [126]. Another German trial for seasonal allergic rhinitis also observed that the treatment effect of acupuncture at acupoints was superior to sham acupoint [127]. Acupuncture at specific acupoints of the stomach meridian was found to be superior to nonspecific acupoints and sham acupoint for FD patients [16]. Furthermore, neuroimaging studies provided similar evidence for this theory [128–131].

However, there is growing evidence show that the sham acupoints used in trials may also have therapeutic effects or that there is no significant difference between verum acupoints and sham acupoints [132–134]. In several acupuncture RCTs, some sham acupoints are defined as being as close as 1 cun (ca. 1.5 cm) to verum acupoints [135]. According to acupuncture textbooks for the description of acupoint location, many acupuncturists or researchers assume that the verum acupoints are small and must be located precisely. In 2008, the localization of 86 acupoints were represented by the WHO Standard on Acupuncture Point Locations in the Western Pacific Region [136]. Nonetheless, according to TCM theories and clinical practices, acupoints are not only some sites, but also various for locations. Because many acupuncturists rely on eliciting the *Deqi* sensation, and therefore, would produce adjustments to their point localization and the angle of needle insertion to achieve treatment effect [137]. Molsberger et al. [138] examined the localization of 23 commonly used acupoints by 71 physicians who were experienced and trained. They reported significant variability in point size range from 2.7 to 41.4 cm^2, suggesting that the term "acupuncture field," rather than "acupuncture point." Hence, the distance (1 cun) between sham points and verum acupoints or fields in some trials may not far enough to compare, which showed no significant difference between verum acupoints and sham acupoints [9,139,140]. Other explanations for the efficacy of sham acupuncture include nonspecific effects such as positive patient expectations, patient-practitioner interaction, the experience of an invasive needling technique, as well as specific biologic effects of skin palpation and needling [137]. It has been speculated that the size of the nonspecific effects associated with acupuncture may be larger than that associated with other interventions (sham acupuncture and placebo acupuncture) [141,142]. Among these effects, patient expectations, patient-practitioner interaction, and the therapeutic ritual are likely to have the most prominent role [9,143,144]. In summary, there is a lack of clear understanding of the mechanisms of acupuncture and of what constitutes an acupuncture point. Well-designed studies are needed to elucidate the complex factors involved and allow the design of appropriate control procedures in clinical studies of acupuncture [140].

Conclusion

In summary, acupoints may release certain substances or incur some changes, which could adjust the function of organs, maintain homeostasis, or treat disease. These changes or functions reflect the local and the systemic effects of acupoints from different perspectives. In addition, we also discuss the verum versus sham acupoints. At present, research evidence is insufficient to draw definitive conclusions regarding the existence of acupoints as distinct physiological entities or as to their clinical relevance. Sufficient evidence exists to suggest that acupoints may have distinct physical properties, which justifies continued research to explain these phenomena. Further research into the identity of acupoints is warranted, and multidisciplinary methods using novel technologies may yield significant advances over existing knowledge.

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