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The Molecule Mechanism of Acupuncture and Moxibustion for Alleviating Pain from The Perspective of Purinergic Signals, A Short Review

Qiuping Ye[1], Yong Dai[2], Jiahui Hu[2] and Zulin Dou[1]*

[1]*Department of Rehabilitation Medicine, The Third Affiliated Hospital of Sun Yat Sen University, China*

[2]*Guangzhou University of Traditional Chinese Medicine, Clinical Medical College of Acupuncture moxibustion and Rehabilitation, China*

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***Corresponding author:** Zulin Dou, The Third Affiliated Hospital of Sun Yat-sen University, Department of rehabilitation medicine, China, Email: douzulin@mail.sysu.edu.cn

Abstract

The underlying mechanism of acupuncture and moxibustion of pain was reviewed from the perspective of purinergic signals, which was studied mainly in three pains. In this process, electroacupuncture (EA) could decrease the expression of ATP-acting P2 receptors and increase the expression of adenosine receptors, both of which belong to purinergic signals. Among them, inflammatory factors (such as Interleukin-1 beta) and SP (substance P) could be inhibited by EA to take an analgesic effect and changed with the increase or decrease of purinergic signals, including A1R, A2aR, A2bR, A3R, P2X3R, P2X4R, P2X2R and P2X7R. The same effect was proved in moxibustion treatment for various pains. However, the selection of acupuncture points varied greatly in acupuncture or moxibustion, among which Zusanli (ST36) was the most used. In total, the purinergic signals in both the periphery and the central nervous system participated in acupuncture and moxibustion treatment for alleviate pain.

Keywords: Molecule mechanism; Acupuncture and moxibustion; Pain; Purinergic signals and review

Introduction

As a common clinical symptom, pain makes people uncomfortable and anxiety, which could result in insomnia and finally influence life and work. For its Therapy, drugs, physical therapy, transcutaneous electrical nerve stimulation (TENS), and acupuncture (including electroacupuncture) were mainly used, which has been shown to alleviate various chronic pain [1,2]. Electroacupuncture (EA) has been confirmed to integrate afferent signals from local acupuncture points and painful areas, which are transmitted to the central nervous system (CNS) for analgesia [3]. It is widely believed that the mechanism of EA-induced analgesia was related to opioid receptors [1,4], whose effect was similar to morphine analgesia, which was always putative to take analgesia by activating adenosine, which belongs to purinergic signals [5].

Purinergic signals include purinergic receptors, adenosine triphosphate (ATP) and its metabolites adenosine diphosphate (ADP), adenosine monophosphate (AMP), and adenosine. Purinergic receptors included the following two categories: adenosine-acting P1 receptor and the ATP-acting P2 receptor, while the P2 receptor also included ligand-gated cationic channel P2X receptors and G protein-coupled P2Y receptors [6]. Until now, types of purinergic receptors have been shown to be analgesics in both humans and animals. Related studies had appeared early in 1994 and demonstrated that purinergic signals were involved in the mechanism of EA for analgesi [7], especially for alleviating chronic pain. However, how are these purinergic signals involved in the process of EA and moxibustion to relieve different types of pain? We will elaborate on this in the review.

Main content

Inflammatory pain is attributed to the release of inflammatory mediators induced by stimulation of variety damage. For its treatment, EA could activate the adenosine 2 receptor (A2R) to produce an anti-inflammatory effect in collagen-induced arthritis [8], in conjunction with the reduction of inflammatory factors, such as tumor necrosis factor alpha (TNF-ą), which was

confirmed to be suppressed by A2R agonists [9]. This effect was also demonstrated in moxbustion treatment for inflammatory pain [10]. Furthermore, A1R had a similar analgesic effect in EA treatment for inflammatory pain [11], and this effect was consistent with that of opioid peptides to elevate the inflammatory pain threshold. In another study, the A1R antagonist can inhibit the adenosine dephosphorylation process and produce antinociceptive effects by EA [12]. For purinergic receptor 2 (P2XR), its expression could be inhibited during the regulation of acute pain by EA and moxibustion, including P2X3R and P2X7R [13]. Furthermore, the concentration of P2X3R in the peripheral region was affected by opioid substances that had been shown to involve the process of analgesia by EA [14], as was the SP [15]. However, other purinergic receptors that have been verified to participate in the process of analgesia for inflammatory pain, such as A3R, P2Y1R, P2Y6R, and P2Y11R, have not been shown to be associated with EA analgesia [16,17].

Neuropathic pain is defined as the pain caused by a lesion or disease of the somatosensory system [18]. For neuropathic pain, it can be relieved by EA via lowing P2X7R in spinal microglia, which results in depressing the symptoms of tactile allodynia and thermal hyperalgesia, as well as the decrease in Interleukin-1 beta (IL-1β) and interleukin-18 [19]. P2X4R and P2X3R showed the same effect, in which EA could decrease their expression, improve tactile allodynia, thermal and mechanical threshold in neuropathic pain [19,20]. Furthermore, A1R, a purinergic receptor that could be activated by the afferent nerve, was necessary in EA treatment to reduce mechanical and thermal hypersensitivity [21]. Moreover, the antagonists of A1R could reverse the anti-nociceptive effect of EA by increasing the glial fibrillary acid protein (GFAP), which indicated that A1R participated in EA for neuropathic pain [22].

Visceral pain could be induced by mechanical traction, spasm, ischemia, or inflammation. EA treatment for visceral pain involved adenosine receptors that can reverse the expression of SP and IL-1β [23]. A previous study indicated that the A1R antagonist could alter the effect of EA that lowering the mechanical threshold, and a similar effect was found in A2aR and A3aR, except for A2bR [24]. Among those, the A2bR antagonist has been shown to enhance the effect of EA on inhibition of SP and IL-1βexpression but remains controversial [25]. For other purinergic receptors, EA can decrease the expression of P2X7R and P2X4R to improve hypersensitivity [26]. So was the P2X2R and P2X3R in DRG, those effects were found in both the peripheral [27], the anterior cingulate cortex and the prefrontal cortex [28]. Regarding the therapeutic effect of moxibustion on visceral pain induced by irritable bowel syndrome (IBS), the expression of P2X7R mRNA could be depressed to inhibit nociceptive transmission. But the mechanism of moxibustion treatment for visceral pain is complex, including the expression of GFAP that reversed with moxibustion to take the analgesic effect in visceral pain [29].

In EA treatment for other pains, nociceptive receptors, including acid sensing ion channel subunit 3 (ASIC3), Nav1.7, and Nav1.8, could be regulated by EA via the same opioid and adenosine pathways in fibromyalgia (FM) pain [30]. EA could also down-regulate ATP and P2X7R to alleviate thermal hyperalgesia in neck incision pain [31]. A similar effect was found in the process of analgesic effect of EA treatment for myocardial pain by inhibiting the expression of P2X3R [32]. Recently, EA could relieve bone cancer by reducing the expression of P2X3R and inhibiting calcium influx [33]. Those studies showed the prospect of acupuncture treatment for bone cancer pain.

Regarding acupoints and parameters in the EA and moxibustion treatment for analgesia, ST36 was the most widely used acupionts, regardless of inflammatory pain, neuropathic pain, visceral pain, etc. [34,35]. The parameters were inclined to 1mA/2mA and 2Hz/15Hz for at least 15 min or 30 min every day, lasting for 7 consecutive days. Furthermore, Dachangshu (BL25), L3 and L5 (Hua Tuo Jia Ji), Huantiao (GB30), Sanyinjiao (SP6), and Taichong (LV3) were also used in the EA treatment for various pains. Among those, a special Chinese medicine method, called contralateral acupuncture (Juci), was also selective, such as ST36 and GB34. In total, the acupuncture acupionts selected for the treatment of different pains are regular and the matching acupuncture points based on the theory of Traditional Chinese Medicine are popular.

Conclusions

In total, purinergic signals, including adenosine and ligand-gated cationic channel P2X receptors, are both involved in the analgesia by acupuncture and moxibustion treatment, which work through increasing the expression of adenosine receptors or reducing the expression of P2 receptor.

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References

1. Li Y, Yu Y, Liu Y, Yao W (2022) Mast Cells and Acupuncture Analgesia. Cells 11.
2. Chung SH, Dickenson A (1980) Pain, enkephalin and acupuncture. Nature 283: 243-244.
3. Ren W, Tu W, Jiang S (2012) Electroacupuncture improves neuropathic pain: Adenosine, adenosine 5'-triphosphate disodium and their receptors perhaps change simultaneously. Neural Regen Res 7: 2618-2623.
4. Jiang QY (2016) Electroacupuncture relieves labour pain and influences the spinal dynorphin/kappa-opioid receptor system in rats. Acupunct Med 34: 223-228.
5. Ye JH, L, YL, Kong QX (2001) Effects of electroacupuncture on cAMP and cGMP contents in different brain regions of rats. Journal of Zhejiang University of Traditional Chinese Medicine 06: 1-23.

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6. von Kugelgen I, Hoffmann K (2016) Pharmacology and structure of P2Y receptors. Neuropharmacology 104: 50-61

7. Liu CN, Zhao FY, Zhu LX (1994) Purines participate in analgesia of weak electroacupuncture in rats. Acupuncture research 01: 59-62.

8. Li QH (2015) Adenosine A2A Receptors Mediate Anti-Inflammatory Effects of Electroacupuncture on Synovitis in Mice with Collagen-Induced Arthritis. Evid Based Complement Alternat Med 2015: 809560.

9. Hamano R, Takahashi HK, Iwagaki H, Kanke T, Liu K et al. (2008) Stimulation of adenosine A2A receptor inhibits LPS-induced expression of intercellular adhesion molecule 1 and production of TNF-alpha in human peripheral blood mononuclear cells. Shock 29: 154-159.

10. Yue YQ (2017) Study on the analgesic effect of Adenosine A2a receptor mediated moxibustion. Chengdu University of TCM 83.

11. Yin HY, Peng Fan Y, Liu J, Tong Li D, Guo J et al. (2023) Purinergic ATP triggers moxibustion-induced local anti-nociceptive effect on inflammatory pain model. Purinergic Signal.

12. Julie K H, Mark JZ (2012) PAPupuncture has localized and long-lasting antinociceptive effects in mouse models of acute and chronic pain. Mol Pain 8:28.

13. Zhang Y, Huang L, Kozlov SA, Rubini P, Tang Y et al. (2020) Acupuncture alleviates acid- and purine-induced pain in rodents. Br J Pharmacol 177: 77-92

14. Chai W, Tai Y, Shao X, Liang Y, Zheng GQ et al. (2018) Electroacupuncture Alleviates Pain Responses and Inflammation in a Rat Model of Acute Gout Arthritis. Evid Based Complement Alternat Med 2018: 2598975.

15. Tain XN (2014) Study on the correlation between Moxibustion Zusanli Analgesia and spinal cord P2X3 receptor and substance P expression. Chengdu University of TCM 54.

16. Teixeira JM, Bobinski F, Parada CA, Sluka KA, Tambeli CH (2017) P2X3 and P2X2/3 Receptors Play a Crucial Role in Articular Hyperalgesia Development Through Inflammatory Mechanisms in the Knee Joint Experimental Synovitis. Mol Neurobiol 54: 6174-6186.

17. Barragan-Iglesias P, Luis Mendoza-Garcés, Jorge Baruch Pineda-Farias, Verónica Solano-Olivares, Juan Rodríguez-Silverio et al. (2015) Participation of peripheral P2Y1, P2Y6 and P2Y11 receptors in formalin-induced inflammatory pain in rats. Pharmacol Biochem Behav 128: 23-32.

18. Jensen TS, Baron R, Haanpaa M, Kalso E, Loeser JD et al (2011) A new definition of neuropathic pain. Pain 152: 2204-2205

19. Xu J, Chen XM, Zheng BJ, Wang XR (2016) Electroacupuncture Relieves Nerve Injury-Induced Pain Hypersensitivity via the Inhibition of Spinal P2X7 Receptor-Positive Microglia. Anesth Analg 122: 882-892.

20. Xiang X, Wang W, Liu X, Du J, Fang J et al. (2019) Electroacupuncture Stimulation Alleviates CFA-Induced Inflammatory Pain Via Suppressing P2X3 Expression. Int J Mol Sci 20 (13): 3248.

21. Liao HY, Hsieh CL, Huang CP, Lin YW (2017) Electroacupuncture Attenuates Induction of Inflammatory Pain by Regulating Opioid and Adenosine Pathways in Mice. Scientific Reports 7: 15679.

22. Zhang M, Dai Q, Liang D, Li D, Chen S et al. (2018) Involvement of adenosine A1 receptor in electroacupuncture-mediated inhibition of astrocyte activation during neuropathic pain. Arq Neuropsiquiatr 76: 736-742.

23. Sjölund KF SA, Segerdahl M (1997) Intrathecal adenosine analog administration reduces substance P in cerebrospinal fluid along with behavioral effects that suggest antinociception in rats. Anesth Analg 85: 627-632.

24. Hou T, Xiang H, Yu L, Su W, Shu Y et al. (2019) Electroacupuncture inhibits visceral pain via adenosine receptors in mice with inflammatory bowel disease. Purinergic Signal 15: 193-204

25. Zhou M, Wu J, Chang H, Fang Y, Zhang D et al. (2022) Adenosine signaling mediate pain transmission in the central nervous system. Purinergic Signal 19(1): 245–254.

26. Weng ZJ, Hu SX, Zhang F, Zhang ZY, Zhou Y et al. (2022) Spinal cord astrocyte P2X7Rs mediate the inhibitory effect of electroacupuncture on visceral hypersensitivity of rat with irritable bowel syndrome. Purinergic Signal 19(1): 43–53.

27. Weng Z, Luyi Wu L, Lu Y, Wang L, Tan L et al. (2013) Electroacupuncture diminishes P2X2 and P2X3 purinergic receptor expression in dorsal root ganglia of rats with visceral hypersensitivity. Neural Regen Res 8: 802-808.

28. Weng ZJ, Wu LY, Zhou CL, Dou CZ, Shi Y et al. (2015) Effect of electroacupuncture on P2X3 receptor regulation in the peripheral and central nervous systems of rats with visceral pain caused by irritable bowel syndrome. Purinergic Signal 11: 321-329.

29. Takeda M, Takahashi M, Matsumoto S (2009) Contribution of the activation of satellite glia in sensory ganglia to pathological pain. Neurosci Biobehav Rev 33: 784-792.

30. Yen LT, Hsieh CL, Hsu HC, Lin YW (2017) Targeting ASIC3 for Relieving Mice Fibromyalgia Pain: Roles of Electroacupuncture, Opioid, and Adenosine. Sci Rep 7: 46663

31. Gao YH, Li CW, Wang JY, Tan LH, Duanmu CL et al. (2017) Effect of electroacupuncture on the cervicospinal P2X7 receptor/fractalkine/CX3CR1 signaling pathway in a rat neck-incision pain model. Purinergic Signal 13: 215-225.

32. Yan Q, Zhang Y, Liu YS (2014) Effect of electroacupuncture at Neiguan point on P2X3 receptor in myocardium and hypothalamus in rats with myocardial pain. Journal of Hubei University of Chinese Medicine 16: 5-8

33. Tian SX (2022) Analgesic effect of electroacupuncture on bone cancer pain in rat model: the role of peripheral P2X3 receptor. Purinergic Signal.

34. Cheng RD, Tu WZ, Wang WS, Zou EM, Cao F et al. (2013) Effect of electroacupuncture on the pathomorphology of the sciatic nerve and the sensitization of P2X3 receptors in the dorsal root ganglion in rats with chronic constrictive injury. Chinese Journal of Integrative Medicine 19: 374-379.

35. Goldman N, Chen M, Fujita T, Xu Q, Peng W et al. (2010) Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. Nat Neurosci 13: 883-888.

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