

The Impact of Acupuncture and Moxibustion on the Microenvironment

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Acupuncture therapy is an essential part of traditional Chinese medicine that is being recognized by an increasing number of countries due to its convenience, effectiveness, and low risk of adverse reactions. The microenvironment is important in the occurrence, development, treatment, and rehabilitation of diseases, and has recently become a focus of research in the field of various diseases. Acupuncture's therapeutic effect on the human body begins in the microenvironment (acupoints) and ends in the microenvironment (lesions). Many reports on the mechanism of acupuncture and moxibustion are written with the impact of acupuncture on the microenvironment of different systems or parts in mind. Several diseases that have been widely reported in recent years, such as osteoarthritis, spinal cord injury, and tumors, have been chosen as examples.

Keywords: Acupuncture; Moxibustion; Microenvironment; Traditional Chinese Medicine; Acupoints; Diseases

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Introduction

TRADITIONAL Chinese Medicine (TCM) includes acupuncture and moxibustion as forms of acupuncture therapy. Acupuncture and moxibustion both treat specific parts (meridians, acupoints) under the guidance of TCM theory in order to treat or prevent diseases by adjusting “yin” and “blood”, warming meridians, and balancing “yin” and “yang” (1, 2). Acupuncture is being recognized, accepted, promoted, and used in an increasing number of countries as a green therapy with simple operation, broad indications, definite curative effect, and no adverse reactions. This review examines the recent effects of acupuncture and moxibustion on the microenvironment

of various systems or parts.

The therapeutic effect of acupuncture and moxibustion on the human body begins in the microenvironment (acupoints) and ends in the microenvironment (lesions) (3). The microenvironment in which acupuncture and moxibustion produce therapeutic effects can be divided roughly into three parts: local acupoints, deep viscera of acupoints, and remote points.

Acupoints' Local Microenvironment Undergoes Changes

The acupoints and meridians are components of acupuncture and moxibustion, and their local multiple tissue structures are

the carriers of the acupoints' biological effects. Currently, advanced instruments and methods can study the microscopic tissue structure and chemical composition of acupoints from a morphological standpoint, which is also an important way to reveal the mechanism of acupuncture and moxibustion (4, 5). Cupping and acupuncture have the same mechanism of action, that is, stimulating the body surface to change the local microenvironment, converting physical signals into biological signals, the signals interact and influence each other in the body, and signal cascade amplification activates the neuroendocrine immunity system, resulting in an overall adjustment effect (6). The initiation of acupuncture information, including the activation of cell functions, the release of chemicals, and the excitation of afferent nerves, is the specific response change caused by acupuncture in the local microenvironment of acupoints. Xu et al. labeled and observed skin tissue in the Taichong acupoint area of rats using fluorescent histochemical staining and immunohistochemical counterstaining in conjunction with microscopic imaging technology (7).

Changes in the Deep Visceral Microenvironment near Acupoints

Acupoints have a near-treat effect, which means they have a therapeutic effect on the tissue system around them. Jiang et al. conducted a comparative study in rats using moxibustion at Guanyuan point and discovered a high number of tryptase-lysosome-related membrane protein 1 co-expressions in the small intestine tissue, indicating that their mast cells are activated and hypertrophy (8). The presence of neuropeptide Y-positive nerve fibers and calcitonin gene-related peptide around the cells suggests that the therapeutic effect of acupuncture at Guanyuan point is related to the activation of sensory, sympathetic, and mast cells in the small intestine. Zhang and coworkers used fluorescent labeling tracing technology to reveal the regular distribution of Shenshu acupoint and adrenal-related innervation in rats from sympathetic nerve, sensory nerve, and motor nerve perspectives, as well as the neuroanatomical link between the two (9). It demonstrates that the Shenshu point and the adrenal gland are linked to the first-level nerves. Acupuncture Shenshu point affects not only the kidney function, but also the adrenal gland.

Alters the Microenvironment of Distant Sites or the Entire System

Acupoints have the effect of treating distant diseases, according to the theory of meridian circulation and the relationship between internal and external organs, which is referred to as the "remote treatment effect." Accordingly, a gut microbiota-immune imbalance can cause low-grade inflammation in the gut, such as irritable bowel syndrome (10, 11). Electroacupuncture has been shown to increase the balance and diversity of intestinal microorganisms, restore and maintain the stability of the intestinal environment, and protect the host from inflammatory damage. Based on the understanding of the physiological and digestive processes of "preacher," studies have investigated about the "large intestine, the organ of preacher" in the transmission of immune information during the disease occurrence and development process (12, 13). The large intestine

is thought to be involved in the transmission of internal signals as well as the transmission of visible drugs. In terms of immune information transmission and immune regulation, the large intestine has the advantage of anatomy and physiology.

Acupuncture and Diseases Osteoarthritis

The microenvironment is closely related to the occurrence, development, and recovery of various orthopedic diseases, and the literature frequently uses terms such as "bone destruction microenvironment," "bone reconstruction microenvironment," "cartilage matrix microenvironment," "adverse osteoarthritis microenvironment," "joint immune microenvironment," and others. Mechanical and biological changes in the joint disrupt the original microenvironment's balance, resulting in an adverse microenvironment. Chondrocytes generate inflammatory responses in order to adapt to or resist changes in the cartilage matrix microenvironment by activating related transcription factors and signaling pathways, which creates a vicious cycle (14). Szychlinska et al. summarized that the balance of the intestinal microenvironment had been disrupted, resulting in the occurrence of many diseases, including osteoarthritis (15). Acupuncture plays a role in restoring the relative balance and stability of intestinal microecology in the treatment of osteoarthritis by regulating the brain-gut axis (16).

Spinal Cord Injury

Acupuncture and moxibustion are effective in restoring patients' function after spinal cord injury, but the mechanism is still unknown. Wang and colleagues demonstrated in rats that using Du meridian electroacupuncture in conjunction with early decompression can improve the microenvironment of spinal cord injury and the symptoms of spinal cord injury by inhibiting cell apoptosis and promoting nerve movement recovery after upper cervical spinal cord injury (17). Stem cell transplantation is a relatively effective treatment after the acute phase, but the harsh microenvironment reduces transplant survival. As summarized by Fan et al. that the possible mechanisms of acupuncture therapy for SCI include decreased oxidative stress, suppression of inflammation and neuronal apoptosis, modulation of the expression and activity of endogenous biological mediators, and increased creation of regenerative stem cells (18).

Encephalopathy

Cerebrovascular accident, Alzheimer's disease, anxiety, depression, and other mental and psychological diseases are all examples of encephalopathy. Fu et al. studied the effect of Jing-well point bloodletting on the neuronal microenvironment in the middle cerebral artery area by using enhanced magnetic resonance imaging technology to measure the parameters of extracellular space and interstitial fluid flow in the brain (19). Liu et al. used the hanging moxibustion method on "Baihui," "Dazhui," and "Shenting" points to remove blood stasis and dredging collaterals (20). After three courses of treatment, the BDNF in each group's brain tissue was detected using immunofluorescence/TrkB expression for statistical analysis. The findings indicated that moxibustion for removing blood stasis and dredging collaterals is an effective treatment for vascular dementia. This

therapy can increase BDNF/TrkB protein expression in the neurovascular niche microenvironment, co-regulating the NSCs-EPCs coupling mechanism, promoting neurogenesis, and repairing damaged nerves. The final fate of transplanted neural stem cells is also dependent on the host's microenvironment, making neural stem cell transplantation a promising clinical approach for the treatment of Alzheimer's disease. Acupuncture combined with oral administration of TCM was used in a study by Zhou et al. (21). Their findings revealed that synaptophysin mRNA and protein levels in the hippocampus were significantly increased, increasing the survival of stem cell transplantation and effectively improving the symptoms of dementia mice. It demonstrates that electroacupuncture can disrupt the rat hippocampal microenvironment, increase ERK signaling pathway activation, and promote the proliferation of adult hippocampal neural precursor cells, resulting in obvious antidepressant therapeutic effects.

Tumor

The tumor microenvironment has emerged as a novel concept in cancer research in recent years. Tumor cells, tumor stromal cells (including immune cells, smooth muscle cells, adipocytes, fibroblasts), neuroendocrine cells, endothelial cells, microvessels, and so on are all part of the tumor microenvironment. Stromal cells also include cytokines and extracellular matrix. A suitable microenvironment can promote tumor occurrence and development by inducing genomic instability *in vivo*, providing scaffolds and barriers, generating immune-privileged regions, and inducing bidirectional differentiation, among other things. Tumors form and grow as a result of interactions between cancer cells (seeds) and the tumor microenvironment (soil) (22-24). Yang et al. discovered that acupuncture achieves targeting by altering tumor microvessels and the microenvironment (25). Another study found that acupuncture may repair peripheral nerves damaged by chemotherapy, promote the release of neurotransmitters or neuropeptides from sympathetic nerve endings in the bone marrow, regulate the hematopoietic microenvironment, and act on hematopoietic stem and progenitor cells indirectly or

directly to restore hematopoietic stem and progenitor cells (26).

Infertility

Infertility can be caused by endocrine, immune, uterine, and fallopian tube factors, as well as genetics, environment, and stress. The normal fallopian tube microenvironment is free of abnormalities such as inflammation and adhesion, and it keeps the tube open. Endometrial blood perfusion is adequate, and endometrial thickness is appropriate (good receptivity), resulting in a favorable internal environment for implantation. Because of thin endometrium, poor endometrial morphology, or insufficient endometrial blood supply, some infertile patients frequently cancel their cycles. Endometrial receptivity is one of the most important factors in transplant success. Acupuncture at the Shenshu and Ciliao points, according to Ruonan and Yinping, can promote the metabolism of local inflammatory substances, improve the microenvironment, such as fallopian tube and endometrial blood supply, increase endometrial thickness, and aid infertility (27).

Conclusion

The microenvironments are closely related, which confirms TCM's holistic view theory. The whole and the parts are inseparable, and the local microenvironment of acupoints can be examined from various angles, including the nervous system, endocrine system, and circulatory system. As a result, in disease treatment, different "microenvironments" must be properly integrated in order to identify the dominant "microenvironments" at various stages of disease development and then guide clinical treatment of targeted conditioning.

Studies have shown that acupuncture can change the observed indicators in a positive direction; that is, yin and yang tend to be balanced in TCM, indicating that acupuncture has a two-way regulating effect on the dynamic balance of the microenvironment. As a result, the impact of such factors on experimental results should be considered in future research that is more scientific and effective. ■

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