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Research Progress on the Mechanism of Acupuncture in the Treatment of PTSD

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Abstract: ***At present, there is a lot of room for increase in acupuncture treatment of Post-traumatic Stress Disorder, both in terms of research and the number of articles published. This article reviews the clinical and mechanism of acupuncture treatment of PTSD at home and abroad in recent years. Clinical studies have shown that acupuncture can effectively alleviate PTSD-related symptoms and is an effective means of treating PTSD. Experimental studies have shown that the mechanism of acupuncture therapy for PTSD may involve regulating neural loops, neurotransmitter and receptor expression, signaling pathways, apoptosis, immune cytokin and endogenous cannabinoids. This can provide a reference basis for the clinical application of acupuncture treatment of PTSD and provide new ideas for future in-depth clinical research.***

Keywords: Acupuncture, Post-traumatic stress disorder, Mechanism of action, Application progress**.**

1. Introduction

Post-traumatic stress disorder (PTSD) refers to a group of diseases caused by extraordinary threatening and catastrophic events that are mainly a variety of mental abnormalities or disorders and are closely related to psychological stress [1]. At least 50% of the population may experience more than one traumatic event in their lifetime [2]. According to epidemiological surveys, the prevalence rate of PTSD in post-traumatic people is about 15.4%, and about 3 to 4% of people worldwide suffer from this disease every year [2]. Typical symptoms of PTSD include re-experience, escape and excessive excitement, which undoubtedly increases the psychological pain of patients and seriously affects the quality of life of patients. At the same time, the disease is accompanied by depression, anxiety and drug abuse [3], causing a serious financial burden. In recent years, natural and man-made disasters such as earthquakes, terrorist attacks, traffic accidents, sexual assaults and other natural and man-made disasters have been frequently reported, making PTSD the focus of post-disaster psychosocial research. At present, the international front-line treatment for PTSD is psychological intervention and drug treatment, but due to certain side effects and individual differences, most patients are still unable to obtain satisfactory treatment results [3]. As an important part of the motherland's medicine, acupuncture has rich experience and certain effects in the treatment of mental and psychological diseases. A series of recent case studies have shown that acupuncture has potential benefits for PTSD and depression [4]. Other studies show that in the treatment of PTSD, compared with conventional treatment, acupuncture It is well tolerated, safe, economical and effective for patients with thorn treatment. Based on this, the author has sorted out the relevant literature on acupuncture treatment of PTSD in recent years, and summarized and explained its mechanism of action in the treatment of PTSD, in order to provide reference for clinical work, so that acupuncture therapy can better serve PTSD patients.

2. PTSD's Traditional Chinese Medicine Understanding

According to the clinical characteristics of PTSD, traditional Chinese medicine classifies the disease as "depression syndrome" [5], which can also be seen in sleeplessness, irritability, lily disease and other diseases. The symptoms of patients diagnosed with PTSD are common dizziness, headache, insomnia and dreaminess, palpitation and timidity, frightening fear, pulse count, etc., accompanied by dry tongue, constipation and other complications [6]. The pathology of PTSD is in the heart and brain, which is closely related to the liver, spleen, kidney and other organs. The clinical symptoms are mostly mixed with deficiency. The empirical evidence is mainly phlegm depression and qi depression. The deficiency syndrome is mainly heart, spleen deficiency and heart and kidney deficiency [7]. The pathological mechanism is often reflected in panic injury to the kidney, heart and mind loss, and yin and yang disorders of the viscera. Traditional Chinese medicine believes that this kind of emotional disease is caused by emotional disorder and loss of mind, and acupuncture has a good effect on healing and conditioning. At present, the acupuncture treatment form of PTSD is mainly electric acupuncture. Usually, acupuncture points such as Taichong, Dumai, Baihuihe Shenting, and Sutra Outside the Four Shencong are selected to drain the liver and regulate the qi and regulate the spirit. Supplemented by the inner gate, Sanyin Jiao, Shenmen and other acupuncture points to strengthen the heart and spleen, and reconciliate yin and yang [8].

3. Clinical Research Progress of Acupuncture for PTSD

Acupuncture can be adjusted from both physical and mental aspects to treat mental disorders, which has a good effect on PTSD [9]. Common clinical scales objectively evaluate the efficacy of acupuncture in the treatment of PTSD. Common

scales include: Post-traumatic Stress Disorder Screening Form Fifth Edition (PCL-5), Clinical PTSD Scale (CAPS), Post-traumatic Stress Disorder Self-Assessment Scale Civilian Edition (PCL-C) and Hamilton Anxiety Scale (HAMA) [10,11]. The study found that acupuncture treatment can improve emotional and memory disorders, abnormal behavior, hallucinations and other symptoms in patients with PTSD. Clinical studies have shown that [12] the efficacy of electroacupuncture combined with moxibustion in the treatment of PTSD is significantly better than that of paroxetine, and can reduce the adverse reactions caused by drugs. Wang Zhongheng et al. [13] found that electroacupuncture combined with paroxetine can safely and effectively treat PTSD. Zhou Ping [14] used the post-traumatic stress disorder checklist and the Hamilton Anxiety scale to evaluate the efficacy. The results showed that the antidepressant sertreline combined with electroacupuncture treatment can significantly improve the reappearance of PTSD, increased alertness and anxiety symptoms, and have good safety and tolerance. Kim YD et al. [15] systematic research shows that for patients with PTSD, acupuncture treatment and psychotherapy have a similar effect and can last for at least 3 months. Related meta analysis [16] shows that acupuncture treatment of PTSD is better than oral SSRI. Evidence-based medical research also shows that the effect of electric acupuncture head Shenting, Sishencong, Baihui, Fengchi and other Anshentong acupoints for the treatment of PTSD is better than that of paroxetine, and it is simple and safe, which can be used as an advantageous choice for PTSD patients. Zhao Guijun et al. [17] found that for female PTSD patients, Yishen Tongdu electroacupuncture therapy (frequency of 100 Hz, 30 minutes per day, 6 times a week for acupuncture points such as Baihui, Dashi, Shenyu) can not only play a clinical effect similar to Western medicine treatment (20 mg/tablet, 1 time a day), but also significantly reduce the anxiety score of patients' anxiety score and SCL-90 somatization symptoms, and have small side effects, low price, and good compliance with good compliance. In addition, Ran Qiang et al. and others [12] randomly divided 116 patients with PTSD after fracture into 52 cases and 64 cases in the treatment group. The control group was treated by simple oral paroxetine. In addition to oral paroxetine, the treatment group was treated with electric needle combined with moxibustion. Shenting, Sishencong, Baihui and so on.

4. Research on the Mechanism of Acupuncture Treatment of PTSD

Studies [18] show that the pathogenesis of PTSD is closely related to changes in brain anatomy and neural loops, neuroendocrine system disorders, immune system dysfunction, etc. Therefore, in recent years, the mechanism of acupuncture treatment of PTSD is mainly in the following aspects.

4.1 The Effect of Acupuncture on the Neural Structure and Loop of the Brain

The hippocampus belongs to the limbic system of the brain, which is the main brain area involved in learning memory, and is involved in eliminating fear and regulating the body's neuroendocrine function under stress. The prefrontal cortex is the main brain area for emotional regulation, and the amygdala plays an important role in fear memory. The study found that patients with PTSD showed functional changes in the hippoma and prefrontal cortex in the process of learning and memory. Zheng Chengqiang et al. [19] selected Baihui, Shenting, Sishencong and Fengchi to treat PTSD patients with the "awake-up brain" acupuncture method. The results show that the mechanism of improving PTSD symptoms may inhibit the functional connection of the hipporpompal and hipporal lateral return and amygdala, enhance the connection between the apietal lobe and the hippoma, and indirectly affect its It is related to the function of the brain area. In addition, functional magnetic resonance imaging technology was used to analyze the whole brain functional connection of PTSD patients with bilateral amygdala as the area of interest. It was found that the improvement mechanism of electrically for the clinical symptoms of PTSD patients may be related to the regulation of the functional connection network of PTSD amygdala by electroacupuncture. Other studies have found that the regulation of PTSD amygdala functional connection network by acupuncture may be achieved by promoting the enhancement of amygdala-frontal functional connection and inhibiting the enhancement of amygdala-temporal lobe functional connection.

The experimental study found [21] that the self-discharge level of neurons in the hippocampus of PTSD rats was significantly inhibited, which seriously affected the discharge activity of neurons in the hippocampus. Neuron information coding is completed by a cluster. Its characteristics are shown in the time and spatial characteristics of the activity of the neuron cluster. Waveform amplitude, discharge frequency and number of emission are intuitive characteristics of the waveform space-time mode. Neuron discharge amplitude can reflect the strength of neuron electrical activity. In addition, experimental studies have shown that [22] PTSD rats have the characteristics of sleep disorders such as difficulty falling asleep, increased awakening time, and reduced sleep time. The increpation period of rapb sleep and the increpation period of non-rapb sleep can reflect the quality of sleep. The sleep in latency period increases, but the sleep time decreases. Yu Chao et al. found [23] that PTSD sleep disorder rats increased during the rapid sleep incination period and the non-rapid eye movement sleep incination period, and decreased after "liver-tuning" acupuncture treatment. The amplitude of hippocampus CA1 and CA3 in rats with PTSD sleep disorder decreased, and the prognosis increased through acupuncture and moxibustion. It is suggested that the acupuncture method can significantly improve the sleep quality of rats with PTSD sleep disorder by reversing the discharge activity of neurons in the hippocampus of rats with PTSD sleep disorder and restoring the cell structure of neurons. It can be seen that acupuncture has a good regulating effect on the function and structure of the PTSD hippocampus.

4.2 Effect of Acupuncture on the Expression of Neurotransmitters and Receptors

The pathological mechanism of PTSD is related to the dysfunction of the pituitary gland-adrenal axis of the hypothalamus, the defects of the awakening and sleep regulation system. Patients with PTSD continue to be highly active due to strong traumatic stimulation, and the content of

the associated hormones CRH, ACTH and GC is increased, thus showing negative emotions such as depression and anxiety. Studies show that [24] the monoamine transmitter 5-hydroxytryptamine is involved in PTSD. Monoamine oxidase is a key enzyme that regulates serotonin and plays an important role in the degradation and metabolism of monoamine neurotransmitters. Deacetylation enzyme is an important regulatory enzyme for monoamine oxidase gene transcription. Studies have shown that the occurrence of PTSD-like behavior is related to the abnormal increase in the activity of the hippocampal monoamine oxidase gene, and the inhibitor monoamine oxidase gene may maintain the internal environmental stability of serotonin through transcriptional inhibition of monoamine oxidase, thus playing a therapeutic role in PTSD. Li Fenglei and other research results show that [25] Electroacupuncture pretreatment may alleviate the anxiety behavior of PTSD rats by lowering the level of monoamine oxidase gene in PTSD rats and reducing the expression of monoamine oxidase. Inhibitory γ-aminobutyric acid is the most important inhibitory amino acid neurotransmitter in the central nervous system. Type A GABA receptor is one of the important GABA receptors, which is widely distributed in the central nervous system. Zhu Xiuling et al. found [33] that the electric needle may inhibit the upregulation of PTSD to the GABA receptor α1 in the medial frontal cortex of rats, regulate neuronal activity, restore the function of relevant neural loops, and promote the elimination of PTSD conditional fear. The study found that [26] neuron-type nitric oxide synthase was involved in PTSD. Inhibiting the activity of nNOS can regulate the content of nitric oxide in the body, thus having a regulatory effect on neurological diseases. Inhibiting nNOS can improve the scenario-related fear response of mice.

4.3 Effect of Acupuncture on Signal Conduction Pathway

4.3.1. Effect of acupuncture on Keapl-Nrf2 signaling pathway

Kelch-like chlorohydroxide-related protein 1-nucleo-factor E2-related factor 2/heme oxygenase 1 is an endogenous antioxidant stress pathway in cells. The study found that [27], the Keapl-Nrf2-HO-1 signaling pathway participated in PTSD. Nrf2 is a key transcription factor that regulates cells against foreign bodies and oxidative damage, and plays an important role in improving the antioxidant capacity of cells. When the body is stimulated to undergo oxidative stress, Nrf2 is activated and dissociated from Keapl. The activated Nrf2 enters the nucleus to promote the expression of HO-1 protein and play an antioxidant role. HP-1 is one of the downstream key target genes regulated by Nrf2 and plays an important role in antioxidant stress damage. Adenylate-activated protein kinase is a silk/threonine protein kinase that can positively regulate the Nrf2 pathway.

4.3.2 Effect of acupuncture on mTOR signaling pathway

The study found that the mammalian rapamycin target protein signaling pathway is involved in PTSD. mTOR is a protein kinase that regulates the initial stage of protein translation, which plays an important role in protein translation, ribosomal formation, cell apoptosis, etc. mTOR regulates cell growth, proliferation and synaptic plasticity by activating protein synthesis. The activation of mTOR is related to the synthesis of local proteins in synapses. Post-synaptic dense protein 95 is the synaptic core protein of neurons and an important molecular basis for synaptic plasticity. Synaptin 1 is a glycoprotein closely related to synaptic structure and function, and is a specific molecular marker at the end of the synaptic. Growth-related protein 43 is a neuron-specific envelope phosphoprotein, which plays an important role in the growth, differentiation and regeneration of nerve fibers, as well as axon growth and synaptic formation. Long-term enhancement is also an important indicator to measure the synaptic plasticity of hippocal neurons. Experimental studies showed that the expression of PSD95, Syn1 and GAP43 in PTSD rats decreased. By observing the effect of acupuncture on the depressive and anxiety-like behavior of PTSD rats, some scholars found that acupuncture points can significantly relieve the depression and anxiety-like behavior of PTSD rats, and acupuncture can regulate the protein translation in the mTOR signaling pathway and enhance the activity of hippocampal synaptic proteins PSD95, Syn1 and glutamate receptor 1, indicating that acupuncture may be the protein synthesis needed to increase synaptic plasticity through the hippocampus mTOR pathway, which has antidepressant and anti-anxiety effects on PTSD.

4.3.3 Effects of acupuncture on apoptosis and brain-derived neurotrophic factors

The hippocampus injury and volume reduction in patients with PTSD are positively correlated with the severity of PTSD. Experimental studies found that [30] there was obvious apoptosis in PTSD rat hippocampus. Bcl-2 and Bax are the most representative genes that inhibit apoptosis and promote apoptosis in the bv1-2 family, respectively, and are involved in the pathogenesis of PTSD. The c-fos gene is an immediate early gene, which plays an important role in regulating cell growth, division, proliferation, differentiation and even procedural death. Liu Qianru et al. [31] found that electroacue may improve the learning and memory ability of PTSD rats by adjusting the hippocampus Bcl-2/Bax ratio of PTSD rats. Liu et al. found that [32] After electroaquetherapy, the time for PTSD rats to open their arms in the open area of the open field experimental center and the elevated cross labyrinth experiment significantly increased the expression of c-fos in the antectoid, indicating that electroabulence improved the anxiety-like behavior of PTSD rats, which may be related BDNF is an important member of the neurotrophic factor family, which can influence the formation, consolidation and regression of fear memory and participate in regulating the pathogenesis of PTSD. Zhu Xiuling et al. [33] used immunohistochemical methods to observe the expression of BDNF in the medial frontal cortex of PTSD rats. They found that the immune response of BDNF was significantly enhanced after electroacupuncture treatment, suggesting that electroacupuncture may play a role in the prevention and treatment of PTSD by suppressing PTSD to the downmodulation of BDNF of the medial frontal cortex. Function. The study also found [33] that the number and intensity of BDNF-positive neurons in PTSD rat amygdala decreased, and the intensity and number of BDNF increased after electroacupuncture treatment. The results show that the electric needle may play a role in treating PTSD by promoting BDNF expression.

4.4 Effect of Acupuncture on Endogenous Cannabinoids

In recent years, the endogenous cannabinoid system has been regarded as a new target for future drug treatment of PTSD. The endogenous cannabinoid system is mainly composed of type I cannabinoid receptors and type II cannabinoid receptors, as well as N-arachidonic acid ethanolamine and 2-anyl triglycerides. Type I cannabinoid receptors are mainly distributed in the central nervous system, and the activation of type I cannabinoid receptors plays an important role in promoting memory regression. 2-Aricyl triglycerides are mainly synthesised by diacylglycerol lipase, and the absence of diacylglycerin lipase synthesis can negatively affect the emotional state of animals, leading to increased anxiety, stress and fear reactions [34]. By observing the preventive effect of early electroa needle intervention in PTSD rats' anxiety-like and fear learning behavior, it was found that early electroacupine intervention could improve PTSD-like behavior and increase the expression of hippocampal BDNF, DAGLα and CBIR. However, short hair clip RNA knockout DAGLα or CBIR can eliminate the neuroprotective effect of early electric needle intervention. In addition, the effects of different electric needle parameters on the expression of daGLα and CBIR in hippocys glial cells were also observed. The results showed that electric needles can improve the expression of the two and have a certain neuroprotective effect.

4.5 Effect of Acupuncture on Immune Cytokines

The study found that [35] the inflammatory cytokine interleukin-1β and tumor necrosis factor-αhydrapine increased significantly in patients with PTSD. Cytokines play an important role in regulating the response of the immune system. They can regulate changes in neurobiology, neuroendocrine, neuroplasticity and behavior, and affect the occurrence and development of neurological diseases. The dynamic balance of pro-inflammatory cytokines and anti-inflammatory cytokines is of great significance for the degree of inflammatory response and clinical prognosis. Data showed that PTSD patients had significant immune disorders, increased inflammatory response, and serum levels of IL-6, IL-1β, TNF-α, and cyclooxygenase-2 increased significantly, and IL-4 levels decreased significantly. Steady imbalance of the immune system is involved in the pathogenesis of PTSD, and the occurrence of inflammatory reactions makes it easier for the body to develop into PTSD. It is reported that electroacupoint PTSD rats can significantly improve anxiety-like behavior and reduce IL-6 levels in the prefrontal cortex of rats, but has no significant effect on IL-1β, suggesting acupuncture to improve PTSD-like behavior, which may be related to the reduction of IL-6 in the prefrontal cortex.

5. Look Ahead

The pathological mechanism of post-traumatic stress disorder is not completely clear at present, and the research of acupuncture in the field of PTSD is basically in its infancy: (1) There is insufficient direct literature and relevant evidence. At present, most of the research on acupuncture treatment of PTSD draws on the progress of acupuncture and moxibustion in the treatment of anxiety, depression and sleep disorders. It lacks obvious relevance, the scope and content of the research are not detailed enough, and the basic experimental research is obviously lagging behind. (2) A randomized controlled trial with a lack of multi-center, large samples and sufficient follow-up time. (3) There is less theoretical analysis of acupuncture and moxibustion in the treatment of PTSD. (4) Most of the research is mainly based on electroacupuncture, and there are few reports of simple acupuncture treatment. Intervention and treatment for trauma exposure and post-traumatic stress disorder is now regarded as a "global public health problem". So far, the international first-line treatment of PTSD is still psychological intervention and drug treatment, but some studies have shown that the recovery rate of patients receiving psychological treatment is only 56% [35]. The current effect of drug treatment is also not optimistic. At present, there are only two drugs - selective 5-hydroxytryptin reuptake inhibitors (SSRIs), Sertraline hydrochloride and Paroxetine hydrochloride, which are PTSD oral drugs approved by the U.S. Food and Drug Administration (FDA). Studies by Hoskins M et al. [38] show that although SSRIs are better than placebos in relieving PTSD symptoms, they are less effective. What is more worrying is the toxic side effects caused by long-termSSRI treatment. Cross-sectional observational study [40] showed that the incidence of sexual dysfunction in patients treated with SSRI was 36% to 43%. In addition, many social factors, especially language, culture and economic level, also seriously affect the treatment choices and treatment effects of PTSD patients. Therefore, finding an effective, safe and universal PTSD treatment plan has become a medical and health problem shared by experts in many fields around the world.

6. Brief Summary

Recent studies have shown that acupuncture treatment of PTSD has a relatively satisfactory clinical effect. Its mechanisms of action include: improving the neural structure and loop of the brain, regulating the expression of related neurotransmitters and receptors and the endogenous cannabinoid system, regulating the Keapl-Nrf2 signaling pathway and mTOR signaling pathway, regulating the apoptosis of hippocampal neurons and neurotrophic factors, regulating immune cytokines, etc. The pathological mechanism of PTSD is complex. With the in-depth study of the mechanism of acupuncture treatment of PTSD, the mechanism of acupuncture to improve PTSD symptoms through multi-target and multi-level will be clearer.

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