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A Mathematical Model for the Instigation and Transmission of Biological and Neural Signals in Response to Acupuncture

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Abstract. Acupuncture has been in clinical practice in China for thousands of years and its analgesia effect is worldwide accepted. However, the mechanism of acupuncture effect is not well understood. The study focus on signaling pathways induced by acupuncture, analyzes the cooperative action of the acupoints' structure and the associated chemical mediators during acupuncture, establishes a mathematical model clarifying the roadmap of electroneurographic signal startup and transmission mechanism induced by acupuncture, quantitatively analyzing the response in acupoints to acupuncture. These work contribute to reveal the activation and transmission mechanism of neural signals induced by acupuncture from systems biology perspective, lay the foundation for the integration of acupuncture theory and modern science and further guide the clinical treatment and experimental research of acupuncture.

AMS subject classifications: 92C10, 92C05, 92C42, 92B05

Key words: Mast cell, nerve cell, Ca^{2+} signaling, biological mediators release, acupuncture.

1 Introduction

Although Traditional Chinese Medicine (TCM) is treated with considerable skepticism, the analgesic effect of acupuncture is well accepted. In 1997, NIH panel issued consensus statement on acupuncture, the 12-member panel concluded that there are a number of pain-related conditions for which acupuncture may be effective as an adjunct therapy, an acceptable alternative, or as part of a comprehensive treatment program [1]. We have

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retrieved over 1,000 international papers investigating acupuncture analgesia in recent years, which encouraged us to believe that the mechanism of acupuncture analgesia may be revealed by scientific methods [2, 3].

Acupuncture is a penetration and manipulation of specific anatomic locations on the skin, called acupuncture points (acupoints), by thin, solid, generally metallic needles. Recent studies on acupoint morphology using various approaches, such as MRI, anatomy, and XCT, have shown that the structural basis of the acupoints is complex and composed of connective tissue with numerous intertwining blood vessels, nerves, mast cells, and lymphatic vessels [4]. The dermic dense connective tissue and subcutaneous loose connective tissue at acupoint form a three dimensional collagen fiber network, connecting the surface of the body to internal organs. Under normal conditions, collagen fibers wind together and arrange interlaced [5]. By observing collagen and elastic fibers winding and tightening around the needle during acupuncture, Langevin proposed that needle manipulation transmits a mechanical signal into connective tissue via the needle/tissue coupling [6, 7]. We devised a mechanical sensor to detect the real-time force on the needle during acupuncture manipulation and found if the structure of the collagen fibers at Zusanli (ST36) was destroyed by injection of type I collagenase, the force caused by rotation or lift-thrusting manipulations of the acupuncture needle declined and the analgesic effects was attenuated accompanying the restraint of the degranulation of mast cells [8]. The results indicated that the collagen fibers participated in the initiation of manual acupuncture signal in the acupoints by increasing mast cells' degranulation. Further experiments showed acupuncture resulted in a remarkable increase in degranulation of the mast cells, pretreatment of the acupoints with disodium chromoglycate (DSCG, mast cell stabilizer) not only counteracted the phenomenon of degranulation but also reduced analgesic effect of acupuncture [9]. Acupuncture analgesia depends on the neural system, and there's no acupuncture effect when the acupoint is narcotized [10]. Meanwhile, we found that acupuncture at ST36 can trigger peripheral nerve cell discharge [11], and Han et al. found that acupuncture at ST36 can cause the corresponding neural electrical activity of spinal cord dorsal root, which suggest that there exists the electroneurographic signal startup mechanism at acupoint and transmission mechanism in the nerve cell networks [12].

These studies analyzed the mechanism of acupuncture analgesia effect from collagen fibers, mast cells, nerve cells and neurotransmitters respectively, there was no research combining all the aspects, clearly explaining the mechanotransduction pathway induced by acupuncture and revealing the mechanism of acupuncture analgesia effect. Above researches suggest acupuncture (mechanical stimuli) can activate mast cells to release biological mediators through collagen fiber deformation, biological mediators accumulate in extracellular space (ECS) around acupoint and activate nearby nerve cells, then modulate the multiple pain-processing pathways in response to acupuncture. To explain this process clearly, we suppose to set up a mathematical model and qualitatively describe cellular signaling and biological mediators' dynamics and draw a roadmap of the pain modulating pathways [5].