

Research Progress and Reflections on External Treatments of Traditional Chinese Medicine for Post-Stroke Fatigue

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Abstract: Post-stroke fatigue (PSF) is a common yet frequently overlooked complication that severely impacts patients' quality of life and rehabilitation progress. In recent years, external therapies of Traditional Chinese Medicine (TCM) have gained widespread application in stroke rehabilitation due to their characteristics of being simple, convenient, effective, and cost-effective, emerging as a prominent research focus in the field. This review summarizes advances in TCM external therapies for PSF, including TCM perspectives on PSF, clinically utilized TCM external techniques, and current limitations in research. The aim is to provide a foundation and direction for future studies, as well as a reference for clinical implementation of appropriate TCM external therapies for PSF patients.

Keywords: Stroke; Post-Stroke Fatigue (PSF); Traditional Chinese Medicine; Systematic Review

1. Introduction

According to the Global Burden of Disease Study (GBD)^[1], stroke has surpassed other diseases to become the leading cause of mortality among Chinese residents. China ranks among the countries with the highest stroke prevalence globally, with its incidence, recurrence rate, and stroke-related mortality showing a consistent upward trend, drawing significant societal and healthcare system attention^[2]. Stroke is often accompanied by a range of sequelae, including not only motor dysfunction, language impairment, and cognitive deficits but also negative emotional disturbances such as depression and anxiety^[3]. Among these, PSF, as a prevalent and persistent non-motor symptom, has increasingly become a focus of research among scholars worldwide^[4]. PSF is a pathological state of fatigue, typically characterized by persistent and subjective exhaustion that is disproportionate to prior activity levels and does not resolve with adequate rest. This fatigue manifests at both physiological and psychological levels, significantly impairing functional recovery and quality of life in affected individuals. Globally, the incidence of PSF is as high as 46.79%, while reported rates in China reach 43.5%^[5]. Studies indicate that approximately 43% of stroke survivors consider fatigue their "most unmet care need"^[6]. Furthermore, PSF not only hinders rehabilitation and activities of daily living but also substantially increases psychological and caregiving burdens, emerging as an independent risk factor for poor stroke outcomes^[7]. Consequently, effective interventions for PSF have become a critical research priority and clinical challenge in post-stroke rehabilitation.

Among various therapeutic interventions, TCM external therapies have garnered increasing attention due to their characteristics of being "simple, convenient, effective, and economical." Systematic records of external therapies can be traced back to The Yellow Emperor's Inner Canon·Basic Questions·Great Treatise on the Ultimate Truth (Huangdi Neijing·Suwen·Zhi Zhen Yao Da Lun). TCM external therapies refer to therapeutic approaches that utilize specific medicinal substances, instruments, or manual techniques to stimulate body surface acupoints, thereby regulating visceral functions and qi-blood balance through the meridian system, without requiring oral medication. Currently, TCM external therapies applied in PSF intervention research primarily include acupuncture, moxibustion, auricular acupressure, herbal fumigation, gua sha, cupping, and acupoint application. These modalities can be employed either individually or in combination, demonstrating multiple therapeutic effects such as improving neurological function, modulating immune and metabolic

homeostasis, and alleviating neuropsychological symptoms. Preliminary clinical studies have also shown their definitive efficacy in ameliorating post-stroke fatigue and enhancing patients' quality of life. However, current limitations include insufficient exploration of therapeutic mechanisms, lack of standardized treatment protocols, and inconsistent quality of evidence-based research, all of which necessitate further standardization and in-depth investigation.

Therefore, this review will systematically summarize recent advances in TCM external therapies for PSF intervention, with particular focus on treatment modalities, clinical efficacy, and underlying mechanisms. The findings aim to provide theoretical foundations and research directions for future basic investigations and clinical applications in this field.

2. Traditional Chinese Medicine Perspective on Post-Stroke Fatigue

In TCM, PSF is commonly classified under the categories of "Xie Dai" (lassitude), "Xie Duo" (sluggishness), "Si Zhi Lao Juan" (fatigue of the four limbs), "Xu Lao" (consumptive disease), or "Wei Zheng" (flaccidity syndrome). Its fundamental pathogenesis is rooted in the severe disruption of Qi, Blood, Yin, and Yang, as well as the depletion of Zheng Qi (vital Qi), caused by the acute onset of stroke^[8]. According to TCM theory, the core pathomechanism of PSF is primarily characterized by disharmony of Yin and Yang, obstruction of Qi movement, and disharmony of Qi and Blood. Following stroke, Yuan Qi (primordial Qi) is abruptly damaged, leading to impaired circulation of Qi and Blood, dysfunction of the Zang-Fu organs, and the development of complex pathological patterns such as Qi deficiency with blood stasis, Qi deficiency with phlegm and stasis, and wind-phlegm with blood stasis. Among these, Qi deficiency represents the root, while phlegm and stasis are the manifestations; they interact with and exacerbate each other in a mutually reinforcing manner.

As recorded in Plain Questions (Su Wen), Chapter "Ben Shen", "When the Spleen Qi is deficient, the four limbs will be weak and powerless." The Spleen is regarded as the source of the generation and transformation of Qi and Blood, governing the transportation and transformation of food and water, thereby facilitating the distribution of nutrients throughout the body. After stroke, Spleen Qi is severely impaired, resulting in the inability to generate Qi and Blood. Consequently, the limbs are deprived of nourishment, manifesting as fatigue, excessive sleepiness, and a pervasive sense of tiredness. Ten Treatises of the Eastern Yuan (Dong Yuan Shi Shu) also states^[9]: "When the Spleen and Stomach are weak, one becomes listless, sluggish, fond of lying down, and experiences weakness in the four limbs," further underscoring the pivotal role of Spleen deficiency in the pathogenesis of PSF. The Liver governs the smooth flow of Qi and regulates emotional activity. In patients with stroke, post-stroke functional impairments, social isolation, and changes in life roles may lead to emotional disturbances such as depression and anxiety, which often result in Liver Qi stagnation. This stagnation, in turn, impairs the Spleen's transformative and transportive functions, giving rise to the pattern of "Liver Qi stagnation with Spleen deficiency" (Gan Yu Pi Xu). The failure of the Liver to maintain free flow and the Spleen to perform its transportation function leads to the internal generation of phlegm and dampness, Qi stagnation, and Blood stasis. The subsequent congealing of phlegm and stasis mutually reinforces the pathological burden, thereby exacerbating the state of fatigue^[10].

In addition, modern research has shown that PSF is not only associated with damage to the central nervous system but may also be related to dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis, autonomic nervous system dysregulation, and elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α). In the context of TCM, these pathological changes can be interpreted as manifestations of "deficiency of Zheng Qi (vital Qi) and internal retention of pathogenic Qi," indicating a decline in the body's immunological and neuroregulatory functions^[11]. This aligns with the TCM pathogenesis of "disharmony of Zang-Fu organs and discordance of Qi and Blood," reflecting the convergence of modern biomedical findings and traditional theoretical understanding.

In summary, PSF is classified in TCM as a manifestation of Xu Lao (consumptive disease). Its etiology is primarily attributed to the substantial depletion of Zheng Qi (vital Qi) following stroke, resulting in dual deficiency of the Spleen and Kidney and insufficiency in the generation and transformation of Qi and Blood. Additionally, internal injury caused by emotional disturbances leads to Liver Qi stagnation, further contributing to the formation of intermingled phlegm and blood stasis, dysfunction of the Zang-Fu organs, and ultimately, a clinical presentation dominated by fatigue and physical weakness^[12]. Therapeutic strategies should therefore focus on the principles of tonifying Qi and nourishing Blood, strengthening the Spleen and resolving dampness, soothing the Liver and

regulating Qi, and invigorating Blood circulation to unblock the collaterals. Treatment should be guided by syndrome differentiation, addressing both the root and the manifestation, with the aim of improving patients' quality of life and facilitating their rehabilitation process.

3. Application of External Therapies of Traditional Chinese Medicine in PSF

3.1 Acupuncture Therapy

3.1.1 Needling Techniques

Acupuncture, as a widely recognized and clinically appropriate technique, has extensive therapeutic applications. From the perspective of TCM, one of the key pathophysiological mechanisms of stroke is the deficiency or obstruction of Yang Qi. Persistent post-stroke Yang Qi deficiency is considered a major contributing factor to the development of PSF. Therefore, reinforcing Yang Qi is of critical importance in the treatment of PSF. Baihui (GV20), known as the convergence point of all Yang Meridians and the Governor Vessel (Du Mai), plays a pivotal role in harmonizing the balance of Qi, Blood, Yin, and Yang throughout the body. Stimulation of Baihui is believed to arouse the mind (Xing Nao) and calm the spirit (An Shen), thereby promoting systemic regulation. On the other hand, Qubin (GB7), located at the intersection of the Foot Shaoyang Gallbladder Meridian and the Foot Taiyang Bladder Meridian, serves the dual function of enhancing Yang Qi and regulating the circulation of Qi and Blood. Targeting these two acupoints can effectively improve the status of Yang Qi in post-stroke patients, thus contributing to the alleviation of PSF symptoms^[13]. Sui Ruiqiao et al.^[13] employed the technique of "penetrating Baihui (GV20) to Qubin (GB7)" and observed that it could enhance cerebral cell metabolism, invigorate Yang Qi, and harmonize the balance of Qi, Blood, Yin, and Yang, thereby effectively alleviating fatigue. The study was designed as a randomized controlled trial (RCT), and its findings support the therapeutic significance of the Governor Vessel (Du Mai) and Yang Meridians in the treatment of PSF. However, the relatively small sample size (n = 60) and the lack of long-term follow-up limit the generalizability of the results. Chen Lianghua et al.^[14] focused on PSF of the Qi deficiency pattern and innovatively combined scalp acupuncture (based on the Xingnao Kaiqiao method, with additional points such as Baihui [GV20] and Sishencong [EX-HN1]) with abdominal acupuncture (targeting Yin Qi Guiding to its Origin and Abdominal Four-Gates). The results indicated that this combined therapy was superior to the conventional Xingnao Kaiqiao method alone in improving fatigue severity, quality of life, and TCM syndrome scores. This reflects a therapeutic strategy that integrates spirit-regulation through scalp acupuncture with Qi-regulation through abdominal acupuncture, while also preliminarily addressing the differentiation of TCM patterns—an innovative highlight of the study. Nevertheless, the uniqueness of the theoretical system of abdominal acupuncture and its underlying mechanisms in the treatment of PSF warrant further in-depth investigation. Wang Baoguo et al.^[15] conducted a study to investigate the therapeutic effect of "moxibustion-acupuncture on the Governor Vessel (Du Mai)" in the intervention of PSF. Participants in the control group received repetitive transcranial magnetic stimulation (rTMS), while the treatment group received additional therapy involving moxibustion-acupuncture on the Governor Vessel based on the same rTMS protocol. In the treatment group, selected acupoints included Baihui (GV20), Dazhui (GV14), Shenting (GV24), Fengfu (GV16), Mingmen (GV4), Zhiyang (GV9), and Yaoyangguan (GV3). Dazhui was treated using bloodletting puncture (collateral pricking), Baihui received moxibustion therapy, and the remaining acupoints were stimulated via conventional acupuncture. Each treatment session lasted 30 minutes. After two consecutive weeks of intervention, the results showed that the addition of moxibustion-acupuncture on the Du Mai to rTMS significantly improved fatigue symptoms, sleep quality, and limb motor function. This suggests a potential synergistic effect between traditional acupuncture techniques and modern neuromodulation therapies, providing a novel clinical approach for the management of PSF.

Basic research suggests that acupuncture may exert its therapeutic effects by modulating the expression of microRNAs and influencing associated signaling pathways^[16], as well as by regulating neurotransmitters such as serotonin (5-HT) and dopamine (DA), attenuating neuroinflammation, and improving cerebral blood flow and metabolism. However, studies specifically targeting the mechanistic pathways of acupuncture in the treatment of PSF remain limited. In particular, the differential mechanisms underlying various TCM syndrome patterns (Zheng Xing) and distinct acupoint combinations require further investigation.

3.1.2 Moxibustion Therapy

Moxibustion therapy utilizes the thermal effects and pharmacological activity of ignited *Artemisia argyi* (mugwort) and other combustible medicinal materials, which are applied to specific meridians and acupoints to achieve therapeutic outcomes such as warming and unblocking the meridians, promoting blood circulation, tonifying Yang Qi, dispelling Cold pathogens, and resolving blood stasis [17–18]. This therapy encompasses various techniques and modalities. Depending on the health condition being addressed and the anatomical location of treatment, it is essential to select the appropriate type of moxibustion and to follow the correct sequence of application to ensure efficacy and safety.

Xiao Binxin et al.^[19] randomly assigned patients with PSF into two groups. The control group received standard rehabilitation training and secondary prevention therapy for ischemic stroke, while the observation group received additional constant-temperature moxibustion therapy applied to specific acupoints—Hegu (LI4), Quchi (LI11), and Jianyu (LI15)—along the Hand Yangming Large Intestine Meridian on the affected side. After two consecutive weeks of intervention, the observation group showed significant improvements in both the Modified Barthel Index (MBI) and the Stroke-Specific Quality of Life Scale (SS-QOL), alongside a notable reduction in the Fatigue Severity Scale (FSS) scores. These results indicate enhanced ability in daily living activities, improved quality of life, and alleviation of fatigue. The application of constant-temperature moxibustion to relevant acupoints on the Hand Yangming Large Intestine Meridian demonstrates a positive effect in improving physical function and reducing fatigue in patients with PSF. Xie Gaosheng et al.^[20] conducted a study aimed at evaluating the therapeutic effect of heat-sensitive moxibustion combined with exercise therapy in patients with PSF, as well as its impact on inflammatory cytokines including interleukin-1 β (IL-1 β), tumor necrosis factor-alpha (TNF- α), and C-reactive protein (CRP). A total of 82 patients diagnosed with PSF were enrolled and randomly assigned to an observation group and a control group using a random number table method. On the basis of conventional medical treatment, the control group received standard exercise therapy, while the observation group received additional heat-sensitive moxibustion. Selected acupoints included Hegu (LI4), Quchi (LI11), Sanyinjiao (SP6), Neiguan (PC6), Zusanli (ST36), Guanyuan (CV4), Yanglingquan (GB34), Taichong (LR3), Zhongwan (CV12), and Zhangmen (LR13). After a 4-week intervention, the observation group demonstrated significant improvements in fatigue reduction and motor function, along with marked decreases in serum levels of IL-1 β , TNF- α , and CRP. These findings suggest that inhibition of the inflammatory response may be one of the key mechanisms by which heat-sensitive moxibustion combined with exercise therapy alleviates PSF.

Modern studies have demonstrated that moxibustion can regulate fatigue-related metabolic byproducts such as blood urea nitrogen (BUN) and blood lactic acid (BLA)^[21]. Additionally, it influences the function of the hypothalamic–pituitary–adrenal (HPA) axis by modulating the release of inflammatory cytokines, including interleukin-1 (IL-1) and interleukin-6 (IL-6)^[22], thereby contributing to the stabilization of the internal milieu and alleviation of fatigue symptoms. Compared to acupuncture, clinical and mechanistic research on moxibustion in the treatment of PSF remains relatively limited. The specific roles of its thermal effects, the pharmacological activity of *Artemisia argyi* (moxa floss) components, and its regulatory impact on autonomic nervous system function in PSF require further in-depth investigation. In terms of safety, the risk of burns must be considered; however, most existing studies provide insufficient reporting on adverse events related to moxibustion.

3.2 Auricular Acupressure

Auricular acupressure, guided by the theoretical framework of TCM, involves the application of smooth, firm round objects—such as Semen Vaccariae, magnetic beads, or herbal pellets—onto specific auricular acupoints on the auricle. Manual pressing or kneading of the seeds is performed to elicit sensations such as soreness, numbness, or distension, thereby stimulating the acupoints^[23]. This method is believed to harmonize the functions of the Zang-Fu organs, nourish the limbs and musculoskeletal system, and ultimately achieve an anti-fatigue therapeutic effect. In addition, modern biomedical studies have shown that auricular acupressure may alleviate fatigue by stimulating peripheral nerve endings in the ear, thereby modulating the neuro–endocrine–immune (NEI) network, promoting the secretion of neurotransmitters, enhancing brain function, and improving systemic metabolism^[24].

Dong Xu et al.^[25] conducted a study to evaluate the effects of auricular acupressure with magnetic pellets on fatigue severity and quality of life in patients with PSF. Participants were randomly assigned to two groups. Both groups received auricular acupoint stimulation at Subcortex, Shenmen (TF4), Heart, Liver, Spleen, and Endocrine points. In the Semen Vaccariae group, traditional Semen Vaccariae

seeds were applied with manual pressing, while the magnetic acupressure group received magnetized pellets (magnetotherapy plasters) for stimulation. Fatigue severity was assessed using the Fatigue Severity Scale (FSS), the Personal Fatigue Intensity Questionnaire (PFIQ), and the Stroke-Specific Quality of Life Scale (SS-QOL), both before and after the intervention. Intragroup comparisons revealed statistically significant improvements in fatigue in both groups. However, post-intervention intergroup comparisons showed that the magnetic acupressure group had significantly lower FSS and PFIQ scores, indicating a superior effect in alleviating fatigue. Additionally, SS-QOL total scores were significantly higher in the magnetic acupressure group, reflecting greater improvements in quality of life compared to the Semen Vaccariae group. These results suggest that although both groups used the same auricular acupoints and both interventions significantly improved fatigue, magnetic acupressure demonstrated superior efficacy in reducing fatigue severity and intensity, as well as enhancing quality of life. This indicates that the biophysical effects of magnetic fields may potentiate the traditional therapeutic effects of auricular stimulation. It also highlights that different stimulation modalities may exert distinct influences on fatigue outcomes, offering a new direction for optimizing auricular therapy in PSF management. Li Ruoxuan^[26] conducted a study to evaluate the clinical efficacy of auricular acupressure in patients with PSF of the Qi deficiency pattern. A targeted auricular acupressure protocol was developed specifically for this TCM pattern and applied in a trial involving 78 patients. The results showed that patients in the Qi deficiency-type auricular acupressure group exhibited significantly greater clinical improvements compared to those in the sham auricular acupressure group. The intervention effectively reduced fatigue severity, improved cognitive function, alleviated TCM syndrome manifestations, and enhanced the ability to perform activities of daily living. These findings are consistent with those reported by Yang Lili et al.^[27].

Current research on auricular acupressure commonly faces several methodological limitations, including a lack of standardized criteria for acupoint selection, ambiguous control over stimulation dosage parameters such as pressing frequency, intensity, and duration, as well as challenges in the design of appropriate placebo controls. While its fatigue-relieving effects are believed to be associated with neuroendocrine modulation, it remains unclear whether additional mechanisms—such as vagus nerve stimulation or involvement of central circuits related to pain and fatigue regulation—are also implicated. Further evidence integrating both basic and clinical research is needed to elucidate these potential pathways.

3.3 Other Therapeutic Approaches

In addition to the aforementioned treatments, traditional Chinese external therapies—including herbal fumigation, acupoint application, and therapeutic massage—have demonstrated efficacy in alleviating fatigue symptoms in PSF patients by regulating qi and blood circulation, unblocking meridians, balancing yin-yang, and harmonizing zang-fu organ functions.

Liang Yahui et al.^[28] investigated the effects of herbal fumigation based on the principles of tonifying qi and activating blood circulation and strengthening the spleen and soothing the liver. Their findings revealed significant improvements in TCM symptom patterns, fatigue severity, sleep quality, depressive mood, and motor function, ultimately enhancing patients' quality of life. Li Jiao et al.^[29] conducted a comparative study in which the control group received early-stage comprehensive rehabilitation exercises, while the observation group underwent additional acupoint application therapy. Results indicated that the combined intervention yielded superior outcomes in fatigue reduction and motor function recovery. Furthermore, some researchers have employed scalp meridian massage combined with herbal acupoint application to treat PSF. This approach facilitates head qi-blood circulation, regulates visceral functions, and promotes mental clarity and sensory awakening, thereby exerting sedative, anxiolytic, and fatigue-relieving effects^[30].

4. Conclusion

Traditional Chinese external therapies have demonstrated multifaceted advantages and considerable clinical efficacy in managing PSF. Acupuncture modulates meridians and regulates qi-blood circulation to restore yin-yang balance, thereby alleviating fatigue symptoms; Auricular acupressure leverages the somatotopic correspondence between the ear and bodily systems to regulate physiological functions through auricular stimulation; Herbal fumigation combines pharmacological and thermal effects to permeate through the skin, warming meridians, harmonizing qi-blood, and reinforcing healthy qi while eliminating pathogens; Therapeutic massage employs manual techniques to enhance blood circulation,

relieve muscular tension, and regulate psychosomatic states; Acupoint application therapy improves overall patient condition by regulating qi-blood and zang-fu functions. Despite these demonstrated benefits, several limitations persist in current research: 1) Most studies lack PSF-specific syndrome differentiation, resulting in non-individualized treatments and inconsistent clinical outcomes. 2) Standardized protocols for treatment procedures, manipulation techniques, and treatment frequency remain underdeveloped for many external therapies. 3) Current research disproportionately focuses on acupuncture, while other external therapies remain understudied, suggesting the need for broader therapeutic exploration. 4) While effective, symptom recurrence following treatment cessation necessitates the development of post-discharge continuation protocols. 5) Safety concerns (e.g., burns from fumigation or acupuncture-related adverse events) remain insufficiently addressed in most studies. 6) The predominant absence of sham interventions in control groups introduces potential placebo effects and confounding biases.

Future research should prioritize: (1) syndrome-specific treatment protocols, (2) standardization of therapeutic parameters, (3) expansion to understudied modalities, (4) long-term efficacy evaluation, (5) rigorous safety assessments, and (6) implementation of proper sham controls to enhance methodological rigor.

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