

An anti-inflammatory pathway that can explain the role of acupuncture in immune homeostasis

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In the early '90s acupuncture was believed to be an efficient analgesic technique. Many conditions which involve inflammation have been treated with acupuncture, such as tendonitis, osteoarthritis, rheumatoid arthritis. Lately, evidence has accumulated regarding the fact that acupuncture has anti-inflammatory effects in addition to analgesia. Likewise opioids, were found to have powerful anti-inflammatory actions, apart from central nervous system and in periphery, via Kappa-opioid receptors. Finally, Naxolone (an opioid antagonist) only partially blocks the effect of acupuncture.

Inflammation is a homeostatic response, a reaction to infection, injury or trauma. The onset of inflammation is characterized by release of pro-inflammatory mediator (TNF, IL-1, adhesion molecules, vasoactive mediator and reactive oxygen species). Although inadequate production of anti-inflammatory cytokines leads to ongoing (and chronic) inflammation, excessive production can be injurious to the organism. Homeostatic response is balanced by anti-inflammatory factors such as IL-10, IL-4, IL-1 receptor antagonists etc.

All these peripheral molecules, apart from pro and anti-inflammatory action, signal inflammation to the brains' neuro-endocrine pathways, and more specific to the hypothalamo-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS). Both laboratory and clinical evidence have shown the presence of a cross talking, negative feedback between the autonomic nervous system (mainly sympathetic) and the innate immunity.

Recently, *Kelvin J. Tracey et al*, described the anti-inflammatory role of the vagus nerve in animal models, as a new pathway of neural inhibition of inflammation. They proved that cytokines transmit signals to the brain through the vagal sensory neurons (vagotomy inhibits the stimulation of the HPA axis and norepinephrine axis).

This is the first reference for the existence of a parasympathetic control on systemic and/or local inflammation. Acetylcholine, the neurotransmitter of the vagus nerve, binds to the $\alpha 7$ subunit of the acetylcholine receptor ($\alpha 7nAChR$) on macrophages. Stimulation of the afferent pathway of the vagal nerve induces immunosuppression controlling TNF production of the spleen macrophages.

The description of the neural arc reflex (afferent and efferent pathway) through which the vagus nerve participates in immunological homeostasis was the critical step in understanding this pathway. The noradrenergic splenic nerve fibers and the cholinergic vagus fibers are the neural connection between the immune response and the spleen macrophages. Animal experiments indicate that the vagus nerve drives organisms to achieve rapid and precise control of the inflammation (systemic cytokine production) through the celiac-superior mesenteric plexus ganglia.

The question for medical acupuncturist was: Is acupuncture a treatment through which the cholinergic anti-inflammatory reflex controls inflammation (decreasing TNF production)? In our review we will describe the auricular and body acupuncture points which act as immunoregulators through the vagus nerve. These points are used for centuries by Chinese therapist for the control of symptoms such as fever, anorexia, fatigue, somnolence (cytokine overproduction) and they are considered as a potentially useful treatment of various chronic inflammatory disorders; Crohn's disease, rheumatoid arthritis, autoimmune (allergic) diseases, colitis, inflammatory bowel disease, arthritis, type 2 diabetes, atherosclerosis, multiple sclerosis, Alzheimer's disease etc., where cytokine overproduction has been implicated.

To conclude, we will mention the role of the spleen in controlling inflammation as the prominent source of TNF-alpha circulation. Our statement proves that the spleen as an organ is more significant than believed. This perspective comes more in accordance to its role in Traditional Chinese Medicine.

This decade opens up a new chapter for the research in the field of acupuncture regarding the biological mechanisms involved in its anti-inflammatory action. In the near future, acupuncture will be an absolute indication for an inflammation –regardless the cause. It will not surprise us the use of acupuncture as an adjunct therapy to the conventional medical treatments of a number of chronic inflammatory and autoimmune diseases.