Acupoints Initiate the Healing Process

Heming Zhu, MD(China), PhD, CMD, MAc, LicAcu

ABSTRACT

Background: As an important modality of Traditional Chinese Medicine, acupuncture has been widely accepted by the Western world in the past 4 decades because of this modality's efficacy and safety. A vast amount of acupuncture research has been done. However, the mechanisms of acupuncture actions are still elusive. It is believed that the effects of acupuncture treatment begin from the moment of needle insertion.

Methods: This review focuses on the acupuncture points and the three major reactions at the acupuncture points when needling is performed. These initial reactions may be the beginning of the healing process that initiates downstream effects through neuronal and humoral pathways. In addition to the physical reactions, this article also discusses the possibility of the effects of acupuncture on the healing process through a holistic pathway.

Conclusions: Needling is the first step of traditional acupuncture therapy. Needling reactions— neuronal, biophysical, and biochemical—are the beginning of healing. The messengers of the three reactions involved may include neurotransmitters, cytokines, hormones, and inflammatory factors. Healing may be potentiated through these messengers in neuronal and humoral pathways. The reactions manifest as erythema and De Qi— both of which are common phenomena used as positive signs in acupuncture treatment. Acupuncture may also play a role in the healing process through the holistic pathway, which needs further study.

Key Words: TCM, Acupoints, Needling Reactions, Healing Process

INTRODUCTION

ACUPUNCTURE IS ONE OF SIX MAJOR MODALITIES in Traditional Chinese Medicine (TCM). TCM has been practiced for ~3000 years and is a complete system of medical theory and practice. Since the 1970s, acupuncture has developed rapidly and has become a widely accepted medical modality in Western countries. Increasing research has provided solid evidence that acupuncture can be used to treat a number of diseases and symptoms effectively and safely, such as chronic pain, arthritis, and menopause. The National Institutes of Health (NIH) has recognized the value of acupuncture and advocated its inclusion into conventional medicine.¹ Many prestigious institutions have started integrative medicine centers to utilize acupuncture and Chinese herbs. Some complementary and alternative medicine

(CAM) schools aim for integrative health care that will incorporate multiple traditional medicines into the existing allopathic health care system. Acupuncture is rapidly becoming an integral part of mainstream medicine and integrative health care.²

However, many questions remain as we study acupuncture. In clinical trials, the main challenges come from the design of the studies, using sham acupuncture, placebo, double-blinded needling techniques, dosages of treatment, dosages of timing, and the methods of outcome assessment.^{2,3} In basic research, the most difficult question to answer is concerning the existence and functions of acupuncture points and meridians. This review discusses the existence and functions of acupuncture points (acupoints).

According to TCM theory, Qi is vital energy that flows in the meridians throughout the whole body. Qi helps animate

Department of Integrative Health Sciences, Maryland University of Integrative Health, Laurel, MD.

body, mind, and spirit and protects human beings from illness and disease. A blockage, Deficiency, or imbalance of Qi results in disease. Acupoints are the sites in the meridians where Qi is able to flow, enter more deeply, and exit. Acupoints are permeated and irrigated by the Qi flowing in the meridians.⁴ Stimulation at acupoints may reduce pathologic conditions by unblocking Qi Stagnation and rebalancing Qi movement in the meridians so that healing can occur, and balance–harmony of Yin and Yang can be fulfilled.

There are specific modalities in TCM that are used to stimulate the acupoints and meridians, resulting in healing. These major modalities include acupuncture, moxibustion, cupping, *Gua Sha*, and acupressure. The procedure of acupuncture treatment is to insert sterile disposable needles into the skin and manipulate the needles in order to regulate Qi in the meridians. Therefore, the acupoints should be the locations that initiate the healing process. Studying the acupoints in the framework of bioscience is an imperative first step to expand the understanding of acupuncture and ancient science that was begun thousands of years ago.

The Anatomy of Acupoints

This section describes structures that may respond to acupuncture stimulation according to widely accepted bioscience knowledge.

When acupuncture needles are inserted into the human body, the needles may go through multiple layers including the skin (epidermis and dermis), subcutaneous tissue, and muscles. Each of these layers contain special structures and cells that may respond to needling.

There are abundant blood vessels, hairs and hair follicles, oil glands, and sweat glands in the dermis. More meaningful structures that may respond to needling would be special neural receptors. These are free nerve endings, follicular nerve endings, Merkel's complexes, Meissner's corpuscles, Ruffini corpuscles, and Pacinian corpuscles. Among them, the free nerve endings are in the dermis and epidermis; these endings are thermal receptors and nociceptors that are responsible for sensations of pain, heat, and cold, and chemical irritability. The follicular nerve endings serve as position receptors. The last four corpuscles are mechanoreceptors. The Merkel complexes are located in the dermis but are close to the bottom of the epidermis and function to sense sustained pressure, such as wearing glasses or holding a pen. Meissner's corpuscles are located close to the bottom of the epidermis and sense fine texture and pressure, while working with Meissner's complexes. Ruffini corpuscles are in the middle of the dermis and sense shearing stress or drag, especially on hairy skin. The Pacinian corpuscles are close to the bone and sense bone vibration. Those special receptors respond broadly to different types of mechanical stimulation that may include acupuncture needling.

The subcutaneous tissue contains a number of cells, fibers, sympathetic nerve-rich blood vessels, and lymphatic

vessels. The common cells and fibers are fibroblasts, mast cells, macrophages, plasma cells, collagen fibers, elastic fibers, and reticular fibers. The cells and fibers in the connective tissue and cells in the skin are likely to respond to acupuncture stimulation in different ways, either biochemical or mechanical.

Muscle spindles and Golgi tendon organs are mechanical receptors that serve as stretch receptors in muscles and tendons. The intramuscular connective tissue also contains free nerve endings that are responsible for sensing pain in the muscles.

The first known book of Chinese medicine, the *Huangdi Neijing* (*The Yellow Emperor's Canon of Internal Medicine*, ~2500 BC), states that the points are the sites where vital Qi flows, goes deeper, and exits; they are not skin, muscles, tendons, and bones, and that the 12 meridians travel in the fascia and are invisible.⁴ Nerve trunks, nerve branches, and nerve plexuses in the walls of blood vessels have been well-observed at the acupoints in anatomy research. Most of the acupoints and meridians are located along the blood vessels and nerves. However, nerves and blood vessels are not considered to be the acupoints or meridians.

After examining the aforementioned neural structures at the acupoints, researchers who performed histologic studies found that acupoints had relatively dense and concentrated neural structures in comparison to adjacent areas.⁵ This indicates that the neural structures may be closely related to acupuncture stimulation and essential mechanisms.

However, there is still no convincing evidence of novel structures at the acupoints and in the meridians.

Reactions at the Acupoints When Needling Is Performed

The needling reactions of aforementioned structures determine their roles at the acupoints and in the healing process. A vast amount of research has been conducted in experimental and clinical studies in the past 4 decades. Collectively, these studies show that there are three kinds of possible reactions at the acupoints when needling. These reactions are discussed in the sections below.

Neuronal reactions. When a needle is inserted and manipulated either manually or electronically, the local free-nerve endings and specialized neural receptors receive the stimulation that is then transformed into nerve impulses. In turn, these impulses are sent to the central nervous system (CNS) through afferent neural pathways. Every level of the CNS responds to the signals, leading to downstream effects—a possible healing process. The crosstalk of the nervous system with the endocrine system and immune system may amplify and enhance these effects. This interaction within the neuro-immuno-endocrine network has drawn attention and is well-addressed in many TCM research publications.^{6–8} Recently, it was reported that innate

immunity was regulated by dopamine and electrical acupuncture (EA) in mouse experiments.⁹ It is widely accepted that EA activates nerve impulses by stimulating various receptors in the skin, subcutaneous tissue, and muscles. Most nociceptive signals are transmitted by unmyelinated C fibers and thin myelinated A δ fibers. Most mechanical signals are transmitted through A δ fibers. Therefore, the nervous system receives different types of stimulation through different receptors and fibers, includes possible stimulations produced by needling.^{10–13}

Biophysical reactions. Acupuncture needling may be a noxious stimulus sensed by the nociceptors, but it is also mechanical stimulation received by the mechanical receptors. The needle insertion and needle manipulation techniques (thrust, lift, rotation, twist, scrape, shake, and flick) may cause mechanical signal transduction and connective tissue deformation that leads to downstream effects.^{14–17}

In rat experiments, Langevin et al. observed winding of connective tissue around the needle after rotating the needle.¹⁴ The main structure within the connective tissue that wound around a needle was collagen, as shown by a special staining technique. There were four significant changes in the connective tissue after rotating the needle:

- (1) Fibroblasts were aligned with collagen fibers.
- (2) Fibroblasts were more spindle-like in shape.
- (3) Collagen fibers were straighter and more parallel to each other.
- (4) More actin proteins were expressed in the fibroblasts.

Mechanical signals are transduced through connective tissue deformation to remote sites. The deformation activates the mechanoreceptors and nociceptors when the waves of the mechanical signal spread to remote sites. That may explain the propagation of the needling sensation along the meridians and in distant places. Based on these results, the common mechanism proposed for the effect of acupuncture needling is mechanical signaling through connective tissue.¹⁴

The activation of the mechanical receptors is well-studied in mice and human beings. The muscle-stretch receptors also play an important role in the remote transduction of the needling effect. The distant effect of needling is mainly obtained by shear force- and stress-induced tissue displacement during manual manipulation.^{16,17} The aforementioned techniques of manual manipulation produced greater distant effects on sarcous stretch receptors than on cutaneous mechanoreceptors. Among the manual techniques twist/rotation was the strongest technique that caused the greatest distant effects on the cutaneous receptors, deeper mechanoreceptors, and sarcous stretch receptors. Twist/rotation at the muscle-rich acupoints produced stronger distant effect.^{18,19} This is probably why manual manipulation or electrical stimulation on the inserted needles at the muscle-rich acupoints can often produce strong sensation transduction in

acupuncture treatments. Therefore, it is understandable that Langevin used the rotation to produce connective tissue deformation as the model of mechanical signal transduction.

Electrical properties at the acupoints were studied by Nakatani and others.^{20–23} These studies revealed that the acupoints have higher electrical conductance and lower impedance than adjacent points. Electricity measurements at the acupoints have been shown to have clinical significance in health and diseases such as coronary heart disease,²⁴ lung cancer,^{25,26} and chronic pelvic pain.²⁷ Normalization of acupoints electricity leads to therapeutic outcomes in patients with heart stress,²⁸ obesity,²⁹ joint pain,³⁰ and other conditions.^{31,32}

A narrative review of 29 studies of electrical conductance measurement at the acupoints stated that electrodermal activity (EDA) testing at auricular acupuncture points may distinguish pathology-related acupuncture points from nonpathology-related points, and decreased skin conductance correlates with tiredness or low energy. The review also suggests that EDA testing at the *Jing-Well* acupuncture points, on the tips of the fingers and toes, may assist in monitoring the effectiveness of acupuncture treatment. This review also highlighted the heterogeneity of approaches to EDA assessments and the discrepancies between common clinical practice and the scientific evidence to support that practice.³³

Therefore, although some types of instruments for acupoints' electrical conductance measurement are available on the market—and are used by some acupuncturists to help diagnose Qi imbalance, guide treatment strategies, and evaluate treatment outcomes—reliable and wide use of these instruments in patient care deserves further investigation.³³ About 5 years ago, a multichannel system for continuous measurement of skin resistance and capacitance at acupoints was developed in a research setting for obtaining accurate and reliable measurements.³⁴

Biochemical reactions. In addition to the biophysical reactions, needling at the acupoints may produce a series of biochemical reactions.

Needling-produced tissue injury is minimal and self-heals, according to clinical observation. More importantly, the injury initiates a healing process. In other words, the small needle injury treats greater pain and health issues. Needling stimulation greatly increases the concentration of many neural and nonneuronal bioactive factors, such as noradrenaline,^{35–37} β -endorphin,^{38,39} acetylcholine,⁴⁰ and somatostatin.⁴¹

Acupuncture stimulation may activate free nerve endings and local cells including mast cells, fibroblasts, macrophages, lymphocytes, and keratinocytes. All of these release bioactive factors, such as neurotransmitters; neuromodulators; hormones; cytokines; and inflammatory factors, such as substance P, calcium gene-related peptide (CGRP), histamine, serotonin (5-hydroxytryptamine), interleukin

(IL)-1, IL-4, IL-6, IL-8, tumor necrosis factor- α , and prostaglandin. These factors may, directly or indirectly, affect and influence their neural receptors, target cells, or tissues locally and systematically.⁴²⁻⁴⁵

Exploring the possible bioactive factors involved in acupuncture needling may provide a new avenue for understanding the mechanism of action of acupuncture treatment. In 2010, Goldman et al. reported that acupuncture at ST 36 (*Zusanli*) in mice significantly reduced chronic pain in the ipsilateral paw and increased the extracellular concentration of adenosine triphosphate and adenosine in the acupoints' tissues.⁴⁶ Local application of an adenosine A₁-receptor agonist replicated the analgesic effect of acupuncture. The antinociceptive action of adenosine requires adenosine A₁-receptor expression. Inhibition of the enzymes involved in adenosine degradation potentiated the acupuncture-elicited increase in adenosine as well as its antinociceptive effect. These observations indicate that adenosine mediates the effects of acupuncture and that interfering with adenosine metabolism may prolong the clinical benefit of acupuncture.⁴⁶

Autoreceptor-negative feedback is a local mechanism mediated by bioactive factors released by local cells. This mechanism is proposed for acupuncture pain management.⁴⁷ The neuropeptides substance P and CGRP are often co-contained and co-released with excitatory neurotransmitter Glu (glutamate) by afferent nerve terminals.⁴⁸⁻⁵¹ Acupuncture increases substance P and CGRP in peripheral nerve terminals and in blood in humans and rats.⁵²⁻⁵⁶ Nonneural substance P and CGRP are also expressed in rodent peripheral tissues.^{57,58} The elevated substance P and CGRP at the acupoints may activate the negative feedback mechanism by acting at corresponding autoreceptors, which, in turn, inhibit afferent-fiber excitability at the acupoints.⁴⁷

Collectively, there are more than 20 bioactive factors that may be induced by acupuncture needling. They have their corresponding receptors on afferent nerve terminals.⁴⁷ Through the receptors, the bioactive factors play a key role in producing downstream effects.

In an acupuncture treatment, the neuronal, biophysical and biochemical reactions take place after needling. Then, certain changes may be manifested in patients, such as erythema at acupoints and special sensations at the acupoints or along the meridians. Erythema is a visible phenomenon, and the special sensations are perceptible phenomena. The following two sections address how the needling-induced reactions play role in the healing process.

Erythema—Inflammation That May Initiate the Healing Process

Erythema around needles is common in acupuncture treatment, particularly in the back and the abdominal area. The Five Element tradition of acupuncture regards the er-

ythema/flare at the *Back Shu* points after needling as a sign of a positive clinical outcome. The flare may remain for a few minutes and become a white wheal. The majority of patients who receive Aggressive Energy (AE) treatment report feeling better. They report beneficial effects, such as having a clearer mind, feeling lighter, and feeling more relaxed and balanced. Anxiety tends to diminish and the patient feels a sense of "my old self returning."⁵⁹ It is well-documented that erythema is mediated by an axon reflex.^{42,60} While acupuncture stimulation causes a nociceptive sensation in the primary sensory cortex via afferent pathways, the bifurcation of the afferent fibers releases substance P. Substance P causes dilatation of arterioles that, in turn, cause the erythema or flare. Substance P also activates mast cells to release histamine. In turn, histamine increases capillary permeability, leading to a local accumulation of tissue fluids—the wheal response. Thus, as a form of inflammation, erythema may be seen as an early sign of a therapeutic outcome.⁵⁹

Increased blood flow is observed at the acupoints. One-sided needling at LI 4 may cause a blood flow increase at LI 4 on the opposite side of the body.^{61,62} Thus, in addition to a local mechanism (axon reflex), a systematic mechanism must be involved and deserves more study.

De Qi—Positive Signs for Treatment

De Qi means *Qi arrival* or *needling sensation*. When Qi is regulated by acupuncture stimulation, Qi arrives and manifests as some special sensations, such as soreness, numbness, heaviness, distension, warmth, and aching around the inserted needles and along the meridians. It is widely accepted in TCM that De Qi is one of the most important effective therapeutic factors. The specific sensations induced by acupuncture are more important than the specific stimulation sites for inducing cerebral hemodynamic and autonomic responses. The autonomic responses during acupuncture, which might be important for therapeutic efficacy, may be mediated through brain-activity changes, as exemplified by the cerebral hemodynamic responses during acupuncture.⁶³ The needling sensation may lead to significant changes in neuroimaging results,^{64,65} electroencephalogram results,⁶⁶ and clinical outcomes.^{67,68} De Qi is regarded as an imperative indication required to obtain effective results in TCM acupuncture.

It is well-demonstrated that needling sensations are mediated by specialized neural receptors in the skin and muscles and transmitted by different afferent fibers. The aching and soreness are highly related to cutaneous-receptor-rich acupoints with a predominance of nociceptors, and are transmitted by A δ and C fibers. The numbness, heaviness and distension are closely associated with muscle-spindle and Golgi tendon-rich acupoints and are transduced by A β and A δ fibers.⁶⁹⁻⁷¹ These results match clinical observations. Needling muscle-rich acupoints causes more

numbness, heaviness, and distension. Superficial needling within the skin leads to more aching and soreness.

In conclusion De Qi is a strong predictor for positive healing outcomes, although perception of the needling sensation may vary widely in individuals and with different needle techniques. Healing is a very complex process that may be mediated by neuronal and humoral pathways induced by acupuncture stimulation, in addition to other modalities, such as acupressure, massage, and moxibustion. Positive responses may also relate to an individual's health state and lifestyle. However, De Qi indicates a beginning of healing, and consistent treatment is needed to embody the functions of the neuro-immuno-endocrine network, which deserve to be well-discussed in research.

DISCUSSION

Acupuncture is becoming widely accepted in the West mainly because of its efficacy and safety. However many more questions regarding why and how it works are challenging acupuncture researchers and practitioners. Traditionally, needle insertion is the first step in acupuncture treatment. This review has offered significant evidence that, in this first step, three types of reactions occur at the acupoints and mediate healing processes. The study of neural and humoral pathways could have profound implications in clinical and basic research. With further study on these effects and mechanisms, solid explanations will be provided to patients and other medical professionals and more people will receive the benefits of acupuncture.

Similar to other modalities in conventional medicine, Chinese medicine and acupuncture can be used to treat a variety of physical diseases and symptoms. The disease-centered health care system uses acupuncture as a technique or a tool in its regimen. On the one hand, biomedical science study in acupuncture indeed provides some solid scientific explanations. On the other hand, unfortunately, the beauty of the ancient wisdom gets lost. That is the true mission of a medicine system—healing of the body and mind. Chinese medicine as a form of holistic medicine particularly emphasizes wholeness of body, mind, and spirit. Although this review focused on the acupoints at the physical levels—neural reactions, biophysical reactions and biochemical reactions—it is important for holistic medicine practitioners to know that many other factors may affect healing. Therefore it is necessary to discuss what constitutes healing under a bigger umbrella of *healing* instead of focusing on *physical disease* if we wish to pursue healing physically, mentally, and emotionally in patients.

Healing means *to restore to wholeness, wellness and soundness in body and mind*. The healing process is initiated not only by physical needling but also from good rapport, emotions, communication, lifestyle changes, and wellness coaching. A recent systematic review reported

that evidence of a relationship between indices of psychologic stress and biologic parameters was limited and inconsistent. There was some evidence of a consistent relationship between natural-killer cells and lymphocyte subpopulations.⁷² However, physical perception of emotion in the human body triggers conscious emotional experiences, indicating clear interactions among body, mind, and emotion. With special techniques, a bodily map of emotions may be drawn.⁷³ More holistic research is absolutely warranted for addressing the interactions of body, mind, and emotions, and empowering clinicians to treat patients as whole persons and promote health and wellness.

CONCLUSIONS

Needling is the first step of traditional acupuncture therapy. Needling reactions are the beginning of the healing process. There is existing research on the three major needling reactions. These reactions are neuronal, biophysical, and biochemical in nature. The messengers of the three reactions involved may include neurotransmitters, cytokines, hormones, and inflammatory factors. Healing may be potentiated through the messengers in neuronal and humoral pathways. The reactions manifest as erythema and De Qi—both of which are common phenomena used as positive signs in acupuncture treatment—which provide interesting evidence regarding the mechanisms of acupuncture actions. Acupuncture may also play a role in the healing process through the holistic pathway, which needs further study.

ACKNOWLEDGMENTS

Sincere thanks to Karin Holt, MAc, Christina Tian, MDM, James Snow, MA, and Xiaoming Tian, MD CMD, for the English editing, comments, and suggestions.

DISCLOSURE STATEMENT

No competing financial conflicts exist.

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Address correspondence to:

Heming Zhu, MD(China), PhD, CMD, MAc, LicAcu
 Department of Integrative Health Sciences
 Maryland University of Integrative Health
 7750 Montpelier Road
 Laurel, MD 20723

E-mail: hzhu@muih.edu