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Research Progress on the Mechanism of Acupuncture Treatment for Sciatica

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Abstract: ***Sciatic neuralgia, a prevalent neuropathic pain condition, has been the focus of numerous clinical studies. Current treatment methods for sciatica encompass acupuncture, catgut embedding at acupoint, physical therapy and surgery. Among these, acupuncture therapy has demonstrated notable therapeutic efficacy, not only in alleviating pain symptoms but also in effectively managing the progression of the disease. Notably, acupuncture therapy exhibits a low recurrence rate and is characterised by a high degree of safety. The aim of this paper is to review the research literature on the mechanism of acupuncture in treating neuropathic pain at home and abroad in recent years, and to summarise its mechanism from the perspectives of the spinal cord, centre and periphery, in order to provide a theoretical basis for clinical acupuncture treatment of sciatica.***

Keywords: Acupuncture, Sciatica, Chronic compressive sciatica (CCI), Neuropathic pain, Mechanism research.

1. Introduction

Traditional Chinese Medicine (TCM) categorizes sciatica under the scope of lower back and leg pain as well as bi syndrome, often employing therapies such as acupuncture, massage, and thread embedding [1,2]. Acupuncture, as an effective treatment, exerts its analgesic effects through mechanisms involving both peripheral and central nervous systems, as well as multiple factors including neural, immune, and endocrine systems. However, the exact mechanisms remain unclear. This article aims to outline the analgesic mechanisms of acupuncture in the treatment of sciatica, with the goal of providing a theoretical basis for clinical treatment.

Sciatica is classified as neuropathic pain in modern medicine, characterized by spontaneous pain, hypersensitivity, and allodynia. This condition typically manifests as recurrent and persistent episodes, and it is one of the most difficult symptoms to eradicate in clinical practice, significantly affecting patients' daily lives. Neuropathic pain arises from lesions or dysfunctions in the somatosensory nervous system, and it constitutes a complex pain disorder whether the lesion occurs in the peripheral or central nervous system. The high prevalence of this condition is partly due to the insufficient treatment options available. Currently, widely used opioid analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) do not provide complete relief for such pain, and their effectiveness is limited, benefiting only a minority of patients [3]. The mechanism of pharmacological treatment primarily involves inhibiting the activation of spinal microglia, regulating voltage-gated ion channels in the dorsal root ganglia, and affecting the p38 MAPK pathway in the hippocampus to achieve analgesic effects. Acupuncture, an ancient therapeutic method, has a history of thousands of years in China. It works by stimulating specific acupuncture points to regulate the flow of Qi (energy) and blood, unblock meridians, and balance organ functions. In the treatment of conditions such as sciatica and other pain-related disorders, acupuncture gradually shows unique therapeutic advantages by improving local blood circulation, reducing inflammation, and regulating nerve function. Modern medical research has increasingly confirmed the effectiveness of acupuncture and has explored its mechanisms through the lens of neurobiology.

Acupuncture is believed to achieve its therapeutic effects by unblocking meridians and adjusting the flow of Qi and blood. However, advancements in modern science, particularly in neurobiology and physiology, have provided a deeper understanding of acupuncture's mechanisms. Research shows that acupuncture works through multiple pathways, including the central nervous system, peripheral nerves, and immune system.

2. Spinal Cord Analgesic Mechanism of Acupuncture for Sciatica

The spinal cord plays a critical role in pain transmission, as it is not only regulated by the central nervous system but also serves as the first site for processing and modulating nociceptive information [4,5]. In this process, microglial cells in the dorsal horn of the spinal cord play a crucial role in abnormal pain perception triggered by nerve injury. Under physiological conditions, microglial cells remain in a "resting" state; however, when exposed to noxious stimuli, these cells become activated. Studies show that peripheral nerve injury leads to morphological changes in microglial cells, as well as an increase in the expression of the microglial marker OX-42, which is considered a key indicator of microglial activation. Once activated, microglial cells secrete a variety of bioactive substances, including adenosine triphosphate (ATP), brain-derived neurotrophic factor (BDNF), and the pro-inflammatory cytokine interleukin-1 (IL-1). The release of BDNF increases the expression of gamma-aminobutyric acid (GABA), causing a shift in inhibitory signals to excitatory signals within the first lamina of the spinal dorsal horn, leading to chloride ion efflux and depolarization excitation, ultimately resulting in pain hypersensitivity [6,7].

Additionally, the expression levels of specific receptors on microglial cells increase, activating their state through

signaling pathways. Targeting the blockade of these receptors holds significant potential for the treatment of neuropathic pain. Studies have shown that purinergic substances, such as P2X receptors, play a critical role in pain induced by peripheral injury, particularly the function of the P2X4 receptor. After peripheral injury, the expression of the P2X4 receptor in spinal cord microglial cells rapidly increases, and its upregulation is synchronized with the development of neuropathic pain. Blocking the function of the P2X4 receptor can effectively alleviate this type of pain, while P2X4 receptor agonists can significantly induce tactile hypersensitivity and persistently affect this process [8-10]. Activated microglial cells release a large number of pro-inflammatory factors like ATP, which activate P2X4 receptors and lead to increased expression, closely associated with the onset of neuropathic pain [11]. Chen [12] et al.'s study indicated that acupuncture improves abnormal tactile pain after peripheral nerve injury by reducing the overexpression of γ-interferon in spinal cord microglial cells in CCI rats and decreasing P2X4 receptor expression After peripheral nerve injury, the expression of P2X4 receptor protein in the dorsal horn of the spinal cord significantly increases. Therefore, blocking the expression of P2X4 receptors in microglial cells may be one of the strategies for treating neuropathic pain.

As research into the analgesic mechanisms of acupuncture deepens, cellular and molecular signaling pathways have been gradually revealed. The known members of the MAPK family include extracellular signal-regulated kinase (ERK) 1/2, p38 mitogen-activated protein kinase (p38MAPK), phosphoinositide 3-kinase (PI3K), cyclic adenosine monophosphate response element-binding protein (CREB), protein kinase A/protein kinase C (PKA/PKC), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) [13,14]. These signaling pathways interact with neuromediators and inflammatory mediators related to neuropathic pain through cascade reactions, thereby mediating the process of central sensitization. p38MAPK plays a key role in the plastic changes of spinal dorsal horn neurons and the transmission of nociceptive information. Research has shown that electroacupuncture at the Zusanli acupoint can increase the pain threshold in neuropathic pain rats and reduce the necrosis of spinal dorsal horn neuronal fibers. This phenomenon may be associated with a reduction in the expression level of p-p38MAPK in the spinal dorsal horn [15].

3. Central Mechanisms of Acupuncture in Treating Sciatica

The central mechanisms of acupuncture analgesia involve the activation of specific functional regions or nuclei in the brain. These areas include parts of the limbic system, such as the anterior cingulate cortex [16], amygdala, and hippocampus, all of which play roles in pain regulation. As a part of the limbic system, the hippocampus not only plays a crucial role in learning, memory, and emotional regulation but also plays an essential role in the processing of pain information and the acupuncture analgesia process.

Acupuncture analgesia involves various neurotransmitters and mediators, such as serotonin (5-HT), GABA, opioid peptides, and their corresponding receptors. Glutamate, as one of the main excitatory neurotransmitters in the central nervous system, has its N-methyl-D-aspartate (NMDA) receptors sensitive to Ca2+ permeability, which can induce Ca2+ influx, thereby activating Ca2+/calmodulin-dependent protein kinase II or protein kinases, promoting signal transduction in postsynaptic neurons. The excitatory glutamate produced in the hippocampus plays a key role in chronic pain, especially in pain accompanied by emotional, mood, and cognitive disorders, with NMDA receptor-mediated central sensitization being one of the primary causes of neuropathic pain [17]. Acupuncture treatment can inhibit the expression of glutamate in the hippocampus of CCI rats and increase the content of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the periaqueductal gray (PAG), suggesting that acupuncture analgesia is closely related to the increase in GABA receptors in the hippocampus and PAG. Therefore, acupuncture can regulate the expression of excitatory and inhibitory neurotransmitters and their related receptors in the hippocampus, thereby alleviating neuropathic pain in brain regions [18].

The hippocampus plays a key role in pain perception and regulation. Studies have shown that the granule cell layer of the hippocampus contains neurons that are sensitive to pain. These neurons not only participate in pain information processing but also in pain modulation [19]. Electrical stimulation of the hippocampal region can increase an individual's pain threshold. Nitric oxide (NO), as a lipophilic gas neurotransmitter, can transmit information between neurons through diffusion and is involved in various physiological and pathological processes, including nociception and hyperalgesia. Research indicates that electroacupuncture can inhibit glial cell activation and the release of excitatory neurotransmitters, regulate the function of nitric oxide synthase (NOS) in the spinal cord, and influence synaptic plasticity changes, modulating the expression of pro-inflammatory and anti-inflammatory factors as well as pain-related receptors. Additionally, the onset of neuropathic pain is closely related to inflammation and excessive NOS expression in locally recruited macrophages, Schwann cells, and glial cells. An increase in NOS levels exacerbates abnormal mechanical and thermal hyperalgesia in CCI rats, possibly linked to the excessive release of glutamate from pain afferent nerve endings, which activates NMDA receptors and NOS, increasing neuronal excitability. The increase in NO generated from the breakdown of NOS further promotes glutamate release, intensifying pain. This release of chemical stimuli may worsen secondary hyperalgesia and abnormal pain, possibly playing a crucial role in central nervous system sensitization processes [20].

4. Conclusion

The study of the mechanisms underlying acupuncture treatment for neuropathic pain is of theoretical significance for the clinical treatment of sciatica. This treatment mechanism involves spinal analgesia, primarily including the activation of microglial cells, cell signaling pathways, and hippocampal-related molecular pathways for central analgesia. Additionally, peripheral effects involve the participation of inflammatory factors and ion channels. Although considerable progress has been made in the study of

neuropathic pain mechanisms, many unresolved issues remain. In acupuncture research for sciatica, standardization and unification are still needed in aspects such as electroacupuncture parameters, treatment duration, model selection, and acupuncture point selection. At present, the interrelationships between these factors have not been thoroughly studied, which may lead to variations in analgesic effects. Therefore, it is necessary to adjust research parameters to further uncover the mechanisms and effects of acupuncture analgesia, providing a new alternative strategy for clinical drug treatment of sciatica.

In both acute and chronic pain models, the NO/PKG signaling pathway within hippocampal cells may play a role in the cumulative analgesic effects of electroacupuncture, significantly influencing the induction and maintenance of tactile hypersensitivity. For CCI-induced neuropathic pain rats, repeated electrical stimulation of the Zusanli (ST36) and Yanglingquan (GB34) acupoints demonstrates cumulative analgesic effects, which are closely associated with a decrease in hippocampal synaptophysin immunoreactivity and an improvement in hippocampal synaptic plasticity. Blocking the primary afferent or efferent pathways of the hippocampus effectively reduces pain behaviors. The hippocampus plays a crucial role in pain and electroacupuncture-induced analgesia, with its function closely linked to the activation of the mitogen-activated protein kinase kinase 1 (MEK1) family signaling in neuropathic pain. The MEK1 signaling pathway within the hippocampus is involved in the cumulative analgesic effects induced by electrical stimulation, and the relevant molecules in this brain region play an important role in the process.

In summary, the research background of acupuncture for treating sciatica involves not only the history of traditional Chinese medicine but also the continuous exploration of its mechanisms through modern biology. With the ongoing development of modern medicine and scientific advancements, conducting in-depth research on the therapeutic effects and mechanisms of acupuncture for sciatica can provide more theoretical support and practical guidance for clinical treatment.

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