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Post-stroke Depression Combined with Constipation: Research Progress on Pathogenesis of Traditional Chinese and Western Medicine and Acupuncture Therapy

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Abstract: ***Depression and constipation are two common complications during the recovery period after stroke. These two disorders frequently coexist and interact to form a vicious cycle, impairing patients' physical and mental health as well as quality of life and hindering rehabilitation. At present, western medicine mainly adopts symptomatic medications for depression and constipation separately. Such treatment only achieves limited and short-term symptom relief; long-term medication is prone to diverse adverse reactions and fails to simultaneously improve emotional and intestinal lesions, resulting in unsatisfactory overall efficacy. Benefiting from holistic syndrome differentiation and multi-target regulation, acupuncture of traditional Chinese medicine matches the pathological feature of simultaneous brain-gut impairment and synchronous brain-gut treatment. This paper systematically reviews the pathogenesis of post-stroke depression combined with constipation from both western and Chinese medical perspectives, summarizes the clinical application of various acupuncture regimens, and elaborates the unique advantages of acupuncture in brain-gut synchronous therapy, so as to provide theoretical evidence for standardized clinical management and further relevant researches of this comorbidity.***

Keywords: Post-stroke depression complicated with constipation, Middle-aged and elderly, Brain-gut axis, Pathogenesis, Acupuncture therapy.

1. Research Background

Post-stroke depression (PSD) is one of the highly prevalent complications of stroke [1]. It is a syndrome featuring emotional disorders developed on the basis of stroke manifestations, which severely impairs patients' rehabilitation process and quality of life. The prominent manifestations of PSD include persistent low mood, loss of interest, and obvious somatic symptoms; in severe cases, patients may have suicidal tendencies. Post-stroke constipation (PSC) [2] refers to a range of constipation symptoms occurring after stroke onset, such as prolonged defecation intervals, straining during defecation, anal distension and obstruction, and incomplete defecation sensation. Epidemiological studies have indicated that the incidence of PSC reaches 48% [3], and it is positively correlated with the progression of stroke [4].

Middle-aged and elderly stroke patients commonly suffer from varying degrees of impaired activities of daily living. During rehabilitation, most patients experience insufficient physical activity and prolonged bed rest. Long-term immobilization and bed rest directly slow intestinal peristalsis. Combined with post-stroke dietary changes and inadequate dietary fiber intake, patients are prone to digestive complications including constipation. Meanwhile, partial or complete loss of self-care ability severely disrupts the psychological status and self-perception of middle-aged and elderly patients, rendering them susceptible to self-denial, pessimism and other negative emotions. Some patients even develop self-abandonment and resistance to rehabilitation, resulting in depressive disorders that further delay the recovery of limb and neurological functions. Current clinical studies reveal that the coexistence of physical complications and emotional disorders is highly prevalent among stroke patients in the recovery phase. Such complications are closely associated with patients' physical conditions and mental status, and are jointly influenced by multiple factors including family care patterns and insufficient treatment adherence of patients and caregivers. This comorbidity has become an intractable clinical challenge that cannot be overlooked in comprehensive stroke rehabilitation.

PSD and PSC exhibit high comorbidity, shared pathological mechanisms and bidirectional interactions. They are interrelated and reciprocally causative in terms of pathogenesis, clinical manifestations and prognosis, forming a self-perpetuating vicious cycle that substantially increases the rehabilitation burden of middle-aged and elderly stroke patients. Clinical epidemiological data indicate high incidence rates of both PSD and PSC in middle-aged and elderly populations: depression occurs in 30%–65% of patients, while constipation affects 40%–85%. More than half of middle-aged and elderly stroke patients develop both conditions simultaneously. Greater severity of depression correlates with higher risk and worse severity of constipation. In turn, persistent defecation difficulty, abdominal distension and sleep disturbances exacerbate low mood, anxiety, irritability and feelings of worthlessness, leading to progressive deterioration of depressive symptoms.

2. Epidemiology

The comorbidity of PSD and PSC among stroke patients is not randomly distributed but presents obvious population clustering. Its prevalence is closely associated with age, stroke

location and severity, bedridden status, underlying chronic diseases and medication use. Middle-aged and elderly patients aged over 45 constitute the highest-risk population. Degenerative central nervous system changes, reduced intestinal peristalsis and impaired autonomic nerve regulation in this population predispose individuals to gut-brain axis dysfunction. Coupled with emotional fragility and drastically reduced physical activity after stroke, the risk of concurrent PSD and PSC rises markedly.

Stroke patients with severe neurological deficits and long-term bed rest accompanied by hemiplegia frequently experience insufficient physical activity, weakened defecation muscles [5][6], and poor dietary intake that reduces gastrointestinal motility. Suboptimal rehabilitation outcomes also trigger anxiety and depression, creating a vicious cycle of mutually aggravated constipation and depression. Middle-aged and elderly patients suffer from visceral hypofunction and a constitution characterized by deficiency and blood stasis. Additional factors including polypharmacy and psychological stress further weaken nerve repair, intestinal peristalsis and emotional regulation, aggravating PSD-PSC comorbidity. PSD and PSC share pathological pathways involving cerebral injury, neurotransmitters, autonomic nerve function, inflammation, endocrine regulation and the gut-brain-microbiota axis, forming a pathological closed loop. This provides theoretical evidence for simultaneous regulation of brain and viscera as well as integrated brain-intestine therapy in clinical practice.

3. Modern Medical Mechanisms

Stroke is a prevalent central nervous system injury disorder [7]. Besides neurological deficits such as hemiplegia, cognitive impairment and aphasia, stroke frequently induces a spectrum of neurogastrointestinal dysfunctions, among which PSD-PSC comorbidity is particularly common. The two conditions interact synergistically to worsen clinical outcomes and drastically reduce patients' rehabilitation efficiency and quality of life. Their internal correlation is primarily mediated by disrupted bidirectional signaling along the gut-brain axis.

The gut-brain axis [8]is a bidirectional information network linking the central nervous system, enteric nervous system, endocrine system and intestinal microbiota. It mediates brain-intestine communication via neural, immune, endocrine and metabolic pathways [9]. Structural cerebral damage caused by stroke disrupts gut-brain axis homeostasis, acting as the initiating factor for concurrent PSD and PSC. At the central level, stroke lesions often involve core brain regions regulating the gut-brain axis, including the frontal lobe, insula, amygdala, brainstem vagal nuclei and paracentral lobule. On one hand, these lesions directly damage neural circuits governing emotional regulation in the brain, disrupting synthesis and release of key neurotransmitters such as 5-HT [10], dopamine and γ-aminobutyric acid, which leads to core depressive symptoms including low mood, anhedonia, anxiety and irritability. On the other hand, cerebral injury interrupts autonomic nerve signaling to the intestines [11], resulting in impaired afferent and efferent vagal function and overactive sympathetic tone. This inhibits gastrointestinal smooth muscle peristalsis and intestinal gland secretion, weakens defecation reflexes, and consequently causes hard stools and difficult defecation.

Furthermore, stroke induces chronic neuroinflammation [12] characterized by excessive activation of central microglia and massive release of pro-inflammatory factors including tumor necrosis factor-α and IL-6. Inflammatory signals propagate downward through the gut-brain axis to the intestines, disrupting intestinal mucosal barrier integrity and reducing intestinal motility. Conversely, intestinal inflammation transmits inflammatory mediators upward to the central nervous system via blood circulation and the vagus nerve, amplifying central neuroinflammation and progressively worsening depression. This inflammation-mediated cascade creates a vicious cycle of gut-brain axis dysfunction.

Dysbiosis of the intestinal microbiota [13] serves as a critical intermediate mediator linking the gut-brain axis to PSD-PSC comorbidity. Post-stroke prolonged bed rest, eating disorders, insufficient dietary fiber intake, and medications including antiepileptics, sedatives and dehydrating agents drastically alter intestinal microbiota composition and abundance. Beneficial bacteria such as Bifidobacterium and Lactobacillus decrease while pathogenic bacteria proliferate, disrupting microbial metabolism. First, insufficient production of microbial metabolites short-chain fatty acids (SCFAs) [14] removes regulatory control over intestinal peristalsis rhythm and mucosal repair, exacerbating constipation. Loss of SCFAs also abolishes their neuroprotective effects on the central nervous system [15], accelerating central neurotransmitter imbalance and neuroinflammation to induce and worsen PSD. Second, intestinal microbiota synthesize over 90% of peripheral 5-HT [16]. Dysbiosis directly reduces peripheral 5-HT secretion [17], which fails to stimulate intestinal peristalsis for stool evacuation and cannot replenish central neurotransmitter reserves through the gut-brain axis, further aggravating both depression and constipation.

Overactivation of the hypothalamic-pituitary-adrenal (HPA) axis [18], a key manifestation of gut-brain axis disturbance, further drives PSD-PSC comorbidity progression. Cerebral injury after stroke [19] and depressive mood trigger HPA axis hyperactivity and excessive cortisol secretion. Elevated cortisol not only suppresses central neurotransmitter synthesis and exacerbates depression [20], but also directly inhibits gastrointestinal peristalsis, reduces intestinal mucus secretion and delays gastric emptying, markedly worsening constipation. In turn, persistent constipation-related physical discomfort including abdominal distension and painful defecation increases psychological burden, triggering anxiety, irritability and inferiority complex. This forms a pathological closed loop: depression → HPA axis hyperactivity → constipation → intensified negative emotions → simultaneous deterioration of depression and constipation.

In recent years, continuous advancement of the gut-brain-microbiota axis theory has comprehensively supplemented the internal mechanisms underlying this comorbidity. Central emotional dysfunction suppresses intestinal function via top-down signaling pathways [21], while intestinal dysbiosis, insufficient SCFA production and reduced synthesis of 5-HT precursors disrupt central nervous function through bottom-up pathways [22], resulting in

bidirectional regulatory imbalance.

Higher brain centers controlling defecation [23] are mainly distributed in the cerebral cortex, hypothalamus and brainstem, which coordinate with spinal lower centers to complete the defecation reflex. As the supreme regulatory center [24], the cerebral cortex mediates defecation sensation, voluntary bowel control and defecation inhibition. The paracentral lobule, located on the medial cerebral hemisphere, governs bladder, rectal and pelvic floor muscle function; lesions here readily cause defecation and urination disorders (constipation or incontinence). The hypothalamus modulates autonomic nerves (sympathetic and parasympathetic) to regulate intestinal peristalsis velocity and anal sphincter tension. Brainstem defecation control relies on the pons and medulla oblongata. The medulla oblongata [25] acts as a vital integrative hub of autonomic nerves and a transmission pathway for defecation reflexes; brainstem lesions disrupt gastrointestinal peristalsis and induce constipation. Defecation regulation [26] relies on coordinated abdominal muscle contraction, pelvic floor and anal sphincter relaxation, and stable trunk and pelvic posture to facilitate stool evacuation.

Stroke patients complicated with underlying diseases including diabetes, hypertension and dyslipidemia frequently develop microvascular lesions and autonomic neuropathy, further aggravating intestinal dysmotility and central neurotransmitter imbalance. Long-term clinical administration of anticholinergic agents such as sedative-hypnotics, tricyclic antidepressants and certain antiepileptics significantly inhibits intestinal peristalsis and impairs emotional regulation [27], worsening both constipation and depression.

4. Western Medical Treatment

Western medicine primarily treats PSD with selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors.

For constipation, symptomatic interventions include osmotic laxatives, gastrointestinal prokinetic agents and enema therapy [28]. However, middle-aged and elderly stroke patients exhibit weak gastrointestinal motility, impaired hepatic and renal function, and widespread polypharmacy. Long-term combined medication frequently causes adverse reactions including nausea, vomiting, dizziness, headache, abdominal pain, diarrhea, electrolyte disturbance, drug dependence and high recurrence rates after drug withdrawal.

Current therapeutic regimens only target either emotional symptoms or intestinal dysfunction separately, lacking standardized protocols for concurrent PSD and PSC. Clinical evidence for novel interventions such as neuromodulation and microecological regulation remains insufficient [29], and large-sample trials are required to verify their long-term efficacy and safety.

5. Analysis of Etiology and Pathogenesis in Traditional Chinese Medicine (TCM)

TCM categorizes this comorbidity under the diagnostic categories of "Stroke", "Depression Syndrome" and "Constipation". Its core pathogenesis consists of malnutrition of brain spirit, liver qi stagnation, impaired spleen transportation and blocked intestinal qi movement. The disease locates in the brain, liver, spleen and large intestine, characterized by root deficiency and branch excess with intermingled deficiency and excess that reciprocally induce each other.

Following stroke, cerebral vessel stasis disrupts mental function, compounded by emotional discomfort leading to liver qi binding. Impaired liver dispersion further weakens spleen transportation and large intestinal conduction, ultimately generating concurrent emotional stagnation and difficult defecation. Stroke is predominantly caused by qi deficiency and blood stasis, as well as wind-phlegm obstructing collaterals. The brain houses the primordial spirit; occluded cerebral vessels disrupt mental governance. Dysfunction of mental regulation induces emotional imbalance and visceral dysfunction, forming the shared pathological basis for PSD and PSC. Liver qi stagnation and qi binding constitute the core pathogenesis. Post-stroke limb disability and loss of independent living readily trigger emotional distress and liver qi stagnation. The liver governs dispersion; stagnated liver qi obstructs intestinal qi movement and impairs large intestinal conduction to produce constipation. Prolonged liver qi stagnation generates internal fire that consumes body fluids and deprives intestines of lubrication, aggravating constipation.

Impaired spleen transportation leads to insufficient qi and blood generation. Liver stagnation invades the spleen, or prolonged bed rest after stroke induces spleen qi deficiency and weakened transportation. Qi deficiency lacks propulsive force to eliminate intestinal waste; alternatively, spleen deficiency generates dampness and phlegm obstruction, both of which cause constipation. TCM holds that qi, blood and body fluids are fundamental substances sustaining human life, originating from the same source yet exerting distinct functions with mutual interdependence and transformation. Therefore, patients with PSD accompanied by constipation commonly present varying degrees of deficiency in qi, blood and body fluids.

Yin and blood deficiency deprives intestines of lubrication. Stroke consumes liver and kidney yin-blood, compounded by yin injury from fire generated by liver stagnation and chronic physical deficiency. Insufficient yin-blood fails to moisten intestines, resulting in dry, hard stools. Deficient yin-blood also fails to nourish the heart spirit, intensifying irritability and depressive emotions. Intermingled phlegm and blood stasis block intestinal qi movement; liver qi stagnation further exacerbates phlegm and blood coagulation. Phlegm-stasis obstructs collaterals and gastrointestinal tracts to block intestinal qi, generating intractable constipation. Upward disturbance of phlegm-stasis confuses clear orifices and clouds the heart spirit, rendering depression refractory.

Middle-aged and elderly patients present insufficient healthy qi and liver-kidney deficiency, dominated by qi deficiency and dual yin-yang deficiency as the root, with qi stagnation, phlegm turbidity and blood stasis as secondary manifestations. Treatment should simultaneously tonify and unblock with

mild harmonizing therapy, avoiding harsh purgative attack. Common syndrome patterns include liver stagnation and spleen deficiency, qi deficiency and blood stasis, liver-kidney insufficiency, internal obstruction of phlegm turbidity, and yang qi deficiency.

6. Clinical Application of Acupuncture Therapy

Stroke patients in the rehabilitation phase are highly susceptible to concurrent emotional disorders and intestinal dysfunction. PSD aggravates gastrointestinal qi stagnation, while prolonged constipation worsens emotional binding, forming a vicious cycle. Western medicine relies on antidepressants and gastrointestinal prokinetic agents for symptomatic relief, which are limited by slow onset and abundant adverse effects. Based on meridian and acupoint theories, acupuncture adopts therapeutic principles of regulating spirit and unblocking fu-organs, soothing the liver and invigorating the spleen, and integrated brain-intestine therapy. It achieves dual therapeutic effects through holistic regulation with advantages including safety, efficacy, high treatment adherence and suitability for long-term rehabilitation.

The Spirit-Regulating and Fu-Organ-Unblocking Acupuncture Method [30] is formulated based on the gut-brain axis theory, with core therapeutic principles of soothing depression via spirit regulation and moistening intestines via fu-organ unblocking. This acupuncture protocol targets concurrent PSD and PSC by balancing spirit regulation and intestinal unblocking acupoints. The spirit-regulating group consists of Yintang (EX-HN3), Shangxing (GV23), Baihui (GV20), Neiguan (PC6) and Sanyinjiao (SP6), focusing on nourishing brain spirit. The fu-organ-unblocking group includes Zhongwan (CV12), Tianshu (ST25) and Zusanli (ST36), prioritizing regulation of intestinal qi. Additional acupoints including Shangwan (CV13), Zhongwan (CV12), Xiawan (CV10) and Liangqiu (ST34) are selected based on individual conditions to invigorate spleen-stomach function and restore the pivot of qi ascent and descent. Qihai (CV6) and Guanyuan (CV4) are added to regulate systemic qi movement, ultimately soothing brain spirit and descending intestinal qi.

Beyond the above protocol, multiple acupuncture modalities including electroacupuncture, warm acupuncture, auricular point therapy and abdominal acupuncture are widely applied clinically with confirmed efficacy. Shen et al. Reported [31] that electroacupuncture significantly improves defecation frequency and stool properties in stroke patients, accompanied by marked reductions in NIHSS and HAMD-17 scores before and after treatment. This therapy remodels intestinal microbiota structure, elevates abundance of beneficial bacteria including Bifidobacterium and Lactobacillus, inhibits pathogenic proliferation, and corrects gut dysbiosis in stroke patients. Wang et al. applied electroacupuncture during the acute phase of ischemic stroke to effectively promote gastrointestinal peristalsis and intestinal conduction [32], alleviating abdominal distension and difficult defecation to facilitate subsequent rehabilitation. Wang et al. [33] treated post-stroke constipation with warm acupuncture, transmitting thermal moxibustion stimulation through acupuncture needles to warm unblock meridians, promote qi movement, guide stagnation and moisten intestines for defecation. Compared with routine acupuncture, warm acupuncture effectively relieves deficiency-cold symptoms of yang deficiency constipation and improves clinical efficacy. Zhao et al. combined auricular point pressing with repetitive transcranial magnetic stimulation (rTMS) for PSD patients [34]. The integrated non-invasive neural electrical stimulation and TCM auricular therapy significantly reduced depression scale scores, upregulated serum 5-HT and TRPC1 expression, downregulated S100β levels, alleviated neural injury, and achieved an overall effective rate of 93.3%. Guided by gut-brain axis theory, Huang et al. integrated auricular acupuncture for spirit regulation and abdominal acupuncture [35] for fu-organ unblocking to bidirectionally modulate emotional activity and intestinal conduction, providing theoretical support for acupuncture treatment of cerebrovascular sequelae combined with gastrointestinal discomfort.

Existing research demonstrates that acupuncture exerts regulatory effects at multiple levels. In neural modulation, it regulates functional activity of advanced central regions including the frontal lobe and insula to balance secretion and release of gut-brain peptides such as 5-HT [36] and dopamine [37], alleviating depression and anxiety while repairing defecation reflex pathways. In visceral qi regulation [38], acupuncture dredges meridians, harmonizes visceral function and restores large intestinal conduction capacity. It also remodels intestinal microbiota composition, ameliorates gut-brain axis communication disorders [39][40], and interrupts the pathological cycle of mutually aggravated depression and constipation.

Acupuncture monotherapy or combined regimens with western medicine and rehabilitation training exhibit prominent comprehensive advantages. Integrated TCM-WM protocols lower depression scale scores, relieve constipation, reduce stroke recurrence risk, and exert critical effects on limb functional recovery and psychological intervention, accelerating patients' return to family and society. Compared with single western medication, psychological intervention or physical therapy, acupuncture combined with drugs or rehabilitation yields superior efficacy with fewer adverse reactions, higher patient acceptance and treatment adherence, representing a preferred clinical intervention for post-stroke comorbidity.

7. Conclusion

Concurrent PSD and PSC constitute a high-burden comorbidity that severely impairs rehabilitation and quality of life among middle-aged and elderly stroke patients, while western therapeutic approaches remain limited and single-targeted. Centered on integrated brain-intestine therapy via spirit regulation and fu-organ unblocking, acupuncture features safety, efficacy, dual-target intervention and high adherence, forming a clinical treatment system anchored on the gut-brain-microbiota axis. Current research is restricted by insufficient clinical evidence specific to middle-aged and elderly populations, inconsistent technical standards and superficial mechanistic exploration. Future research should target this elderly comorbid population, standardize

therapeutic protocols, deepen mechanistic investigations, and advance integrated rehabilitation. Characteristic TCM therapies combined with modern medical technologies will serve as core supportive interventions for full-cycle rehabilitation of middle-aged and elderly stroke patients, providing TCM-based solutions to address population aging challenges.

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