

The Intervention Mechanism of the "Regulating Marrow and Awakening Spirit" Method on the Efficacy of Awakening Vegetative Patients

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Abstract: Vegetative patients (Persistent Vegetative State, PVS) represent a severe form of Prolonged Disorders of Consciousness (pDoC). It refers to a special state of unconsciousness without perception that occurs after brain injury due to various causes. Currently, most scholars believe that PVS is defined as a vegetative survival state lasting for more than one month without any signs of awakening [1]. Subsequently, some scholars argued that, out of humanitarian considerations, the term "unresponsive wakefulness syndrome" should replace "vegetative state" for naming this condition [2]. Due to the patients' inability to cooperate with physical examinations and tests, the misdiagnosis rate for such patients is as high as over 40% [3]. However, with the intervention of current medical approaches, there is still a possibility of vegetative patients waking up. On this basis, the costs generated during the awakening process and subsequent supportive treatments have become a major concern. Currently, Western medicine has limited treatment methods for awakening vegetative patients, and no new treatment means have emerged in recent years. The treatment of traditional Chinese medicine is gradually showing its advantages, especially acupuncture treatment. This article is based on the theory of "Marrow Damage and Spirit Injury" proposed by Chief Physician Chen Xiao [4], combined with modern neuroinflammatory mechanisms, covering aspects such as the theoretical basis of traditional Chinese medicine, modern medical mechanisms, and clinical research evidence. It systematically reviews the intervention mechanism of the Tiaosui Xingshen Method (TSXSF) in awakening vegetative patients. Research shows that TSXSF regulates the IL-10/NF- κ B signaling pathway by acupuncture at specific acupoints (such as Shuigou, Neiguan, Baihui, etc.), inhibits the neuroinflammatory response, improves cerebral blood flow and neural functional connectivity, thereby promoting the recovery of consciousness. This article integrates clinical research data and molecular biological evidence to clarify the multi-target intervention mechanism of TSXSF, aiming to provide a more in-depth theoretical basis and practical reference for the treatment of vegetative patients.

Keywords: Tiaosui Xingshen Method, Vegetative Patients, Arousal Promotion, Intervention Mechanism

1. Introduction

According to relevant statistics, the number of vegetative patients and those with chronic disorders consciousness is on the rise globally. In the United States, there are approximately 100,000 - 300,000 such cases, and in China, the conservative estimate is over 500,000, with an annual increase of 70,000 - 100,000 cases. This not only imposes a heavy economic and psychological burden on the patients' families but also exerts great pressure on social medical resources. Currently, the treatment methods for vegetative patients in Western medicine are limited, mainly including drug therapy, hyperbaric oxygen therapy, nerve electrical stimulation, etc., but the overall efficacy is unsatisfactory. Traditional Chinese medicine has unique theories and practical experiences in the treatment of awakening vegetative patients, and the Tiaosui Xingshen Method is one of the much - concerned therapies. An in - depth exploration of the intervention mechanism of the Tiaosui Xingshen Method in awakening vegetative patients is of great significance for improving the treatment effect and prognosis of vegetative patients.

A vegetative patient, that is, in a Persistent Vegetative State (PVS), suffers from a severe chronic disorder of consciousness. The patient's cerebral cortex function is lost, and only brainstem functions remain. They are in a state of unconscious wakefulness, with periodic awakenings (such as opening their eyes) but a lack of the ability to perceive themselves and the environment. According to the

guidelines [5], a disorder of consciousness with a duration of more than 28 days can be defined as a Prolonged Disorder of Consciousness (pDoC), and the Vegetative State (VS) is one of its main types. Globally, the incidence of pDoC is increasing year by year. There are about 100,000 - 300,000 patients in the United States, and in China, the conservative estimate of the number of patients is over 500,000, with an annual increase of 70,000 - 100,000 cases. Such patients rely on long - term medical support, imposing a heavy economic burden on families and society [6]. Currently, Western medicine treatment mainly focuses on multidisciplinary comprehensive interventions, including drugs (such as dopamine agonists), hyperbaric oxygen, median nerve electrical stimulation, and rehabilitation training. However, the efficacy varies significantly and lacks specificity. Therefore, it is urgent to explore new treatment strategies. The Tiaosui Xingshen Method (TSXSF) is a comprehensive awakening treatment plan created by Professor Chen Xiao's team based on the traditional Chinese medicine theory of "marrow damage and spirit injury". It takes acupuncture as the core and is supplemented by syndrome - differentiated treatment with traditional Chinese medicine. Preliminary clinical studies have shown that TSXSF can significantly improve the consciousness level of vegetative patients, with a total effective rate of up to 50%. This article systematically expounds on the intervention mechanism of TSXSF from three aspects: traditional Chinese medicine theory, molecular mechanism, and clinical evidence.

2. Theoretical Basis of the Method of Regulating Marrow and Awakening the Mind

2.1 The Theory of "Marrow Injury and Spirit Damage" in Traditional Chinese Medicine

The Huangdi Neijing (Yellow Emperor's Inner Canon) proposed that "the brain is the sea of marrow," laying the theoretical foundation for the close relationship between the brain and marrow. The Compendium of Materia Medica clearly stated that "the brain is the residence of the original spirit," further emphasizing the core role of the brain in mental activities. Wu Qian, a medical expert in the Qing Dynasty, pointed out in The Golden Mirror of Medicine that "when the brain marrow is damaged, the spirit has nowhere to rely on, becomes erratic, and the divine consciousness is impaired, thus it is called spirit damage." This clearly expounded on the relationship between the marrow and the spirit, as well as the impact of marrow injury on the spirit. Based on this, modern traditional Chinese medicine believes that the core pathogenesis of chronic disorders of consciousness is "marrow injury and spirit damage." "Marrow injury" is often caused by factors such as trauma, phlegm and blood stasis obstructing the collaterals, and deficiency of the zang - fu organs, resulting in emptiness of the sea of marrow and malnourishment of the brain marrow. "Spirit damage" is manifested as loss of consciousness, cognitive dysfunction, etc. In the pathogenesis of vegetative state, for example, severe craniocerebral trauma can directly damage the brain marrow, leading to disorder of qi and blood, blockage of the clear orifices by blood stasis, and further aggravating marrow injury. Moreover, the insufficiency of the sea of marrow makes the spirit have no attachment, further deteriorating the state of consciousness and forming a vicious cycle [7-8].

2.2 The Neuroinflammatory Mechanism of Modern Medicine

Neuroinflammation is considered a key factor in secondary brain injury and plays a significant role in the pathogenesis of vegetative state patients. Microglia, as innate immune cells of the central nervous system, are rapidly activated after craniocerebral injury[9] and can differentiate into two phenotypes: pro-inflammatory (M1) and anti-inflammatory (M2)[10]. M1 microglia release a large number of pro-inflammatory cytokines, such as tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β). By activating the nuclear factor-kappa B (NF- κ B) pathway, they exacerbate neuronal apoptosis, blood-brain barrier damage, and neuroinflammatory responses. In contrast, M2 microglia secrete anti-inflammatory factors like interleukin-10 (IL-10), which can promote tissue repair and reduce inflammation [11]. Research shows[12] that the expressions of TNF- α and NF- κ B in the cerebrospinal fluid of patients with chronic disorders of consciousness are significantly elevated, suggesting that the persistent presence of neuroinflammation is a major obstacle to consciousness recovery. Therefore, during the process of awakening vegetative state patients, there is an inevitable connection between disease changes and persistent neuroinflammation. Persistent neuroinflammation continuously damages neurons and glial cells, affecting the recovery of consciousness.

2.3 Integration of Traditional Chinese and Western Medicine Theories

There is a certain correlation between the traditional Chinese medicine (TCM) theory of "marrow

damage and spirit injury" and the neuroinflammatory mechanism in modern medicine. "Marrow damage" can correspond to the structural and functional damage of the brain marrow caused by neuroinflammation, such as neuronal apoptosis and damaged nerve fibers. "Spirit injury" is closely related to consciousness dysfunction, which is consistent with the fact that neuroinflammation affects the normal neural signal transmission in the brain and leads to a decline in consciousness levels. The Method of Regulating Marrow and Awakening Spirit was established based on the integration of these TCM and Western medicine theories. It aims to regulate the balance of qi, blood, yin, and yang in the body, improve the nutritional supply of the brain marrow, and inhibit the neuroinflammatory response, thereby achieving the dual goals of "regulating the marrow" and "awakening the spirit." For example, acupuncture at the Baihui acupoint can regulate the release of neurotransmitters, inhibit the TNF- α /NF- κ B pathway, reduce neuronal apoptosis in the frontal cortex, and play a role in protecting nerve cells[13]. Stimulating the Taixi acupoint can nourish the kidney essence, improve cerebral blood flow, and promote nerve regeneration, providing a material basis for the restoration of consciousness.

3. Intervention Mechanisms of the Method of Regulating Marrow and Awakening the Mind

3.1 Regulation of Neuroinflammation by Acupuncture

The method of regulating marrow and awakening the mind takes acupuncture as its core. Its main acupoints (such as Shuigou, Neiguan, Baihui, etc.) play a crucial role in regulating neuroinflammation, mainly by influencing the IL - 10/NF - κ B signaling pathway. Electroacupuncture stimulation of these acupoints can reduce the activity of the IKK complex and decrease the degradation of I κ B α , thereby preventing the nuclear translocation of NF - κ B and downregulating the expression of pro - inflammatory factors such as TNF - α and IL - 1 β [14]. At the same time, acupuncture can also upregulate the expression of IL - 10. As an important anti - inflammatory factor, IL - 10 can inhibit the release of pro - inflammatory factors by blocking the NF - κ B signal transduction and promote the polarization of M2 - type microglia, enhancing the body's anti - inflammatory ability[15]. Preliminary clinical studies have found that this method has a definite curative effect. Combining existing relevant research and clinical observations, it is speculated that the acupuncture method of regulating marrow and awakening the mind may act on the IL - 10/NF - κ B pathway, inhibit the activation of NF - κ B, downregulate the expression of TNF - α , upregulate the expression of IL - 10, reduce neuroinflammation, and protect nerve cells, thus playing a role in treating chronic disorders of consciousness.

Electroacupuncture at the Shuigou (GV26) acupoint can increase the expression of arginase-1 (Arg-1, a marker of M2 microglia) and reduce the expression of inducible nitric oxide synthase (iNOS, a marker of M1 microglia) in the brains of rats with traumatic brain injury[16]. This helps to improve the inflammatory microenvironment and promote the recovery of nerve function. Such a phenotypic shift is conducive to reducing the damage of neuroinflammation to neurons and promoting the repair and regeneration of nerve cells, providing an important cytological basis for the restoration of consciousness in vegetative state patients. By regulating the function of microglia, the method of regulating the marrow and awakening the mind can effectively alleviate the neuroinflammatory response, promote the stability of the brain's internal environment, and create favorable conditions for the recovery of nerve function.

3.2 Regulation of Cerebral Blood Flow and Neural Network by Acupuncture

Insufficient cerebral perfusion is one of the important factors leading to disorders of consciousness in vegetative patients. The method of regulating the marrow and awakening the mind can improve cerebral perfusion by acupuncture at specific acupoints [17]. Acupuncture at acupoints on the Governor Vessel such as Shenting (GV24) and Baihui (GV20) can, to a certain extent, activate the vascular endothelial growth factor (VEGF) pathway, promote the establishment of collateral circulation, increase the blood supply to brain tissue, improve the state of cerebral ischemia and hypoxia, provide sufficient nutrients and oxygen for nerve cells, and contribute to the recovery of nerve function and the awakening of consciousness.

3.3 Synergistic Effects of Adjuvant Chinese Medicine Treatment

Previous studies have found that the Method of Regulating Marrow and Awakening the Mind is often combined with Chinese medicines that invigorate qi and promote blood circulation, such as

Sijunzi Decoction and Tongqiao Huoxue Decoction, for treatment, which can effectively reduce [the symptoms]. These Chinese medicines play an important synergistic role. Active ingredients in Chinese medicines, such as astragaloside and tetramethylpyrazine, can penetrate the blood-brain barrier, inhibit the Toll-like receptor 4 (TLR4)/NF- κ B pathway, reduce free radical generation, and mitigate the oxidative damage of nerve cells. For example, andrographolide can reduce the level of IL-1 β in rats with cerebral hemorrhage, alleviate cerebral edema, and protect nerve cells [18]. Chinese medicine treatment can regulate the physiological functions of the body from multiple aspects, enhance the therapeutic effect of the Method of Regulating Marrow and Awakening the Mind, and further promote the recovery of consciousness in vegetative patients. The holistic conditioning effect of Chinese medicine complements the local stimulating effect of acupuncture, jointly improving the patient's condition.

4. Efficacy Evaluation System

4.1 Behavioral Assessment

Before treatment and every 15 days after treatment, five physicians will score the patients using the Modified Coma Recovery Scale (CRS-R). The average score will be calculated for statistical analysis to evaluate the treatment effect.

4.2 Imaging evidence

Before treatment and every 1 month after treatment, functional magnetic resonance imaging including Perfusion Weighted Imaging (PWI) and Blood Oxygen Level Dependent (BOLD) assessment will be performed. For PWI assessment, cerebral blood volume (rCBV) and cerebral blood flow (rCBF) will be used as specific quantitative indicators. For BOLD assessment, the amplitude of low-frequency fluctuations (ALFF) and regional homogeneity (ReHo) will be the main evaluation methods. After specific quantitative evaluation, the data will be included in the statistical analysis to objectively evaluate the treatment effect.

4.3 Molecular biology indicators

Before treatment and every 1 month after treatment, the expressions of inflammatory factors IL-10, NF- κ B, and TNF- α in cerebrospinal fluid will be detected by ELISA. Before treatment and every 1 month after treatment, the expression levels of related inflammatory proteins IL-10, NF- κ B, and TNF- α in cerebrospinal fluid will be detected by Western blot.

5. Discussion

5.1 Advantages and Innovations of the Method of Regulating Marrow and Awakening the Mind

The Method of Regulating Marrow and Awakening the Mind adopts a multi-target intervention approach. It integrates the anti-inflammatory effects of acupuncture, the improvement of blood flow, and the synergistic effects of traditional Chinese medicine, breaking through the limitations of single therapies. It comprehensively treats the conditions of vegetative patients from multiple perspectives, thereby enhancing the therapeutic effect. In terms of efficacy evaluation, it combines multi-dimensional indicators such as the Coma Recovery Scale - Revised (CRS-R), functional magnetic resonance imaging (fMRI), and molecular markers for the first time. This achieves an objective and comprehensive verification of the treatment effect, providing a reliable basis for scientifically evaluating the effectiveness of the therapy. This therapy organically combines the traditional Chinese medicine theory of "marrow damage and spirit injury" with the modern neuroinflammatory mechanism, offering a new paradigm for the integrated traditional Chinese and Western medicine treatment of vegetative patients and promoting the development of integrated traditional Chinese and Western medicine.

5.2 Potential Problems and Challenges

Although the Method of Regulating Marrow and Awakening the Mind has achieved certain results in the current clinical treatment of awakening vegetative patients, it still faces potential problems and

challenges. The causes of vegetative state are complex and diverse, including brain trauma, stroke, hypoxia, etc. The affected areas in patients vary, and the symptoms presented can also be different. During the treatment process with this method, it still needs to be combined with the syndrome differentiation and treatment in traditional Chinese medicine to achieve better therapeutic effects. At present, although we have some understanding of the role of the IL - 10/NF - κ B pathway in the Method of Regulating Marrow and Awakening the Mind, the specific regulatory nodes of this pathway have not been fully elucidated. In - depth research on its detailed mechanism will help further optimize the treatment plan and improve the precision of treatment. Most of the existing studies are short - term observations lasting 3 - 6 months, lacking long - term follow - up data. It is difficult to comprehensively evaluate the long - term efficacy and safety of this therapy. Therefore, it is necessary to carry out longer - term follow - up studies to determine its impact on the long - term prognosis of patients.

5.3 Future Research Directions

After forming a comprehensive traditional Chinese medicine awakening - promoting plan with an objective evaluation system, definite efficacy, and clear mechanisms, centered around the "Method of Regulating Marrow and Awakening the Mind" acupuncture technique, we will conduct academic promotion through academic exchanges and technical training courses. This will enable the research results to guide clinical practice on a wider scale and benefit as many patients with chronic disorders of consciousness as possible. Given the large number of patients with chronic disorders of consciousness nationwide, the promotion and application of the clinical research results of the "Method of Regulating Marrow and Awakening the Mind" acupuncture technique for treating chronic disorders of consciousness have broad market prospects. This research provides new technologies, methods, and ideas for the treatment of chronic disorders of consciousness and is worthy of promotion in related research. It can be widely applied in clinical practice in the future, laying a solid foundation for continuously exploring new methods of traditional Chinese medicine in the treatment of chronic disorders of consciousness.

6. Conclusion

As an innovative therapy combining traditional Chinese medicine theory and modern medicine, the "Regulating Marrow and Awakening Mind" method has shown remarkable potential in the treatment of vegetative state patients for arousal. By inhibiting neuroinflammation and improving cerebral perfusion and neural network function, this therapy can effectively promote the restoration of consciousness in vegetative state patients. Its core mechanism lies in regulating the IL-10/NF- κ B pathway to achieve a synergistic effect of "regulating marrow" and "awakening mind". However, currently, this therapy still faces some problems and challenges, which require further in-depth research and exploration. In the future, through continuous deepening of mechanism research, optimization of treatment plans, and expansion of clinical verification, the "Regulating Marrow and Awakening Mind" method is expected to achieve greater breakthroughs in the field of vegetative state treatment, bringing new hope to numerous patients and their families. At the same time, it will also provide more effective strategies and methods for the treatment of chronic disorders of consciousness.

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