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REVIEW

Application of Acupuncture in Cervical Spondylotic Radiculopathy: An In-Depth Analysis and Outlook on Pathophysiological Basis and Therapeutic Mechanisms

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Abstract: Cervical Spondylotic Radiculopathy (CSR) is a debilitating condition caused by nerve root compression from degenerative cervical changes, leading to pain and dysfunction. Acupuncture, a key non-pharmacological treatment, shows significant clinical promise, yet its biological mechanisms are not fully understood. This article analyzes CSR's pathophysiology and acupuncture's therapeutic actions, based on literature published between 2010 and 2025, with a focus on recent key advancements. The review covers CSR's pathology, including mechanical compression, neuro-inflammation (eg, TNF-α), and neural sensitization. It then elucidates acupuncture's mechanisms: central analgesia via endogenous opioids (eg, β-endorphin), downregulation of pro-inflammatory mediators, enhanced local microcirculation, and modulation of oxidative stress. In conclusion, acupuncture intervenes in CSR's pathology through a multi-target neuro-immune-circulatory network. Future high-quality clinical trials and deeper molecular studies are essential to provide robust scientific evidence for its clinical application.

Keywords: acupuncture, cervical spondylotic radiculopathy, nerve root inflammation, pathophysiology, central sensitization

Introduction

Cervical spondylosis is a common chronic degenerative condition primarily affecting the cervical intervertebral discs, vertebral bodies, facet joints, and related soft tissues. As people age, the structure and function of the cervical spine gradually deteriorate, leading to a series of clinical symptoms, including neck pain, stiffness, dizziness, and numbness in the upper limbs. In recent years, the incidence of cervical spondylosis has significantly increased due to changes in modern lifestyles. Depending on the location of the lesion and clinical manifestations, cervical spondylosis can be classified into various types, including cervical type, nerve root type, spinal cord type, vertebral artery type, and mixed type.[1] Among these, cervical spondylotic radiculopathy (CSR) is the most common and severe, as it often results in nerve root compression, causing radiating pain and numbness.

Acupuncture is a therapeutic modality with a long history of clinical application for musculoskeletal conditions, including cervical spondylosis. The practice involves the insertion of fine needles into specific anatomical locations (acupoints), which are often characterized by a high density of neurovascular structures. While its historical roots are extensive, modern scientific investigation has been crucial in validating its application and elucidating its physiological mechanisms.[2] Contemporary research indicates that acupuncture's therapeutic effects extend beyond pain relief to include the improvement of local blood circulation and potent modulation of the nervous system.[3] The therapy appears particularly effective for patients whose symptoms are strongly associated with impaired microcirculation and myofascial tension, leading to significant reductions in neck pain and stiffness and enhancing the patient's quality of life.[4] Furthermore, acupuncture is noted for its high safety profile and minimal side effects, making it a valuable option for long-term treatment and management.

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However, a significant gap remains in the literature. While numerous studies have explored CSR's pathology and acupuncture's mechanisms independently, there is a lack of a comprehensive review that systematically connects the dynamic, stage-specific pathophysiology of CSR with the diverse repertoire of acupuncture techniques available. Furthermore, as medicine advances towards a paradigm of precision and personalization, it is crucial to understand how mechanistic insights can be translated into tailored therapeutic strategies.

Therefore, the primary objective of this review is twofold. First, we will synthesize existing evidence to construct a clear framework linking the core pathological stages of CSR—from acute inflammation to chronic neurodegeneration—with the multi-target mechanisms of acupuncture. Second, we will bridge this mechanistic understanding to clinical application, exploring how different acupuncture modalities can be strategically employed and how emerging biomarkers, such as those from neuroimaging, can pave the way for precision acupuncture in CSR management. In doing so, this paper seeks to provide not only a profound interpretation of acupuncture's scientific basis but also a forward-looking perspective for future research and optimized clinical practice.

Epidemiology

CSR is a common neurological condition caused by compression of cervical nerve roots.[5] As the most predominant type of cervical spondylosis, CSR accounts for 60–70% of all cases, and its growing public health significance is demonstrated by the 14.76% average annual growth rate in related research publications since 2015.[6]

Advanced age is the primary risk factor, with signs of cervical spondylosis present in approximately 85% of individuals over 60.[7] The annual incidence of CSR is well-established by multiple studies at approximately 107 per 100,000 in males and 64 per 100,000 in females.[5] Its prevalence ranges from 1.07 to 1.76 per 1,000 in males and 0.63 to 5.8 per 1,000 in females, with specific figures varying by diagnostic criteria and geographical location.[8] The peak age of onset is 50–54 years, which aligns with the mean age of 51.35 years observed in clinical studies.[9]

The etiology is multifactorial, including degenerative changes, trauma, inflammation, and genetic factors.[6] However, lifestyle and occupational factors are major accelerators, particularly neck strain from prolonged electronic device use and occupations such as office work and manual labor.[10]

Clinical Manifestations

Neck Pain

One of the primary symptoms of CSR is neck pain. This pain can be persistent or intermittent and often worsens with neck movement.[11] The nature of the pain can vary, ranging from a dull ache to a burning or sharp sensation, and it frequently radiates from the neck to the shoulder, upper back, and upper limbs. Radiating pain typically follows the distribution of the affected nerve root, often involving the arm and fingers. This pain severely impacts the patient's daily life and work and can even affect their sleep quality and psychological state.[12]

Numbness and Tingling in the Upper Limbs

Patients with CSR often report numbness and tingling in the upper limbs. These sensory disturbances typically accompany pain and are located in the distribution area of the affected nerve root. The numbness and tingling may be intermittent, but as the disease progresses, these sensations may become persistent. Patients frequently describe these sensations as a prickling feeling, similar to being poked with needles, which significantly impacts their daily activities and sleep. Certain postures may exacerbate these symptoms, while rest or adjusting posture may provide some relief.[13]

Muscle Weakness and Atrophy

Due to nerve root compression, CSR patients may experience muscle weakness and atrophy. This weakness usually manifests as reduced strength in the upper limbs, particularly during daily activities such as gripping objects, lifting arms, or performing fine motor tasks.[14] Patients may find it increasingly difficult to perform these tasks as easily as before, with a noticeable decrease in grip strength and difficulty lifting the arm. Prolonged nerve compression can lead to gradual

muscle atrophy in the affected area, further limiting the patient's mobility. Muscle atrophy not only impacts function but also leads to visible changes such as muscle indentation or asymmetry, increasing the patient's psychological burden.[15]

Abnormal Tendon Reflexes

Abnormal tendon reflexes are a significant clinical manifestation in patients with CSR. Normally, tendon reflexes are elicited by gently tapping specific tendons to assess nerve and muscle function.[16] In CSR patients, tendon reflexes in the affected area may be diminished or absent, which is a key sign of nerve root compression.[17]

Neck Stiffness and Limited Mobility

Patients often experience neck stiffness, especially upon waking in the morning or after maintaining a fixed posture for an extended period. This stiffness is usually accompanied by pain, which limits the range of motion in the neck, making simple movements such as turning the head or bending the neck difficult.[18] Limited neck mobility not only affects daily life but can also lead to further muscle tension and increased pain, creating a vicious cycle. Patients may avoid certain activities due to pain and stiffness, further impacting their work and social life.[19]

Symptoms of Spinal Cord Compression

In severe cases of CSR, symptoms of spinal cord compression may occur.[20] These symptoms include gait instability, weakness in all four limbs, and loss of bladder or bowel control. Spinal cord compression is typically caused by a herniated disc or osteophyte directly pressing on the spinal cord, which requires urgent medical intervention.[21] Gait instability is characterized by an unsteady walk, with patients feeling as if they are walking on cotton. Limb weakness not only affects the upper limbs but can also extend to the lower limbs, making standing and walking difficult. Loss of bladder or bowel control is a severe sign of spinal cord compression, indicating the need for rapid diagnosis and treatment to prevent permanent nerve damage.[22]

Disease Progression and Staging of CSR

The natural course of CSR is a dynamic process, evolving through distinct stages. Understanding this progression, where the underlying pathology directly shapes the clinical picture, is critical for appropriate diagnosis and staged treatment. For clarity, the disease course is typically categorized into acute, subacute, and chronic phases.

The Acute Stage

The acute stage is defined by the sudden onset of severe, sharp, and often unbearable radicular pain. This intense pain is not merely from mechanical compression but is primarily driven by a severe local inflammatory response following irritation of the nerve root.[23] This process involves the release of pro-inflammatory mediators like TNF-α, leading to significant nerve root edema and a disruption of the BNB.[24] This biochemical irritation is often the principal cause of the severe symptoms, manifesting as pain that follows a specific dermatomal pattern and is characteristically aggravated by neck movements, coughing, or sneezing.[25] Clinically, this is accompanied by significant protective muscle spasms in the neck and shoulder girdle, and special provocative tests, such as the Spurling's test, are typically strongly positive.[26]

The Subacute Stage

As the initial inflammatory storm begins to subside, the disease enters a transitional subacute phase where the pathology shifts towards early-stage tissue remodeling. Activated fibroblasts initiate perineural fibrosis, leading to adhesions around the nerve root, while persistent abnormal afferent signals begin to induce the onset of central sensitization.[27] This pathological shift is reflected clinically as the nature of the symptoms changes. The sharp, intense pain may lessen, often replaced by a persistent, nagging ache. During this stage, sensory deficits such as numbness and paresthesia ("pins and needles") in the affected limb often become more prominent than the pain itself, and emerging motor weakness or abnormal reflexes become more apparent.[28] Consequently, while a patient's pain score may decrease, their functional disability, measured by tools like the Neck Disability Index, can remain significant.[29]

The Chronic Stage

The chronic stage is characterized by persistent symptoms driven by established, and often irreversible, pathological changes. Prolonged compression and inflammation lead to structural nerve damage, including axonal degeneration and demyelination, which can be verified by electrophysiological studies.[30] Furthermore, perineural fibrosis becomes dense and central sensitization becomes solidified, creating a state where pain can be disproportionate to, or independent of, the peripheral stimulus. This underlying pathology manifests as a constellation of chronic symptoms. The pain is typically a dull, diffuse ache that is harder to localize, but the most significant clinical features are established neurological deficits, including measurable muscle atrophy, persistent sensory loss, and diminished or absent deep tendon reflexes.[31] These chronic impairments significantly impact the patient's quality of life and can lead to secondary complications like depression and anxiety.[32] In severe cases, progressive compression may lead to the far more serious condition of cervical spondylotic myelopathy.[33]

Pathological Mechanisms of CSR in Modern Medicine

Intervertebral Disc Degeneration and Osteophyte Formation

Intervertebral disc degeneration and osteophyte formation are key pathological mechanisms in CSR, closely related and interacting with each other.[34] This mechanism typically develops with aging or the accumulation of chronic mechanical loading, progressively exacerbating nerve root compression and leading to a range of neurological impairments. The initial manifestation of intervertebral disc degeneration involves gradual structural damage.[35] The intervertebral disc, which is crucial for connecting the vertebral bodies, serves to absorb pressure and maintain spinal stability. Composed mainly of the annulus fibrosus and nucleus pulposus, the latter is rich in water content, which helps disperse pressure applied to the spine. Over time, the water content in the disc gradually decreases, resulting in reduced elasticity and loss of disc height.[36] This change compromises the disc's ability to effectively absorb mechanical pressure.

The degeneration of the intervertebral disc directly impacts the development of CSR. As the disc degenerates, it loses its ability to absorb and distribute pressure, leading to the collapse of the disc height and increased pressure on the adjacent nerve roots.[37] This mechanical compression is one of the primary causes of nerve root irritation and the subsequent pain and neurological dysfunction characteristic of CSR. The progression of disc degeneration often leads to disc herniation, where the nucleus pulposus protrudes through fissures in the annulus fibrosus, further compressing or irritating the cervical nerve roots.[38]

At the early stage of degeneration, the annulus fibrosus gradually thins and develops fissures, while dehydration of the nucleus pulposus accelerates the process. As the degeneration progresses, the nucleus pulposus may protrude through the fissures, resulting in a herniated disc. The herniated disc directly compresses adjacent nerve roots, triggering intense neurological symptoms such as pain, numbness, and muscle weakness.[39] Additionally, the protruding nucleus pulposus may also induce local inflammatory responses. Studies have shown that the release of inflammatory mediators from the herniated nucleus pulposus can activate local immune responses, further exacerbating nerve root damage and clinical symptoms.[40] These inflammatory mediators not only intensify the perception of nerve root compression but also contribute to the continuous transmission of pain signals, making the symptoms more severe and persistent.

As intervertebral disc degeneration worsens, spinal stability further declines, and the intervertebral spaces become narrower, leading to increased instability.[41] In response, the spine forms osteophytes as a compensatory mechanism to restore stability. Osteophyte formation is a typical adaptive response to degenerative changes, occurring at the vertebral margins and joint surfaces.[42] Osteophytes arise due to vertebral instability, as the mechanical stress across the spine is not effectively dissipated, leading to bone overgrowth. Although the primary function of osteophytes is to increase spinal stability, their growth has detrimental effects. As osteophytes enlarge, they gradually occupy space within the spinal canal, increasing pressure on the nerve roots or spinal cord, thereby exacerbating nerve root compression and potentially leading to spinal cord damage.[43] The growth of osteophytes is a significant contributor to the aggravation of nerve root compression in the context of spinal degeneration.[44] This process directly links osteophyte formation to the pathophysiology of CSR, as it plays a crucial role in increasing the severity of nerve root compression and contributing to the neurological deficits observed in affected patients.

Simultaneously with osteophyte formation, the persistent inflammatory response induced by intervertebral disc degeneration and nerve root compression causes a series of pathological changes in the nerve roots and surrounding tissues. As osteophytes proliferate, the space within the spinal canal narrows further, increasing pressure on the nerve roots.[45] This compression results in reduced blood supply to the nerve roots, leading to ischemia and insufficient nourishment, which further exacerbates nerve function impairment.[46] Chronic nerve root compression may result in nerve degeneration and death, ultimately causing permanent sensory loss and motor dysfunction.

Moreover, intervertebral disc degeneration and osteophyte formation are mutually reinforcing. The instability caused by disc degeneration leads to osteophyte formation, and the subsequent growth of osteophytes further exacerbates disc degeneration, creating a vicious cycle.[47] As the pathological process progresses, intervertebral disc degeneration and osteophyte formation not only cause nerve root compression but may also result in widespread spinal cord damage, especially in cases of central spinal stenosis. This narrowing often leads to more severe neurological impairments, including weakness in the limbs and gait instability.[48] Thus, intervertebral disc degeneration and osteophyte formation represent critical mechanisms in CSR, working together through mechanical compression and inflammatory responses to exacerbate nerve root damage and drive the onset and progression of clinical symptoms.[49]

Nerve Root Inflammation and Damage

Nerve root inflammation and damage is a critical mechanism in CSR, particularly after disc herniation or osteophyte formation, where localized compression triggers a complex inflammatory response.[23] This inflammation not only exacerbates nerve root damage through mechanical effects but also intensifies it through immune system activation, thereby complicating and worsening the clinical presentation.

When mechanical compression occurs, particularly from a herniated disc, the extruded nucleus pulposus is recognized as a foreign substance by the immune system. This stimulates local macrophages, mast cells, and disc cells to release the primary inflammatory instigators: TNF-α and IL-1β.[50]

These cytokines initiate a powerful cascade, inducing the production of other pro-inflammatory mediators like IL-6 and PGE2, the latter being a key molecule responsible for inducing pain hypersensitivity. This cascade activates and recruits immune cells, such as macrophages and T-cells, to the site of injury,[51] which in turn release more pro-inflammatory factors that perpetuate the local inflammatory response. The involvement of this inflammatory cascade makes the pathological process significantly more complex than mechanical compression alone.[52]

The release of these inflammatory mediators directly alters the microenvironment of the affected tissue, with edema formation being a key event.[53] Specifically, cytokines like TNF-α and IL-1β act directly on the microvascular endothelial cells around the nerve root, disrupting their tight junctions and increasing the permeability of the BNB.[54] This allows inflammatory cells and plasma proteins to leak into the nerve's inner layers, leading to intraneural edema. The resulting tissue swelling further compresses the nerve root, exacerbating nerve dysfunction and leading to intensified pain, numbness, and weakness. As this pressure persists, it restricts local blood flow, causing ischemia and reducing oxygen and nutrient supply, which further compromises nerve root function.[55]

In addition, chronic inflammation promotes the process of fibrosis. As the edema fluid accumulates and persists, it transforms into fibrous tissue. This process involves excessive collagen deposition and the proliferation of fibrous tissue, causing the nerve roots to adhere tightly to surrounding structures. This fibrosis not only limits the range of motion of the nerve roots but also severely hinders their ability to repair and regenerate.[56] Chronic fibrosis can lead to permanent nerve root dysfunction, manifested clinically as persistent pain and motor deficits.[57]

Furthermore, inflammation causes direct damage to the nerve root by sensitizing neurons and degrading their protective structures. Inflammatory mediators like TNF-α directly act on sensory neurons in the Dorsal Root Ganglion (DRG), upregulating the expression and sensitivity of specific ion channels, such as TRPV1.[58] This lowers the neuron's activation threshold, causing an exaggerated pain response to normal stimuli (peripheral sensitization) and even spontaneous, abnormal firing without any stimulus (ectopic discharges), which is the direct cause of radicular pain.[59] Concurrently, the inflammatory environment induces significant damage to the myelin sheath, the protective covering of nerve fibers crucial for rapid signal transmission.[60] Myelin damage leads to delayed or disrupted nerve signals, resulting

in impaired sensation and motor function. In severe cases, this progresses to axonal injury, which can cause neuronal degeneration and make the restoration of normal nerve function exceedingly difficult.[61]

These pathological changes are not limited to the local nerve root but also induce adaptive changes in the central nervous system. Chronic peripheral inflammation and pain signals can lead to central sensitization, a state of hyperexcitability in the spinal cord and brain that amplifies and maintains the pain experience, causing hyperalgesia and persistent neurological dysfunction.[62] This prolonged inflammation can lead to neurodegenerative changes, further diminishing the nervous system's capacity for recovery and potentially resulting in permanent sensory loss and motor deficits.[63]

Chronic inflammation also creates an increasingly hostile local cellular environment. In this environment, enzymes such as Matrix Metalloproteinases (MMPs) are activated, which degrade the extracellular matrix, including collagen and proteoglycans, surrounding the nerve root.[64] This action not only worsens the structural damage but also facilitates the migration and infiltration of more inflammatory cells, disrupting the supportive structures necessary for nerve repair. The continued accumulation of immune cells and the excessive release of cytokines create an environment that becomes progressively more hostile, further increasing the severity of the nerve damage.[65]

Thus, nerve root inflammation in CSR involves a cascade of destructive molecular and cellular mechanisms. It progresses from an initial trigger by key cytokines like TNF-α and IL-1β to a state of chronic damage characterized by edema from a compromised BNB, direct neuronal sensitization causing pain, and tissue destruction via fibrosis and MMP activity. Understanding these specific mechanisms—how inflammation releases mediators, forms edema, degrades myelin and axons, and induces fibrosis—is essential for developing effective therapeutic strategies aimed at controlling inflammation, promoting nerve repair, and improving patient outcomes.[66]

Blood Supply Disorders

Blood supply disorders are a critical factor in the development and progression of CSR, primarily caused by prolonged mechanical compression and local inflammatory responses that impair blood flow to the nerve roots.[67] The nerve roots receive blood supply through small arteries and a delicate microvascular network.[68] Compression or occlusion of these vascular structures disrupts blood flow, leading to ischemia and a reduction in the delivery of oxygen and nutrients to the nerve tissue. This ischemic environment triggers a series of cellular and molecular events that exacerbate nerve root damage.[69]

Ischemia induces oxidative stress, a state in whichROS are generated in excess. ROS, including superoxide anions and hydrogen peroxide, damage cellular structures such as lipids, proteins, and DNA, accelerating the process of neuroinflammation.[70] This damage promotes the activation of microglial cells and macrophages, which secrete pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6. These cytokines further exacerbate neuronal injury by amplifying the inflammatory response and disrupting neuronal signaling.[71] Oxidative stress also impairs mitochondrial function, further reducing ATP production and contributing to cell death via necrosis or apoptosis.[72]

Ischemia triggers the upregulation of angiogenic factors like VEGF, promoting new blood vessel formation. However, these vessels are often structurally abnormal and hyperpermeable, increasing inflammation and edema. The abnormal vessels can further compress nerve roots, worsening the initial ischemic injury. Additionally, the ischemic environment impairs immune response efficacy, making macrophages less effective in clearing apoptotic cells and inflammatory debris. This delays tissue repair, prolongs inflammation, and exacerbates nerve root damage, leading to chronic pain, weakness, and sensory disturbances.[73]

As blood supply continues to be impaired, the regenerative capacity of nerve roots diminishes, contributing to the chronic nature of CSR.[74] The failure of these nerve roots to repair themselves or regenerate efficiently increases the difficulty of treating CSR, whether through conservative methods or surgical intervention.[75] Blood supply disorders, therefore, play a central role in the pathophysiology of CSR, exacerbating nerve damage, hindering recovery, and making the condition more difficult to treat over time.

Muscle and Soft Tissue Changes

Nerve root compression can cause reflexive muscle spasms in the neck and shoulder muscles, leading to muscle stiffness and pain. Muscle spasms occur reflexively as the nerve roots are stimulated, causing continuous contraction of local muscles to reduce further damage.[76] However, prolonged muscle spasms decrease local blood flow, leading to the

accumulation of metabolic byproducts, which exacerbates pain and stiffness. Prolonged nerve root compression can lead to weakness and atrophy in the muscles of the affected area, impacting the patient's daily activities and quality of life.[77] Muscle weakness occurs due to impaired nerve signal transmission, preventing muscles from receiving adequate nerve stimulation. The surrounding soft tissues, such as ligaments and tendons, may undergo fibrosis and thickening due to prolonged compression and inflammation, leading to reduced elasticity and flexibility, further aggravating nerve root compression and creating a vicious cycle.[78]

Pathogenesis of CSR in Traditional Chinese Medicine

In Traditional Chinese Medicine (TCM), the pathogenesis of CSR is primarily related to Qi stagnation, blood stasis, meridian blockage, and organ dysfunction.[79] In simple terms, these concepts correspond to the obstruction of internal energy (Qi) and blood flow. Factors such as trauma, chronic illness, emotional stress, and prolonged sedentary behavior can disrupt the smooth flow of energy and blood within the body, similar to poor blood circulation and nerve compression in Western medicine.[80] This blockage can result in symptoms such as pain and numbness.[81] TCM also holds that these issues can further affect other functional organs in the body, leading to more complex symptoms.[82] Overall, TCM emphasizes alleviating symptoms and improving the condition by regulating the flow of energy and blood within the body, a concept that parallels the Western approach of improving blood circulation and reducing nerve compression to treat the disease.

Mechanisms of Acupuncture in Treating CSR

The mechanism shown above is illustrated in Figure 1.

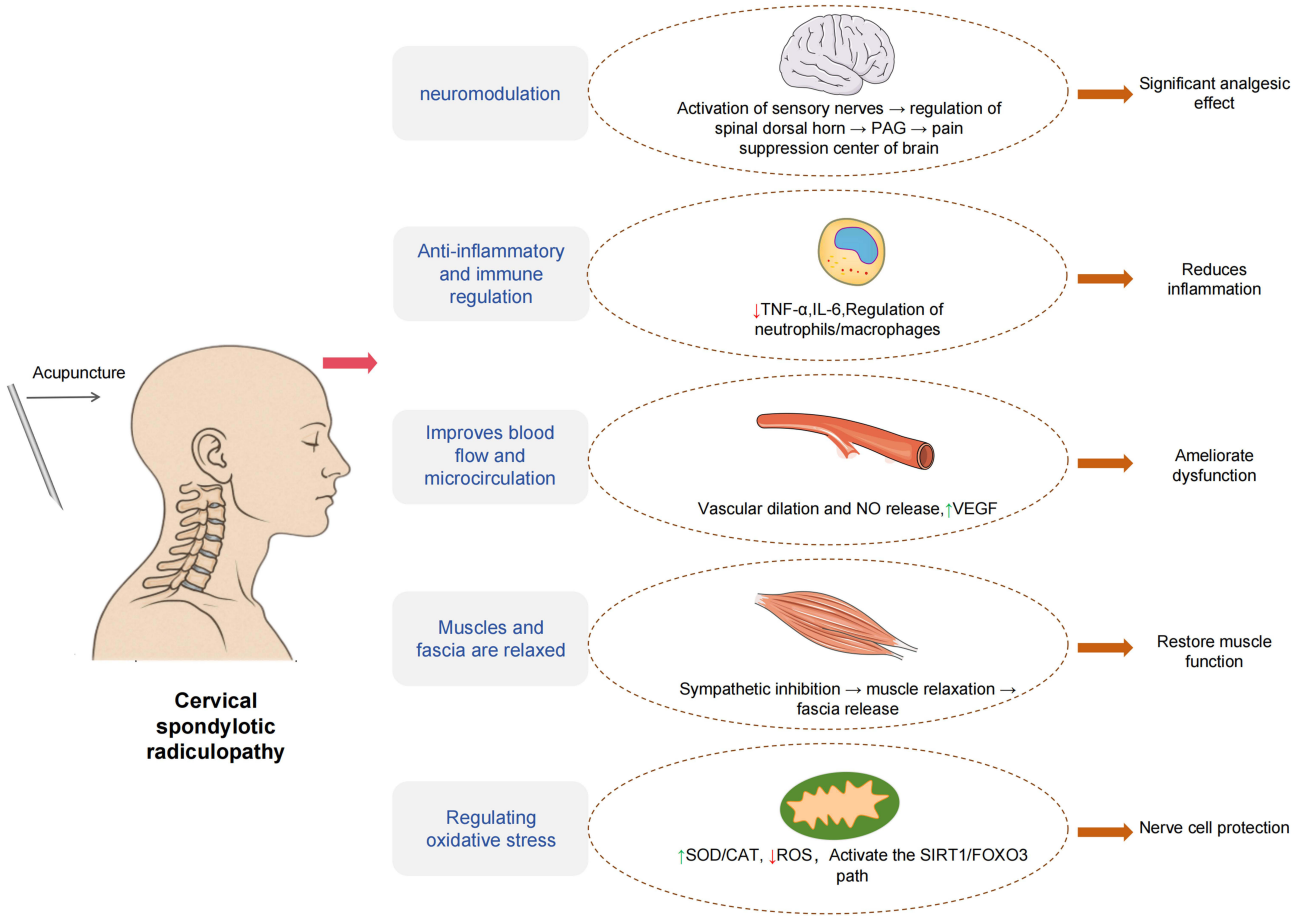

Figure 1 Mechanisms of acupuncture therapy for cervical spondylotic radiculopathy (the red downward arrows indicate inhibitory or down-regulatory effects, while the green upward arrows indicate stimulatory or up-regulatory effects).

Counteracting Nerve Root Inflammation and Damage

As established in Nerve Root Inflammation and Damage, nerve root inflammation, driven by pro-inflammatory cytokines like TNF-α and IL-1β, is a critical pathological driver of CSR. This inflammatory cascade leads to edema from a compromised Blood-Nerve Barrier, myelin sheath damage, and neuronal sensitization. Acupuncture exerts a potent anti-inflammatory effect by directly modulating these pathways.

Firstly, acupuncture treatment has been shown to significantly reduce the release of local and systemic inflammatory mediators, including PGE2, TNF-α, and IL-6.[83] By lowering the levels of these key mediators identified in CSR's pathology, acupuncture directly reduces inflammation, thereby alleviating pain and swelling.[84] This is further supported by evidence that acupuncture inhibits the expression of cyclooxygenase-2, an enzyme that synthesizes prostaglandins and promotes inflammation.[85]

Secondly, acupuncture regulates the body's cellular immune response. It can balance the levels of pro-inflammatory and anti-inflammatory cytokines, and modulate immune cell activity, such as reducing the infiltration of neutrophils and macrophages at the site of nerve compression.[86–88] This neuro-immune modulation is also achieved via the hypothalamic-pituitary-adrenal (HPA) axis. By stimulating specific acupoints, acupuncture can regulate the activity of the HPA axis, increasing cortisol release, which contributes to its systemic anti-inflammatory and immunomodulatory effects.[89,90]

Modulating Nociceptive Pathways and Central Sensitization

The intense radicular pain characteristic of CSR stems from both direct nerve compression and the subsequent peripheral and central sensitization of the nervous system, as discussed in Nerve Root Inflammation and Damage. Acupuncture's most well-documented effect is its powerful analgesic capability, which operates at multiple levels of the nervous system to interrupt these pain signals.

At the spinal level, nerve impulses from acupuncture activate inhibitory interneurons in the dorsal horn, which release neurotransmitters like gamma-aminobutyric acid to suppress the transmission of nociceptive signals to the brain. This segmental inhibition effectively "gates" the pain at the entry point to the central nervous system.

Ascending to the brain, these impulses activate key pain-regulating centers, most notably the periaqueductal gray (PAG). As demonstrated by Wang Q, electroacupuncture activates proopiomelanocortin neurons in the arcuate nucleus to release β-endorphins, which then act on the PAG to produce a strong, systemic analgesic effect.[91] This modulation of the endogenous opioid system is a cornerstone of acupuncture analgesia.[92] Furthermore, acupuncture influences other crucial neurotransmitters like serotonin and norepinephrine, which are involved in descending pain inhibition pathways that further suppress pain signals at the spinal level.[93] fMRI studies corroborate these mechanisms, showing that acupuncture alters the activity and functional connectivity of the brain's pain network, including the thalamus and prefrontal cortex.[94,95]

Restoring Impaired Microcirculation and Mitigating Oxidative Stress

Blood Supply Disorders established that impaired microcirculation is a core pathological feature, leading to a vicious cycle of ischemia, hypoxia, and a surge in oxidative stress that further damages nerve roots. Acupuncture directly addresses this cycle through a dual mechanism of improving blood flow and enhancing antioxidant defenses.

Acupuncture stimulation induces local vasodilation, increasing blood flow and the supply of oxygen and nutrients to the ischemic nerve root.[96] This is achieved partly through neural reflexes that balance the autonomic nervous system, promoting systemic vasodilation],[97] and through the local release of vasodilators like nitric oxide.[98] The improved microcirculation also helps to clear accumulated inflammatory mediators and metabolic byproducts.[99]

Concurrently, acupuncture directly counteracts the resulting oxidative damage. It enhances the activity of endogenous antioxidant enzymes like superoxide dismutase and catalase (CAT), which neutralize excess reactive oxygen species (ROS).[100,101] By improving mitochondrial function, for instance through the Sirt1/FOXO3/PINK1/Parkin signaling pathway, acupuncture reduces the primary source of ROS production.[102] This attenuation of oxidative stress slows lipid peroxidation, protecting the structural integrity of nerve cell membranes,[103] and exerts a powerful neuroprotective effect by reducing apoptosis and promoting the release of neurotrophic factors like NGF, which are essential for nerve repair and regeneration.[104,105]

Alleviating Reflexive Muscle Spasm and Fascial Tension

As described in Muscle and Soft Tissue Changes, nerve root irritation in CSR triggers reflexive muscle spasms and fascial tension in the neck and shoulders, which contributes significantly to the patient's pain and limited mobility. Acupuncture provides effective relief by directly targeting these secondary musculoskeletal changes.

The stimulation of specific acupoints modulates the autonomic nervous system, particularly by inhibiting sympathetic nervous system excitability, which reduces overall muscle tone and alleviates spasms.[106] Locally, the mechanical action of the needle and the subsequent improvement in blood circulation helps to relax contracted muscle fibers, increase oxygen supply, and wash out pain-inducing substances.[107] At the fascial level, acupuncture can release adhesions and reduce tension in the connective tissue layers that encase the muscles, thereby improving flexibility and restoring normal movement patterns.[108] By breaking this cycle of pain and tension, acupuncture not only provides symptomatic relief but also reduces the secondary mechanical strain on the cervical spine.

Bridging Mechanisms to Clinical Practice: Towards Precision Acupuncture for CSR

A thorough understanding of acupuncture's mechanisms is crucial, but its true value lies in translating this knowledge into effective and optimized clinical strategies. The traditional "one-size-fits-all" approach to acupuncture is being replaced by a more nuanced, evidence-based paradigm. This section provides a critical perspective on how to tailor acupuncture therapy for CSR by considering different techniques, the specific stage of the disease, and the principles of precision medicine.

Differentiating Acupuncture Modalities for Targeted Effects

While often grouped together, different acupuncture techniques exert distinct physiological effects, making them suitable for different pathological targets in CSR.

Manual Acupuncture (MA)

As the most traditional form, MA's primary strength lies in its ability to alleviate reflexive muscle spasms and fascial tension (Alleviating Reflexive Muscle Spasm and Fascial Tension) by targeting local trigger points (Ashi points) and anatomically significant acupoints (eg, Jiaji, GB21).[109] Its effect on microcirculation is also well-documented, making it a foundational treatment across all stages.

Electroacupuncture (EA)

EA offers superior modulation of nociceptive pathways (Modulating Nociceptive Pathways and Central Sensitization) due to its continuous and controllable stimulation. Critically, the choice of frequency allows for targeted neurochemical responses. Low-frequency (2 Hz) EA preferentially stimulates the release of β-endorphins and enkephalins, ideal for the dull, aching pain characteristic of the chronic stage.[110] Conversely, high-frequency (100 Hz) EA primarily releases dynorphins, which may be more effective for the sharp, intense pain of the acute inflammatory stage.[111] This makes EA a powerful tool for targeted analgesia.

Warm Needle Acupuncture

This technique combines MA with moxibustion, applying heat directly to the needle. This is particularly relevant for addressing the impaired microcirculation and ischemia discussed in Blood Supply Disorders. The thermal effect enhances local vasodilation, promotes the clearance of inflammatory mediators, and alleviates the deep-seated muscle stiffness common in the subacute and chronic stages.[112,113]

A Stage-Specific Approach to Treatment

Based on the disease progression outlined in Disease Progression and Staging of CSR, a more effective clinical approach involves tailoring the treatment strategy to the dominant pathology of each stage.

Acute Stage Strategy

The primary goals are potent anti-inflammation and strong analgesia. Treatment should focus on techniques that powerfully modulate the nervous and immune systems.[114] High-frequency EA on distal acupoints known for their systemic anti-inflammatory effects could be prioritized to avoid aggravating local inflammation.[115] This approach aims to control the "inflammatory storm" and interrupt central sensitization before it becomes established.

Subacute and Chronic Stage Strategy

As the pathology shifts towards tissue remodeling, fibrosis, and established neurological deficits, the focus should move to promoting local microcirculation, nourishing the nerve root, and releasing chronic muscle tension.[114,115] Local acupoints (eg, Jiaji, cervical segment points) combined with warm needle acupuncture would be highly beneficial. Low-frequency EA can be used to manage persistent neuropathic pain and promote the release of neurotrophic factors essential for nerve repair.[116]

The Future: Precision Acupuncture Guided by Biomarkers

The ultimate goal is to move towards precision acupuncture, where treatment is individualized for maximal efficacy. Neuroimaging offers a promising avenue for achieving this. Recent fMRI studies have demonstrated that the pre-treatment functional connectivity of key brain regions involved in pain processing, such as the periaqueductal gray (PAG), can predict the analgesic response to acupuncture therapy.[117,118] This suggests that neuroimaging profiles could one day serve as biomarkers to identify patients who are most likely to respond to acupuncture. By integrating such objective biomarkers with clinical presentation, practitioners could develop highly personalized treatment prescriptions, selecting the optimal acupuncture modality, acupoints, and stimulation parameters for each individual, thereby cementing acupuncture's role in modern, evidence-based medicine.

Conclusion

This review systematically bridges the pathophysiology of CSR with the multi-target therapeutic mechanisms of acupuncture. We have established that acupuncture is not a monolithic treatment but a versatile intervention that can modulate the neuro-immune-circulatory network at the core of CSR's pathology. Its actions, ranging from down-regulating key inflammatory mediators like TNF-α and modulating central pain pathways via endogenous opioids to restoring local microcirculation, directly counteract the destructive processes of the disease.

More importantly, this review argues for a critical shift from a generalized to a precise and stage-specific application of acupuncture. By differentiating modalities like electroacupuncture for targeted analgesia and warm needle acupuncture for chronic ischemia, and tailoring these tools to the dominant pathology of the acute, subacute, and chronic stages, clinical efficacy can be significantly enhanced. Looking forward, the integration of objective biomarkers, particularly from neuroimaging studies that can predict treatment responders, holds the key to unlocking true personalization in acupuncture therapy.

To solidify its role as a mainstream, evidence-based treatment, future research must move beyond simply asking "if" acupuncture works, to answering "how, when, and for whom" it works best. Rigorous clinical trials designed to compare these tailored, stage-specific protocols, coupled with translational studies to validate predictive biomarkers, are essential for building a robust scientific foundation that will fully integrate acupuncture into the modern management of CSR.

Abbreviations

CSR, Cervical Spondylotic Radiculopathy; TCM, Traditional Chinese Medicine; GABA, gamma-aminobutyric acid; POMC, proopiomelanocortin; ARC, arcuate nucleus; PAG, periaqueductal gray; ROS, reactive oxygen species; HPA, hypothalamic-pituitary-adrenal; BNB, blood-nerve barrier; PAG, periaqueductal gray.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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