

Science-based Mechanisms to Explain the Action of Acupuncture

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Abstract

Although acupuncture has been practiced for thousands years in China, it is still not recognized by and incorporated in the conventional (Western) medicine in many countries. One of the reasons is lack of clear science-based mechanistic explanation for the action of acupuncture. There are some hypotheses on how acupuncture works: local mechanotransduction, neurohumoral theory and morphogenetic singularity theory, etc. Needling in the skin elicits a local mechanical deformation and body's reaction results in a self-healing process. According to the neurohumoral theory, acupuncture stimulates the release of various neurochemical substances, which have an analgesic and overall relaxing effect. The gate-control theory, believes that acupuncture blocks pain signals from reaching the brain by generating a competing stimulus in the spinal cord. The morphogenetic singularity theory states that acupuncture points and meridians originate from the organizing centers in the developing embryo. The rationale and plausibility of each theory is briefly discussed.



Acupuncture is thousands years old and presumably not only developed in China, but also in Egypt and Europe in parallel, but there it disappeared. In China, the practitioners of Traditional Chinese Medicine (TCM) refined acupuncture in hundreds of years based on the yin-yang philosophy. Since President Nixon's visit to China in 1971, the Western world showed interest in acupuncture. Up until now, there is still a lot of skepticism, even though the World Health Organization (WHO) recognizes that acupuncture does work for many diseases. How about the scientific evidence for acupuncture? Numerous clinical studies are published showing that acupuncture is effective for various diseases. Less is known about the exact biological mechanisms how acupuncture works. From a Western Medicine point of view, there are several theories to explain how acupuncture works. This paper will explore these theories and discuss which theory/theories is/are most plausible in authors' opinion and why acupuncture is still regarded by many as a supplementary therapy, next to the fundamental science-based Western medicine.

1. Objective measurable effects of acupuncture

Acupuncture is based on pricking (puncture) a needle (acus) in and through the skin on specific places (acupuncture points). This leads to different biological reactions in the body, which can be objectively measured. These reactions can be observed on the punctured point, e.g. redness, lowering of the skin resistance, but also distal from the point, for example in nerves and in the brain (Kuo, 2004; Hsieh, 2001). Acupuncture affects all kinds of organ functions, e.g. heart rate, blood pressure, bowel movements, action of the autonomous nervous system, release of hormones in blood and chemical substances in the brain (Nishijo, 1997; Ouyang 2004; Stux, 2001). Thus, puncturing a needle in the skin can have measurable effects on the whole body. Changes locally around the acupoints, in the brain, in the spinal cord and systemically are measurable after acupuncture.

In modern western medicine, animal models are often used to test whether a therapy like acupuncture works, before clinical application. They can give us a clue what the underlying mechanisms are. However, even when the therapy works in an animal model, this does not mean that it will be effective for patients too. It is important to investigate whether these effects of acupuncture also can help the patients. Otherwise, there is only proof that acupuncture works, but does not help. Therefore, studies need to be done in humans. These kind of clinical trials which meet the requirements to be accepted by the modern western medicine are quite difficult and laborious. Furthermore, acupuncture is not simply a pill, but a special form of individualized treatment in which many factors play a role. Adapted forms of clinical trials have shown that acupuncture has a beneficial effect in different diseases: chronic neckpain, chronic (lower) backpain, tennis elbow, osteoarthritis of the knee, myocardial infarction, migraine, tooth pain, nausea and vomiting after an operation, difficult labor and malposition of the foetus (Birch, 2004). In addition, acupuncture helps often to relieve symptoms of chronic diseases. The patient often sleeps better, feels more relaxed, less tired and has more energy, which results in a better quality of life. Even if acupuncture is viewed as abracadabra or placebo, the important thing is that it helps! Still, the pure scientist will wonder how acupuncture works.

2. Local mechanotransduction theory

In 1961, the French physician Niboyet wrote in his thesis that acupuncture points have a much lower electrical resistance than the surrounding skin (Niboyet, 1961). Normally, dry skin has a resistance in the order of 200.000 to two million ohms. At acupuncture points this resistance is down to 50.000 ohms (Becker, 1976). In 1977 it was discovered that the distribution of these points with a lower resistance was exactly the same as the localization of the Chinese acupuncture points, whereas the ancient Chinese did not have the techniques to check resistances (Hyvarinen, 1977). Melzack and Katz found no difference in

conductance between acupuncture points and nearby control points in patients with chronic pain (Melzack, 1984). This phenomenon can be explained by the dynamic nature of the acupoints. In a healthy person, resistance of the acupoints is the same as that of non-acupoints. In a chronically sick person, the acupoints transit from the latent phase (healthy tissue) to the passive phase (tender or sensitized tissue) in a predictable sequence and location. The sensitive area of acupoints is getting larger in chronic conditions, which contributes to high electrical conductance and low resistance (Ma, 2005).

Acupuncture inoculates minute intrusive “traumas” or lesions into the tissues, which stimulates many survival mechanisms of the body. A research team demonstrated that manipulation promotes tissue healing by producing biomechanical, vasomotor, and neuromodulatory effects on interstitial connective tissue (Langevin, 2002; Langevin, 2001).

When a needle is inserted into the body tissue, there is mechanistic deformation. In response to this, cells generate cascades of cellular and molecular events, including cytoskeletal reorganization, cell contraction and migration, autocrine release of growth factors, and activation of intracellular signaling pathways and of nuclear binding proteins that promote the transcription of specific genes, leading to changes in the extracellular milieu surrounding needed tissues and finally promotes local healing. These effects may expand to distant connective tissue to spread the healing process with long(er)-term effects (Langevin, 2001; 2006).

Thus, acupuncture needling and its induced lesions activate a self-healing mechanism, including restoring homeostasis, facilitating repair mechanisms such as anti-inflammatory reaction and tissue regeneration, and pain modulation. Mechanical signals produced by simple needle manipulations generate cascades of downstream physiologic healing effects. After the needles are removed, the needle-induced lesions continue to stimulate the body until the lesions heal (Langevin, 2001; Ma, 2007).

3. Neurohumoral theory

Critics of acupuncture believe that if acupuncture works, it is merely a placebo effect. Several pain studies in human and animals, however, show that this is not true (Vincent, 1986; Pomerantz, 1976; Chan, 1975; Chen, 1980). One study for example, investigated the effect of acupuncture on acute pain. Reduction of pain was accomplished by needling the true acupuncture points, whereas needling in a non-acupuncture point a much weaker effect was observed (Brockhaus, 1990). Another research group found that the analgesic effect of acupuncture could be blocked by naloxon, an opiate antagonist, which implies that the action of acupuncture could be based partly on stimulating the endogenous painkilling substances (Goldstein, 1975; Mayer, 1977). If it is not just a placebo effect, what is really happening in the body then?

In the 1980's the neurohumoral theory was introduced. This is the most well known theory to describe mechanistic actions of acupuncture. According to this theory, the analgesic effect of acupuncture is explained by production of endogenous, painkilling opiate substances, *i.e.* endorphins, enkephalins and dynorphins, and other neurotransmitters, serotonin and

noradrenalin, which are released in the synapses, the connecting points of nerves (Cabyoglu, 2006).

4. Gate-control theory

A pain signal is transmitted through the spinal cord to the sensory cortex of the brain, where the pain is perceived (Fig. 1). Pain signals of the skin are transferred to the spinal cord via thin nerves, so-called C-fibers. Stimulation by acupuncture is conducted to the brains by another way than pain. An acupuncture stimulus in skin and muscle is converted to an impulse, which is transmitted along thicker nerves, myelinated A δ fibers. Therefore, needling an acupuncture point induces a different sensation, *e.g.* warm, heavy, tingling feeling, than a pain stimulus. In addition, these sensations are often accompanied by physical and mental relaxation. The impulse following acupuncture through A δ fibers causes release of the body's own painkillers. This mechanism is called the ‘Gate-control theory’ of Melzack and Wall (1965). In this theory, a ‘gate keeper’ in the substansia gelatinosa of the spinal cord controls what impulses are let through. Pain signals are transmitted to warn what is happening, but this does not occur continuously. The gate keeper can be warned by acupuncture and stop the pain signal by stimulating production of enkephalines and dynorphines in the spinal cord. The gate keeper is activated and alerted by the extra stimulation of acupuncture needling.

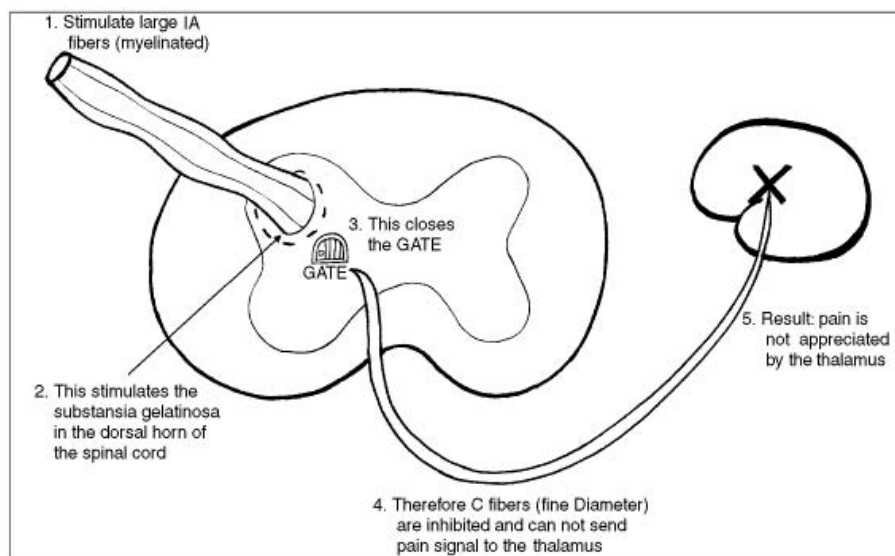


Figure 1. Gate-control theory. This theory states that in the nervous system, there exist nerve fibers that both transmit (C-fibers) and inhibit (A δ fibers) pain. These nerve fibers come together in the spinal cord. Acupuncture stimulates the pain inhibitory nerve fibers, which lowers the pain input and therefore, relieves the pain.

Source:

<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=physmedrchab&part=A10811>

The acupuncture stimulus induces a train of impulses along the A δ fibers as long as the needle is in place. Secretion of β -endorphin in the blood by the pituitary dampens pain. This hormone spreads through the whole body, resulting in a feeling of comfort and decreased pain sensation. Lower expression of β -endorphin receptors in mice and administration of antibodies to β -endorphin to rabbits, make them less sensitive for the analgesic effects of acupuncture (Peets, 1978; Xie, 1983).

5. Postsynaptic inhibition

Next to production of opiates in the spinal cord, acupuncture also affects processes in the brain (Fig. 2). An acupuncture stimulus is conducted to the rafe nuclei in the periaqueductal grey matter, which produce serotonin, accommodated by the presence of enkephalin. Disinhibition of the rafe nuclei induces impulses down to the place in the spinal cord, where the pain signal entered in the first place, and serotonin and noradrenalin are released to dampen the pain stimulus even more. This is called postsynaptic inhibition (Stux, 2000). This principal of negative feedback also occurs in the case of intense pain, *e.g.* loss of extremity during war. The pain impulse stimulates this tract and blocks the pain sensation. In this way, the body protects itself in acute situations of extreme stress and pain, to survive.

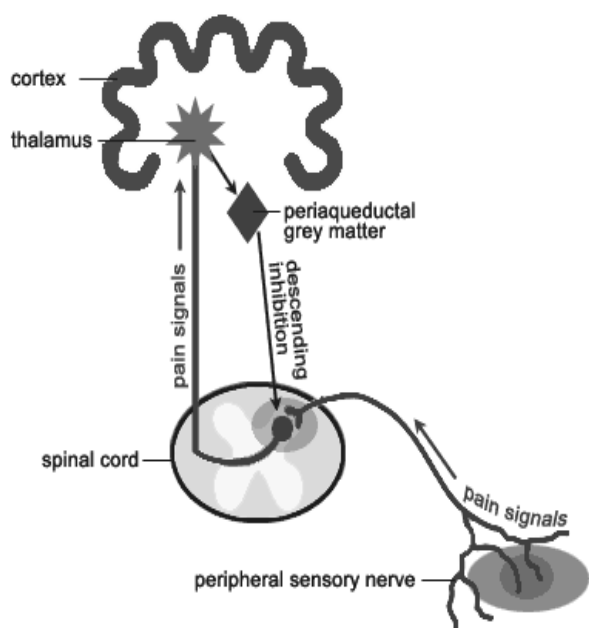


Figure 2. Pain transmission pathways between spinal cord and brain. In the spinal cord, information on pain is received by cells in the dorsal horn and is passed on to higher centres in the brain along tracts in the spinal cord. It is in the thalamus and cerebral cortex where the appreciation or conscious awareness of pain is to be found. On the other hand, descending pathways from the brain can reduce and even abolish some forms of pain.

Source:

http://www.ccac.ca/en/CCAC_Programs/ETCC/Module10/07.html

Needling ashi points have beneficial effects on the levels of spinal cord and in the brain (mesencephalon, pituitary, hypothalamus), whereas distal acupuncture points affect mainly the brain and induce a more general analgesic effect (Teitelbaum, 2000; Medeiros 2003). Thus, ashi and distal points act synergistically in relieving pain.

6. Autonomous nervous system

Besides affecting production and release of neural substances, acupuncture also calms the overactive 'fight-and-flight' sympathetic nervous system and beneficially influences the 'rest-and-digest' parasympathetic nervous system, in stressed animals. Several studies have shown that acupuncture inhibits the sympathetic nervous system and activates the parasympathetic system (Nishijo, 1997; Sugiyama, 1995; Sakai, 2007). The sympathetic nervous system is normally activated during danger and stress, whereas the parasympathetic system

calms the body, *e.g.* lowering the heart frequency, blood pressure, muscle tension, and brain activity. It helps during the phase of recovery. Thus, acupuncture relaxes the body.

Nitric oxide (NO), the smallest neurotransmitter molecule of all, is produced by NO synthetases (NOS). Stimulation of ST-36, Zusanli, with electroacupuncture in a rat results in the release of NOS in the brain (Ma, 2005). A higher concentration of NO in the brain nucleus tractus solitarius, lowers the sympathetic activity in the body and consequently the blood pressure. So, a well-known effect (of many) of ST-36 is lowering blood pressure, which can be explained by production of NO by NOS in the brain. Electroacupuncture of ST36 also induces an analgesic effect in pain experiments in rats, in which the tail is exposed to a heat and the amount of time taken for the animal to flick its tail away from the heat is recorded (Medeiros, 2003).

Also systemically, NO was found to play a role in the mechanism behind the action of acupuncture (Chen, 2006). Acupuncture points in the skin of rats had a higher concentration of noradrenalin, a hormone released during stress, than normal skin and NO stimulated the release of noradrenalin in the acupuncture points. When an NOS inhibitor was administered, NO is not produced and the noradrenalin concentration was reduced.

7. Morphogenetic singularity theory

Acupuncture is not only used to relieve pain. It can also regulate, and if needed corrects (bidirectionally), other processes in the body, which are transmitted from acupuncture points through meridians to the internal organs, according to the traditional Chinese medicine theory. Conventional nerve stimulation usually results in a unidirectional effect. For example, parasympathetic vagal stimulation slows down the heart rate and opioids inhibit gut motility. However, acupuncture at PC-6 accelerates bradycardia and decelerates tachycardia. Acupuncture at ST-36 suppresses hyperfunction (as in diarrhea), and stimulates hypofunction (as in constipation) of the gut motility (Li, 1992).

Moreover, the neurohumoral theory does not give an explanation for the localization of acupuncture points and the existence of meridians, as they do not follow the course of the anatomical nervous system. In addition, the ear does not have important nerves connected with the spinal cord; it nevertheless has the highest density in acupuncture points. One study shows that patients suffering from myocardial infarction, which received acupressure at Shenmen point in the ear compared to a sham ear point in the ambulance, felt less anxiety and more positive expectations regarding the recovery (Kober, 2003). Similar effects are observed in heart failure patients, parents before operation of their child and elderly undergoing shock wave crushing of kidney stones (Middlekauff, 2002; Wang, 2004; Mora, 2007). According to the World Health Organization, 43 auricular points have proven of therapeutic value, which make up 10% of the acupuncture points on the whole body (WHO, 1991).

The 'morphogenetic singularity theory' explains these effects of acupuncture (Shang, 1989; Shang, 2001). The basic idea of this theory is that acupuncture points and meridians are remnants of the growth control system, the first physical communication system in an embryo. This growth control system directs the embryonic development, next to the genetic imprinting. As every cell has its own place and function in the growing fetus, communication between cells is essential. Experiments with

cells growing between a positive and negative electrode, have shown that cells mainly grow in the direction of the negative electrode (McCaig, 1987). Even during fertilization, electric waves determine the place where the first cell is divided into two cells. Cells can communicate with each other via gap-junctions (Levin, 2007). During the multiplication of cells, communication between cells is impeded due to the increasing distance between cells. When a critical distance is reached, two groups of cells are formed, which coordinate the cell growth around them. These groups are called organizing centers and determine the differentiation of other cells. They are characterized by more gap-junctions, a lower resistance, more superficial location on the embryo and a more negative charge compared to the other cells. Collagen fibers can transport impulses and form the communicating network between organizing centers.

Acupuncture points and organizing centers are similar in several ways, *i.e.* the presence of many gap junctions, a low resistance and a high conducting capacity. According to this theory, acupuncture points originated from organizing centers and are found on similar places on the body. Their network (connecting collagen fibers) is reflected in the meridian system. Many think that meridians are imaginary, abstract lines, but they may be really present (Ahn, 2005). They can become visible by injecting radioactive tracers into acupuncture points (Vernejoul, 1984; Meng, 1989; Kovacs, 1992). In contrast, when injecting the tracers in random non-acupuncture points, only a small area of vague staining around the injected location is observed, and the specific, centrifugal spread along the meridian does not appear. Subsequently, infrared measurements were used to visualize the meridian system (Liu, 1988). Even without experimental interventions, linear rashes can be visible along the course of meridians. An English dermatologist for example, described that he observed red lines on the skin of a patient, with the track of the pericardium and kidney meridian (James, 1993).

Based on the phase gradient model in developmental biology, many organizing centers are at the extreme points of curvature on the body surface such as the locally most convex points or concave points (Goodwin, 1969; Shang, 1989). Similarly, almost all the extreme points of the body surface curvature are acupuncture points; for example, the convex points include EX-UE 11 Shixuan, EX-LE Qiduan, ST-17 Ruzhong, ST-42 Chongyang, ST-45 Lidui, SP-1 Yinbai, SP-10 Xuehai, GV-25 Suliao, and EX-HN3 Yintang. The concave points include CV-17 Danzhong, KI-1 Yongquan, LI-5 Yangxi, LU-5 Chize, LU-7 Lieque, LU-8 Jingqu, LU-10 Yuji, SI-19 Tinggong, TE-21 Ermen, GB-20 Fengchi, GB-30 Huantiao, BL-40 Weizhong, HT-1 Jiquan, SI-18 Quanliao, BL-1 Jingming, CV-8 Shenque, and ST-35 Dubi.

8. Visible Evidence

Modern techniques like functional Magnetic Resonance Imaging (fMRI)-scans are developing rapidly. These methods give insight in the effects of acupuncture on the brain. In healthy subjects BL-67, Zhiyin, was stimulated with laser acupuncture (Siedentopf, 2002). The control group received the same treatment, except that the laser light was off; the subject could not see the laser light. One of the functions of BL-67 is to 'make the eyes clear', which is explained by the course of the bladder meridian. fMRI showed that stimulation of BL-67 resulted in a specific activity in the visual area of the brain. In another study, fMRI was applied to examine the effect of

electrostimulation of GB-34, Yanglingchuan, on the brain (Wu, 2002). As controls, no stimulation, electrostimulation on a sham point and minimal stimulation of GB34 were used. Electroacupuncture of GB-34 resulted in a significant higher activity in the hypothalamus, the primary sensory and motor, visual and auditory brain areas, which correspond with the distribution of the gall bladder channel. A new concept was introduced in 1998 in which the brain is seen as the 'missing link' to explain the effects of acupuncture on organs (Fig. 3).

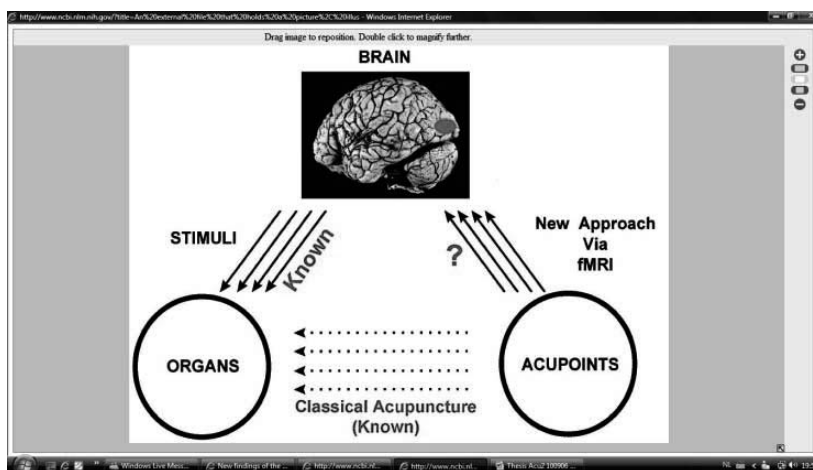


Figure 3. Relationship between acupoints, brain and organs. A large amount of experimental data obtained by fMRI demonstrates the effects needling acupuncture points on the brain. In addition, areas in the brain correspond with certain organic functions. Therefore, the concept was arisen that acupuncture stimulation activates functional areas of the brain cortex and thereby influences organic function. Source: Cho, 1998.

These modern imaging techniques indicate that both the morphogenetic singularity theory (course of a meridian) and the neurohumoral theory (action on the brain) are involved in the biological effects of acupuncture.

9. Comparison of theories

The mechanotransduction-based theory to explain acupuncture effects is very plausible and most easy to understand in my opinion. Needling and needle-induced lesions are foreign invaders to our body. Inoculation of minute "traumas" or lesions into the body increase the number and the activity of immune cells and control the inflammatory process to restore the mechanisms of self-healing, including autonomic homeostasis, tissue healing, and pain relief.

Needling also reduces bodily stress by stimulating the parasympathetic nervous system, thereby relaxing the cardiovascular and muscular systems, and restoring the physiologic and autonomic balance which includes normalizing visceral functions that are impaired during stressful assault. The neurohumoral theory mainly explains analgesic effects of acupuncture via an enhanced secretion of neurochemical substances, *e.g.* endorphins, but does not give a reason for the localization of many acupuncture points, the existence of meridians and their mediating function in regulating internal organs.

The morphogenetic singular theory presumes that acupuncture points and meridians are remnants of the embryonic growth control system and therefore also explains the existence and purpose of meridians. It gives a reason for the bidirectional action of acupuncture points in adjusting bodily processes and

restoring normal function by activating the network of organizing centers in the organism. The activation of the self-organizing activity may induce normal physiological processes. It is therefore less likely to cause the adverse effects resulting from directly antagonizing a pathological process, with the risk of an 'overshoot effect' of the therapy.

There is more scientific proof for the local mechanistic reaction after acupuncture and the neurohumoral theory. An important reason is that the morphogenetic theory is much more difficult to study, because research in developing embryos is burdensome. In my opinion, the major advantage of the morphogenetic theory compared with the neurohumoral theory is that it also explains the regulating effects of acupuncture and the course and function of meridians in the connection between acupuncture points and organs, even without the presence of an anatomic (nerve) structure. Taken together, as with many explanations of phenomena, the combination of theories is most probably closest to the truth, as can be conceived from modern imaging techniques, e.g. fMRI.

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Biography

Man-Chi Wong, born in The Hague, The Netherlands, entered the University of Leiden in 1999 to study biomedical sciences and graduated in 2004. Two years later, she obtained her master's degree in medicine and became a resident Internal Medicine at the St. Antoniusshove hospital in Leidschendam. Her current job as PhD student at the Departments of Endocrinology and Pulmonology of the Leiden University Medical Center is to study the relationship between atherosclerosis and pulmonary emphysema in experimental mouse models. She started the acupuncture course at Shenzhen Open TCM University in 2007.

