**Science of Acupuncture: Review of recent data.**

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Acupuncture is part of an ancient medical health care system that has its roots in antiquity. Through the years, the theories behind “Eastern” acupuncture have been solidified. Starting with blunt stone implements and progressing to the use of modern, fine filiform needles, acupuncture has demonstrated the ability to treat a variety of disease states in man and animals. With the introduction to the West and with the popularization after President Nixon’s historic trip to China, “Western” acupuncture has sot to scientifically evaluate acupuncture and establish a better understanding of its principles. Acupuncture is now accepted in the West as a valid therapy for a number of medical conditions and in particular the control of pain through established neural mechanisms. These neurophysiologic conditions are similar to those achieved using transcutaneous nerve stimulators (TENS) units. Modern acupuncture including “dry” needle techniques (use of small needles placed in specific points in the body), aquapuncture (injection of certain materials at specific points in the body) and electrical acupuncture (stimulating needles placed in the skin at specific points in the body). While there are other techniques, these are the most common.

Perhaps the earliest record of acupuncture in the West dates to the “Ice-Man” found in the Italian Alps, who had a tattoo over a known acupuncture point which had to have been placed there by another person. On magnetic resonance imaging (MRI), the Ice-Man had an intervertebral disc herniation which should have been painful and which might have responded to acupuncture treatment at the tattooed point.

Recently there have been 2 surges in acupuncture interest in the West. Prior to 1972, there were few cites related to acupuncture recorded on PubMed since it began in 1966 with less than 20 cites per year. After 1972, the number of cites increased to an average of around 300 per year. However, in 1991, Public Law 102-170 provided funds to the National Institutes of Health (NIH) to establish an office and advisory panel to recommend a research program that would investigate promising unconventional medical practices. Then, in 1993, Public Law 103-43, the NIH Revitalization Act of 1993, established the Office of Alternative Medicine (OAM) within the Office of the Director of NIH. The purpose of the Office was to facilitate the evaluation of alternative medical treatment modalities and to disseminate information to the public via an information clearinghouse. Finally, in 1998, Public Law 105-277, the Omnibus Consolidated and Emergency Supplemental Appropriations Act, elevated the status and expanded the mandate of the OAM by authorizing the establishment of the National Center for Complementary and Alternative Medicine (NCCAM). This provided an infusion of funds and resources for the study of complementary and alternative medicine. With the support of the NCCAM and growing interest in acupuncture throughout the World, the number of cites concerning acupuncture has increased to over 16,000 with an increase at around 1000 cites per year. Granted, not all of these are on animals and not all are scientific, but there are now in excess of 2500 which would represent systematic reviews, meta-analyses or randomized clinical controlled trials. Over 50 of these scientific papers are on animals, realizing that many studies in animals are well controlled studies; but are not clinically directed; rather they are directed at basic acupunctural mechanisms.

 Understanding acupuncture in today’s terms must take into account the history of acupuncture and the changes in technology that developed as acupuncture theory evolved. Today, we can look into the body in non-invasive ways using techniques like MRI, while in ancient times; science was limited to observations of the world at the time. For example, we now know the location of nerve pathways throughout the physical body which were not known to the ancients. On the other hand, early acupuncturists documented and characterized acupuncture points which lie on the nerves that we know today. As such, to know acupuncture is to know the nervous system. Certainly, we know that for acupuncture to work it requires an intact nervous system and acupuncture is not effective if the nervous system is damaged beyond repair.

 From a modern prospective, acupuncture represents a form of nerve stimulation. Local counter-irritation cause by needle insertion (or other form of acupuncture point stimulation) leads to microtrauma of the tissues. What follows is a complex, yet integrated series of reactions that leads to stimulation of the nervous system. Depending upon the acupuncture point selected and the method of stimulation, there will be sequential and simultaneous activation of local, segmental and super-segmental neural pathways. These changes ultimately lead to altered blood flow, altered humeral responses and affects within the immune system.

 The volume of work which describes these effects individually or in aggregate is enormous and can be confusing due to conflicting, yet cohesive data. What is represented here is an overview (with support of selected studies) of a prevailing, integrated view of acupuncture based upon recent advances in understanding functional neurophysiology and how it relates to acupuncture. Included are some findings about TENS since these modern devices represent another form of acupuncture. In animals, it is much easier to place a needle directly through the haired skin to achieve TENS than to apply external electrodes to accomplish the same effects.

 The events of acupuncture will be discussed anatomically and functionally somewhat in isolation, but the reader should remember that all of the events of acupuncture take place (under normal circumstances) together at the same time.

 While acupuncture in human beings and domestic livestock are referenced in China for over 2000 years, recently some have criticized that acupuncture in dogs and cats in perhaps only 25 years-old. This may be true, since dogs and cats were not considered important animals in ancient China and certainly were not an integral part of the household as they have become in the West until recently.

 Successful application acupuncture depends upon three important factors: the acupuncture point; the method of stimulation; and the response observed. Modern experiments have shown that acupuncture points occur where nerves penetrate tissue planes or where nerves, themselves, divide. As such, there are 4 major types of acupuncture points. Type I (motor) points are the most common and exist where nerves penetrate muscles. Type II points are located where nerves intersect on the dorsal and ventral midlines of the body. Type III points are located where superficial nerves branch. Finally, Type IV points are located where nerves penetrate tendons (Golgi tendon organ). , Most acupuncture points are located at areas of low electrical resistance and high electrical conductance of the skin. Deep in the point, there are accumulations of free nerve endings; small arterioles, veins and lymphatics; and tissue mast cells. Stimulation of these points results in degranulation of the mast cells, activation of the inflammatory cascade, alterations of blood and lymph flow, and conduction of nerve impulses to the central nervous system. This results in a local response which spreads over time throughout the entire neural axis evoking numerous biochemical changes within the nervous system and eventually the whole body. The initial sensation is termed, “de Qi”, meaning, “the arrival of Qi”. In this context, Qi can be interpreted as “energy”.

 Many important studies have been done to indicate how acupuncture works and what physiologic mechanisms are involved in its actions. One complaint has been that many studies have not been performed in a double-blinded manner, particularly when it comes to acupuncture where an acceptable sham procedure has not been developed. On the other hand, studies where the results are not based upon subjective data (like, “How did it feel?”), but upon objective results of measurable test values (like, changes in blood cell numbers) are not subject to the placebo effect. As such, many of the studies of acupuncture upon animals are valid scientifically.

 Recently, using functional MRI (fMRI), the basic tenets of acupuncture have been proven. Those are that acupuncture is based upon the point selected, the method of stimulation and the duration of stimulation. Stimulation of various acupuncture points result is specific special changes in the central nervous system (CNS). The change is mild when only acupuncture needles are used and become more pronounced if electrical acupuncture is added. While the change initially is more limited, over time, the entire neural axis becomes involved. In a separate study using fMRI, it was shown that acupuncture points that have analgesic properties associated with them tend to activate specific pain-associated brainstem regions. Non-analgesic acupuncture points do not activate these regions; rather they activate other regions of the brain. Although fMRI has only been used to examine about 15 different points, the experience has been enlightening. An additional study on the effects of acupuncture on equine colic demonstrated that while both needles and electrical acupuncture provide relief of clinical signs, but only electrical acupuncture results in system endorphin release. One new study indicated that the benefits of acupuncture, particularly in relationship to pain control, were independent of placebo in human beings since the response was present even when the regions of the brain which are associated with placebo effect were not activated. On the other hand, placebo activation does enhance both acupuncture and exogenous opioid treatment responses.

 Reviewing the recent literature, the National Institutes of Health (NIH) developed a consensus statement about acupuncture and its efficacy. NIH said that there was compelling evidence that acupuncture was usefully in the management of osteoarthritis and musculoskeletal pain. It can be helpful in treating many gastrointestinal problems, including inflammatory bowel disease, diarrhea, ulcerative colitis, peptic ulcers, dyspepsia, abdominal pain, nausea and vomiting. Acupuncture can help with management of pulmonary disease including colds and asthma. The immunomodulation of acupuncture can reduce inflammation, elevate WBC, and increase interleukin-2 production. Finally, acupuncture can help in treating reproductive disorders, decreasing uterine bleeding and regulating ovulation. While most of these studies reviewed the effectiveness of acupuncture in human patients, much of the data was based upon animal experimentation. Moreover, the conditions for which NIH thinks acupuncture can be effective are the same conditions which veterinarians treat with acupuncture.

Local Effects of Acupuncture

 Acupuncture (Greek: acus needle; pungare to pierce: to puncture the skin with a needle) may be defined as the insertion on needles into specific points on the body to cause a desired healing effect. In TCM, acupuncture includes using fine-needle (dry needles) acupuncture, hemoacupuncture (blood-letting), moxibustion (burning of the herb, Artemisia vulgaris, over acupuncture points), pneumoacupuncture (insertion of air under the skin), acupressure, and firing (counter-irritation with heat). In modern times, constant stimulation of the needles has been replaced by electrical acupuncture. Acupuncture (injection of dilute solutions into acupuncture points) and gold-bead implants (insertion of small metallic particles at certain acupuncture points) have also become popular. Low-power lasers and static magnets can also be used to stimulate certain superficial acupuncture points.

Most acupuncture points have been identified to be one of four basic types of points. All of these points are located along the nervous system. Although the ancients did not know the location or function of the peripheral nervous system, they mapped it by finding the location of the acupuncture points. The anatomic nature of acupuncture points represents neural vascular bundles: containing free nerve endings, an artery and vein, a lymphatic channel, and numerous mast cells. Most acupuncture points in animals also represent regions of low electrical resistance and high electrical conductance in the skin over the point. Most are also found in palpable depressions. When a needle is placed in an acupuncture point, there is local tissue trauma which activates Hageman’s tissue factor XII. This in turn results in the activation of local coagulation cascade and the complement cascade, leading to the production of plasminogen, protein kinins, and prostaglangins. Further, the trauma causes mast cell degranulation which releases histamine, heparin, proteases and bradykinin. As such, acupuncture can be thought of as a form of counter-irritation where the process sets up a local reaction that ultimately results in increase blood flow to the area, increased local immune responsiveness, and relaxation of the muscles and tissues in the area.

Studies at acupuncture points have provided evidence that they can have profound influences on the body and its function. GV (Governing Vessel) 26 which is located on the midline at a point equal to the bottom of the nostrils has numerous effects. If it is twisted, there is endorphin release leading to relaxation and calming of the animal. On the other hand, if it is manipulated by rapidly moving a needle in and out (bouncing off the bone), there is a release of epinephrine, which can result in revival of a patient. When experimental dogs had 50 percent of their blood volume rapidly removed, 75 percent of those who received stimulation of GV 26 survived, while 100 percent mortality was produced in the control animals. Pericardium (PC) 6, located on the midline above the wrist (2 cun [Chinese body inches]), is well known for its anti-nausea effects. In addition, a recent study showed that stimulation of PC6 resulted in decrease lipid peroxidation of the heart, increase coronary blood flow and stabilization of cardiac rhythm.

Segmental and Super-segmental Responses to Acupuncture

 Once the local acupuncture point is stimulated, nerve impulses will travel up the sensory nerves to enter the spinal cord. For the most part, the fibers are part of the pain pathways, although proprioceptive fibers also are part of the overall activation by acupuncture stimulation. The concept that the acupuncture points were connected by some sort of channel is part of TCM theory. These eventually became know as meridians when the acupuncture maps of the body were made by French physicians. There does seem to be a close correlation between meridians and nerve pathways, particularly those in the extremities. Many of the properties ascribed to meridians are present in the peripheral nerves. Research in China has demonstrated that meridians may exist as formal structures. If radioisotopes are injected into one acupuncture point along a meridian and the meridian is stimulated, the radioisotope migrates and accumulates at other acupuncture points along the meridian. Stimulation of one point along a meridian tends to alter the resistance (usually lowers it) at other points along the meridian. If a radio signal is introduced at one acupuncture point on the meridian, the signal can be heard at other acupuncture points along the meridian. In each of these examples, the changes were not seen at non-acupuncture points or at other acupuncture points that were not on the meridian being studied. These facts suggest that acupuncture points are interconnected in some manner.

Acupuncture stimulates nerve fibers in the muscle which send impulses to the spinal cord and activate three centers (spinal cord, midbrain, and hypothalamus/pituitary) to cause analgesia. The spinal site uses enkephalin and dynorphin to block incoming messages with stimulation at low frequency and other transmitters (perhaps gammaaminobutyric acid, or GABA) with stimulation at high frequency. The midbrain uses enkephalin to activate the raphe descending system, which inhibits spinal cord pain transmission by a synergistic effect of the monoamines, serotonin, and norepinephrine. The midbrain also has a circuit which bypasses the endorphinergic links at high frequency stimulation. Finally, at the third, or hypothalamus/pituitary center, the pituitary releases (3-endorphin into the blood and CSF to cause analgesia at a distance. Also, the hypothalamus sends long axons to the midbrain and activates the descending analgesia system via beta endorphin. This third center is not activated at high frequency stimulation but only at low frequency.

Overwhelming evidence supports an endorphin hypothesis for acupuncture analgesia. Acupuncture analgesia is reversible with naloxone but stress analgesia is only partly antagonized by large doses of naloxone. Plasma cyclic adenosine monophosphate (cAMP) levels decrease during acupuncture analgesia, but rise during stress analgesia. The periaqueductal gray is essential for acupuncture analgesia, but not for stress analgesia. Finally, dorsolateral spinal cord lesions eliminate acupuncture analgesia, but not stress analgesia.

Pain sensation is carried in the lateral spinothalamic tract. Unmyelinated fibers from pain, pressure and thermoreceptors in the periphery enter through the nerve roots and pass 1-2 segments caudally and 3-4 segments cranially in the substantia gelatinosa. These then penetrate to synapse in the gray matter of the dorsal horn. Some fibers innervate locally the motor neurons of the spinal segment (including those on the contralateral half of the spinal cord), while the remainder of these second order neurons pass, for the most part, across the mid-line in the ventral white commissure to build up on the contralateral spinal cord in the ventromedial aspect of the lateral funiculus. The spinothalamic tract then proceeds cranially where the sensation for the head is placed in the pathway by way of the spinal tract of CNV (cranial nerve V) until it terminates in the thalamus. Along the way, many branches are given off in the reticular formation which assists in altering the cortex through the reticular activating system.

When needles are placed close to the site of pain or in the tender (trigger, or Ah Shi) points, they are maximizing the segmental circuits operating within the spinal cord while also bringing in cells in the brainstem. When needles are placed in distal points far from the painful region, they activate the midbrain and hypothalamus-pituitary without the benefit of local segmental effects. Moreover, the brainstem produces analgesia throughout the body, while spinal segments primarily produce analgesia only locally. On the other hand, local segmental needling usually gives a more intensive analgesia than distal non-segmental needling because it uses all three centers. Generally, the two kinds of needling (local and distal) are used together on each patient to enhance one another.

 Pain is an extremely important biologic sensation. It alerts animals to hostile conditions in the environment. It make adaptive sense that this pathway travels up the contralateral spinal cord, since if the leg is immobile from paralysis, it is important to be able to feel it, so the opposite limb can be used to get away from environmental threats. On the other hand, if a limb is moving, it may leave a hostile environment before extensive damage might be done. Superficial pain can be tested by pinching the webbing between the toes; however, deep pain is best tested by clamping a hemostat on the joints of the digits so that the periosteum will be stimulated. Withdrawal of the limb is only a spinal reflex. Stimulation of the lateral spinothalamic tract and subsequent transfer of information to the cerebral cortex will result in a behavioral response. This may be crying, snapping or change in autonomic activities. Unless one or more of these behavioral responses is seen, deficiency of pain pathways must be considered.

 The biochemistry of acupuncture is the same as that from TENS methods and involves the complex interaction of the endogenous opiod compounds with substance P, acetylcholine, serotonin, norepinephrine and gamma amino butyric acid (GABA) to name a few. It is generally agreed that TENS and acupuncture both stimulate nerve endings which in turn alters segmental and super-segmental spinal pathways. This leads to changes within the brainstem and the cortical regions and eventually affects the entire neural axis. Melzac and Wall suggested that stimulation of mixed sensory nerves results in transmission of proprioceptive information which arrives at the spinal cord before the pain information can be received due to the difference in their respective nerve conduction velocities. The proprioceptive information, then, through pre-synaptic inhibition, blocks the transmission of the pain information at the local level. In acupuncture, it may be the A delta fibers and type II proprioceptive fibers that are responsible for local analgesia rather than the large 1a and 1b proprioceptive fibers that have been associated with the effects of TENS units. On the other hand, the results are the same, both techniques produce analgesia. At one level, acupuncture is just another form of TENS. It is much easier to apply needles through the skin of animals that have hair than trying to glue electrodes on their shaved skin. When combined with electrical stimulation, acupuncture is the ultimate TENS technique.

Another aspect is the frequency effect. Low frequency (2-4 Hz) needling works through the endorphin system and acts in all three centers, while high frequency (50-200 Hz) needling only activates the brainstem, bypassing the endorphin system. Numerous studies have shown that the types of analgesia produced by these two approaches are quite different: the low frequency method produces an analgesia of slower onset and, more importantly, of long duration, outlasting the 20minute stimulation session by 30 minutes to many hours. Also, its effects are cumulative, improving increasingly after several treatments. In contrast, the high frequency analgesia is rapid in onset but of very short duration and with no cumulative effects. Because low frequency analgesia produces a cumulative effect, repeated treatment produces more and more benefit for the patient. This could be due to long-lasting effects of endorphins in the low frequency system. High frequency stimulation’s effect is of short duration and wears off after some months of continuous use, because tolerance develops.

 The segmental analgesia from acupuncture utilized several neurochemical systems depending upon the stimulus applied. With electrical acupuncture at low frequency (4-20 Hz) the predominant reaction is due to activation of enkaphalin neurons. This frequency also results in the release of endorphins from the brainstem in to the circulation as a super-segmental reaction. Both of these compounds and their effects can be blocked by naloxone (a morphine antagonist). At frequencies around 100 Hz, the primary mediator of segmental analgesia is due to dynorphins, which is not blocked by naloxone. At even higher frequencies (200Hz), the segmental effects are influenced greatly by descending serotonergic neurons which can be block by serotonin antagonists. This differential control of segmental analgesia depending upon the stimulus frequency partially explains the different results reported by some investigators in dealing with segmental pain control. There is litle doubt that the monoamines (serotonin and norepinephrine) play a role in acupuncture analgewsia. Serotonin projections from the raphe to higher centers may help mediate acupuncture analgesia while descending projections to the spinal cord appear to work synergically with descending norepinephrine effects to block pain transmission in the spinal cord.

 Because of the neurochemistry involved in acupuncture, a number of pharmaceutical compounds can alter the effects of acupuncture. Corticosteroid medications tend to lower endorphin levels and reduce acupuncture efficiency. Substance P, cyclic-GMP and histamine potentiate acupuncture whereas GABA and cyclic-AMP inhibit it. As such, anti-histamines, xanthene compounds like aminophyline, and GABA angonists like diazepam can all reduce the efficacy of acupuncture. Cholinergics and alpha-blockers enhance the effects of acupuncture, whereas anti-cholinergcis and beta-blockers reduce acupuncture efficacy. Clearly, it is important to know the patient’s medication status to determine how effective acupuncture can be potentially.

 Since CNS neurochemistry is altered, it is not surprising that CNS function will change. Endorphins are highly concentrated in the pituitary gland where alterations will lead to changes in the release of many pituitary hormones. Through the release of these hormones into the systemic circulation, regulation of internal homeostasis can be achieved. Body metabolism and immunologic responsiveness will be altered.

Some patients will never respond to acupuncture for various reasons; non-responders may be genetically deficient in opiate receptors. Mice genetically lacking endorphin receptors respond poorly to acupuncture. Other failures may be due to deficiency in endorphin molecules; rats lacking endorphin compounds respond poorly to acupuncture. Some non-responders can be converted to responders by treatment with phenylalanine, which potentiates endorphins.

 Segmentally, there is convergence of somatic and visceral afferent information. An example of this convergence is the presence of “referred pain” areas where visceral discomfort is manifest by sensitivity of somatic dermatomes. By reversing the process, visceral pain may be suppressed by stimulating appropriate somatic receptors which correspond to acupuncture points. Moreover, organ blood flow and activity of the autonomic nervous system regulating visceral function in the segment can be altered beyond mere pain relief.

In conclusion, there is no doubt that acupuncture can lead to many changes within the body. The greatest effect appears to be when the local segments are directly stimulated. The acupuncture system requires an intact and functioning nervous system in order to generate its many effects. The effects of acupuncture have temporal, spatial and methodological tenets which must be met to be effective; however, if these are met, acupuncture can have profound effects upon the patient. Scientific evidence is growing which clarifies how acupuncture works and how ancient wisdom can be explained with modern technology.