MedCrave Step into the World of Research
International Journal of Complementary & Alternative Medicine

Mini Review

Biomedical effects of acupuncture

Abstract

Biomedical effects of acupuncture

Introduction: The use of acupuncture as a method of pain relief in western medicine is based on a wide range of clinical trials, and there is no doubt that it has significant effect in the treatment of acute and chronic pain.

Method: We were going a summary on past decades performed acupuncture studies on effects. Studies found that in chronic pain the concentration of endorphins in the spinal fluid is markedly reduced. Cholecystokinin octapeptide has been shown to function in the CNS as a neuropeptide with potent antiopioid activity. Electro acupuncture stimulation caused a substantial increase of immunoreactivity in CSF perforates of the rat spinal cord. The diffuse noxious inhibitory controls may be involved in the mechanisms. DNIC are part of the biological pain control system. Our summary examines the analgesic effect of the TRR 469 adenosine receptor agonist. Upon acupuncture points stimulation Zu San Li (St 36) significantly higher concentrations of adenosine were recorded.

Results: Acupuncture induces a variety of biological responses, which occur both locally as well as in a remote location. Studies on the stress response show that acupuncture techniques can reduce the neither concentration of nor adrenaline at cerebral perfusion and in the blood circulation, reduce the production of epinephrine in animals exposed to restraint stress, induce long-term behavioural and cardiovascular depression in behaviour and anxiolytic effects common in animals in captivity. Forced restraint has shown to be a simple physiological stressor that causes significant increase of heart activity, blood pressure and levels of nor epinephrine and epinephrine, activation of the simpatico-adrenal system and the hypothalamic-pituitary axis.

Discussion: CCK 8 is in fact increasingly released at frequencies from 100 Hz to 15 Hz. Opioid peptides are activated and CCK 8 is not produced at low frequencies 1-2 Hz. The known effect of the endogenous opioids which are produced in electro acupuncture stimulation and hindered by naloxone does not apply unequivocally, since the low frequency EA stimulation have been found to activate opioid peptides derived from propio-enkephalins, while the high frequency of 100 Hz activates the preprodynorphin group, in laboratory animals as well as in humans. The needle stimulation or low frequency electro acupuncture was effective in certain nociceptive some states, whereas the high frequency stimulation proves more effective in comparison with manual acupuncture. The lack of acupuncture effectiveness may be attributed to the high levels of cholecystokinin opioid antagonist in the brain.[1]

Conclusion: Acupuncture and associated therapies have come to the fore. More further basic and applied researches need for deeper understand its effect. They are always related to the patient`s lifestyle for elevate QoL.

Keywords: acupuncture, endogenous opioids, pain, tens, cholecystokinin, a(1) adenosine receptors,stress

Volume 2 Issue 1 - 2015

Alena Ondrejkovicova, Gabriel Petrovics , Hegyi Gabriella
Pecs University, Hungary

Correspondence: Hegyi Gabriella, University of Pécs, Faculty of Health Sciences, Pécs Campus, H-7623 Pécs, Vörösmarty str 4, Hungary, Tel 36-72-513-671, Email drhegyi@hu.inter.net

Received: September 01, 2015 | **Published:** November 27, 2015

Introduction

The use of acupuncture as a method of pain relief in Western medicine is based on a wide range of clinical trials, and there is no doubt that it has significant effect in the treatment of acute and chronic pain, as to the pain classification. Acupuncture has been recognized as a pain relief method in most countries and is commonly used in general practice and at pain relief clinics in addition to conventional therapy. The introduction of Melzack`s gate-control theory and endogenous opioids facilitated the recognition of acupuncture. It is necessary to point out that any effect of acupuncture must be based on a physiological and/or psychological mechanism. Stimulation of the cutaneous or subcutaneous tissue, where the acupuncture points are situated, by needles and other tools (soft laser, moxibustion, etc.) is effective in case of pain, allergies, functional conditions and others.

Pain and acupuncture

Research in acupuncture suggests that somatic sensory stimulation engaging various body mechanisms can have multiple effects that explain the results of this treatment in certain pain conditions. Particularly good results of treatment by acupuncture can be achieved in functional disorders. A common feature in many of the methods used for the pain relief is the activation of somatic afferent nerves; for example in the transcutaneous electrical nerve stimulation (TENS), vibration stimulation and massage the receptors or nerve fibers are excited in the stimulated tissue. TENS and acupuncture by manual or electrical stimulation are effective at triggering nerve impulses. According to TCM (Traditional Chinese medicine) , the needle stimulation in the active acupuncture point needs to produce a specific feeling (called "Deqi"), which is experienced as numbness, heaviness, radiating paraesthesia, sensation of muscle pain. It is a

sign of the thin myelinated A-delta nerve fibers activation. The low-frequency electrical stimulation (electro acupuncture) of sufficient intensity causes muscle contraction, while activating the high-threshold and low-threshold mechanoreceptors in muscles and other tissues. Particular significance is attributed to the group of receptors in skeletal muscle with a high threshold for mechanical stimulation, which are innervated with A-delta fibres and C-fibres. These are physiologically activated by strong muscle contraction, which can be functionally excited by dynamic movements. It is possible to argue that acupuncture and physical exercise with repetitive muscle contractions similarly activate these receptors and afferent nerve fibres. Functional modulation, as well as therapeutic effects attributed to acupuncture, occur also during muscular exercise.[2]

One of the main effects of acupuncture is the release of not only the endogenous opioids, beta-endorphins, enkephalins, dynorphins but also non-opioid compounds, such as serotonin, norepinephrine, GABA, and also the oxytocin which seems to be essential for the induction of functional changes in various organs.[3]

Moreover, the studies in human volunteers and animals have shown that the diffuse noxious inhibitory controls (DNIC) may be involved in the mechanisms of acupuncture. DNIC are part of the biological pain control system [4]. Several types of endogenous opioids have been identified and proved to have an affinity for a variety of opioid receptors. Particular attention was paid to the beta-endorphins that have a high affinity for μ-receptors and represent a vital factor in pain control and in the regulation of blood pressure and body temperature (Figure 1).

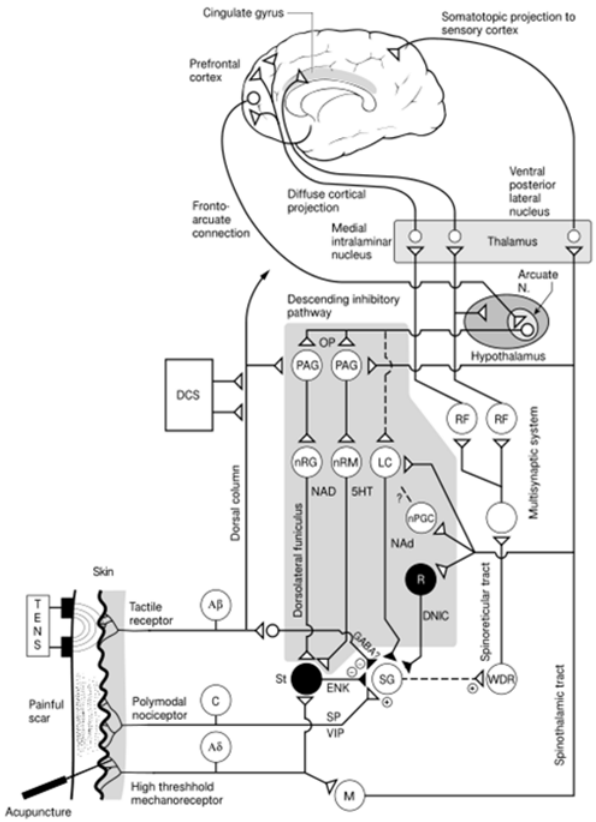

Figure 1 Local and systemic effects of acupuncture.[16]

Abbreviations: M: Marginal cells; SG: Spinal Cord; nPGC: Nucleus Para-Gigantocellularis Lateralis; NRM: Nucleus Raphe Magnus; LC: Locus Ceruleus; NAD: Noradrenergic Axons; OP: Opioid Peptids; DCS: Dorsal Colums Stimulation; GABA: Gamma-Aminobutiryc Acid

Endogenous opioid beta-endorphin is released by two different systems - neural network and blood. The first system includes the hypothalamus and the neural network leading to the midbrain and brainstem and this way it can affect the pain sensitivity as well as autonomous functions. There is evidence that the hypothalamus nuclei play a vital role in the mediating effect of acupuncture. Damage in the arcuate nucleus eliminates the analgesic effect of low-frequency but not of high-frequency electro acupuncture. Low-frequency electrical stimulation induced circulatory changes in multiple tissues. These effects are eliminated after hypothalamic damage. Increase in the beta-endorphin levels was observed in the animal brain tissue both after the acupuncture treatment and muscular exercise. Although the details are still unknown, experimental and clinical evidence indicates that acupuncture can also affect the sympathetic nervous system on the hypothalamus-hypophysis level (Figure 2).

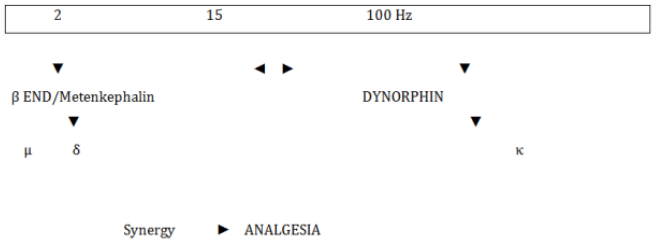

Figure 2 Effects of electro acupuncture stimulation on secretion of opiate neurotransmitters.[4]

The second system includes the release of the beta-endorphin levels into blood. Proopiomelanocortin in the hypophysis produces the equimolar amount of beta-endorphin and ACTH after muscular exercise and also after acupuncture treatment and its modifications in the active acupuncture point. These agents affect various target organs. The two beta-endorphin systems may work independently, but both can be stimulated by afferent nervous activity. It was found that stress could cause increased concentrations of beta-endorphin and ACTH levels in blood, regardless of their increase in the brain. Since the blood-brain barrier is relatively impermeable to the circulating peptides, the concentration of beta-endorphin in plasma may not be relevant to the opioid receptors in the brain. The effects of endorphins are important because endorphins are secreted during both the acupuncture and muscular exercise and may induce changes similar to the effects of morphine agonist and naloxone, which is a non-specific antagonist of beta-endorphins.

The effects of both energetic muscular exercise and the afferent neural stimulation fall into two phases. First, there is the excitation of the sympathetic nervous system with increased heartbeat and the regional vasoconstriction with elevated blood pressure resulting in more efficient muscle perfusion, while the blood flow in multiple internal organs and in the skin can be reduced. These activities enable adaptation to muscle workload provided that the stimulation of the muscle receptors by muscular exercise or acupuncture needles continues for a sufficient time, while releasing endogenous opioids.

In the 1970s and 1980s a large experimental research by a group of Chinese scientists in Beijing demonstrated that the cerebrospinal fluid collected from rabbits after acupuncture analgesia also induced analgesia when applied to the fourth brain chamber of other rabbits. This proved the humoral basis of the analgesic effect of acupuncture, although the nature of the substance was unknown at that time. Later on, a group of Toronto scientists led by B. Pomeranz, Mendeson and Ehrenpreis established the analgesic effect of acupuncture via endogenous opioids. The importance of the periaqueductal gray in the

Citation: Ondrejkovicova A, Petrovics G, Gabriella H. Biomedical effects of acupuncture. *Int J Complement Alt Med.* 2015;2(1):231–234.
DOI: 10.15406/ijcam.2015.02.00048

nociception is well known and various clinical trials pointed to electro stimulation analgesia in cases of chronic pain, wherein high levels of endorphins in cerebrospinal fluid were recorded during electro stimulation, while the analgesia was suppressed by naloxone. It was also found that the long-term stimulation weakened the analgesic effect and the increase in endogenous opioids was also lower; this was resolved by administration of the L-tryptophan amino acid, a precursor of the serotonin biosynthesis in the CNS. The connection between serotonin and pain regulation is significant; the stimulation of the periaqueductal gray leads to the activation of the descending inhibitory serotonergic system, which is linked to the raphe nuclei in the brain stem. The descending inhibitory track (tractus reticulospinalis) is involved in the regulation of pain threshold to nociceptive impulse at the substantia gelatinosa posterior horn level (Figure 2).

Studies of the Swedish pharmacologists[4] found that in chronic pain the concentration of endorphins in the spinal fluid is markedly reduced. Cholecystokinin octapeptide (CCK 8) has been shown to function in the CNS as a neuropeptide with potent antiopioid activity. It hinders opioid analgesia and facilitates opioid tolerance. The studies of the authors Zhou, Han, Sun, Hammes, Flatau, Bäcker, Ehinger and many others have found that electro acupuncture stimulation caused a substantial increase of immunoreactivity in CSF perfusate of the rat spinal cord. The CCK8 increase was more marked in electro acupuncture stimulation at 100 Hz and15 Hz and the least marked at 2 Hz stimulation. Since the CCK 8 was found to have potent anti opioid activity at the spinal level, it would be expected to reduce the electro acupuncture analgesia[5] which is opioid-mediated.[6,7]

It was found that CCK 8 is in fact increasingly released at frequencies from 100 Hz to 15 Hz. Opioid peptides are activated and CCK 8 is not produced at low frequencies 1-2 Hz. The known effect of the endogenous opioids which are produced in electro acupuncture stimulation and hindered by naloxone does not apply unequivocally, since the low frequency EA stimulation have been found to activate opioid peptides derived from propio-enkephalins, while the high frequency of 100 Hz activates the pre-prodynorphin group, in laboratory animals as well as in humans. Recent research suggests that there is another category other than nociceptive and neurogenic pain . Pain, in relation to pathological reaction that occurs by exposure to chemical compounds and infectious agents and consequent major changes, is transformed while developing increased sensitivity, which is described as chronic pain syndrome.[8] In clinical trials, acupuncture needle stimulation or low frequency electro acupuncture were effective in certain nociceptive some states, whereas the high frequency stimulation proves more effective in comparison with manual acupuncture. The use of needles is usually ineffective in patients with chronic pain syndrome and high anxiety. The lack of acupuncture effectiveness may be attributed to the high levels of cholecystokinin opioid antagonist in the brain. It was also found that patients respond to acupuncture treatment better when they are not under stress[9-11] (Table 1).

Table 1 Participation of the opioid neurotransmitters and their receptors in pain therapy.[20]

Endorphins	Opioid Receptors	Stimulation Frequency (Hz)	Supra Spinal Effects	Spinal Effects
BEndorphin	δ, μ	210	+	+
Metenkephalin	δ, (μ)	210	+	+
Dynorphin	K	100	+	+
Orphanin Q	ORL 1	100		+
Endomorphin	M	100	not found	+

+ Potentiation of the acupuncture analgesia

Lack of effectiveness of the acupuncture analgesia

The results of some clinical trials in human volunteers and in animals provide evidence of the involvement of the nervous and endocrine system in acupuncture. Studies in animals and in human volunteers have found that acupuncture induces a variety of biological responses, which occur both locally as well as in a remote location (off-center). Studies on the stress response in animal models show that acupuncture techniques can reduce the concentration of noradrenalin at cerebral perfusion and in the blood circulation, reduce the production of epinephrine in animals exposed to restraint stress, induce long-term behavioural and cardiovascular depression in behaviour and anxiolytic effects common in animals in captivity. The physical and psychological stressors may cause various behavioural and biochemical changes in the body, including the effects on cardiac function, blood pressure, and systemic release of catecholamines. Forced restraint has shown to be a simple physiological stressor that causes significant increase of heart activity, blood pressure and levels of norepinephrine and epinephrine, activation of the sympatico-adrenal system and the hypothalamic-pituitary axis.[12-15]

Another possibility how to alleviate pain is the A (1) adenosine receptor (ARs). There are four types of adenosine receptors, which all belong to the G protein-binding group and are located in the whole body. Therefore, they participate in the most of physiological as well as pathological processes. Adenosine, which binds to these receptors, is produced by the degradation of adenosine triphosphate (ATP) released in the mechanical and chemical stimuli as a vital source of energy. The pain is suppressed upon the binding of adenosine to the A (1) receptor.[16,17] This would suggest that the A1 receptor agonists have analgesic effect. A recent study by Vincenzi et al. (2014) examines the analgesic effect of the TRR469 A (1) adenosine receptor agonist in acute and chronic pain in animal models. TRR469 effectively inhibited nociceptive response, which was comparable to the effect of morphine analgesia. When combined with morphine TRR 469 potentiated the analgesic effect of morphine. A group of scientists observed the antinociceptive effect of acupuncture in relation to the adenosine concentration. Upon acupuncture points stimulation Zu San Li or Zusanli (Chinese: , ST36) significantly higher concentrations of adenosine were recorded, and this effect persisted even 60 min after acupuncture treatment.[18-21]

Conclusion

The prevention but also the pain treatment options have expanded substantially. Among the non-pharmacological methods, acupuncture and its associated therapies have come to the fore. The pain treatment by acupuncture and other medical treatments relating to physical activity, diet modification or non-pharmacological intervention must be applied throughout the patientslife.

Thetreatment outcomes are always related→the patients life.

Thetreatment outcomes are always related→the patients lifestyle.

Citation: Ondrejkovicova A, Petrovics G, Gabriella H. Biomedical effects of acupuncture. *Int J Complement Alt Med.* 2015;2(1):231–234.
DOI: 10.15406/ijcam.2015.02.00048

Currently, many studies have examined the effects of acupuncture. They are often discussed in the context of traditional Chinese medicine.[22] Further qualitative studies are needed for deeper understanding of its mechanism.[23]

Acknowledgements

The present scientific contribution is dedicated to the 650th anniversary of the foundation of the University of Pécs, Hungary.

Conflicts of interest

None.

Funding

None.

References

1. Ulett GA, Han S, Han JS. Electroacupuncture: Mechanisms and Clinical Application. *Biol Psychiatry*. 1998;44(2):129-138.
2. Kotani N1, Hashimoto H, Sato Y, et al. Preoperative intradermal acupuncture reduces postoperative pain, nausea and vomiting, analgesic requirement, and sympathoadrenal responses. *Anesthesiology*. 2002;95(2):349-356.
3. Martuliak I. Pain pathology in clinical practice. (1st edn), Banská Bystrica, Dali-BB, Slovakia. 2014. p.310.
4. Pomeranz B, Chiu D. Naloxone blockade of acupuncture analgesia: Endorphin implicated. *Life Sci*. 1976;19(11):1757-1762.
5. Mann F. Acupuncture analgesia. Report of 100 experiments. *Brit J Anaest.* 1974;46(5):361-364.
6. Zhou Y, Sun YH, Shen JM, et al. Increased release of immunoreactive CCK-8 by electroacupuncture and enhancement of electroacupuncture analgesia by CCK-8 Antagonist in rat spinal cord. *Exp Neurol*. 1988;24(3):554-562.
7. Han JS. Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. *Trends Neurosci.* 2003;26(1):17-22.
8. Lundeberg T, Stener-Victoria E. Is there a physiological basis for the use of acupuncture in pain? *Intern CongressSeries*. 2002;1238. p.3-10.
9. Kalso E, Mcquay HJ, Wiesenfeld H. Opioid sensitivity of chronic non-cancer pain. *IASP Press*. 1999;14:30.
10. Kulichová M. Algesiology. (1st edn), Žilina EDIS, Slovakia. 2005. p.298.
11. Kulichová M, Bernadič M, Ondrejkovičová A. Tumor pain. *Eurorehab, Slovakia*. 2000;10(3):131-135.
12. Rokyta R, Krisiak M, Kozak J. Pain. (Bolesť) (1st edn), Prague, Tigis. 2006. p. 664.
13. Šmirala J. Practical acupuncture. (1st edn), Martin: Education. 1991. p. 461.
14. Šmirala J. A compendium of acupuncture 1. (1st edn). Martin: Education. 2005. p.447.
15. Šmirala J, Ondrejkovičová A. A compendium of acupuncture 2. (1st edn), Martin: Education. 2011. p. 441.
16. Trincavelli ML, Daniele P, Martini C. Adenosine receptors: what we know and what we are learning. Curr,Top Med, Chem 10.9. 2010. p.860-877.
17. Bernadič M, Kulichová M. Pain, pathophysiology, diagnostics, treatment. Extended edition, Bratislava, SAP. 2001. p.104.
18. Goldman N, Chen M, Fujita T. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nature Neurosci*. 2010;13. p.883-888.
19. Mccaffery M. Understanding your pain patients. Nursing. 1980;80. p.26-31.
20. Melzack R, Bond R, Simpson HK. Pain, its nature and treatment. Edinburgh Churchill Livingstone Elsevier, London. 2006. p.309.
21. Ondrejkovičová A, Petrovics G, Bangham H. Pain and Acupuncture. In: Rehabilitation. 2001; 34(5):293-297.
22. Zhang X. General guidelines for methodologies on research and evaluation of traditional medicine. Document of WHO, Geneva, Switzerland. 2000. p.137.
23. Hegyi GA. Acupuncture, TCM as part of the EBM, in the current state of research: achievements, doubts, solutions. *Health Academy*. 2015;6(1):22-36.

Citation: Ondrejkovicova A, Petrovics G, Gabriella H. Biomedical effects of acupuncture. *Int J Complement Alt Med.* 2015;2(1):231–234.
DOI: 10.15406/ijcam.2015.02.00048