

Research Progress on Common Neurological Diseases Accompanied by Depression in Both Chinese and Western Medicine

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Abstract: *Depression is one of the most common comorbid conditions associated with various prevalent neurological disorders, including stroke, Parkinson's disease, epilepsy, Alzheimer's disease, and insomnia. It significantly impairs prognosis, functional recovery, and quality of life of the primary diseases, and markedly increases suicide risk and caregiver burden. Its pathogenesis involves shared mechanisms such as disruption of monoamine neurotransmitter pathways, hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, neuroinflammation, and disconnection of neural circuits. Conventional Western medicine primarily relies on antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and psychological therapies; however, these approaches are limited by delayed onset of action, suboptimal response in some patients, and potential drug interactions. In Traditional Chinese Medicine (TCM), based on the holistic concept of "unity of body and mind," such comorbid depression is categorized under "depression due to underlying illness." The core pathological mechanisms involve liver qi stagnation, phlegm-blood stasis obstructing orifices, deficiency of heart and spleen, yin deficiency with fire exuberance, and kidney deficiency leading to marrow depletion. Each syndrome pattern has corresponding representative herbal formulas. Classical TCM formulas such as Chaihu Jia Longgu Muli Tang, Suanzaoren Tang, have accumulated substantial clinical evidence in alleviating depression through individualized treatment based on pattern differentiation. Their multi-target effects include modulation of monoamine neurotransmitters and neurotrophic factors, suppression of neuroinflammation, restoration of HPA axis negative feedback regulation, and modulation of the gut-brain axis. The integrated strategy of traditional Chinese and Western medicine can achieve enhanced efficacy with reduced toxicity. This article provides a systematic review of recent research progress on depression associated with common neurological disorders from both traditional Chinese and Western medical perspectives, aiming to offer reference for optimizing clinical decision-making.*

Keywords: Neurological diseases, Depression, Classical Chinese herbal formulas, Integrative medicine, Advances in diagnosis and treatment.

1. Introduction

Depression accompanied by neurological diseases is an extremely common clinical phenomenon. Epidemiological data show that the incidence of depression after stroke is about 31% [1], Parkinson's disease depression is 40%~50% [2], the lifetime risk of depression in epilepsy patients is 20%~30% [3], the incidence in Alzheimer's disease is 40%~50% [4], and about 40%~50% [5] of insomnia disorders meet the criteria for depressive status. Depression is not only a symptom accompanying neurological diseases, but also a syndrome with independent pathological significance and far-reaching harm. In patients with neurological diseases, the presence of depression significantly worsens the harm caused by the underlying disease, creating a vicious cycle. Specifically, post-stroke depression can worsen neurological deficits, delay rehabilitation, and increase long-term disability and mortality rates; Parkinson's disease depression accelerates the worsening of motor symptoms and cognitive decline, causing a sharp decline in quality of life; Epilepsy with depression not only increases the frequency of seizures, but also raises the risk of suicide to three to five times that of the general population; Alzheimer's disease accompanied by depression accelerates cognitive loss, worsens psychiatric and behavioral symptoms, and greatly increases the burden on caregivers; The depression associated with insomnia is often mutually causal, making the disease chronic and difficult to treat, and significantly reducing social functioning and work ability. Moreover, depression severely affects patient treatment adherence, increases medical resource consumption, and

leads to higher rates of unplanned readmissions. Even more severe, depression is one of the main causes of suicide, with the incidence of suicidal ideation and suicide deaths among patients with neurological disorders far higher than in the general population. Therefore, early identification and effective intervention of depression associated with neurological diseases not only relates to mood improvement but also to the prognosis of the underlying disease and the patient's safety.

However, in clinical practice, such comorbid depression is often missed or mistakenly classified as the "normal response" of the primary disease, with a recognition rate of less than half. Although selective serotonin reuptake inhibitors are first-line treatment, they take 2 to 4 weeks to take effect, about one-third of patients respond poorly, and long-term use carries risks of interactions with antiepileptic drugs and anti-Parkinsonian drugs [6]. Against this backdrop, integrated Chinese and Western medicine has received increasing attention for its holistic regulation, multi-target interventions, and relatively safe profiles. In particular, the precise treatment concept of "prescription-syndrome correspondence" in classical medicine offers new ideas for individualized diagnosis and treatment of complex cases accompanied by depression. This article systematically reviews the advances in diagnosis and treatment of depression in five common neurological diseases: Stroke, Parkinson's disease, epilepsy, Alzheimer's disease, and Insomnia, covering the progress of Chinese and Western medicine in diagnosis and treatment.

2. Current Status of Western Medicine Diagnosis and Treatment

2.1 Overview of Pathogenesis

Disorders of the monoamine transmitter system are the earliest identified mechanisms. Stroke lesions can disrupt the ascending 5-hydroxyserotonin and norepinephrine pathways in the nucleus sutures and plaque coeruleus in the brainstem [7], leading to neurotransmitter deficiency in the prefrontal and limbic systems. Parkinson's disease degenerates the substantia nigra–striatum dopamine pathway and the ventral tegmental region–nucleus accumbens reward pathway, directly causing anhedonia⁸. Temporal lobe epilepsy leads to decreased density of 5-HT1A receptors in the amygdala and hippocampus. Long-term insomnia further depletes synaptic cleft monoamine neurotransmitters, creating a vicious cycle. Overactivation of the hypothalamic-pituitary-adrenal axis plays a central role. The storm of inflammatory cytokine storms caused by various neurological diseases continuously stimulates the hypothalamus to secrete adrenocorticotropin -releasing hormone, leading to sustained elevation of cortisol levels [9]. Excessive glucocorticoids damage hippocampal neurons, inhibit neurogenesis, and impair neuroplasticity by lowering brain-derived neurotrophic factors, resulting in a susceptibility to depression.

Neuroinflammation is a key bridge connecting nerve damage and depression. Activated microglia release large amounts of inflammatory factors, activating the kynurenine pathway, causing tryptophan metabolism to shift neurotoxic products, reducing serotonin synthesis, and damaging synapses. In models of Alzheimer's disease, Parkinson's disease, and stroke, NLRP3 inflammatory body activation was observed to occur simultaneously with depressive-like behaviors [10].

2.2 Clinical Features of Depression in Various Diseases

Post-stroke depression mostly occurs 3 to 6 months after stroke, with lesions in the left frontal lobe, basal ganglia, and dominant hemisphere as independent risk factors, while aphasia and cognitive impairment further increase the risk. Clinical manifestations are characterized by decreased interest, low mood, and fatigue. In severe cases, suicidal ideation may occur. The degree of depression worsens with neurological deficits and functional dependenc [11]. Parkinson's depression centers on anhedonia, decreased motivation, pessimism, and despair, often accompanied by anxiety, fatigue, and sleep disturbances. The “closing period” of its movement fluctuations coincides with a high level of emotional downturn. It is noteworthy that depression and anhedonia often appear years before motor symptoms and are considered precursors to non-motor symptoms of Parkinson's disease [12]. Epilepsy-related depression can be divided into interparoxysmal depression, interparoxysmal depression, and periepisaric mood disorder, with interparoxysmal depression being the most common. Patients with temporal lobe epilepsy and drug-refractory epilepsy have a particularly pronounced risk of depression, with suicide risk three to five times higher than in the general population. Patients often experience inter-episode agitation disorder, characterized by irritability and emotional instability [13]. Alzheimer's disease accompanied by depression often intertwines with

psychobehavioral symptoms such as apathy and agitation, increasing caregiver burdens and accelerating cognitive decline. Their depressive symptoms are often atypical, mainly showing reduced interest, social withdrawal, and changes in appetite, with few actively expressing low mood [14]. Insomnia and depression form the most closely linked “bidirectional comorbidity.” About 40% to 50% of insomnia patients meet the criteria for depression, and among depressed patients, the incidence of insomnia is as high as 80% to 90%. Difficulty falling asleep, waking up early, and shallow sleep are the core complaints [15].

2.3 Diagnostic Assessment and Current Treatment Status

Diagnosis is mainly based on ICD-11 criteria [16]. Special attention should also be paid to distinguishing between the primary disease symptoms and the overlap of depressive core manifestations. For example, Parkinson's disease has a “masked face” that may mask emotional expression, and post-stroke aphasia affecting emotional self-narrative. Common screening tools include the Patient Health Questionnaire Depression Scale, Hamilton Depression Scale, etc. Recommendations include comprehensive psychiatric interviews, caregiver observation information, and polysomnography for comprehensive assessment.

The preferred drug treatment is selective serotonin reuptake inhibitors such as sertraline and escitalopram [17], which provide sufficient evidence for post-stroke depression. Norepinephrine and serotonin reuptake inhibitors such as venlafaxine and duloxetine may be more advantageous for those with chronic pain. In Parkinson's disease, the dopamine receptor agonist pramipexole also has antidepressant effects. Insomnia with Depression is recommended as a non-pharmacological first-line intervention. However, existing treatments have multiple limitations: onset delays of 2 to 4 weeks, and about one-third of patients respond inadequately; Elderly patients are prone to hyponatremia, weight gain, and fall risks; Pharmacokinetic interactions with warfarin, antiepileptic drugs, levodopa, etc. [18]; Some medications may worsen tremors or trigger spasms. Although psychotherapy is effective, some patients find it difficult to implement due to aphasia, cognitive impairment, or mobility difficulties.

3. Advances in the Diagnosis and Treatment of Traditional Chinese Medicine

3.1 Etiology and Pathogenesis in Traditional Chinese Medicine

Ancient traditional Chinese medicine (TCM) texts do not have a direct corresponding disease name; based on main manifestations, it can be categorized as “Yu syndrome” or “Chan Yu” (trembling and stagnation). “Depression caused by illness” is the core pathogenesis of this type of associated depression [19]. The Jingyue Quanshu · Yu Zheng points out: “When the five qi are stagnant, all diseases exist; this is stagnation caused by illness.” “Neurological diseases first damage the body—stroke causes qi and blood to reverse, and the brain vessels become stagnant; Tremor syndrome refers to advanced age, kidney deficiency, marrow loss, and internal wind causing internal movement; In epilepsy, wind-phlegm

obstructs the orifices and gradually invades the collaterals; Dementia is rooted in kidney deficiency, with phlegm, turbidity, and blood stagnation affecting the orifices; Insomnia causes yang to fail to enter yin, and the spirit loses its storage. When these illnesses persist, qi and blood are disrupted, organs are disharmonious, and the heart gradually spreads, eventually leading to depression and loss of interest. The overall pathogenesis can be summarized as: the primary disease causes damage to the brain collaterals, deficiency of the marrow sea, or yang not entering yin, resulting in liver stagnation and qi stagnation, phlegm and stasis interlocking, deficiency of heart and spleen, yin deficiency with excessive fire, kidney deficiency with reduced marrow, or heart and gallbladder qi deficiency, ultimately leading to “imbalance of form and spirit” and resulting in depression.

3.2 Traditional Chinese Medicine Diagnosis

TCM diagnosis centers on the combined diagnosis of four diagnostic methods, aiming to identify the timeline of “depression caused by illness,” distinguish emotional changes secondary to movement disorders, pain, or cognitive decline, and make a comprehensive judgment based on sleep, appetite, bowel movements, and emotional episodes. Tongue diagnosis and pulse diagnosis provide objective evidence: a dark purple tongue with much blood stasis, a red tongue with little coating and yin deficiency, a thick tongue with many teeth marks and spleen deficiency; A wiry pulse indicates liver stagnation, slippery rapid indicates phlegm-heat, and a deep, thin pulse indicates kidney deficiency. On this basis, syndrome differentiation and classification are conducted based on the characteristics of primary neurological diseases. Common clinical syndromes include: liver qi stagnation syndrome mostly occurs in the early stages of depression after stroke and insomnia accompanied by depression, treated with soothing the liver and relieving depression, with representative formulas such as Chaihu Shugan San [20]; Liver Qi's Transformation into Fire syndrome is mostly seen in insomnia with depression and post-stroke depression accompanied by anxiety and agitation. Treatment involves clearing the liver and draining fire, with representative formulas such as Dan Zhi Xiao Yao San [21]; Liver depression and spleen deficiency syndrome most commonly occur during the recovery period from post-stroke depression and insomnia accompanied by depression. Treatment involves soothing the liver and strengthening the spleen, with representative formulas such as Xiaoyao San [22]; Phlegm-heat internal disturbance syndrome is commonly seen in epilepsy with depression and insomnia with depression. Treatment involves clearing heat and resolving phlegm. Representative formulas include Huanglian Wendan Tang or Chaihu Jia Longgu Muli Tang [23]. In recent years, TCM syndrome scales, tongue imaging instruments, and pulse diagnostic instruments have gradually been applied in clinical practice to help improve consistency in syndrome differentiation.

3.3 Advances in Traditional Chinese Medicine treatment

3.3.1 Post-stroke depression

Post-stroke depression is the most deeply studied area. Chaihu Jia Longgu Muli Decoction is mainly used to treat “chest fullness and fright.” A randomized controlled trial involving

120 patients showed that after 8 weeks of treatment with this formula combined with sertraline, the reduction in Hamilton's depression scale scores was more significant than in the sertraline alone, with onset about one week earlier. Mechanistic studies have confirmed that it can increase hippocampal levels of serotonin 5-hydroxytryptamine and norepinephrine, lower serum cortisol, upregulate the BDNF-TrkB signaling pathway, and inhibit NLRP3 inflammatory body activation [24]. Among later famous formulas, Xiaoyao Powder was the representative formula for liver stagnation and spleen deficiency. A meta-analysis showed that combining SSRIs with the drug group significantly reduced HAMD scores compared to the Western drug group alone. Animal experiments confirmed that it upregulated hippocampal BDNF, inhibited NLRP3 inflammatory body activation, and restored gut microbiota diversity, elucidating the mechanism of remote mood regulation from the perspective of the “gut-brain axis” [25]. Guipi Decoction is suitable for heart and spleen deficiency syndromes; Huanglian Wendan Decoction combined with escitalopram can enhance efficacy. Buyang Huanwu Decoction combined with Gancai Dazao Decoction is used for qi deficiency and blood stasis, while Dihuang Yin Zi is suitable for kidney deficiency and marrow reduction during the sequelae stage.

3.3.2 Parkinson's disease depression

Parkinson's depression emphasizes kidney tonification, marrow-replenishing the liver, calming the liver, and calming the mind. After 12 weeks of treatment with Chaihu Jia Longgu Muli Decoction, both HAMD and UPDRS scores improved simultaneously, related to regulation of mesolimbic dopamine pathways and increased BDNF [26]. Huanglian Ejiao Decoction is mainly used to treat irritability and insomnia caused by yin deficiency and excessive fire; clinical observations showed significant improvements in PSQI and HAMD scores after 8 weeks, with mechanisms related to reduced cortisol and increased GABA content. Lily and Rehmannia Decoction combined with Suanzaoren Decoction are suitable for yin deficiency with internal heat and insomnia. Ganmai Dazao Decoction combined with Si Ni San is used for mild emotional instability and frequent crying. Zi Shui Qing Gan Yin is a representative formula for kidney deficiency liver stagnation; a randomized controlled trial showed HAMD improvement comparable to paroxetine but better improvement in exercise scores. Zuo Gui Wan and Di Huang Decoction are mainly used for kidney deficiency with reduced marrow.

3.3.3 Epilepsy-related depression

Epilepsy-related depression requires phlegm and orifice-opening and calming the mind, as well as soothing the liver and relieving depression [27]. Chaihu Jia Longgu Muli Decoction is the most commonly used prescription, and its “fright” syndrome closely matches postepileptic irritability and inter-episode depression. Clinical reports show that combining this formula with antiepileptic drugs can significantly reduce HAMD and HAMA scores without increasing seizure frequency. Animal experiments show this formula can simultaneously inhibit amygdala discharge and reduce hippocampal IL-1 β , achieving both anticonvulsant and

antidepressant effects. Chaihu Guizhi Decoction is suitable for generalized stiffness and fright, while combined with valproate sodium can reduce seizure frequency and improve depression scores. Suanzaoren Decoction combined with Ganmai Dazao Decoction is used for heart and liver blood deficiency and insomnia. Zhizi Chi Decoction is used for mild heat-type irritability during attacks. Huanglian Wendan Decoction is used for phlegm-heat internal disturbance. Si Ni San combined with Ganmai Dazao Decoction is used for liver qi stagnation syndrome. Gui Pi Tang is used for chronic deficiency of both heart and spleen. Dingxian Wan combined with Anshen Dingzhi Wan is used for wind-phlegm obstruction and combined heart and gallbladder qi deficiency.

3.3.4 Alzheimer's disease with depression

The main treatment principles for Alzheimer's disease with depression are tonifying the kidneys and marrow, resolving phlegm and opening the orifices, and calming the mind and nerves [28]. Suanzaoren Decoction combined with Ganmai Dazao Decoction is suitable for those with early insomnia, nighttime irritability, and emotional instability. Huanglian Ejiao Decoction is used for yin deficiency with excessive fire. Baihe Dihuang Decoction is used for yin deficiency with internal heat, deficiency vexation, and sadness. Zhizi Chi Decoction is mild in nature and suitable for elderly people with restless restlessness. Si Ni San combined with Ganmai Dazao Decoction is used for liver qi stagnation syndrome. Banxia Houpo Decoction is used for those with a foreign body sensation in the throat and low mood. The later formula Dihuang Yinzi is a representative formula for kidney deficiency with reduced marrow, which can simultaneously improve MMSE scores and reduce depression scale scores. Zuo Gui Wan combined with An Shen Ding Zhi Wan is used for kidney essence deficiency. Qifu Yin is used for heart and kidney deficiency syndromes. Tongqiao Huoxue Decoction is used for blood stasis obstructing the orifices type vascular dementia with depression.

3.3.5 Insomnia accompanied by depression

Insomnia accompanied by depression is generally guided by "calming the mind and stabilizing the will, and connecting yin and yang." Suanzaoren Decoction is the core classic formula, mainly treating "deficiency fatigue and irritability, insomnia." A randomized controlled trial involving 160 patients showed that after 4 weeks of treatment, PSQI dropped by 6.4 points and HAMD by 7.8 points, comparable to the zopiclone combined with sertraline group, but significantly reduced daytime sleepiness and dry mouth. Pharmacological studies have revealed that jujube seed saponins can positively regulate GABAA receptors, upregulate 5-HT1A receptors, and lower cortisol [29]. Huanglian Ejiao Decoction mainly treats "vexation in the heart and inability to lie down," suitable for yin deficiency with excessive fire. After 8 weeks of treatment, PSQI and HAMD scores improved better than the alprazolam combined with fluoxetine group. Zhizi Chi Decoction is mainly used to treat 'inability to sleep due to deficiency vexation' and 'vexation in the heart.' It acts quickly and is suitable for those characterized by chest heat and restlessness when sitting or lying down. Chaihu Jia Longgu Muli Tang is suitable for those with anxiety and panic. Lily and Rehmannia Decoction combined with Suanzaoren

Decoction is suitable for yin deficiency with internal heat. Ganmai Dazao Decoction combined with Si Ni San is used for mild emotional instability. Guizhi Jia Longgu Muli Decoction is used for heart yang deficiency and floating and unrestrained spirit. Later, Fang Tianwang Heart Supplement Dan combined with Suanzaoren Decoction was used for heart yin deficiency syndrome. Gui Pi Tang is the representative formula for both heart and spleen deficiency syndromes. Xuefu Zhuyu Decoction is used for stubborn insomnia accompanied by blood stasis. Jiaotai Pills combined with Huanglian Ejiao Decoction is used for the syndrome of heart-kidney disharmony.

4. Integrated Chinese and Western Medicine Diagnosis and Treatment Strategie

4.1 Combining Disease and Syndrome, Harmonizing Form and Spirit" Diagnosis and Treatment Model

Currently, integrated Chinese and Western medicine programs have formed a diagnosis and treatment model centered on "combining disease and syndrome, staging treatment, and combined use of acupuncture and medicine" [30,31]. Taking post-stroke depression as an example, during the acute phase, the main focus is to activate blood circulation, resolve blood stasis, resolve phlegm, and unblock the channels. Prescriptions include Bu Yang Huan Wu Tang or Hua Tan Tong Luo Tang, combined with low-dose SSRIs and acupuncture at Baihui, Yintang, and Taichong; During recovery, liver stagnation and spleen deficiency appeared, so Xiaoyao San combined with Gui Pi Tang was used to remediate, supplemented with moxibustion at Zusanli and Sanyinjiao; For patients with kidney deficiency and marrow reduction during the sequelae phase, use Rehmannia Drink combined with Anshen Dingzhi Pills combined with scalp acupuncture. Parkinson's disease depression emphasizes kidney tonification and marrow filling throughout. Early treatment uses Zishui Qinggan Drink or Chaihu Jia Longgu Muli Decoction to soothe the liver and tonify the kidneys; middle to late stages mainly uses Zuo Gui Wan or Dihuang Ying Zi to nourish marrow. For epilepsy and depression, Chaihu Jia Longgu Muli Decoction or Chaihu Guizhi Decoction are the dominant formulas, combined with antiepileptic drugs, and acupuncture techniques should be mild. For insomnia accompanied by depression, treatment is based on symptoms such as Suanzaoren Decoction, Huanglian Ejiao Decoction, and Zhizichi Decoction, combined with CBT-I and auricular acupressure to press beans.

4.2 Synergy, Toxicity Reduction, and Drug Interactions

The core goal of combined Chinese and Western medicine is to "enhance efficacy" and "reduce toxicity" [23]. In terms of efficacy, Chaihu Jia Longgu Muli Decoction combined with sertraline can show antidepressant effects about a week in advance. For detoxification, Ganmai Dazao Decoction or Suanzaoren Decoction combined with SSRIs can alleviate side effects such as nausea, insomnia, and dry mouth. Huanglian Wendan Decoction combined with a small dose of atypical antipsychotic can reduce the latter dosage and lower the risk of extrapyramidal reactions. It is important to note that some components of Chinese medicines may affect liver

enzyme activity. Clinically, it is recommended to select combinations of classical formulas with long-term practice and good safety, and to follow pharmacopoeia dosage guidelines.

4.3 Early Prevention and “cure before disease”

Based on the disease course pattern of “illness-induced depression,” early intervention in TCM has been explored as an effective secondary prevention strategy. Intervention with liver-soothing and blood-activating injections during the acute phase of stroke can reduce the incidence of moderate to severe depression by about 12% after 6 months. During the prodromal phase of Parkinson’s disease, tonifying the kidneys and soothing the liver can delay the onset of anhedonia. In the early stages of insomnia, using Suanzaoren Decoction or Zhizi Chi Decoction to regulate sleep can reduce the risk of depression later on. This approach of shifting the focus of prevention and treatment forward reflects the core value of traditional Chinese medicine: ‘preventing illness before it occurs, and preventing deterioration after illness’ [32].

5. Issues and Prospects

Despite significant progress in research, there are still shortcomings in this field. First, the criteria for differentiating syndromes have not been standardized, and the objectification of these syndromes is lacking. Most studies use self-developed traditional Chinese medicine syndrome scales, the reliability and validity of which have not been rigorously tested. In the future, it is necessary to develop and validate assessment scales specifically tailored to depression in neurological diseases, and to uniformly use internationally recognized scales as primary outcome indicators. Second, the quality of clinical research is inadequate; high-quality studies involving large sample sizes, multi-centers, and placebo controls for the treatment of such conditions are particularly scarce. In the future, pre-registration systems should be implemented, random assignment procedures should be strictly enforced with blind methods used throughout the research process, and follow-up periods should be extended. Third, there is a lack of systematic integration in mechanistic studies; most research focuses on single pathways or individual indicators. In the future, multidisciplinary approaches such as metabolomics and metagenomics should be utilized to explore the interrelationships between traditional Chinese medicine formulas, syndromes, brain function, and microbiota. Fourth, the collaborative process between traditional Chinese and Western medicine has not yet been standardized. Multidisciplinary teams consisting of neurologists, psychiatrists, and traditional Chinese medicine practitioners need to be established on a systematic basis. Clinical pathways specifically tailored to address depression associated with various major neurological disorders urgently need to be developed and promoted.

6. Conclusion

The high incidence of common neurological disorders accompanied by depression is the result of multi-level damage to brain networks. Single-target treatments often struggle to address all pathological aspects. Traditional Chinese Medicine (TCM) is based on the holistic concept that “form

and spirit are one,” with a core principle of precise treatment that corresponds to specific TCM formulas and syndromes. Through the application of representative formulas such as Bupleurum with Dragon Bone and Oyster Shell Decoction, Spine Date Seed Decoction, and Coptis with Donkey-hide Gelatin Decoction, rich clinical evidence has been accumulated in the treatment of stroke, Parkinson’s disease, epilepsy, Alzheimer’s disease, and insomnia with depression. Modern research has begun to reveal how these formulas regulate multiple targets, including monoamine neurotransmitters and neurotrophic factors, inhibit neuroinflammation, restore neural plasticity, and modulate the gut-brain axis. The integrated approach of TCM and Western medicine, which combines disease-specific treatment strategies, staged therapy, and the use of both acupuncture and medication, leverages their complementary strengths to potentially improve the response rate to antidepressant treatments, shorten the onset time of effects, reduce adverse reactions, and provide synergistic protective effects on the primary neurological disorder. In the future, with advances in high-quality clinical research and breakthroughs in understanding these mechanisms, TCM-based integrated treatment plans are expected to become the preferred approach for neurological disorders accompanied by depression, bringing new hope for the comprehensive recovery of patients with neuropsychiatric comorbidities.

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