

Research Progress in the Treatment of Substance Use Disorders with Traditional Chinese Medicine

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Abstract—Substance Use Disorder (SUD) has become a global public health crisis. Existing Western medical treatments have limitations such as significant side effects, poor adherence, and high relapse rates. Traditional Chinese Medicine (TCM), with its advantages of multi-target effects, minimal side effects, and holistic management of body and mind, provides new approaches for the treatment of SUD. This article systematically reviews 18 related studies, summarizing TCM's understanding of the etiology and pathogenesis of SUD. It holds that 'addictive toxins' damage qi, blood, and yin-yang, leading to disharmony among the internal organs, mainly affecting the heart, liver, spleen, and kidneys, often accompanied by pathological products such as phlegm, blood stasis, and dampness. Based on this, the article reviews clinical and experimental evidence of TCM interventions, including herbal formulas (such as Compound 511, modified Shenling Baizhu decoction, and Anshen formula), acupuncture (including electroacupuncture and auricular acupuncture), tuina (such as Yizhi Chan massage technique), and guiding exercises, in alleviating withdrawal symptoms, reducing psychological cravings, improving comorbid anxiety and depression, and restoring cognitive function. The mechanisms of action are discussed, primarily including regulation of neurotransmitter levels in the mesolimbic dopamine system (such as DA, 5-HT, NE, GABA), modulation of the BDNF signaling pathway to repair neuronal plasticity, regulation of circRNA expression profiles, and regulation of neuroinflammatory responses. This review finds that TCM treatment for SUD is effective and possesses unique advantages, restoring the body's homeostasis through multi-level, multi-target integrated regulation.

Keywords—substance use disorder, traditional Chinese medicine, acupuncture, tuina, neurotransmitters

I. INTRODUCTION

Substance Use Disorders (SUDs), encompassing the abuse and dependence on addictive substances such as opioids, alcohol, and methamphetamine, have become a major public health issue threatening human health and social stability [1, 2]. Although existing substitution therapies represented by methadone and buprenorphine can alleviate acute withdrawal symptoms, their long-term use has drawbacks such as drug dependence, increased

tolerance, significant side effects, and poor patient compliance, resulting in persistently high relapse rates after detoxification [3]. Therefore, it is particularly urgent to explore safe and effective complementary and alternative therapies that can fundamentally reduce the risk of relapse.

As a treasure of traditional Chinese medicine, Traditional Chinese Medicine (TCM) has accumulated rich experience in the prevention and treatment of SUD. Its core concepts of "holistic view" and "syndrome differentiation and treatment" emphasize restoring health by adjusting the balance of qi, blood, yin, and yang, and the functions of the internal organs, which align closely with the complex etiology and pathogenesis of SUDs. In recent years, a large number of studies have confirmed the intervention effects of TCM on SUD at both clinical and experimental levels. This article aims, based on the literature provided, to systematically review the research progress of TCM in the treatment of SUD, with a focus on its theoretical basis, treatment methods, and modern biological mechanisms, in order to provide a reference for further research and clinical practice in this field.

II. RESEARCH ON THE MECHANISMS OF TRADITIONAL CHINESE MEDICINE IN TREATING SUBSTANCE USE DISORDER

Traditional Chinese Medicine (TCM) treatment for Substance Use Disorder (SUD) is characterized by multi-target and multi-pathway actions. Existing research primarily reveals its biological mechanisms on three levels: first, regulating neurotransmitter imbalance and reward circuit function; second, repairing neural plasticity damage caused by chronic addiction; and third, modulating emotion, cognition, and neuroinflammatory responses. The following systematically summarizes the research progress in these three aspects.

A. Regulation of Neurotransmitters and Reward Circuits

The mesolimbic dopamine system is a key pathway for addictive reward. Traditional Chinese medicine can act by modulating the neurotransmitters in this pathway.

Compound 511 can reverse morphine-induced downregulation of BDNF and TrkB in the VTA, regulate the ERK, PI3K-Akt, and PLC γ 1 pathways, and repair the structure of dopaminergic neurons [1]. Tui Na (therapeutic massage) can increase serum levels of DA, 5-HT, and NE in addicts [4–6], as well as enhance GABA levels, restoring the excitatory/inhibitory balance [7]. Acupuncture regulates dopamine release through the endogenous opioid system (2 Hz stimulates enkephalins and β -endorphins; 100 Hz stimulates dynorphins), thereby alleviating withdrawal symptoms and cravings [2, 8].

B. Repairing Neural Plasticity

Chronic addiction leads to changes in neuronal plasticity in brain regions such as the VTA, NAc, and prefrontal cortex. Acupuncture can affect neural plasticity by modulating the reward, salience, and executive control networks [8]. Compound 511 can reverse morphine-induced atrophy of VTA dopaminergic neuron cell bodies [1]; electroacupuncture can increase BDNF expression in the VTA of morphine-withdrawn rats, thereby promoting neuronal repair [2].

C. Regulating Emotion, Cognition, and Neuroinflammation

Patients with SUD often have comorbid anxiety, depression, and cognitive impairment. Tuina and Daoyin therapy alleviate depression and anxiety by regulating levels of 5-HT, NE, β -EP, and other neurotransmitters [4, 9]. The modified Shenling Baizhu Decoction can improve diarrhea in patients with alcohol addiction while enhancing cognitive function by regulating BDNF and reducing IL-1 β and TNF- α [10]. Acupuncture can regulate the HPA axis and the sympathetic-adrenal medullary axis, lower CRF levels, and play roles in anti-stress, anti-anxiety, and alleviating neuroinflammation [8]. Tuina can also increase serum DA, 5-HT, and NE in individuals undergoing detoxification to improve psychological problems [6].

III. CLINICAL EVIDENCE OF TRADITIONAL CHINESE MEDICINE IN TREATING SUBSTANCE USE DISORDERS

A. Intervention Studies of Traditional Chinese Medicine Formulas and Single Herbs

TCM formulas, characterized by multiple components and multiple targets, are widely used in the treatment of SUDs. Zhang Han's study showed that Formula 511 (composed of ginseng, astragalus, Corydalis yanhusuo, etc.) can effectively inhibit morphine-induced Conditioned Place Preference (CPP), behavioral sensitization, and self-administration in mice, as well as alleviate acute withdrawal symptoms precipitated by naloxone, indicating that it can suppress both psychological dependence and physical dependence [1]. Regarding alcohol addiction, Wen [11] found that the Anshen Formula (composed of Schisandra, Polygala, Ziziphus seeds, etc.) can significantly inhibit alcohol-induced CPP and the formation of behavioral sensitization in mice, lower the contents of Dopamine (DA) and Glutamate (Glu) in the mesolimbic region, increase GABA

content, and has no addictive properties itself. Clinical research by Luo [10] indicated that the modified Shenling Baizhu Formula (based on Shenling Baizhu San with added Coptis, Shenqu, Astragalus, Bupleurum, Citrus peel, and Cuscuta) can effectively treat diarrhea in alcohol-dependent patients with spleen deficiency and dampness excess, improve gastrointestinal symptoms, and significantly enhance patients' cognitive functions (such as immediate memory, visual span, verbal ability, etc.), with efficacy superior to that of Shenling Baizhu San and conventional treatment groups. Furthermore, research by Sonam *et al.* [12] found that Tibetan medicine comprehensive therapy (using a series of Tibetan medicinal formulas from "Detox No. 1" to "Detox No. 10") can effectively improve withdrawal symptoms during the maintenance period, as well as psychological symptoms such as anxiety and depression in opioid-addicted individuals.

B. Intervention Studies of Acupuncture Therapy

The efficacy of acupuncture for addiction treatment is clear, and there are various methods. In methamphetamine addiction, clinical research by Gu [13] shows that electroacupuncture (targeting bilateral T5 paraspinal points, Shenshu, Neiguan, Shenmen, Zusanli, Sanyinjiao, Baihui, and Yintang) can significantly improve the psychological cravings, withdrawal symptoms, and anxiety and depression of addicts in the early detoxification stage, with efficacy superior to conventional detoxification treatment. The review by Lian and Zhou [2] points out that acupuncture can intervene in alcohol addiction by regulating monoamine neurotransmitters (such as 5-HT and DA), GABA, and the endogenous opioid system. The review by Zhang *et al.* [8] further elaborates that acupuncture can treat alcohol addiction by modulating functional networks (such as the reward network), neurotransmitters (monoamines, peptides, amino acids), spinal-brain communication pathways, and neuroendocrine-immune interactions.

Auricular acupuncture (NADA ear acupuncture protocol) is another widely used therapy. A prospective trial by Carter *et al.* showed that NADA ear acupuncture (bilateral stimulation of the Sympathetic point, Shenmen (HT7), Kidney (CO4), Liver (CO18), and Lung (CO14) points) combined with conventional treatment can significantly alleviate symptoms such as cravings, depression, anxiety, anger, and physical pain in patients with SUD [14]. A meta-analysis by Grant *et al.* [15] further confirmed that compared to the control group, acupuncture had a statistically significant advantage in improving craving and anxiety symptoms in patients with SUD (SMD -0.57), although no significant differences were found in relapse, frequency/amount of substance use, or treatment dropout. A survey by Qeadan *et al.* [16] of SUD treatment facilities in the United States found that although only 5.5% of facilities offered acupuncture treatment, facilities operated by the federal government, tribal governments, and those in the western region were more likely to provide this service.

C. Intervention Studies of Tuina and Daoyin Therapy

Tuina, as a non-invasive and accessible therapy, has unique advantages in SUD rehabilitation. Yizhichen Tuina is a representative school among them. Research by Li [5] shows that Yizhichen Tuina (targeting Baihui, Sishencong, Zhongwan, Qihai, Guanyuan, Neiguan, Shenmen, Hegu, Zusanli) can significantly improve clinical symptoms in patients with anxiety after drug addiction, with a total effective rate of 95.0%, higher than 76.9% in the control group, and can increase the levels of DA, 5-HT, NE, and GABA in serum. Research by Zhao [4] also confirmed that Yizhichen Tuina (targeting Baihui, Neiguan, Shenmen, Zusanli, Sanyinjiao, etc.) can effectively treat depression after drug addiction, with a total effective rate for females (85%) significantly higher than that for males (65%), which may be related to the regulation of serum β -Endorphin (β -EP), 5-HT, DA, Epinephrine (E), and Leptin (LP) secretion. Research by Cui [6] shows that Yizhichen Tuina can effectively improve the total score and factor scores of the SCL-90 scale in individuals undergoing detoxification (including somatization, depression, anxiety, and compulsiveness) while also increasing serum concentrations of DA, 5-HT, and NE. Another study by Li and Shi [7] also confirmed that Tuina manipulations can upregulate the expression of the endogenous neurotransmitter GABA, thereby alleviating anxiety symptoms in individuals with opioid addiction.

Dao Yin exercises combine movement, breathing, and mental focus, and are a traditional practice that harmonizes body and mind. Research by Miao Di found that traditional Chinese Dao Yin exercises (including self-massage of the head, face, chest, abdomen, and acupoints on the limbs, combined with breathing and guided mental focus) can effectively treat anxiety disorders secondary to drug addiction, with women showing better therapeutic effects than men. The mechanism lies in raising the serum levels of DA, 5-HT, NE, and GABA, while also improving anxious mood, tension, insomnia, and musculoskeletal symptoms. Chang and others also found that relaxation response (RR, similar to Dao Yin) and auricular acupuncture can effectively reduce craving and anxiety levels in U.S. veterans with substance use disorders, with significant effects observed even after a single intervention.

IV. CONCLUSION

In summary, based on existing literature, TCM shows promising potential in the treatment of SUDs. Its core advantage lies in its multi-target, multi-level integrative regulatory effects. TCM intervenes in multiple aspects of addiction through the “neuro-endocrine-immune” network: first, alleviating withdrawal symptoms by regulating neurotransmitters such as GABA and 5-HT, reducing discomforts like anxiety, insomnia, and pain during withdrawal; second, reducing psychological cravings by regulating the DA system and BDNF signaling pathways, inhibiting the reward circuits, and weakening the pathological memory and desire for addictive substances; third, repairing neural damage by upregulating neurotrophic factors such as BDNF, promoting structural and functional remodeling of neurons in addiction-related

brain regions; fourth, improving comorbid disorders by regulating the HPA axis and reducing neuroinflammation, thereby treating accompanying depression, anxiety, and cognitive impairment. Different therapies, including Chinese herbal medicine, acupuncture, tuina (therapeutic massage), and guiding exercises, each have their focus, but all reflect the TCM philosophy of “supporting the healthy and dispelling the pathogenic” and “harmonizing body and mind.”

However, research in this field still faces numerous challenges. Firstly, high-quality, large-sample Randomized Controlled Trials (RCTs) are still lacking, and the sample sizes of existing studies are generally small [4, 9, 10, 13]. Secondly, interventions in traditional Chinese medicine (such as acupoint combinations and acupuncture parameters) lack standardization, making it difficult to compare and replicate study results [15]. Thirdly, although mechanistic studies have made progress, they are mostly limited to verifying a few neurotransmitters and signaling pathways [1, 4, 5], and further in-depth exploration is required to clarify how TCM systematically regulates complex addiction-related networks. Future research should verify the efficacy and safety of traditional Chinese medicine in treating SUDs through rigorous randomized controlled trials, use multi-omics techniques to reveal its multidimensional regulatory mechanisms, and explore optimized strategies such as combining acupuncture and herbal medicine with long-term follow-up to reduce relapse rates. As a unique healthcare resource of China, traditional Chinese medicine holds great potential in this field.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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