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The Role and Mechanism of Acupuncture Analgesia in the US Opioid Crisis Research

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Abstract: The US opioid crisis has become a serious public health issue, causing tens of thousands of deaths and tremendous economic loss annually. Acupuncture, as a traditional non-pharmacological method of analgesia, has demonstrated extraordinary value in addressing this crisis. This paper systematically elucidates the causes and impacts of the US opioid crisis and deeply explores the neurobiological mechanisms of acupuncture analgesia, including the activation of the endogenous opioid system, neurotransmitter regulation, and anti-inflammatory and immune modulation via multiple pathways. By analyzing the clinical evidence for acupuncture in the management of acute and chronic pain, opioid dosage reduction, and addiction treatment, we demonstrate the feasibility and efficacy of acupuncture as an alternative to opioid therapy. Research shows that acupuncture can not only effectively relieve various types of pain but also reduce opioid consumption and treat opioid dependence and addiction. However, the promotion of acupuncture in the US still faces multi-faceted challenges, including issues of standardization, limited insurance coverage, and insufficient high-quality evidence. Future efforts should focus on strengthening multidisciplinary research collaboration, improving standardized treatment protocols, and integrating acupuncture into comprehensive pain management systems to provide a safer, more cost-effective, non-pharmacological alternative for resolving the opioid crisis.

Keywords: Acupuncture; Analgesic Mechanism; Opioid Crisis; Pain Management; Non-pharmacological Therapy

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1.Introduction

The US opioid crisis is one of the most severe public health disasters of the 21st century. Since the late 1990s, the over-prescription and misuse of opioid medications have led to a sharp rise in addiction and death rates. According to data from the US Centers for Disease Control and Prevention (CDC), approximately 860,000 Americans died from an opioid overdose between 1999 and 2023 [1]. Approximately 105,000 people died from drug overdose in 2023, nearly 80,000 of which involved opioids (approximately 76%). The number of people who died from an opioid overdose in 2023 was nearly 10 times the number in 1999 [2]. This crisis has not only caused massive human casualties but has also imposed a heavy burden on the socioeconomic structure, with estimated annual losses exceeding trillions of dollars. On August 10, 2017, President Trump declared the opioid crisis a national public health emergency. It was estimated that the economic cost of the US opioid crisis in 2017 was $1.021 trillion, including an estimated $471 billion for the cost of opioid use disorder and an estimated $550 billion for the cost of fatal opioid overdose [3].

The root of the opioid crisis lies in the imbalance of pain management strategies. For a long time, opioids were considered the primary treatment for chronic pain, but their high addictiveness and serious side effects have become increasingly apparent. Finding safe and effective non-pharmacological methods for analgesia has become an urgent priority. Against this backdrop, on July 13, 2017, the US National Academies of Sciences (NAS), Engineering (NAE), and Medicine (NAM) jointly released a report, "Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use," which dedicated a chapter to the clinical study of acupuncture for various types of pain, recognizing it as a potentially effective non-pharmacological therapy for pain [4]. Subsequently, the American Society of Acupuncturists (ASA) and six collaborating organizations jointly published a white paper titled "The Role of Acupuncture in Addressing the Opioid Crisis: Evidence, Cost and Health Services Feasibility of Acupuncture as a First-Line Non-Pharmacological Therapy for Treatment and Control of Pain" [5, 6].

In response to the risks of pharmacological treatments for acute and chronic pain and the ongoing opioid crisis, the US CDC and the Food and Drug Administration (FDA) recommend non-pharmacological pain management methods as first-line care. Acupuncture has been listed as a preferred first-line option by the Army Surgeon General's Pain Management Task Force and the American College of Physicians (ACP). The Agency for Healthcare Research and Quality (AHRQ), the National Institutes of Health (NIH), and the National Academy of Medicine have all included acupuncture as part of comprehensive pain care [7]. Acupuncture, a traditional Chinese medical therapy with thousands of years of history, has received increasing attention due to its significant analgesic effects, minor side effects, non-addictive nature, and low cost.

This paper aims to comprehensively analyze the role and mechanisms of acupuncture analgesia in addressing the US opioid crisis. It demonstrates that integrating acupuncture into the pain management system can not only alleviate the American healthcare burden but also offer patients more treatment options, reduce opioid dependence, and thereby lower the risk of addiction and mortality.

2.Overview of the US Opioid Crisis

2.1 Analysis of the Crisis's Causes

The etiology of the opioid crisis is complex and multi-factorial. The initial catalyst was the healthcare system's reliance on pharmacological solutions, compounded by the intense pressure on clinicians to alleviate pain—a measure categorized by the World Health Organization (WHO) as the "fifth vital sign," alongside standard metrics like blood pressure and temperature. Pharmaceutical corporations aggressively promoted their products, using deceptive marketing to assure the medical community that opioids were safe for the extended management of chronic non-cancer pain, minimizing concerns about dependency.

This challenge was subsequently magnified by inadequate regulatory oversight. Early, lax standards for opioid prescriptions permitted physicians to readily dispense substantial drug quantities, while the absence of effective patient education and robust risk assessment mechanisms meant many individuals initiated use without recognizing the significant addiction risks. Furthermore, the problem was intensified by a dearth of accessible alternative treatments; safer options, such as physical therapy and acupuncture, were frequently underutilized due to insufficient insurance coverage and limited availability. Finally, socioeconomic factors provide an underlying context, as economic hardship, unemployment, and social isolation are strongly correlated with heightened drug abuse risk, leading to opioid addiction rates significantly exceeding the national average in regions experiencing economic downturn.

2.2 Scale and Impact of the Crisis

The magnitude of the opioid crisis is staggering, representing a pervasive societal issue that transcends specific demographics, affecting individuals across all ages, racial groups, and socioeconomic strata. While its reach is broad, certain populations have been disproportionately impacted, notably middle-aged white males, residents of rural areas, and low-income communities.

The resultant economic toll is immense, extending far beyond direct healthcare expenditures. The overall financial burden encompasses substantial costs related to diminished labor force productivity, expenses within the criminal justice system, and greatly increased child welfare expenditures. The widespread prevalence of opioid addiction has driven a dramatic surge in social crises, including increased family dissolution, child neglect, and abuse. Furthermore, the crisis has led to a noticeable

decline in labor force participation across numerous communities, directly undercutting regional economic vitality and growth.

3.Neurobiological Mechanisms of Acupuncture Analgesia

3.1 Activation of the Endogenous Opioid System

One of the core mechanisms of acupuncture analgesia is the activation of the body's endogenous opioid peptide system. Research indicates that needling stimulation promotes the release of endogenous opioid peptides such as β-endorphin, enkephalin, and dynorphin from the central nervous system. These substances bind to opioid receptors (μ、δ、κ type) to produce analgesic effects, raising the pain threshold and decreasing pain sensitivity. Animal experiments confirm that the use of the opioid receptor antagonist naloxone can partially block the analgesic effect of acupuncture. Other studies have shown that intracerebroventricular or intrathecal injection of cholecystokinin octapeptide (CCK-8), an endogenous opioid antagonist, can block the analgesia induced by morphine or electroacupuncture (EA) in rats [8]. This suggests that an opioid mechanism is involved in mediating acupuncture analgesia. Different frequencies of electroacupuncture stimulation can selectively release different endogenous opioid peptides. Low-frequency EA (2 Hz) is mediated by μ and δ opioid receptors, stimulating the CNS network to release β-endorphin, enkephalin, and endorphin, while high-frequency EA (100 Hz) is mediated by κ opioid receptors, releasing dynorphin [9]. The alternating use of high and low-frequency EA stimulation may offer additional analgesic benefits by activating both systems simultaneously [10]. This frequency-dependence provides a theoretical basis for the individualization and precision of acupuncture treatment.

3.2 Regulation of Neurotransmitters

In addition to the opioid peptide system, acupuncture also produces analgesic effects by regulating multiple neurotransmitters. The 5-hydroxytryptamine (5-HT) system is an important descending inhibitory pathway, and serotonin (5-HT) was hypothesized as an analgesic neurotransmitter in early studies [11]. Research shows that acupuncture can increase the pain threshold, and this analgesic effect is attenuated after injection of p-chlorophenylalanine (a serotonin synthesis inhibitor) [12]. Therefore, serotonin is considered to play a major role in acupuncture analgesia.

The norepinephrine (NE) system is also involved in acupuncture analgesia. Norepinephrine-containing neurons originate from various brain regions, including the raphe nuclei, locus coeruleus, periaqueductal gray, and the A1, A2, and A4-A7 nuclei of the brainstem. These neurons project to the forebrain and descend along the dorsolateral funiculus of the spinal cord, playing a role in pain modulation. Acupuncture can activate the locus coeruleus in the brainstem, increasing NE release, and inhibiting nociceptive transmission in the spinal dorsal horn via α 2-adrenergic receptors [13]. Recent research has also found that acupuncture can regulate the adenosine system. Adenosine concentration is significantly elevated in local tissues after needling, producing a local analgesic effect by activating the A1 receptor. This finding reveals the peripheral mechanism of acupuncture's action, providing a new perspective for understanding the immediate analgesic effect of needling [14].

3.3 Neuroinflammation and Immune Regulation

Chronic pain is often accompanied by neuroinflammatory responses. Acupuncture has anti-inflammatory effects. Studies indicate that chronic electroacupuncture (EA) can decrease the activity of T and B lymphocytes in the lymph nodes of mice with collagen-induced arthritis [15]. In another study, the activity of splenic Natural Killer (NK) cells was enhanced in mice after chronic EA, an effect that could be eliminated by injecting the endorphin antagonist naloxone [16]. Furthermore, studies have found that acupuncture can reduce the release of pro-inflammatory factors and increase the production of anti-inflammatory factors. In addition, acupuncture can regulate the vagus nerve-cholinergic anti-inflammatory pathway. This is a crucial neuro-immune regulatory pathway that suppresses peripheral inflammatory responses by releasing acetylcholine. Needling specific acupoints can activate this pathway, producing a systemic anti-inflammatory effect [17]. These immune regulatory effects help to alleviate inflammatory pain.

3.4 Inhibition of Central Sensitization

A key pathological mechanism of chronic pain is central sensitization, which is the enhanced responsiveness and lowered threshold of the central nervous system to painful stimuli. Numerous documented studies indicate that the signaling system of glutamate and its receptors is crucial in the processing of spinal nociception and central sensitization [18]. Acupuncture can

suppress central sensitization through multiple pathways. Firstly, needling can reduce the release of excitatory amino acids (such as glutamate), decreasing the excitability of spinal dorsal horn neurons. Secondly, immunochemical studies revealed that 2 Hz electroacupuncture (EA) administered to rats with neuropathic pain not only alleviated the pain but also reduced the expression of the NMDA receptor subunit NR1 in the spinal dorsal horn [19]. Choi et al. used a similar method but studied CFA-induced inflammatory pain rats and found that the expression of both NR1 and NR2A NMDA receptor subunits was reduced in the spinal dorsal horn [20]. This suggests that acupuncture can regulate the expression and function of NMDA receptors, which are key molecular mechanisms in the formation of central sensitization.

Long-term repeated acupuncture treatment can reverse neuroplastic changes caused by chronic pain. After nerve injury, hyperexcitability similar to long-term potentiation (LTP) may occur in spinal nociceptive synaptic transmission, which may be the basis for neuropathic pain. Animal studies show that long-term depression (LTD) of synaptic strength in the spinal dorsal horn may be the underlying mechanism for the differential analgesic effects of low- and high-frequency EA in neuropathic pain. Therefore, the direction of long-term synaptic plasticity, similar to LTP or LTD, in the spinal dorsal horn may determine the onset or inhibition of neuropathic pain [21]. Acupuncture can restore the function of inhibitory neurons in the spinal cord and brain, re-establishing the excitation-inhibition balance, thereby alleviating chronic pain states. This action may explain the long-term efficacy of acupuncture in chronic pain.

In summary, the neurobiological mechanisms of acupuncture analgesia are multi-target and multi-level, involving multiple systems from the periphery to the central nervous system. By mechanically stimulating acupoints, afferent nerve signals are activated, leading to the release of analgesic substances from the central nervous system (especially the endogenous opioid system) and modulating brain regions related to pain perception, emotion, and cognition, thus achieving a multi-level, holistic analgesic effect.

4.Clinical Application of Acupuncture in Pain Management

4.1 Evidence for Acupuncture Treatment of Acute Pain

Research indicates that acupuncture not only has significant therapeutic effects on various chronic pains, but its role in acute pain is even more striking. It is reported that over 50% of chronic opioid use begins in an acute pain care setting, and acupuncture may be able to reduce this risk. Arya Nielsen et al. conducted a study on acupuncture therapy as an evidence-based, non-pharmacological strategy for integrated acute pain care, updating the evidence base for acupuncture in acute pain by reviewing 22 systematic reviews and meta-analyses on post-operative and peri-operative pain (including opioid-sparing effects) and acute non-surgical and traumatic pain (including acute pain in the Emergency Department). The study found that acupuncture therapy is an effective strategy for treating acute pain, with the potential to avoid or reduce reliance on opioids. Acupuncture treatment for acute pain has a very low risk and is an important strategy in comprehensive acute pain care [22].

4.2 Evidence for Acupuncture Treatment of Chronic Pain

Chronic pain is the main indication for opioid prescriptions and the most widespread area of acupuncture application. Extensive clinical studies and systematic reviews confirm the effectiveness of acupuncture in treating various types of chronic pain.

4.2.1 Chronic Low Back Pain:

This is one of the most common types of chronic pain and a major reason for opioid prescriptions. Cochrane reviews and other systematic reviews consistently show that acupuncture is more effective in reducing pain intensity and mildly improving function in patients with chronic low back pain compared to no treatment or usual care (such as medication, rest advice). Multiple high-quality Randomized Controlled Trials (RCTs) show that acupuncture treatment for chronic low back pain is superior to conventional treatment or sham acupuncture [23]. A prominent large-scale study involving 1,162 patients found that those receiving acupuncture had significantly better pain relief and functional improvement than the control group, with effects lasting at least 6 months [24].

4.2.2 Osteoarthritis Pain:

Knee and hip osteoarthritis are major sources of chronic pain in the elderly. Acupuncture shows good results in the management of osteoarthritis pain. A meta-analysis of 16 RCTs involving 3,498 patients with knee and hip osteoarthritis showed that

acupuncture significantly reduced pain and improved joint function compared to sham acupuncture [25]. Clinical guidelines from the American College of Rheumatology list acupuncture as a conditional recommendation for knee osteoarthritis treatment.

4.2.3 Chronic Neck Pain:

Acupuncture also has a definite effect on chronic neck pain. A systematic review of 18 RCTs explicitly noted that acupuncture, as an adjunctive therapy, provides sustained pain relief for at least 3 months and shows efficacy in improving functional disability that lasts beyond 3 months . This is a distinct advantage of acupuncture's efficacy, indicating that it positively impacts the improvement of patients' daily activities and functional limitations [26].

4.2.4 Migraine and Tension-Type Headaches:

Acupuncture has a long history in the prevention and treatment of headaches. A Cochrane systematic review including 22 RCTs with 4,985 migraine patients found that acupuncture can reduce the frequency of migraine attacks, with effects comparable to prophylactic medication but with fewer side effects [27]. For tension-type headache, acupuncture also shows good results, superior to usual care and sham acupuncture [28].

4.3 Evidence of Acupuncture Reducing Opioid Use

A growing number of studies are focusing on the role of acupuncture in reducing opioid use. This has direct implications for addressing the opioid crisis. A study evaluated 172 adult patients who received acupuncture treatment at a US Air Force Medical Center for at least 4 times over a year. The assessment measured changes in the volume of prescriptions for opioids, muscle relaxants, benzodiazepines, and non-steroidal anti-inflammatory drugs (NSAIDs) in the 60 days before the first acupuncture treatment and the corresponding 60 days one year later, as well as changes in "Measure Yourself Medical Outcome Profile" scores for symptoms, activity, and quality of life. The results found that patients' opioid prescriptions decreased by 45%, muscle relaxants by 34%, NSAIDs by 42%, and benzodiazepines by 14%. Additionally, patients showed improvement in symptom control, functional capacity, and well-being. This study demonstrates the feasibility of acupuncture as an opioid-sparing strategy [29].

In post-operative pain management, acupuncture has also shown an effect in reducing opioid use. Reports suggest that acupuncture can reduce post-operative opioid requirements by over 60% [5]. Acupuncture can also reduce common side effects like nausea and vomiting. This has been verified in various types of surgeries, including neurosurgery, gynecological surgery, and abdominal surgery [30].

A preliminary randomized controlled trial also showed that in patients with non-malignant chronic pain, electroacupuncture reduced opioid use by 39%, an effect that persisted for 8 weeks after the EA treatment stopped [31]. Another study targeting cancer pain patients found that acupuncture and/or acupressure in six randomized controlled trials was significantly associated with reduced cancer pain and decreased use of morphine analgesics [32]. These studies demonstrate that acupuncture can effectively reduce patient pain and opioid consumption in both non-malignant and cancer pain, improving patients' quality of life, further proving that acupuncture can serve as an effective complementary or alternative therapy to opioids.

4.4 Application of Acupuncture in Opioid Addiction Treatment

Acupuncture can not only reduce opioid use but also be used to treat opioid addiction. Auricular acupuncture is the most commonly used method, especially the NADA (National Acupuncture Detoxification Association) protocol, which involves needling five points on the ear: Shenmen, Sympathetic, Kidney, Liver, and Lung.

Clinical studies show that acupuncture can alleviate opioid withdrawal symptoms, including anxiety, insomnia, muscle pain, and irritability. A study by Guangzhou University of Chinese Medicine indicated that acupuncture treatment could significantly reduce methadone maintenance dosage and opioid craving, and improve sleep quality to a certain extent. This research provides reliable clinical evidence for acupuncture intervention in methadone dose reduction [33]. This demonstrates that acupuncture can increase the success rate of withdrawal and reduce relapse rates in patients with opioid addiction.

The mechanism of acupuncture in opioid addiction treatment may include: regulating the dopamine system, reducing drug craving; activating the endogenous opioid peptide system, alleviating withdrawal symptoms; regulating stress response, improving emotional state; and improving sleep quality, promoting recovery. Many detoxification centers have integrated

acupuncture into their comprehensive treatment programs as a complement to medication-assisted treatment.

4.5 Safety of Acupuncture Treatment

A major advantage of acupuncture is its high safety profile. Large-scale studies show that the incidence of serious adverse events from acupuncture is extremely low, at approximately 7.98 per 1 million treatments. Minor adverse events occur 9.4 times per 100 treatments. Half of these adverse events are localized bleeding, pain, or redness at the needling site, which are often considered expected treatment responses and are usually self-limiting, requiring no special handling [34]. Compared to opioids, acupuncture has no risk of addiction, respiratory depression, constipation, or other severe side effects. This makes acupuncture particularly suitable for patients requiring long-term pain management, as well as those sensitive to drug side effects or with a history of substance abuse.

5.Current Status and Challenges of Acupuncture Application in the US

Acupuncture's integration into the United States healthcare system began in the 1970s and is now a well-established practice, with all fifty states regulating and licensing an estimated 50,000 practitioners who provide millions of treatments annually. Its acceptance is expanding significantly, with prestigious institutions like the Mayo Clinic and Cleveland Clinic offering these services, and the Centers for Disease Control and Prevention (CDC) recommending it as a non-pharmacological option to address the opioid crisis. A major step toward broader access was the 2020 decision by Medicare to cover acupuncture for chronic lower back pain. However, widespread utilization faces several persistent barriers: the inconsistent insurance coverage often results in high out-of-pocket costs that undermine the sustainability of long-term treatment. On the patient side, the fear of needles remains an obstacle for many potential users. Finally, a significant lack of public awareness means many beneficiaries are unaware of the conditions acupuncture can treat or how to find a qualified provider.

6.Integration of Acupuncture with Comprehensive Pain Management

Modern pain medicine increasingly champions a multimodal or comprehensive approach to managing pain, acknowledging its multifaceted nature which encompasses physiological, psychological, and social dimensions. This strategy mandates the synergistic use of diverse treatment modalities to enhance efficacy. Typically, comprehensive pain management incorporates a range of therapies, including prescribed medication, physical rehabilitation, exercise regimens, psychological counseling, massage, and acupuncture. This multi-pronged technique allows clinicians to target various pain aspects simultaneously, thereby augmenting overall treatment effectiveness and mitigating the limitations and adverse effects associated with reliance on a single intervention.

Acupuncture serves as a particularly effective non-pharmacological treatment, lending itself well to integration with other therapies for more holistic pain relief. It functions as a valuable alternative or complement to opioid medications, aiding in the reduction of drug dependency while simultaneously improving both emotional distress and physical discomfort. Notably, the military and Veterans Health Administration (VA) systems have been pioneers in integrating this approach. Numerous VA medical centers and military installations have successfully implemented programs, such as "Battlefield Acupuncture," to offer rapid pain relief to veterans and injured service members. The successful deployment and experience garnered from these initiatives provide a practical model for adoption within the civilian healthcare sector.

7.Future Research Directions and Policy Recommendations

Despite the substantial advancements achieved in research concerning acupuncture analgesia, several critical questions remain unanswered, necessitating further investigation and systemic change.

Primarily, there is an urgent need for more high-quality, large-sample randomized controlled trials (RCTs) to precisely evaluate acupuncture's efficacy across various pain conditions. These studies must move beyond assessing immediate pain reduction to focus on long-term effectiveness and robust cost-effectiveness analyses, particularly through direct comparative studies against current standard pharmacological treatments.

Secondly, realizing the full potential of acupuncture as a key strategy to mitigate the opioid crisis requires stronger policy support. Crucial governmental actions include expanding insurance coverage for acupuncture services, increasing dedicated funding for research into its mechanisms and applications, and strengthening the professional standards for acupuncturist

training and certification. Concurrently, enhancing public awareness through comprehensive public education initiatives is vital to foster broader acceptance and greater utilization of this valuable non-pharmacological treatment option.

8.Conclusion and Outlook

The ongoing US opioid crisis remains a formidable public health issue demanding an urgent, comprehensive, and multi-faceted strategic response. Within this framework, acupuncture, recognized as a safe and effective non-pharmacological analgesic, demonstrates unique value and immense potential.

Future direction lies in the integration of acupuncture into comprehensive pain management protocols. By incorporating it into a multi-modal system—synergizing with medication, physical therapy, and psychological intervention—clinicians can offer patients more personalized and thorough treatment choices. The establishment of dedicated integrated pain centers and integrative medicine facilities provides the necessary infrastructure for this integration.

The role of acupuncture in tackling the opioid epidemic is expected to significantly expand as research deepens, evidence accumulates, and policy support grows. It is poised to become one of the mainstream options for managing chronic pain, helping numerous individuals avoid or overcome opioid dependence and achieve safer, more effective analgesia.

Crucially, acupuncture is not a standalone remedy; it must function as a component of a comprehensive treatment strategy. In some cases, opioids remain necessary and appropriate treatment choices, with the key being rational use and avoiding misuse. Ultimately, resolving the opioid crisis requires a unified effort across the entire healthcare system and society, involving the reform of pain management practices, stricter prescription regulation, the expansion of alternative treatment options, the provision of robust addiction services, and the resolution of underlying socioeconomic disparities.

As a vital and increasingly integrated component of this expansive strategy, acupuncture can make a unique contribution. Through continued scientific investigation, supportive policy, collaborative professional efforts, and public awareness campaigns, we are confident that acupuncture will play a progressively significant role in improving patient health outcomes, reducing opioid-related harm, lessening the burden on the US healthcare system, and enhancing overall public well-being.

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The authors declare that there is no conflict of interest regarding the publication of this paper.

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