

Treating Depression-Related Fatigue from the Perspective of “The Liver is the Basis of Resistance to Fatigue”

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Abstract: *Through an in-depth analysis of the theoretical connotation of “the liver is the basis of resistance to fatigue” (“baiji zhi ben”), this paper proposes that the physiological functions of the liver in regulating blood and governing qi movement play essential roles in the body’s ability to tolerate physical and mental fatigue. The development of depression-related fatigue is closely related to dysfunction of the liver in governing free coursing and storage. In terms of pathogenesis, the manifestation lies in the “basis of resistance to fatigue,” the root lies in the disorder of the liver’s substance and function, and the key mechanism lies in the instability of the ethereal soul (“hun”). Regarding treatment, attention should be paid to three aspects: soothing the liver to relieve depression and regulating qi movement; nourishing blood, strengthening the spleen, reinforcing yang, and tonifying deficiency; and regulating the spirit (“shen”), calming the ethereal soul, and harmonizing body and spirit. It is hoped that such approaches may contribute to the treatment of depression-related fatigue.*

Keywords: Liver, Basis of resistance to fatigue, Depression, Fatigue.

1. Introduction

Depression is a common mental disorder characterized by “four highs”: high prevalence (lifetime prevalence of approximately 15–20% globally), high recurrence rate (>40% within three years), high disability rate (ranked by the WHO as the leading cause of disability worldwide), and high risk of suicide (approximately 15% of patients eventually die from suicide) [1]. Epidemiological surveys show that there are 280 million people with depression worldwide [2], of whom more than 95 million are in China, with an incidence rate of 6.8%, making depression the leading cause of disease burden among mental disorders [3].

Modern psychiatric diagnostic systems have clear criteria for the symptomatic characteristics of depression. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) of the American Psychiatric Association lists somatic fatigue as a typical manifestation of the motor inhibition symptom cluster in depression [4]. In the International Classification of Diseases, 10th revision (ICD-10), motor inhibition symptoms, together with low mood, loss of interest, and anhedonia, constitute the core diagnostic elements of depression [5]. Currently, the pathogenesis of depression-related fatigue remains unclear, possibly involving dysregulation of neural circuits in the brain, immune dysfunction, and inflammatory factors [6]. Clinical intervention strategies mainly include non-pharmacological and pharmacological approaches. Non-pharmacological interventions, such as exercise therapy, psychological intervention, and dietary modification, have shown certain efficacy. Pharmacological interventions are primarily based on antidepressants, which act by regulating neurotransmitter levels. However, existing treatments generally have limitations, including limited efficacy and significant adverse drug reactions [7]. Studies have shown that approximately 20% of patients treated with selective serotonin reuptake inhibitors (e.g., fluoxetine) experience fatigue and other side effects, and similar reactions are also common with tricyclic

antidepressants such as clomipramine [8]. Therefore, exploring the treatment of depression-related fatigue from the perspective of traditional Chinese medicine (TCM) holds important clinical and practical significance.

In TCM, depression is classified under the categories of “depression syndrome” (“yu zheng”) or “depression disease” (“yu bing”), while depression-related fatigue falls under the category of “consumptive disease” (“xu lao”). The liver is closely related to depression-related fatigue, and liver depression is the root cause of depression syndromes. As stated in the “Suwen·Six Component Spleen Theory”: “The liver is the basis of resistance to fatigue and the residence of the ethereal soul.” This indicates that the liver plays a fundamental regulatory role in the body’s response to physical and mental fatigue. This paper explores the etiology, mechanism, and treatment of depression-related fatigue based on the theory of “the liver is the basis of resistance to fatigue,” aiming to provide new insights and methods for its clinical management.

2. Theoretical Connotation of “the Liver Is the Basis of Resistance to Fatigue”

The “Suwen·Six Component Spleen Theory” states: “The liver is the basis of resistance to fatigue (“baiji zhi ben”) and the residence of the ethereal soul.” There has long been academic debate regarding the meaning of “baiji zhi ben”, with various interpretations among physicians throughout history. From the perspective of philology, it is more accurate to interpret it as “the basis of ability to endure fatigue” (“nengji zhi ben”). “Ability to endure fatigue” refers to the body’s capacity to tolerate fatigue, and human motor function depends on the activity of the sinews. According to TCM visceral manifestation theory, the liver governs the functions of the sinews and regulates limb movement. Therefore, the liver is indeed the foundation of the body’s ability to resist fatigue [9]. The “Erya·Yi” records: Pi” refers to the female

bear, which is particularly fierce.” From the perspective of ancient philology, the character “ji” often denotes the highest degree or extremity. Regarding the physiology of the liver, the “Suwen·Treatise on Flaccidity” states: “The liver governs the fascia of the body.” The “Yimen Falü·Zangfu Fu” says: “Human movement relies on the strength of the sinews; the liver nourishes the sinews, hence it is called the basis of resistance to fatigue.” Later physicians have provided new interpretations of the connotation of “baiji”. A review of the literature [10-12] indicates that the essential meaning can be summarized as follows: the liver, through its blood-storing function, maintains the normal movement of springing qi and plays an important regulatory role in the circulation of qi and blood. At the same time, liver blood storage is also the material basis for tolerating and alleviating fatigue. From a pathological perspective, Wang Hongtu [13] proposed that “ba” is interchangeable with “pi”, meaning laziness or relaxation, while “ji” is interchangeable with “ji”, indicating urgency or urgency. Contraction of the sinews makes them tense and powerful, whereas relaxation makes them weak and flaccid; the coordination of these two states enables normal limb movement. Li Jinyong [14] argued that “ba” is a miswriting of “neng” and should be read as “nai”, meaning to endure, while “ji” is interpreted as fatigue, emphasizing the liver’s important role in eliminating fatigue and tolerating physical strain.

3. Exploration of the Etiology and Pathogenesis of Depression-Related Fatigue Based on “the Liver Is the Basis of Resistance to Fatigue”

3.1 The Manifestation Lies in the “Basis of Resistance to Fatigue”

Factors such as emotional frustration and dietary injury can lead to dysfunction of the liver, spleen, and kidney, resulting in abnormal generation and distribution of qi, blood, and body fluids, giving rise to pathological products such as qi stagnation, blood stasis, and phlegm-dampness. Phlegm can cloud the orifices of the heart, and stasis can obstruct the collaterals of the brain. Among these, liver qi stagnation plays an initiating role in the development of depression. Fatigue is a major clinical manifestation of depression and an important sign of sinew fatigue [15]. The “Jisheng Fang·Various Deficiency Patterns” states: “The patterns of five types of consumption and six types of injury... are mostly caused by failure to maintain health, beginning with overexertion.” Excessive strain depletes the body’s vital qi, manifesting as yin-yang imbalance, qi-blood disharmony, meridian obstruction, and visceral dysfunction. Regarding the liver, the “Suwen·Yinyang Yingxiang Dalun” says: “The liver generates the sinews.” The “Leijing·Twelve Meridian Sinews and Branches” states: “All the sinews of the body are generated by the liver.” Human movement relies on sinew strength. When the liver’s qi, blood, yin, and yang are harmonious, the sinews are supple and strong, movement is appropriately tense and relaxed, and the body can tolerate fatigue. If liver qi is deficient, liver blood is insufficient, or liver yin is depleted and liver yang is weakened, the sinews and fascia lose nourishment, thereby affecting the physiological function of “resistance to fatigue” and rendering the body prone to fatigue. At the same time, disharmony of liver qi, blood, yin, and yang can affect the heart (the mother

organ affecting the child), leading to malnutrition of the heart spirit and clouding of the ethereal soul, presenting as a state of both physical and mental fatigue. Therefore, clinically, patients with depression not only exhibit physical abnormalities such as fatigue and lassitude, tightness and heaviness of the limbs, and muscle or joint pain but also experience mental disturbances such as low mood, cognitive symptoms, and sleep disorders. As described in the “Piwei Lun”: “Shortness of breath, inability to speak, fatigue and weakness, silence, sleeplessness, lack of appetite, aversion to heat, and restlessness triggered by movement...” Thus, depression-related fatigue is a condition involving both body and spirit, characterized by concurrent mental exhaustion and physical decline.

3.2 The Root Lies in the Disorder of the Liver’s Substance and Function

The concept that the liver is “yin in substance and yang in function” is a high-level summary of the liver’s physiological functions in governing free coursing and storing blood. The liver governs free coursing, regulating the movement of qi throughout the body, ensuring the unimpeded flow of qi in the viscera, meridians, limbs, and orifices. When liver qi is harmonious, emotions are mild, qi and blood flow smoothly, and the sinews and bones are appropriately tensed and relaxed. The “Lingshu·Ben Zang” states: “When blood is harmonious, the meridians flow smoothly, the yin and yang are restored, the sinews and bones are strong, and the joints are clear and functional.”

Only when liver blood is sufficient and free coursing is appropriate can qi be distributed to the sinews, nourishing them, and enabling their normal physiological functions. Thus, the substance and function of the liver are interdependent and mutually reinforcing: sufficient blood ensures proper free coursing, and smooth qi flow ensures orderly blood circulation, collectively maintaining the supple state of the sinews and allowing sustained physical activity without fatigue. The “Waijing Weiyan” records: “When encountering frustrating matters, the liver tends to become qi-stagnated.” Depression arises from disordered qi movement, specifically liver qi stagnation. The development of the disease often follows a progressive course. Initial symptoms mainly include low mood and depression, accompanied by somatic manifestations such as reduced energy, fatigue, and sleep disturbances. As the disease progresses, prolonged liver depression impairs the spleen (the liver overacting on the spleen), leading to impaired transportation and transformation and dysfunction of ascending and descending. Clinically, this manifests as gastrointestinal symptoms such as poor appetite, loose stools or constipation, nausea, and vomiting. The “Suwen·Treatise on Flaccidity” says: “The spleen governs the muscles of the body.” The spleen controls the limbs and is associated with the muscles. When the generation of qi and blood is insufficient, the muscles lack nourishment and moisture, resulting in clinical manifestations such as fatigue, weakness, slow response, and even progressive wasting and disuse. At the same time, spleen disease can also affect the liver, leading to the pathological change of “earth congestion causing wood depression.” Spleen-stomach weakness and qi-blood deficiency make it difficult to nourish the liver substance and replenish liver blood. On the one hand, this

progressively worsens the smooth and harmonious nature of the liver, aggravating depressive symptoms. On the other hand, it leads to malnutrition of muscles and sinews, manifesting as significant reduced energy, easy fatigue, and marked psychomotor retardation [16].

3.3 The Key Mechanism Lies in the Instability of the Ethereal Soul

The spirit (shen) is the central governing axis of the body and mind [17], regulating the functions of the viscera and controlling life activities. At the mental level, shen highly corresponds to free will or consciousness in modern psychology [18]. The “Suwen Shiyi” states: “All human movements are due to the actions of shen and the ethereal soul; because the liver stores the ethereal soul, it is called the basis of resistance to fatigue.” The ethereal soul (hun) is the initial qi of shen and thus follows shen. The ethereal soul resembles the subconscious and emotional system. First, the ethereal soul assists the spirit; the liver ethereal soul participates in the decision-making of the heart spirit, influencing the activity of the conscious mind (shen). As Wang Bing said: “The liver stores the ethereal soul, which assists the spirit qi.” Second, the ethereal soul directs qi and the body. The liver ethereal soul, receiving commands from the heart spirit, directs whole-body qi to act on the body. When the heart spirit is clear and calm, the ethereal soul and corporeal soul are harmonious, the will is stable, the ethereal soul follows shen without reckless movement, and the corporeal soul acts in an orderly manner. Thus, spirit is retained internally, and body and spirit are integrated, resulting in neither mania nor depression. As stated in the “Leijing”: “The heart is the great governor of the five viscera and six bowels, governing both the ethereal and corporeal souls and encompassing the will and intent.” Long-term co-morbidity of the liver and spleen leads to inadequate generation or improper circulation of qi and blood, resulting in malnutrition of the heart body or obstruction of heart vessels by phlegm and stasis. This can damage the heart spirit, causing it to become unsettled or even lose its governance. When shen is unclear, the liver ethereal soul moves recklessly, and the soul is no longer settled. At this point, depression progresses to major depressive disorder. Patients exhibit severe low mood, pessimism, hopelessness, low self-esteem, and other manifestations of “weak ethereal soul” [17]. In severe cases, hallucinations, delusions, suicidal tendencies, and other symptoms of “chaotic ethereal soul” [17] may appear. At the same time, previously significant somatic symptoms such as reduced energy, fatigue, and sleep disturbances worsen further, and psychomotor retardation may progress to stupor [19]. As noted in the “Leijing·Point Selection in Four Seasons Inversely Causes Harm”: “The liver stores the ethereal soul; when liver qi is injured, the ethereal soul scatters, causing the patient to want to lie down but be unable to sleep, or to see things while sleeping, referring to strange objects.”

4. Treatment of Depression-Related Fatigue Guided by the Theory of “the Liver Is the Basis of Resistance to Fatigue “

4.1 Soothing the Liver to Relieve Depression and Regulating Qi Movement

The “Chishui Xuanzhu·Treatise on Depression Syndromes” explicitly states: “Wood depression refers to liver depression. ‘Facilitating’ means opening it up... in patients with underlying deficiency, when things do not go as expected, spirit is diminished, sinews are flaccid, presenting as deficiency patterns. One should first relieve depression and regulate qi, then the disease will resolve on its own.” The therapeutic principle for relieving depression is to “facilitate.” Facilitating involves dredging the meridians and regulating qi movement, thereby allowing blood to flow smoothly in the vessels, body fluids to distribute properly, and the limbs, body, orifices, and structures to receive nourishment, achieving the goal of “harmonious qi and blood, with all diseases ceasing to occur.” Clinically, pungent, dispersing, and qi-moving herbs are often used, such as “Chaihu” (*Bupleuri Radix*), “Xiangfu” (*Cyperus Rhizoma*), and “Yujin” (*Curcuma Radix*). Commonly used formulas include Chaihu Shugan San, Xiaochaihu Tang, and Sini San. It is important to note that excessive use of pungent and dispersing herbs may deplete yin and blood. The “Xixi Shuwu Yejie Lu” warns: “If liver qi distension is severe and the distension worsens with dispersing treatment, the liver should be softened.” Therefore, in clinical practice, it is advisable to combine herbs that soften the liver and relieve spasm, such as “Danggui” (*Angelica Sinensis Radix*) and “Baishao” (*Paeoniae Radix Alba*), or to use qi-regulating herbs that do not damage yin, such as “Foshou” (*Citri Sarcodactylis Fructus*) and “Xiangyuan” (*Citri Fructus*). At the same time, “all qi depression belongs to the lung.” The liver ascends and the lung descends; metal and wood mutually restrain. If the liver wood becomes depressed and sinks, it may easily prevent the lung metal from descending, exacerbating qi stagnation and forming a pattern of “wood depression with metal reversal.” The method of “left metal controlling wood” should be adopted, using herbs such as “Baihe” (*Lilii Bulbus*), “Xingren” (*Armeniacae Semen Amarum*), and “Zisuye” (*Perillae Folium*), so that the descending of the lung metal allows the liver wood to ascend and the pivot to be restored. According to the “Yishu”: “Body fluids nourish the sinews; when blood is astringent and fails to flow, phlegm accumulates in the diaphragm, causing weakness of the hands and feet.” Phlegm-stasis is both a pathological product and an important pathogenic factor that aggravates depression. Clinically, phlegm-resolving herbs such as “Fabanxia” (*Pinelliae Rhizoma Praeparatum*), “Zhuru” (*Bambusae Caulis in Taeniam*), and “Baijiezi” (*Sinapis Semen*) can be selected, along with stasis-resolving herbs such as “Danshen” (*Salviae Miltiorrhizae Radix*), “Chuanxiong” (*Chuanxiong Rhizoma*), and “Honghua” (*Carthami Flos*). In addition, adjunctive psychological therapies unique to TCM, such as emotion regulation therapy, mind-regulating therapy, and five-tone therapy [20], can help regulate and soothe liver qi.

4.2 Nourishing Blood, Strengthening the Spleen, Reinforcing Yang, and Tonifying Deficiency

The “Yixue Qiushi” states: “If fatigue and injury affect the middle, or if worry and depression cause stagnation, the spleen yang is trapped, and earth depression leads to wood depression. Wood, being characterized by free coursing, desires to course even more when depressed.” This indicates that while soothing the liver to relieve depression and regulating qi movement, attention should be paid to

nourishing blood and strengthening the spleen. Treating the liver and spleen together can restore normal physiological functions between earth and wood, thereby avoiding the complications of “liver depression overacting on the spleen” and “earth congestion causing wood depression” [21]. Nourishing blood and strengthening the spleen achieves three objectives. First, it promotes the generation of blood, and abundant blood nourishes liver qi, maintaining its harmonious and mild nature and preventing excessive or insufficient free coursing. Second, vigorous qi and blood eliminate somatic symptoms such as fatigue, lassitude, and general pain. Third, when qi and blood are abundant, liver blood is sufficient, and heart vessels are full, the spirit and ethereal soul are calm, and the body and mind are mutually supportive. As stated in the “Jingyue Quanshu·Blood Patterns”: “All functions of the seven orifices, the use of the four limbs, the suppleness of the sinews and bones, the abundance of muscles, the nourishment of the viscera, and the calming of the ethereal soul and spirit... are all functions of blood.” In treatment, qi-supplementing and spleen-strengthening herbs such as “Huangqi” (Astragali Radix), “Danggui” (Angelicae Sinensis Radix), “Dangshen” (Codonopsis Radix), and “Fuling” (Poria) can be used, or formulas such as Xiaoyao San, Sijunzi Tang, and Guipi Wan.

Qin Bowei said in the “Qianzhai Medical Lecture Notes”: “In disease, qi becomes reversed and yang becomes hyperactive, which is generally called liver qi or liver yang. Alternatively, it may manifest as laziness, depression, timidity, headache, numbness, and cold limbs, which are manifestations of liver qi deficiency and liver yang deficiency.” Yang qi is the foundation of shen and the ethereal soul. Deficiency of yang qi, particularly the failure of liver yang to warm and transform, leads to two consequences. First, the ascent of liver qi is impaired, resulting in symptoms such as timidity, easy fright, and depression, resembling liver qi stagnation. Second, shen and the ethereal soul lose warmth and nourishment, leading to manifestations of yang deficiency with mental decline, such as lethargy, weak ethereal soul, and listlessness. Third, the sinews lose warmth and nourishment, leading to physical laziness and weakness. In clinical treatment, the principle of “warming the cold” should be followed, using herbs such as “Guizhi” (Cinnamomi Ramulus), “Xixin” (Asari Radix et Rhizoma), and “Wuzhuyu” (Euodiae Fructus) to warm yang. As the “Lun Gan Bing” states: “In liver diseases, the warming method is used... using “Guizhi” (Cinnamomi Ramulus), “Xixin” (Asari Radix et Rhizoma), “Wuzhuyu” (Euodiae Fructus), and “Chuanjiao” (Zanthoxyli Pericarpium); particularly in deficiency patterns, “Rougui” (Cinnamomi Cortex) is frequently used, as it enters the liver and blood aspect and can promote growth qi.” Representative formulas include Nuanjian Jian, Wuzhuyu Tang, and Sini Tang.

4.3 Regulating the Spirit and Calming the Ethereal Soul: Harmonizing Body and Mind

As stated in the “Zhou Shenzhai Yishu”: “When disease affects the body, it cannot be without affecting the spirit; when disease affects the spirit, it cannot be without harming the body.” Depression-related fatigue involves both physical damage to the viscera and functional impairment of the intangible spirit. Therefore, the therapeutic strategy should prioritize harmonizing body and mind. On the one hand, methods to regulate the body, such as soothing the liver to

relieve depression, nourishing blood and strengthening the spleen, and reinforcing yang and tonifying deficiency, should be used to calm the spirit. On the other hand, methods to regulate the spirit and calm the ethereal soul should be employed to govern the body. In this way, body and spirit mutually support each other, achieving twice the result with half the effort.

Regulating shen includes both invigorating shen and calming shen. The method of invigorating shen aims to stimulate the heart spirit, activate yang qi, and dispel the yin stagnation of emotions, as reflected in the “Neijing” saying: “Yang qi, in its essence, nourishes shen.” Commonly used herbs include warming and yang-reinforcing products such as “Rougui” (Cinnamomi Cortex), “Wuzhuyu” (Euodiae Fructus), and “Bajitian” (Morindae Officinalis Radix). Representative formulas include Wuzhuyu Tang, Mahuang Fuzi Xixin Tang, and Fuzi Tang. Calming shen aims to restrain the floating and hyperactive heart yang and stabilize the restless spirit. This method can quickly resolve mental disturbances such as anxiety, irritability, insomnia with vexation, dream-disturbed sleep, and easy awakening. Commonly used herbs include calcined “Muli” (Ostreae Concha), calcined “Longgu” (Fossilia Osis Mastodi), and calcined “Zhenzhumu” (Margaritifera Concha). Representative formulas include Guizhi Jia Longgu Muli Tang, Cizhu Wan, and Zhenzhumu Wan.

Calming the ethereal soul is an important method for alleviating acute episodes of depression. Methods for calming the ethereal soul include nourishing and restraining the liver ethereal soul and heavy-calming the liver ethereal soul, with differentiation between deficiency and excess. The methods and formulas for nourishing the ethereal soul are the same as those described above for nourishing blood and strengthening the spleen. Restraining the ethereal soul focuses on using sour, astringent herbs to consolidate the liver ethereal soul and control its floating of deficient yang. The preferred herbs are “Suanzaoren” (Ziziphi Spinosae Semen), “Wuweizi” (Schisandrae Chinensis Fructus), and “Wumei” (Mume Fructus), as stated in the “Bencao Beiyao”: “Sour herbs can astringe and descend, thereby calming the ethereal and corporeal souls.” The method of heavy-calming the ethereal soul uses heavy minerals to directly suppress the hyperrebellious liver ethereal soul. This is an emergency measure. When the liver ethereal soul is in turmoil, it most easily disturbs the spirit, and only heavy doses can achieve rapid efficacy. The specific formulas and herbs are the same as those described for calming shen. In addition, attention should be paid to the body-mind interaction, complemented by traditional mind-body practices such as meditation, Tai Chi, Baduanjin, and Wuqinxi [22]. The essence of these practices lies in the integration of movement and stillness, the combination of hardness and softness, and the regulation of qi and blood, achieving the mutual nourishment of body and spirit and internal and external harmony.

5. Conclusion

In summary, through an in-depth exploration of the theory that “the liver is the basis of resistance to fatigue,” this paper suggests that the development of depression-related fatigue is significantly associated with dysfunction of the liver’s

physiological functions. Regarding treatment, interventions can be approached from three aspects: soothing the liver to relieve depression and regulating qi movement; nourishing blood, strengthening the spleen, reinforcing yang, and tonifying deficiency; and regulating the spirit, calming the ethereal soul, and harmonizing body and spirit. These strategies may provide a reference for the clinical diagnosis and treatment of depression-related fatigue.

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