International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Exploration of TCM Comprehensive Treatment of Irritable Bowel Syndrome Based on Pathophysiological Mechanism

Xiaonan Xu[1], Yan Huang[1], Zhuolin Ma[2], Zhaoxia Liu[1]

[1]First Affiliated Hospital of Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang Province, People's Republic of China; [2]Eye Hospital of Heilongjiang Province, Harbin, Heilongjiang Province, People's Republic of China

Correspondence: Zhaoxia Liu, First Affiliated Hospital of Heilongjiang University of Chinese Medicine, 26 heping Road, Xiangfang District, Harbin, Heilongjiang Province, People's Republic of China, Email hlj0451lzx@163.com

Abstract: Irritable bowel syndrome (IBS) is a gastrointestinal disorder that is characterized by abdominal pain and altered bowel habits. The clinical manifestations of IBS include abdominal discomfort; irregular bowel movements; potential bleeding; and various symptoms associated with somatic, visceral, and psychiatric conditions. Presently, the diagnosis of IBS relies on symptomatology and the exclusion of other organic disorders, while treatment modalities include pharmacological interventions targeting primary symptoms, dietary modifications, and psychotherapy. Although the underlying mechanisms contributing to morbidity in IBS remain inadequately understood, potential etiological factors include increased epithelial cell permeability, biological irregularities, inflammation, visceral hypersensitivity, genetic and epigenetic influences, and altered brain-gut interactions. IBS significantly diminishes the quality of life and imposes substantial burdens on patients, healthcare providers, and healthcare systems. Recent academic research has indicated that traditional Chinese medicine plays an increasingly significant role in IBS management. This study aimed to investigate the efficacy and safety of Traditional Chinese Medicine (TCM) in treating IBS, focusing on the pathophysiological mechanisms underlying the disorder, to provide insights into a promising complementary approach for managing IBS, with potential applications in clinical practice to improve symptom management and patient quality of life. Further research into the specific mechanisms of TCM in IBS treatment could pave the way for the development of targeted therapeutic strategies.

Keywords: IBS, abdominal pain, diarrhea, defecation disorder, TCM

Introduction

Irritable bowel syndrome (IBS) is classified as a functional gastrointestinal disorder that significantly affects individuals' quality of life and social interactions.[1,2] The underlying pathophysiology of IBS remains only partially elucidated in contemporary medical research.[3] This condition is prevalent in approximately 5–10% of the general population.[4] IBS is characterized by recurrent abdominal pain associated with alterations in bowel patterns or frequency.[5] Treatment strategies primarily focus on alleviating abdominal pain and normalizing bowel habits, often targeting the most distressing symptoms. First-line therapeutic interventions typically include dietary modifications, incorporation of soluble fibers, and use of antispasmodic medications.[6]

IBS is recognized as a multifactorial disorder, suggesting that the underlying morbidity mechanisms are intricate and have not been fully elucidated at the molecular level. Recent studies have identified various functional alterations associated with IBS, including changes in visceral sensitivity, modifications in brain function, disruptions in intestinal motility, endocrine dysfunction, and somatic and psychiatric comorbidities. Furthermore, investigations into the contributions of various proposed pathological factors have yielded inconsistent results, with particular etiological factors frequently not correlating with specific bowel symptoms.[7] For instance, although some studies have reported evidence of intestinal inflammation in IBS patients, others have failed to replicate these findings despite the presence of similar gastrointestinal symptoms.[8] This variability extends to other potential candidate biomarkers.

Received: 23 December 2024
Accepted: 7 May 2025
Published: 12 June 2025

This review aims to consolidate recent advancements in our understanding of the incidence of IBS, its comorbidities, and the roles of inflammation, genetics, the gut microbiota, and the brain-gut axis in the mechanisms underlying IBS morbidity. Additionally, we will examine current diagnostic methodologies and highlight the application of Traditional Chinese Medicine (TCM) in the treatment of IBS.

Epidemiology of IBS

The Rome IV criteria, which serve as the current symptom-based diagnostic framework for IBS, were established through consensus among experts on functional gastrointestinal disorders. This criterion stipulates that the diagnosis of IBS requires the presence of abdominal pain in conjunction with alterations in the form or frequency of bowel movements for at least six months.[5] Patients were categorized based on their predominant stool pattern using the Bristol Stool Morphology Scale, which classifies them into four groups: IBS with diarrhea, IBS with constipation, IBS with a mixed stool pattern, and IBS not otherwise classified.[9] Accurately determining the incidence of IBS poses significant challenges, particularly because of the lack of universally accepted biomarkers for this condition.[10] Consequently, IBS diagnosis primarily relies on self-reported symptom clusters. Nevertheless, given that organic gastrointestinal diseases are relatively uncommon in the general population, and that the diagnosis of IBS is contingent upon the manifestation of characteristic symptoms, population-based epidemiological studies can offer insights into the actual incidence rates. In most geographical regions, the true incidence of IBS is estimated to range from 5% to 10%.[4]

The application of various iterative diagnostic criteria based on specific symptoms has resulted in discrepancies in the reported incidence of the condition; nevertheless, the impact of the disease remains substantial, even among individuals who self-identify as having IBS but do not fulfill the established criteria.[10] Prior to the introduction of the Rome IV criteria in 2016,[5] two systematic reviews were conducted to assess the global prevalence of IBS.[4,11] The first review indicated a combined prevalence of 11.2%, with rates ranging from 1.1% in Iran to 45% in Pakistan.[11] The second review estimated a global prevalence of approximately 8.8%.[4] However, it is noteworthy that prevalence data from regions such as Africa, Eastern Europe, and Middle East remain insufficient. The prevalence rates exhibit considerable variability, ranging from 1.1% in France and Iran to 35.5% in Mexico. Despite the broadly accepted range of prevalence rates, estimates differ markedly across studies, a phenomenon attributed in part to the heterogeneity of the research methodologies employed.

In 2020, the Rome Foundation conducted a cross-sectional survey encompassing 33 countries to investigate the global incidence and burden of functional gastrointestinal disorders in a cohort of 73,000 patients across 26 nations.[12] According to Rome IV criteria, the incidence of IBS ranges from 1.3% to 7.6%, with a combined incidence of 4.1%. In countries where both the Rome III and IV criteria were applied, the combined incidence decreased from 10.1% in Rome III to 3.8% in Rome IV.

Comorbidities and Overlap of IBS with Other Gastrointestinal and Functional Disorders

Research indicates that there is a significant overlap of at least 20% between IBS subtypes[13] and other functional gastrointestinal disorders affecting both the upper and lower gastrointestinal tracts. This includes conditions such as functional dyspepsia, heartburn, gastroesophageal reflux disease, and nausea[14] as well as diarrhea, incontinence, pelvic floor dyssynergia, and constipation.[15] Furthermore, while the potential overlap between IBS and inflammatory bowel diseases (IBDs), such as Crohn's disease and ulcerative colitis, during periods of remission has been suggested, consensus on this matter[16] has yet to be reached.[17]

Other conditions associated with IBS include functional non-bowel syndromes such as chronic pelvic pain syndrome related to the urinary system, vulvodynia, overactive bladder, prostate pain syndrome, premenstrual syndrome, sexual dysfunction, eating disorders, and malnutrition.[18] Population-based studies have indicated a significant overlap between these syndromes and IBS, often exceeding what is anticipated based on the individual prevalence of each condition. Given that many of these disorders are typically diagnosed in specialized medical centers, there is an ongoing debate regarding the potential classification of certain conditions, such as IBS and chronic pelvic pain, as manifestations of a singular underlying disorder.

Furthermore, numerous epidemiological studies have observed that not only IBS but also conditions associated with IBS exhibit psychiatric comorbidities. The prevalence of these symptoms exceeds the anticipated levels and the general population incidence of IBS.[19] Consequently, the entire spectrum of this disease has been categorized under the designation 'symptomatic disease'.[20]

Risk Factors for IBS

Two systematic reviews have indicated that the prevalence of IBS is significantly higher in females compared than in males.[11] Furthermore, a meta-analysis of 14 studies revealed that the incidence of IBS is lower in individuals aged ≥ 50 years than in those aged < 50 years.[11] Currently, there is a lack of reliable data regarding the relationship between IBS and socioeconomic status. IBS is frequently observed in patients with functional somatic syndromes.[21] Various psychosocial, biological, and environmental factors have been associated with IBS and may affect the severity of symptoms. However, it remains uncertain whether these factors constitute genuine risk factors, as most existing studies are cross-sectional and lack the temporal dimensions necessary to establish causal relationships.

One of the most widely acknowledged risk factors for IBS development, observed in approximately 10% of affected individuals, is a history of acute intestinal infections.[22] This subtype is referred to as postinfectious IBS, and can arise following infections caused by bacteria, viruses, or protozoa. A retrospective cohort study indicated that even nonspecific gastrointestinal infections are linked to an elevated risk of postinfectious IBS, comparable to that associated with culture-confirmed bacterial or viral infections.[23] A meta-analysis encompassing 45 observational studies revealed a four-fold increase in the likelihood of IBS development among individuals exposed to infection within a 12-month period. The identified risk factors for the onset of IBS following infection include female sex, prior exposure to antibiotics, psychological distress preceding the illness, and severity of the infection.[22] While patients diagnosed with postinfectious IBS may exhibit a more favorable prognosis than those with non-infectious forms of IBS, a longitudinal follow-up study indicated that 15% of individuals with postinfectious IBS continued to experience symptoms after an eight-year period.[24]

Biophysical and Psychological Mechanisms in the Pathophysiology of IBS

A biophysical model elucidating the manifestations of abdominal pain and defecation disorders in IBS posits a genetic predisposition influenced by adverse early life events, psychological factors, and gastrointestinal infections. These elements are believed to induce modifications in the enteric nervous system, which governs gastrointestinal motility, sensory perception, mucosal integrity, and secretory functions.

In addition to the psychological aspects of IBS,[25] communication between the gut and brain is bidirectional. Longitudinal prospective studies have indicated that a subset of patients experience gastrointestinal symptoms before the onset of psychological issues (Figure 1). Both gastrointestinal infections and psychological disorders have been identified as distinct risk factors that contribute to the emergence of postinfectious IBS and extraintestinal symptoms commonly associated with this condition.

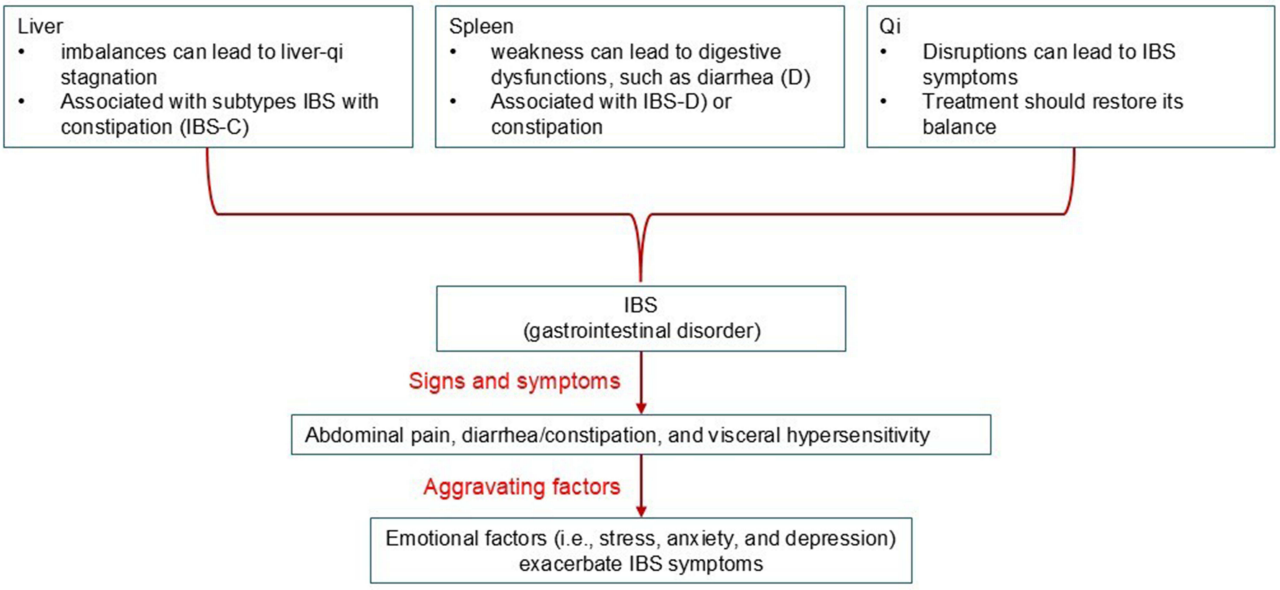

Figure 1 Pathophysiological Mechanisms and Aggravating Factors of IBS.

https://doi.org/10.2147/IJGM.S513906

Visceral sensory alterations in IBS are marked by central abnormalities in brain regions responsible for sensory processing, emotional arousal, and areas beyond the anterior cortex. Additionally, changes in sensory and peripheral mechanisms, which are regulated by descending pathways, have been implicated in the pathophysiology of visceral pain.[26] On average, approximately 60% of patients exhibit heightened sensitivity of the gastrointestinal tract to various physiological stimuli.[27,28] Dyskinesia in IBS is characterized by irregular colonic myoelectrical activity,[29] which manifests as repetitive contractions of the small intestine and colon accompanied by abdominal pain as well as alterations in gastrointestinal and colonic transit.[30,31]

The interplay of various mechanisms, including psychological, sensory, and motor, exacerbates the severity of both gastrointestinal and non-gastrointestinal symptoms, ultimately leading to diminished quality of life in affected individuals.[32,33]

Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) are found in significant quantities in certain fruits, artificial sweeteners, legumes, and green vegetables and are characterized by poor absorption across all individuals. These compounds are both fermentative and osmotic in nature, potentially leading to gastrointestinal symptoms in some patients.[34] Randomized controlled trials (RCTs) have demonstrated that dietary modifications can influence IBS symptoms. However, current evidence does not establish a direct causal relationship between specific foods and symptomatology. Notably, while the intraintestinal water content and colonic volume in individuals with IBS are comparable to those observed in healthy individuals, the symptomatic response in IBS patients is more pronounced, suggesting the involvement of visceral hypersensitivity.[35] Additionally, dietary disaccharide dyspepsia may result in symptoms due to osmotic diarrhea and gas production following fermentation of unabsorbed sugars.[25,36] This condition may be attributed to a deficiency in disaccharidase enzymes or, as evidenced in 4% of patients with IBS, a deficiency in sucrase-isomaltase, which is responsible for the digestion of sucrose and starch.[37]

Although certain studies have indicated that the gastrointestinal microbiome of individuals with IBS differs from that of healthy individuals,[38,39] the precise role of the microbiome in IBS remains uncertain, particularly given the lack of comprehensive knowledge regarding the composition of a healthy microbiome. A systematic review identified a few consistent findings related to IBS, but did not establish a definitive microbiome signature.[40] Antibiotics have been shown to modify the microbial composition of the gastrointestinal tract and are linked to the onset of IBS[41] as well as to small intestinal bacterial overgrowth.[42] However, the role of antibiotics in this context is contentious, primarily because of the limitations inherent in current diagnostic methodologies such as glucose and lactose breath tests[43] and the culture of jejunal aspirates.[43]

Furthermore, up to 25% of patients who fulfill the diagnostic criteria for IBS with diarrhea may actually have idiopathic bile acid diarrhea, as evidenced by abnormal retention rates observed in SeHCAT scans[44] or total fecal bile acid concentrations over a 48-hour period.[45] In a case series, fecal bile acids were found to correlate with fecal quantity, morphology, and colonic transit time.[46] Additionally, a case-control study suggested that elevated fecal bile acids in IBS patients with diarrhea may be linked to a biological abnormality that indirectly enhances Clostridia microbiota.[47]

Acute gastrointestinal infections result in alterations in intestinal permeability and the microbiome.[48] Such modifications may facilitate the activation of immune cells within the gastrointestinal epithelium,[49] which in turn can lead to the release of cytokines that modify the neural regulation of gastrointestinal motility, sensation, and secretion. These pathophysiological changes may persist for extended periods, as evidenced by the sensitivity of neuronal signaling in post-infectious IBS, which can persist for up to two years following the initial infection.[50] Additionally, other researchers have observed increased gastrointestinal permeability accompanied by elevated immune cell counts[51] in IBS patients without an infectious etiology.

The Role of the Enteric Nervous System (ENS), Immune System, and Brain-Gut Axis in IBS

The ENS constitutes a comprehensive network of various intrinsic enteric neurons and glial cells situated between the mucosal layer and circular and longitudinal muscle layers of the gastrointestinal tract. This system encompasses motoneurons, intrinsic primary afferent neurons, and interneurons and is characterized by the presence of nearly all neurotransmitter classes found in the central nervous system (CNS).[52] The neurons within the ENS are organized into two interrelated plexuses: the myenteric plexus, which primarily governs motility, and the submucosal plexus, which

regulates secretory functions.[53] Distinct classes of neurons are chemically differentiated by unique combinations of neurotransmitters and modulators, many of which have been identified in the CNS.[53] The ENS is intricately linked with the gut-associated immune system, the endocrine system, as well as glial and epithelial cells, collectively forming what is referred to as the gut connectome.[54] This connectome illustrates the complex interactions and functional relationships among various cell types within the gut that engage with both the ENS and the CNS.

Recent investigations have indicated that approximately 50% of patients with IBS exhibit abnormal activation of the mucosal immune system, as evidenced by a two- to three-fold increase in mast cell density and significant infiltration of T lymphocytes.[55] This state of low-grade inflammation is directly associated with heightened gut hypersensitivity and motor dysfunction,[56] and is mediated by the activation of TRPV1 channels and serotonin (5-HT) signaling pathways. Polyphenols, such as resveratrol and curcumin, exert their effects through three primary mechanisms: first, they inhibit the NF-κB signaling pathway, leading to a reduction in pro-inflammatory cytokines such as IL-6 and TNF-α by 40% to 60%;[57] second, they facilitate the remodeling of intestinal microbiota, resulting in a 2.8-fold increase in the Bifidobacterium/Firmicutes ratio while suppressing the proliferation of opportunistic pathogens such as Desulfovibrio;[58] and third, they promote the differentiation of CD4CD25FoxP3+ regulatory T cells by modulating dendritic cell (DC) function, thereby enhancing intestinal immune tolerance by 35%.[59] Clinical trial data have demonstrated that a daily intake of 500 mg of olive polyphenol extract led to a 52% reduction in the frequency of abdominal pain among IBS patients and a 67% improvement in abnormal defecation patterns.[60]

At the molecular level, epigenetic studies have confirmed that curcumin can decrease HDAC3 activity by 55%, resulting in a 3.7-fold increase in acetylation of the FoxP3 promoter region, which is crucial for enhancing regulatory T cell function. Concurrently, resveratrol has been shown to significantly improve the intestinal epithelial barrier function[60] by activating the SIRT1 pathway and reducing mitochondrial reactive oxygen species (ROS) production by 68%. Current research is increasingly focused on the triadic interactions among polyphenols, gut bacteria, and the immune system, particularly the antagonistic effects of specific metabolites such as 3,4-dihydroxyphenylacetic acid on the TLR4 receptor. Recent animal studies have revealed that this metabolite can reduce the pathological score in a dextran sulfate sodium (DSS)-induced colitis model by 72%, outperforming the traditional 5-aminosalicylic acid treatment.[61]

The ENS is interconnected with the spinal cord, brainstem, and brain through primary spinal and vagal afferents,[62,63] as well as postganglionic sympathetic and vagal efferents. While the ENS possesses the capability to autonomously regulate all gastrointestinal functions independent of CNS input, the CNS exerts a significant regulatory influence on intestinal behavior,[64] modulating it in accordance with the overall physiological state of the organism and any homeostatic disruptions.[65] Although the ENS is often referred to as the "second brain",[66] it has traditionally been classified as a neural network. However, emerging evidence suggests that specialized neurons that utilize neurotransmitters such as serotonin, catecholamines, and neuropeptides also play a critical role in their function.[67,68] Recent investigations into the human ENS at single-cell resolution have identified a significant gene[69] associated with neuropathic, inflammatory, and extraintestinal diseases. CADM2, which encodes a cell adhesion molecule, is notably expressed in intermuscular regions rather than in the mucosal layer and overlaps with the largest genome-wide association study (GWAS) related to IBS.[70] The intermuscular glial cells are known to regulate neuronal activity,[71] manage oxidative stress and neuroinflammation, and provide nutritional support,[72] among other functions. CADM2 is a member of the synaptic cell adhesion molecule (SvnCAMs) family, which is involved in synaptic organization and signaling.[73] Understanding the mechanisms of communication between glial cells and neurons within the ENS is crucial to elucidate the role of the ENS in both health and disease. Disruptions in this communication may contribute to the dysfunction of the ENS circuitry observed in IBS.[72] Recent comprehensive reviews have extensively examined neuron-glial signaling mechanisms in the ENS, particularly in relation to gastrointestinal diseases, IBS, and visceral pain.[74] Notably, CADM2 is linked to a variety of psychological and neurological characteristics frequently observed in patients with IBS, including psychological behavioral traits, risk-taking tendencies, neurotic features, and neurodevelopmental disorders.[75] Furthermore, synapses are integral to synaptogenesis, axonal guidance, and synaptic plasticity at the fundamental neurodevelopmental level, potentially influencing a range of diseases.[76]

Similarly, NCAM1 has been identified in the largest GWAS to date and is implicated in the development of ENS. Similar to CADM2, NCAM1 has been associated with various aspects of ENS function, including cell migration, neurite outgrowth, neuronal plasticity, and fasciculation,[77] although it has not been studied extensively. Recent cross-tissue mapping utilizing single-core RNA sequencing from eight healthy human organs has revealed that a group of genes, including NCAM1 and

CADM2, are particularly associated with cognitive and psychiatric symptoms, such as general cognitive ability, risk-taking behavior, intelligence, and neuroticism.[78] Although the study did not include tissue samples from the enteric region of the ENS, genes related to cognitive and psychiatric functions were found to be highly expressed in Schwann cells of the esophageal mucosa, interstitial cells of Cajal (ICCs), and neurons within the muscular layer of the esophagus.[78]

An expanding corpus of research, along with clinical observations, underscores the pivotal role of the brain in the onset and persistence of IBS symptoms. Regardless of the initial trigger for symptoms, the brain is fundamentally responsible for the organization and generation of conscious experiences related to abdominal pain, discomfort, and anxiety, which are informed by sensory inputs from the gastrointestinal tract. Early life stressors and traumatic experiences have been shown to elevate the risk of IBS, while psychosocial stressors encountered in adulthood significantly influence the initiation of the first episode, emergence of symptoms, and their severity.[79] Evidence suggests that centrally targeted pharmacological interventions and cognitive-behavioral approaches are among the most efficacious treatment modalities.[80,81] Specific brain functions, including sensory processing, emotional regulation, and cognitive processes, arise from dynamic interactions among various brain regions that operate within extensive neural networks.[82] The characteristics of these central networks have been investigated through neuroanatomical and neurophysiological studies conducted in animal models as well as through a multitude of studies employing diverse structural and functional brain imaging techniques in human subjects.[83,84]

Various types of networks have been identified in the human population, including a functional brain network characterized by evoked responses[85] and the intrinsic connectivity of the brain during resting states.[83,86] Additionally, a structural network has been established based on gray matter parameters[87] and white matter properties as well as an anatomical network derived from white matter connectivity.[88] Research involving both evoked responses and resting state assessments in patients with IBS has revealed abnormalities in regional and task-related networks that are linked to saliency detection,[89,90] emotional arousal,[91,92] central autonomic regulation,[93,94] central executive functions,[95] and sensorimotor processing.[96,97]

Characteristics and Diagnostic Features of IBS

IBS is a multifactorial and heterogeneous disorder; however, it exhibits certain common features. The condition predominantly affects women between the ages of 20 and 40 years; however, in certain regions, a higher prevalence was observed among younger males aged 16 to 30.[98] IBS can manifest at any age.[12] Notably, the average age of the participants in clinical trials for novel IBS treatments was 45 years, reflecting a diverse age range among the affected individuals. Common symptoms associated with IBS include emotional disturbances and extraintestinal manifestations, such as back pain, gynecological and bladder issues, headaches, and fatigue,[99] which may overlap with the symptoms of other functional gastrointestinal disorders.[100] Abdominal pain is a defining characteristic of irritable bowel syndrome (IBS). Consequently, differential diagnosis is extensive, although several features assist in refining this process. First, as IBS is a chronic condition, the etiology of acute abdominal pain is typically excluded. Second, while the pain is recurrent, it is characterized by intermittent episodes rather than a constant presence. Third, pain is generally localized to the lower abdomen, although some patients may experience discomfort in the upper abdominal region.[101] Most importantly, abdominal pain associated with IBS is linked to bowel movements and tends to occur in conjunction with alterations in bowel frequency or consistency.[5] Although IBS is classified based on the predominant bowel pattern, it is important to note that this pattern may fluctuate in many patients.[102]

TCM Perspectives on the Etiology of IBS: Exogenous Factors, Improper Diet, Emotional Disturbances, and Exhaustion

Exogenous Pathogenic Factors

The Yellow Emperor's Canon of Internal Medicine identifies exogenous pathogenic factors such as wind, cold, summer heat, dampness, dryness, and fire". Owing to the distinctive characteristics of these factors, including regional and seasonal variations, it is essential to adhere to the guiding principles of the three causes during treatment. The pathogenic factors most closely associated with IBS are primarily "wind, cold, and dampness".

Improper Diet

The human body functions as an integrated organism, and its life processes require nourishment derived from the essence of grains and serves as the primary source of this acquired essence. Zhang Zhongjing posits that "an appropriate diet benefits the body, while an inappropriate diet can lead to disease", highlighting the significance of dietary habits as a critical pathogenic factor in disease development. Inappropriate dietary practices included overeating, hunger, unclean eating, and food aversion. The spleen and stomach are the principal organs responsible for food digestion. Nutrient absorption relies on the ability of the stomach to decompose food and the role of the spleen in transportation and transformation. When dietary practices are unsuitable, the initial impact is on the functional capacity of the spleen and stomach, leading to dysfunction characterized by the failure of the clear yang to ascend and turbid yin to descend. Consequently, the small intestine may struggle to differentiate between clear and turbid substances, resulting in abdominal pain, distension, and diarrhea.[103]

Emotional Factors

The Yellow Emperor's Canon of Internal Medicine categorizes emotions as "joy, anger, worry, contemplation, sorrow, fear, and surprise". Emotions are intricately linked to innate predispositions, with varying endowments eliciting different emotional responses. The understanding of emotional disorders has evolved, as evidenced by Zhang Jiebin's establishment of a dedicated chapter on "Nine Kinds of Emotions" during the Ming Dynasty, which elucidates the relationship between emotions and diseases. Statistical analyses revealed that 296 medical records in the Clinical Guide Medical Records pertained to emotional factors, encompassing approximately 60 distinct diseases.[104] Qi is essential for normal physiological activities and alterations in its movement can precipitate various ailments. There exists a direct correlation between emotional states and the dynamics of qi movement; for instance, "anger causes qi to rise, while excessive joy leads to a slackening of qi". Emotional disturbances can disrupt normal ascending, descending, entering, and exiting qi, resulting in pain and fullness sensations. Prolonged obstruction of the qi movement can adversely affect the body's water metabolism, leading to conditions such as abdominal pain, distension, and diarrhea.

Exhaustion and Deficiency

Within the framework of the three types of disease causes, fatigue and deficiency are recognized as sources of internal injury stemming from imbalances in yin and yang, qi and blood, and deficiencies in vital qi. This concept encompasses two dimensions: mild fatigue and a more severe strain that can damage visceral organs. Clinical manifestations typically include fatigue, lack of vitality, pallor, and haggard appearance. The human body operates as an interconnected system, in which dysfunction in one area can influence others. Contemporary research has indicated that the spleen, as understood in TCM, plays a crucial role in maintaining the balance of intestinal flora.[105]

TCM Perspectives on the Pathogenesis of IBS: The Role of Spleen, Stomach, Liver Qi, and Qi Regulation

IBS primarily manifests in the large and small intestines, and is significantly associated with the liver, spleen, and kidneys. In TCM, this condition is often associated with the spleen and stomach. Building on this foundation, Zhang Jingyue, during the Ming Dynasty, posited that IBS was also associated with dysuria. Professor Yao Naili[106] emphasized the critical role of spleen and stomach strength, as well as the regulation of qi movement in the management of IBS. Clinical observations by Professor Lv Lin have led to a refined understanding that the root cause of IBS is related to the spleen and stomach, whereas symptomatic expression is attributed to liver-qi stagnation. Furthermore, Zhou Ying[107] suggested that the interconnection between the heart and gallbladder plays a role in regulating emotions and the flow of qi and blood, thereby linking IBS pathogenesis to these organs. Despite varying interpretations among practitioners regarding the etiology of IBS, there is consensus on the importance of harmonizing the spleen and stomach and regulating qi. The TCM perspective on the morbidity mechanism of IBS can be encapsulated as a deficiency in the spleen and stomach induced by various pathogenic factors, leading to a disruption in the normal ascending and descending movements of qi, which ultimately results in abnormal intestinal motility.

Clinical Efficacy of TCM Formulations for Treating IBS Subtypes: Jianpi Zhixie Decoction, Jiawei Tongxie Yaofang, and Zhizhu Pill in IBS-D and IBS-C

Li et al[108] conducted an RCT to assess the clinical efficacy of Jianpi Zhixie Decoction (which includes) in conjunction with Pinaverium Bromide Tablets for the treatment of diarrhea-predominant IBS characterized by liver depression and spleen deficiency. The study involved 96 IBS patients exhibiting symptoms of liver depression and spleen deficiency syndrome, who were randomly assigned to either a control group or an observation group, with 48 participants in each group. The control group received Pinaverium Bromide Tablets, while the observation group was administered the Jianpi Zhixie Decoction in addition to the control treatment. Jianpi Zhixie Decoction includes herbs such as Ren Shen (ginseng), Bai Zhu (atractylodes), and Fu Ling (poria), which help strengthen the spleen, promote digestion, and resolve dampness. Both groups underwent treatment for a duration of four weeks. The clinical efficacy of the interventions was evaluated and comparisons were made regarding TCM syndrome scores, IBS symptom severity scores (IBS-SSS), serum cytokine levels, and intestinal barrier function between the two groups before and after the treatment period. These findings suggest that the Jianpi Zhixie Decoction may effectively inhibit gastrointestinal inflammatory responses, restore intestinal barrier function, and alleviate clinical manifestations, such as abdominal pain and diarrhea.

Zhengyin[109] conducted an RCT to evaluate the clinical efficacy of Jiawei Tongxie Yaofang in treating IBS-D characterized by liver depression and spleen deficiency. The study involved 60 patients diagnosed with IBS-D associated with liver depression and spleen deficiency syndrome who were randomly assigned to either a treatment or control group, with 30 participants in each group. The treatment group received Jiawei Tongxie Yaofang, whereas the control group received Pinaverium Bromide Tablets over a period of four weeks. This formulation typically contains Chao Bai Zhu, Chen Pi, and Dang Gui, which are used to regulate liver qi, improve digestion, and relieve the abdominal pain associated with IBS-D. These ingredients were chosen based on their ability to relieve bloating and regulate bowel movement. The researchers assessed changes in TCM syndrome, irritable bowel syndrome quality of life scale (IBS-QoL), and Hamilton Anxiety Scale (HAMA) scores before and after the intervention in both groups. The overall improvement in symptoms was evaluated using IBS-SSS. Additionally, the study compared the improvement in individual symptoms, such as abdominal pain and diarrhea, as well as the recurrence of symptoms four weeks post-treatment cessation between the two groups. The findings indicated that Jiawei Tongxie Yaofang demonstrated a significant therapeutic effect in IBS-D patients with liver depression and spleen deficiency syndrome, effectively alleviating symptoms of abdominal pain and diarrhea, enhancing TCM syndrome scores, improving patients' quality of life, and reducing anxiety levels.

Xu et al[110] conducted an RCT to evaluate the clinical efficacy of Zhizhu Pill, a traditional formulation used in IBS-C, containing herbs such as Zhi Shi (unripe bitter orange), Bai Shao (white peony root), and Sini Powder, in the treatment of irritable bowel syndrome with liver depression and qi stagnation, as well as their impact on gastrointestinal hormones. This study involved 61 patients diagnosed with IBS-C, characterized by stagnation of liver qi syndrome, who were randomly assigned to either a control group (n = 30) or an observation group (n = 31). In addition to the standard treatment, the control group received oral mosapride citrate dispersible tablets, whereas the observation group was administered oral Zhizhu Pill and Sini Powder over a treatment period of six weeks. The researchers compared TCM syndrome scores, quality of life scores for patients with constipation (PAC-Qol), serum levels of motilin, vasoactive intestinal peptide (VIP), and substance P, as well as clinical efficacy and adverse reactions between the two groups before and after treatment. These findings suggest that pill and powder tablets are more effective than mosapride citrate dispersible tablets in treating IBS-C with liver-qi stagnation, as they alleviate clinical symptoms, enhance mental well-being, and improve quality of life by modulating the serum levels of VIP, motilin, and substance P.

Studies on the mechanism of action of TCM in treating IBS are summarized in Table 1 and were selected due to their rigorous randomized controlled trial (RCT) design and specific focus on IBS subtypes such as IBS-D and IBS-C. These studies are among the most recent and relevant in the field of TCM for IBS treatment, providing insights into the efficacy of these formulations in modulating gastrointestinal motility, inflammation, and emotional symptoms commonly observed in IBS patients. Furthermore, these studies provide robust data on symptom improvement, quality of life, and biochemical markers, which have significantly contributed to the clinical understanding of TCM in IBS management.

Table 1 Efficacy of TCM in the Treatment of IBS

Treatment	Mechanism of Action
Jianpi Zhixie Decoction	Jianpi Zhixie Decoction can effectively relieve clinical signs and symptoms such as abdominal pain and diarrhea, and improve the daily life of IBS patients by inhibiting gastrointestinal inflammatory response and repairing intestinal barrier function.
Jiawei Tongxie Yaofang	Jiawei Tongxie Yaofang can effectively improve the symptoms of abdominal pain, diarrhea and TCM syndrome scores, improve the quality of life of patients, and alleviate the anxiety of patients in the treatment of IBS-D patients with liver depression and spleen deficiency.
Zhizhu Pill and Sini Powder	The curative effect of Zhizhu Pill combined with Sini Powder is better than Mosapride Citrate Dispersible Tablets in the treatment of IBS-C patients with liver depression and qi stagnation syndrome, which may alleviate the clinical signs and symptoms of patients, improve their mental state and improve their quality of life by regulating the levels of VIP, motilin and substance P in serum.

Clinical and Preclinical Investigations of Acupuncture and Electroacupuncture for the Treatment of IBS-D: Mechanisms and Efficacy

Zhan et al[111] conducted an RCT to evaluate the clinical efficacy of acupuncture aimed at regulating the mind and invigorating the spleen in conjunction with electroacupuncture for the treatment of IBS-D. The study involved 60 patients diagnosed with IBS-D who were randomly assigned to either the medication or observation group, with 30 participants in each cohort. The medication group received oral trimebutine maleate dispersible tablets, whereas the observation group received acupuncture combined with electroacupuncture. The researchers assessed changes in the IBS-SSS, IBS-QoL score, Hospital Anxiety and Depression Scale (HADS) score, and activation of mast cells (MCs) in the intestinal mucosa both before and after treatment. A comparative analysis of the clinical efficacy between the two groups was performed. These findings suggest that the combined approach of "Tiaoshen Jianpi" acupuncture and electroacupuncture demonstrates superior clinical efficacy in treating IBS-D compared to the administration of medication alone, as it alleviates clinical symptoms such as abdominal pain, enhances quality of life, mitigates depression, and reduces the activation of mast cells.

Xuemei[112] conducted an RCT to investigate the effects of triple energizer acupuncture on abnormal gastrointestinal motility, as well as the expression of stem cell factor (SCF) and tyrosine kinase receptor (TKR) in the colonic tissue of rats with IBS-D. The study involved male Wistar rats, which were randomly assigned to four groups: blank, model, western medicine, and triple energizer groups, with six rats in each group. All groups, except the blank group, underwent treatment with "glacial acetic acid enema combined with restraint stress" to establish the IBS-D model. The Western medicine group received pinaverium bromide (15 mg/kg) via gavage, whereas the triple energizer group received acupuncture at specific acupoints (Shanzhong, Zhongwan, Qihai, Xuehai bilaterally, and Zusanli bilaterally) for 14 days, and each acupoint was stimulated for 30s daily. The general health of the rats was monitored, and various parameters were measured, including body weight, open-field test results (both transverse and longitudinal movements), loose stool rates, and abdominal retraction reflex (AWR) thresholds. The mRNA and protein expression levels of SCF and C-kit were assessed using RT-PCR and Western blotting, respectively. These findings suggest that triple energizer acupuncture may ameliorate symptoms in IBS-D rats, potentially through the modulation of SCF and C-kit expression in colonic tissue.

In a separate study, Wang et al[113] examined the effects and mechanisms of hilling and inhibiting wood needle therapy on intestinal mucosal barrier function in rats with IBS-D, focusing on the corticotropin-releasing factor (CRF)/CRF receptor 1 (CRFR1) pathway. This study involved 40 female Sprague-Dawley (SD) rats, which were randomly divided into four groups: blank, model, electroacupuncture, and agonist, with ten rats in each group. All groups except the blank group were subjected to gavage with senna extract combined with chronic unpredictable mild stress to induce the IBS-D model. The acupuncture group received acupuncture on one side of "Tianshu" and electroacupuncture on "Zusanli" and "Taichong" (at frequencies of 2 hz and 15 hz) for 20 minutes, alternating every other day for 14 days. The agonist group was administered a CRFR1 agonist, urotropin, 30 min after caudal vein injection using the same acupuncture protocol as the electroacupuncture group. Post-intervention assessments included measuring visceral pain thresholds and Bristol stool scores, evaluating anxiety and depression behaviors through elevated plus-maze and open-field tests, and

Table 2 Acupuncture and Electroacupuncture Effects on IBS-D Symptoms and Mast Cell Activation

Treatment	Mechanism of action
"Tiaoshen Jianpi" acupuncture combined with electroacupuncture	The clinical curative effect of "Tiaoshen Jianpi" acupuncture combined with electroacupuncture on IBS-D is better than that of single oral medication, which can relieve clinical signs and symptoms such as abdominal pain, improve the quality of life, improve depression and reduce the activation of MCs.
Trifocal needling	Triple energizer acupuncture can improve the symptoms of IBS-D rats, which may be related to the regulation of the expression of SCF, C-kit mRNA and protein in the colon tissue.
Earth up and wood suppression needling method	Hilling and inhibiting wood needle method can significantly improve the visceral hypersensitivity, anxiety and depression of IBS-D rats, which may be related to the inhibition of CRF/CRFR1 pathway and the restoration of intestinal tight junction protein expression.

quantifying serum and colonic tissue levels of CRF and CRFR1 using ELISA and immunohistochemistry. The study found positive expression of tight junction proteins ZO-1, Occludin, and Claudin-1. These results indicate that hilling and inhibiting wood needle therapy significantly alleviated visceral hypersensitivity, anxiety, and depression in IBS-D rats, potentially by inhibiting the CRF/CRFR1 pathway and restoring intestinal tight junction protein expression.

The mechanism of acupuncture in the treatment of IBS is summarized in Table 2.

Clinical Efficacy of TCM Interventions in the Treatment of IBS-D: Randomized Controlled Trials on Herbal Formulations, Acupuncture, and Moxibustion

Ying Xuqing[114] designed an RCT to assess the effects of Huangqi Jianzhong Decoction combined with moxibustion on clinical symptoms, inflammation, and gastrointestinal hormone levels in patients with IBS-D. The study included 80 patients with IBS-D who were randomly assigned to an observation group (n = 40) and a control group (n = 40). All participants received standard Western medical treatment; however, the control group underwent moxibustion, while the observation group received Huangqi Jianzhong Decoction in addition to moxibustion. Therapeutic outcomes in both groups were compared. Serum levels of inflammatory markers (soluble interleukin-2 receptor [sIL-2R], tumor necrosis factor-α [TNF-α], and interleukin-1β [IL-1β]) and gastrointestinal hormone markers (gastrin [GAS], motilin [MTL], and somatostatin [SS]) were measured before and after treatment. Additionally, the IBS-QoL and HAMD were used to evaluate the psychological status and quality of life of the patients. These findings suggest that Huangqi Jianzhong Decoction combined with moxibustion effectively improves clinical symptoms, reduces inflammation, enhances gastrointestinal function, and alleviates negative emotional states in IBS-D patients.

Fan et al[115] conducted an RCT to investigate the clinical efficacy and safety of Wuling capsules in conjunction with acupuncture for the treatment of IBS-D. The study involved 140 patients diagnosed with IBS-D, who were randomly assigned to either a control group or an observation group, with 70 participants in each group. The control group received hydrotherapy along with oral trimebutine maleate and Wuling capsules, whereas the observation group received acupuncture in addition to the treatments provided to the control group. Comprehensive therapeutic effects and overall symptom relief were assessed in both the groups. Additionally, the quality of life of patients with IBS-D was measured pre- and post-treatment using the IBS-QOL instrument, while anxiety levels were evaluated using the HAMA. The degree of depression was assessed using the HAMD. Serum levels of diamine oxidase (DAO), D-lactate, intestinal fatty acid-binding protein (IFABP), 5-HT, and calcitonin gene-related peptide (CGRP) were measured using enzyme-linked immunosorbent assay (ELISA). The findings suggest that the combination of Wuling capsules with acupuncture and moxibustion significantly enhances clinical efficacy, improves quality of life, alleviates anxiety and depression in patients with IBS-D, reduces levels of DAO, D-lactic acid, IFABP, 5-HT, and CGRP, and effectively relieves gastrointestinal symptoms while maintaining a high safety profile.

Li et al[116] conducted an RCT to assess the clinical efficacy of warm needling in conjunction with Buzhong Yiqi Decoction for the treatment of female patients with IBS. Sixty female patients with IBS were randomly assigned to either the control or observation group, with each group comprising thirty participants. The control group received treatment

with trimebutine maleate tablets, while the observation group received warm acupuncture alongside Buzhong Yiqi Decoction, in addition to the control treatment. This study evaluated various outcomes, including clinical efficacy, changes in TCM symptom scores, defecation patterns (daily frequency and instances of urgent defecation over ten days), alterations in HAMA and HAMD scores, 5-HT levels, IBS Quality of Life (IBS-Qol) scores, and any adverse reactions. These findings suggest that warm needling combined with Buzhong Yiqi Decoction is an effective, safe, and reliable treatment for IBS in women.

Similarly, Zhang et al[117] designed an RCT to investigate the effects of Tongxie Yaofang combined with moxa stick moxibustion in patients with IBS-D, and its impact on immunoglobulin and serum inflammatory factor levels. In this study, ninety-four patients diagnosed with IBS-D were randomly divided into the observation and control groups, each consisting of forty-seven participants. The control group received Pinaverium Bromide Tablets, while the observation group was treated with Tongxie Yaofang and moxa stick moxibustion for 14 days. The study compared clinical efficacy, TCM symptom scores, IBS-SSS scores, IBS-Qol scores, immunoglobulin levels, and inflammatory factor levels between the two groups, and documented any adverse reactions. The results indicated that the combination of Tongxie Yaofang and moxa stick moxibustion enhanced clinical efficacy in patients with IBS-D, modulated immune responses, controlled inflammation, alleviated pain, and improved symptoms, thereby warranting its application in clinical practice. The mechanism of action of TCM in the comprehensive treatment of IBS is summarized in Figure 2 and Table 3.

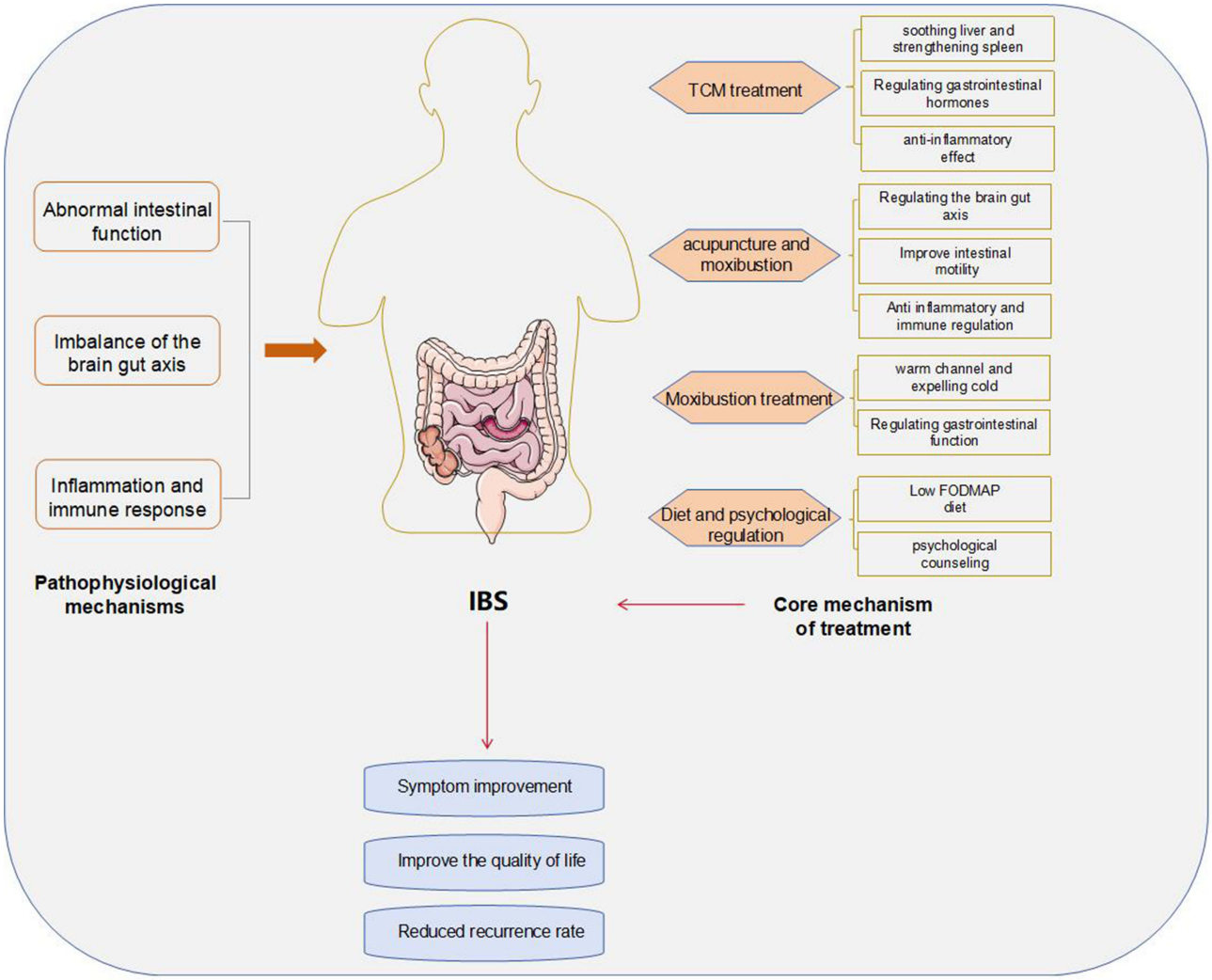

Figure 2 The broader treatment strategies, including psychological and dietary factors, that aim to alleviate IBS symptoms.

https://doi.org/10.2147/IJGM.S513906

Table 3 Clinical Efficacy of TCM Comprehensive Treatment in Irritable Bowel Syndrome-Diarrhea

Treatment	Mechanism of action
Huangqi Jianzhong Decoction combined with moxibustion	Huangqi Jianzhong Decoction combined with moxibustion can effectively improve the clinical signs and symptoms of patients with IBS-D, improve the level of inflammation and gastrointestinal function, alleviate their negative emotions, and improve the quality of life of patients.
Wuling capsule combined with acupuncture	Wuling capsule combined with acupuncture and moxibustion can enhance the clinical efficacy, effectively improve the quality of life and anxiety and depression of IBS-D patients, reduce the levels of DAO, D-lactic acid, IFABP, 5-HT and CGRP, and relieve gastrointestinal symptoms, with high safety.
Warm Needling Combined with Buzhong Yiqi Prescription	Warm needling combined with Buzhong Yiqi Decoction can significantly improve the gastrointestinal function of IBS patients, significantly improve the quality of life of patients, and the treatment is safe and reliable.
Tongxie Yaofang combined with moxa stick moxibustion	Tongxie Yaofang combined with moxa stick moxibustion can improve the clinical efficacy of IBS-D patients, regulate immunity, control inflammation in vivo, and help to alleviate pain and improve symptoms.

Perspectives

TCM offers a holistic and integrative approach to treating IBS, focusing on the balance of the liver and spleen qi, which are central to the pathophysiological mechanisms underlying the disorder. Clinical studies have highlighted the efficacy of TCM formulations, including Jianpi Zhixie Decoction, Jiawei Tongxie Yaofang, and Zhizhu Pill, in providing significant relief for patients with both diarrhea-predominant (IBS-D) and constipation-predominant (IBS-C) subtypes. These formulations address not only the primary symptoms of IBS, but also the underlying imbalances in gastrointestinal motility, inflammation, and emotional regulation that often accompany the condition. In particular, these treatments have demonstrated the potential to improve quality of life, reduce symptom severity, and modulate gastrointestinal hormones, offering an alternative to or complementary therapy alongside conventional treatments. In addition, acupuncture, particularly when combined with moxibustion, has been shown to alleviate abdominal pain and discomfort, regulate bowel movements, and improve psychological well-being by reducing anxiety and depression, which are commonly associated with IBS.

The application of TCM in IBS treatment has immense potential, offering alternative or complementary therapies alongside conventional treatments. However, further research is required to optimize its effectiveness in IBS management. Specifically, future research should focus on clarifying the mechanisms of action underlying individual TCM therapies and their interactions with Western medical treatments. Additionally, investigations into the effects of individual Chinese herbs, as opposed to synergistic formulations, would help to identify more precise therapeutic agents for IBS. Moreover, pharmacokinetic studies examining the absorption, distribution, metabolism, and elimination profiles of these herbs are essential to understand their long-term efficacy and safety.

Limitations

Despite the promising potential of TCM in IBS management, several challenges and limitations persist in its application and scientific validation. One of the primary issues in the research on TCM for IBS is the ambiguity surrounding the classification and assessment of TCM syndromes, particularly in animal model studies. To enhance the effectiveness of follow-up research, it is essential that these models align more closely with specific TCM syndrome types, which will allow for more precise investigations of therapeutic efficacy and underlying mechanisms of action within different IBS subtypes. Currently, the predominant TCM prescriptions are primarily focused on strategies for soothing the liver and strengthening the spleen to manage diarrhea. However, clinical practice incorporates a much broader range of effective treatments that address various syndromes, which are not always adequately explored in research. Thus, clarifying the specific mechanisms underlying the clinical efficacy of these TCM therapies, particularly through foundational and mechanistic research, is vital to bolster the scientific rigor of TCM in IBS management.

Additionally, there is a lack of research examining the effects of individual Chinese herbs on IBS, with much of the existing research focusing on synergistic formulations. However, the role of individual herbs and their specific

contributions to treatment outcomes remain underexplored. Furthermore, studies on the pharmacokinetics of these herbs, including their absorption, distribution, metabolism, and elimination profiles, are limited. Detailed pharmacokinetic studies are necessary to better understand how these herbs interact within the body, their potential long-term efficacy, and elimination half-life. Future research should prioritize these aspects to identify precise therapeutic agents and to evaluate their long-term safety and effectiveness. Additionally, exploring the pharmacological interactions between TCM herbs and conventional drugs could provide valuable insights into the safe integration of these therapies into the comprehensive treatment strategies for IBS.

Conclusions

The application of TCM in treating IBS offers a promising, multifaceted approach that not only focuses on alleviating symptoms, but also addresses the root causes of the condition, such as gastrointestinal motility, inflammation, and emotional factors. While clinical evidence suggests that TCM therapies such as Jianpi Zhixie Decoction, Jiawei Tongxie Yaofang, and acupuncture can be beneficial, there is a need for more rigorous, high-quality research to validate these findings and further elucidate the critical mechanisms of action. Research should focus on bridging the gap between TCM syndromes and modern scientific understanding to ensure that treatment models are more accurately aligned with the underlying pathophysiology of IBS. Furthermore, addressing the current limitations in TCM syndrome classification and research methodology will be crucial for advancing our understanding of the role of TCM in IBS treatment. Collectively, the continued exploration and integration of TCM within modern IBS management paradigms will require a multidisciplinary approach that combines traditional knowledge with contemporary scientific methods.

Abbreviations

IBS, irritable bowel syndrome; TCM, traditional Chinese medicine; IBDs, inflammatory bowel diseases; FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; ENS, enteric nervous system; RCT, randomized controlled trial; CNS, central nervous system; GWAS, Genome Wide Association Study; SvnCAMs, Synaptic Cell Adhesion Molecules; ICCs, interstitial cells of Cajal; IBS-SSS, IBS symptom severity score; IBS-D, diarrhea-predominant predominant irritable bowel syndrome; IBS-Qol, irritable bowel syndrome quality of life scale; HAMA, Hamilton anxiety scale; IBS-C, irritable bowel syndrome with liver depression and qi stagnation; PAC-Qol, quality of life in patients with constipation; VIP, vasoactive intestinal peptide; HADS, hospital anxiety and depression scale; MCs, mast cells; TKR, tyrosine kinase receptor; AWR, abdominal retraction reflex; sIL-2R, soluble interleukin-2 receptor; TNF-α, tumor necrosis factor-α; IL-1β, interleukin-1β; GAS, gastrin; MTL, motilin; SS, somatostatin; DAO, diamine oxidase; ELISA, enzyme linked immunosorbent assay; IFBP, intestinal fatty acid-binding protein; CGRP, calcitonin gene-related peptide.

Disclosure

The authors declare that they have no affiliation with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

References

1. Buono JL, Carson RT, Flores NM. Health-related quality of life, work productivity, and indirect costs among patients with irritable bowel syndrome with diarrhea. *Health and Quality of Life Outcomes*. 2017;15(1):1–8. doi:10.1186/s12955-017-0611-2
2. Frändemark Å, Törnblom H, Jakobsson S, et al. Work productivity and activity impairment in irritable bowel syndrome (IBS): a multifaceted problem. *Off J Am College Gastroenterol*. 2018;113(10):1540–1549. doi:10.1038/s41395-018-0262-x
3. Holtmann GJ, Ford AC, Talley NJ. Pathophysiology of irritable bowel syndrome. *Lancet Gastroenterol Hepatol*. 2016;1(2):133–146. doi:10.1016/S2468-1253(16)30023-1
4. Sperber AD, Dumitrascu D, Fukudo S, et al. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome foundation working team literature review. *Gut*. 2017;66(6):1075–1082. doi:10.1136/gutjnl-2015-311240
5. lacy BE, Mearin F, Chang L, et al. Bowel disorders. *Gastroenterology*. 2016;150(6):1393–407.E5. doi:10.1053/j.gastro.2016.02.031
6. ford AC, Moayyedi P, Chey WD, et al. American college of gastroenterology monograph on management of irritable bowel syndrome. *Off J Am College Gastroenterol*. 2018;113:1–18.
7. Petersen MW, schröder A, jørgensen T, et al. Irritable bowel, chronic widespread pain, chronic fatigue and related syndromes are prevalent and highly overlapping in the general population: danfund. *Sci Rep*. 2020;10(1):3273. doi:10.1038/s41598-020-60318-6

8. Flik CE, Laan W, Smout AJ, et al. Comparison of medical costs generated by IBS patients in primary and secondary care in the Netherlands. *BMC gastroenterol*. 2015;15(1):1–11. doi:10.1186/s12876-015-0398-8
9. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scandinavian J Gastroenterol*. 1997;32(9):920–924. doi:10.3109/00365529709011203
10. Sperber A, Gwee K, Hungin A, et al. Conducting multinational, cross-cultural research in the functional gastrointestinal disorders: issues and recommendations. A Rome foundation working team report. *Alim Pharmacol Therap*. 2014;40(9):1094–1102. doi:10.1111/apt.12942
11. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol*. 2012;10 (7):712–21.E4. doi:10.1016/j.cgh.2012.02.029
12. Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome foundation global study. *Gastroenterology*. 2021;160(1):99–114.E3. doi:10.1053/j.gastro.2020.04.014
13. Ford AC, Forman D, Bailey AG, et al. Irritable bowel syndrome: a 10-yr natural history of symptoms and factors that influence consultation behavior. *Off J Ame College Gastroenterol*. 2008;103(5):1229–1239. doi:10.1111/j.1572-0241.2007.01740.x
14. Yarandi SS, Nasseri-Moghaddam S, Mostajabi P, et al. Overlapping gastroesophageal reflux disease and irritable bowel syndrome: increased dysfunctional symptoms. *WJG*. 2010;16(10):1232. doi:10.3748/wjg.v16.i9.1232
15. Ford A, Bercik P, Morgan D, et al. Characteristics of functional bowel disorder patients: a cross-sectional survey using the Rome III criteria. *Alim Pharmacol Therap*. 2014;39(3):312–321. doi:10.1111/apt.12573
16. long MD, drossman DA. Inflammatory bowel disease, irritable bowel syndrome, or what?: a challenge to the functional–organic dichotomy. *Off J Am College Gastroenterol*. 2010;105(8):1796–1798. doi:10.1038/ajg.2010.162
17. Keohane J, o'mahony C, o'mahony L, et al. Irritable bowel syndrome–type symptoms in patients with inflammatory bowel disease: a real association or reflection of occult inflammation? *Off J Am College Gastroenterol*. 2010;105(8):1789–1794. doi:10.1038/ajg.2010.156
18. Whitehead W, palsson O, Levy R, et al. Comorbidity in irritable bowel syndrome. *Off J Am College Gastroenterol*. 2007;102(12):2767–2776. doi:10.1111/j.1572-0241.2007.01540.x
19. Janssens KA, Zijlema WL, Joustra ML, et al. Mood and anxiety disorders in chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome: results from the lifelines cohort study. *Psych Med*. 2015;77(4):449–457. doi:10.1097/PSY.0000000000000161
20. Barsky AJ. Assessing the new DSM-5 diagnosis of somatic symptom disorder. *Psych Med*. 2016;78(1):2–4. doi:10.1097/PSY.0000000000000287
21. petersen M, schröder A, jørgensen T, et al. The unifying diagnostic construct of bodily distress syndrome (BDS) was confirmed in the general population. *J Psych Res*. 2020;128:109868. doi:10.1016/j.jpsychores.2019.109868
22. Klem F, Wadhwa A, Prokop L, et al. Prevalence, risk factors, and outcomes of irritable bowel syndrome after infectious enteritis: a systematic review and meta-analysis. *Gastroenterology*. 2017;152(5):1042–54.E1. doi:10.1053/j.gastro.2016.12.039
23. Donnachie E, Schneider A, Mehring M, et al. Incidence of irritable bowel syndrome and chronic fatigue following GI infection: a population-level study using routinely collected claims data. *Gut*. 2018;67(6):1078–1086. doi:10.1136/gutjnl-2017-313713
24. Marshall JK, Thabane M, Garg AX, et al. Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery. *Gut*. 2010;59(5):605–611. doi:10.1136/gut.2009.202234
25. Tenghao Z, Shanti E, Amanda LP, et al. Reduced efficacy of low fodmaps diet in patients with IBS-D carrying sucrase-isomaltase (SI) hypomorphic variants. *Gut*. 2019;69(2):397–8.
26. kirsten T, Emeran AM, Jennifer SL. Quantitative meta-analysis identifies brain regions activated during rectal distension in irritable bowel syndrome. *Gastroenterology*. 2010;140(1):91–100.
27. Iris P, Alma S, lina L, et al. Altered rectal perception in irritable bowel syndrome is associated with symptom severity. *Gastroenterology*. 2007;133(4):1113–23.
28. Ritchie J. Pain from distension of the pelvic colon by inflating a balloon in the irritable colon syndrome. *Gut*. 1973;14(2):125–132. doi:10.1136/gut.14.2.125
29. Sullivan MA, Cohen S, Snape WJ. Colonic myoelectrical activity in irritable-bowel syndrome. Effect of eating and anticholinergics. *N Engl J Med*. 1978;298(16):878–883. doi:10.1056/NEJM197804202981604
30. Kellow JE, Phillips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology*. 1987;92 (6):1885–93.
31. Spiller RC, Brown ML, Phillips SF. Emptying of the terminal ileum in intact humans. Influence of meal residue and ileal motility. *Gastroenterology*. 1987;92(3):724–9.
32. Magnus S, Hans T, Olafur SP, et al. Cumulative effects of psychologic distress, visceral hypersensitivity, and abnormal transit on patient-reported outcomes in irritable bowel syndrome. *Gastroenterology*. 2019;157(2):391–402.
33. Lena B, Stine S, Hans T, et al. Self-reported food-related gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. *Am J Gastroenterol*. 2013;108(5): 634–4.
34. Susan JS, Francis CP, Jane GM, et al. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clin Gastroenterol Hepatol*. 2008:6(7):765–71.
35. Giles M, Sue P, Kathryn M, et al. Colon hypersensitivity to distension, rather than excessive gas production, produces carbohydrate-related symptoms in individuals with irritable bowel syndrome. *Gastroenterology*. 2016;152(1):124–3.
36. Louise T, Malte R, Jun W, et al. Sucrase-isomaltase 15Phe IBS risk variant in relation to dietary carbohydrates and faecal microbiota composition. *Gut*. 2018;68(1):177–8.
37. Koldo G-E, Tenghao Z, Ferdinando B, et al. Increased prevalence of rare sucrase-isomaltase pathogenic variants in irritable bowel syndrome patients. *Clin Gastroenterol Hepatol*. 2018;16(10):1673–6.
38. Jonna J-T, Jarkko S, Anne S, et al. Faecal microbiota composition and host-microbe cross-talk following gastroenteritis and in postinfectious irritable bowel syndrome. *Gut*. 2013;63(11):1737–45.
39. Sundin J, Rangel I, Fuentes S. Altered faecal and mucosal microbial composition in post-infectious irritable bowel syndrome patients correlates with mucosal lymphocyte phenotypes and psychological distress. *Aliment Pharmacol Ther*. 2014;41(4):342–351. doi:10.1111/apt.13055
40. Rapat P, Jennifer TL, Yuhong Y, et al. Gut microbiota in patients with irritable bowel syndrome-a systematic review. *Gastroenterology*. 2019;157(1):97–108.

41. Laura Rindom K, Anne Line E, Peter B. Antibiotics: a risk factor for irritable bowel syndrome in a population-based cohort. *Scand J Gastroenterol*. 2018;53(9):1027–30.
42. Pimentel M, Chow EJ, HC L. Eradication of small intestinal bacterial overgrowth reduces symptoms of irritable bowel syndrome. *Am J Gastroenterol*. 2000;95(12):3503–6.
43. Derek Y, Frank C, Stephen V. Combined oro-caecal scintigraphy and lactulose hydrogen breath testing demonstrate that breath testing detects oro-caecal transit, not small intestinal bacterial overgrowth in patients with IBS. *Gut*. 2011;60(3):334–40.
44. Slattery SA, Niaz O, Aziz Q, et al. Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea. *Aliment Pharmacol Ther*. 2015;42(1):3–11. doi:10.1111/apt.13227
45. Andrea S, Michael C, Priya V, et al. Bowel functions, fecal unconjugated primary and secondary bile acids, and colonic transit in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2013;11(10):1270–5.
46. Michael C, Irene B, Andres A, et al. Effect of increased bile acid synthesis or fecal excretion in irritable bowel syndrome-diarrhea. *Am J Gastroenterol*. 2014;109(10):1621–30.
47. Ling Z, Wei Y, Yang C, et al. A Clostridia-rich microbiota enhances bile acid excretion in diarrhea-predominant irritable bowel syndrome. *J Clin Invest*. 2019;130(1):438–5.
48. Marshall JK, Thabane M, Garg AX, et al. Intestinal permeability in patients with irritable bowel syndrome after a waterborne outbreak of acute gastroenteritis in Walkerton, Ontario. *Aliment Pharmacol Ther*. 2004;20:1317–1322. doi:10.1111/j.1365-2036.2004.02284.x
49. Simon PD, David J, Robin CS. Distinctive clinical, psychological, and histological features of postinfective irritable bowel syndrome. *Am J Gastroenterol*. 2003;98(7):1578–83.
50. Balemans D, Mondelaers SU, Cibert-Goton V, et al. Evidence for long-term sensitization of the bowel in patients with post-infectious-IBS. *Sci Rep*. 2017;7(1). doi:10.1038/s41598-017-12618-7.
51. Bashashati M, Moossavi S, Cremon C, et al. Colonic immune cells in irritable bowel syndrome: a systematic review and meta-analysis. *Neurogastroenterol Motil*. 2017;30(1). doi:10.1111/nmo.13192.
52. John BF, Brid PC, Leni RR, et al. The enteric nervous system and gastrointestinal innervation: integrated local and central control. *Adv Exp Med Biol*. 2014;817:1578–83.
53. John BF. The enteric nervous system and neurogastroenterology. *Nat Rev Gastroenterol Hepatol*. 2012;9(5):286–94.
54. Diego VB, Rodger AL. The gut connectome: making sense of what you eat. *J Clin Invest*. 2015;125(3):888—90.
55. Zongchuan L, Nianan Y, Mingya W, et al. Relationship between serum mir-219a-5p and mir-338-3p levels and intestinal microflora and inflammatory factors in patients with irritable bowel syndrome. *J Lab Med Clin Med*. 2024;21(23):3480–3484.
56. Zan L, Xiuxian Z, Yang W. Role of neuro-immune-endocrine network in morbidity of irritable bowel syndrome. *Chin J Gen Med*. 2010;13 (03):334–336.
57. Roudsari NM, Lashgari NA, Momtaz S, et al. Natural polyphenols for the prevention of irritable bowel syndrome: molecular mechanisms and targets; a comprehensive review. *Daru*. 2019;27(2):755–780. doi:10.1007/s40199-019-00284-1
58. Kemperman RA, Bolca S, Roger LC, et al. Novel approaches for analysing gut microbes and dietary polyphenols: challenges and opportunities. *Microbiology* 2010;156(Pt 11):3224–3231. doi:10.1099/mic.0.042127-0
59. Iglesias-Aguirre CE, Cortés-Martín A, Ávila-Gálvez M, et al. Main drivers of (poly)phenol effects on human health: metabolite production and/or gut microbiota-associated metabotypes? *Food Funct*. 2021;12(21):10324–10355. doi:10.1039/D1FO02033A
60. Wicha KA. Health benefits of a polyphenols-rich diet in patients with irritable bowel syndrome–a narrative review. *Gen Med Health Sci*. 2023;29(1).
61. Roopchand DE, Carmody RN, Kuhn P, et al. Dietary polyphenols promote growth of the gut bacterium Akkermansia muciniphila and attenuate high-fat diet–induced metabolic syndrome. *Diabetes*. 2015;64(8):2847–2858. doi:10.2337/db14-1916
62. Kara Gross M, Michael David G, Milena B. Cellular organization of neuroimmune interactions in the gastrointestinal tract. *Trends Immunol*. 2016;37(7):487–501.
63. Meenakshi R, Michael DG. The bowel and beyond: the enteric nervous system in neurological disorders. *Nat Rev Gastroenterol Hepatol*. 2016;13(9):517–28.
64. Kirsteen NB, Alberto RT. Central control of gastrointestinal motility. *Curr Opin Endocrinol Diabetes Obes*. 2018;26(1):11–6.
65. Emeran AM, Jennifer SL, Kirsten T, et al. Towards a systems view of IBS. *Nat Rev Gastroenterol Hepatol*. 2015;12(10).
66. Gershon M. *The second Brain: The Scientific Basis of Gut Instinct and a Groundbreaking New Understanding of Nervous Disorders and Intestines*. New York, NY: Harper Collins Publ; 1998.
67. Kass-Simon G, Pierobon P. Cnidarian chemical neurotransmission, an updated overview. *Comp Biochem Physiol a Mol Integr Physiol*. 2006;146(1):9–25. doi:10.1016/j.cbpa.2006.09.008
68. Caspary DM, Raza A, Armour BL, et al. Immunocytochemical and neurochemical evidence for age-related loss of GABA in the inferior colliculus: implications for neural presbycusis. *J Neurosci*. 1990;10(7):2363–2372. doi:10.1523/JNEUROSCI.10-07-02363.1990
69. Eugene D, Christopher SS, Nicholas VW, et al. The human and mouse enteric nervous system at single-cell resolution. *Cell*. 2020;182 (6):1606–22.
70. Eijsbouts C, Zheng T, Kennedy NA, et al. Genome-wide analysis of 53,400 people with irritable bowel syndrome highlights shared genetic pathways with mood and anxiety disorders. *Nature Genetics*. 2021;53(11):1543–1552. doi:10.1038/s41588-021-00950-8
71. Drokhlyansky E, Smillie CS, Van Wittenberghe N, et al. The human and mouse enteric nervous system at single-cell resolution. *Cell*. 2020;182 (6):1606–22.E23. doi:10.1016/j.cell.2020.08.003
72. Seguella L, Gulbransen BD. Enteric glial biology, intercellular signalling and roles in gastrointestinal disease. *Nat Rev Gastroenterol Hepatol*. 2021;18(8):571–587. doi:10.1038/s41575-021-00423-7
73. Biederer T, Sara Y, Mozhayeva M, et al. Syncam, a synaptic adhesion molecule that drives synapse assembly. *Science*. 2002;297 (5586):1525–1531. doi:10.1126/science.1072356
74. Morales-Soto W, Gulbransen BD. Enteric glia: a new player in abdominal pain. *Cellular Molecular Gastroenterol Hepatol*. 2019;7(2):433–445. doi:10.1016/j.jcmgh.2018.11.005
75. Pasman JA, Chen Z, Smit DJ, et al. The CADM2 gene and behavior: a phenome-wide scan in UK-Biobank. *Behav Gene*. 2022;52(4):306–314. doi:10.1007/s10519-022-10109-8

76. Frei JA, Stoeckli ET. Syncams–From axon guidance to neurodevelopmental disorders. *Molecular Cellular Neurosci*. 2017;81:41–48. doi:10.1016/j.mcn.2016.08.012
77. Fu M, Vohra BPS, Wind D, et al. BMP signaling regulates murine enteric nervous system precursor migration, neurite fasciculation, and patterning via altered Ncam1 polysialic acid addition. *Develop Biol*. 2006;299(1):137–150. doi:10.1016/j.ydbio.2006.07.016
78. Eraslan G, Drokhlyansky E, Anand S, et al. Single-nucleus cross-tissue molecular reference maps toward understanding disease gene function. *Science*. 2022;376(6594):eabl4290. doi:10.1126/science.abl4290
79. Mayer EA. The neurobiology of stress and gastrointestinal disease. *Gut*. 2000;47(6):861–869. doi:10.1136/gut.47.6.861
80. Camilleri M. Diagnosis and treatment of irritable bowel syndrome: a review. *JAMA*. 2021;325(9):865–877. doi:10.1001/jama.2020.22532
81. Ford AC, Quigley EM, Lacy BE, et al. Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis. *Off J Am College of Gastroenterol*. 2014;109(9):1350–1365. doi:10.1038/ajg.2014.148
82. West C, Neufeld K-AM. Animal models of visceral pain and the role of the microbiome. *Neurobiol Pain*. 2021;10:100064. doi:10.1016/j.ynpai.2021.100064
83. Guo CC, Kurth F, Zhou J, et al. One-year test–retest reliability of intrinsic connectivity network fMRI in older adults. *Neuroimage*. 2012;61(4):1471–1483. doi:10.1016/j.neuroimage.2012.03.027
84. Grayson DS, Fair DA. Development of large-scale functional networks from birth to adulthood: a guide to the neuroimaging literature. *Neuroimage*. 2017;160:15–31. doi:10.1016/j.neuroimage.2017.01.079
85. Mayer EA, Aziz Q, Coen S, et al. Brain imaging approaches to the study of functional GI disorders: a Rome working team report. *Neurogastroenterol Motility*. 2009;21(6):579–596. doi:10.1111/j.1365-2982.2009.01304.x
86. Seeley WW, Menon V, Schatzberg AF, et al. Dissociable intrinsic connectivity networks for salience processing and executive control. *J Neurosci*. 2007;27(9):2349–2356. doi:10.1523/JNEUROSCI.5587-06.2007
87. Tijms BM, Seriès P, Willshaw DJ, et al. Similarity-based extraction of individual networks from gray matter MRI scans. *Cerebral Cortex*. 2012;22(7):1530–1541. doi:10.1093/cercor/bhr221
88. Hagmann P, Kurant M, Gigandet X, et al. Mapping human whole-brain structural networks with diffusion MRI. *PLoS One*. 2007;2(7):e597. doi:10.1371/journal.pone.0000597
89. Gupta A, Kilpatrick L, Labus J, et al. Early adverse life events and resting state neural networks in patients with chronic abdominal pain: evidence for sex differences. *Psych Med*. 2014;76(6):404–412. doi:10.1097/PSY.0000000000000089
90. Naliboff BD, Berman S, Suyenobu B, et al. Longitudinal change in perceptual and brain activation response to visceral stimuli in irritable bowel syndrome patients. *Gastroenterology*. 2006;131(2):352–365. doi:10.1053/j.gastro.2006.05.014
91. Bradford K, Shih W, Videlock EJ, et al. Association between early adverse life events and irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2012;10(4):385–90.E3. doi:10.1016/j.cgh.2011.12.018
92. Labus JS, Gupta A, Coveleskie K, et al. Sex differences in emotion-related cognitive processes in irritable bowel syndrome and healthy control subjects. *Pain®*. 2013;154(10):2088–2099. doi:10.1016/j.pain.2013.06.024
93. Farmer A, Aziz Q. Visceral pain hypersensitivity in functional gastrointestinal disorders. *British Med Bulletin*. 2009;91(1):123–136. doi:10.1093/bmb/ldp026
94. Tillisch K, Mayer EA, Labus JS, et al. Sex specific alterations in autonomic function among patients with irritable bowel syndrome. *Gut*. 2005;54(10):1396–1401. doi:10.1136/gut.2004.058685
95. Hong J-Y, Kilpatrick LA, Labus JS, et al. Sex and disease-related alterations of anterior insula functional connectivity in chronic abdominal pain. *J Neurosci*. 2014;34(43):14252–14259. doi:10.1523/JNEUROSCI.1683-14.2014
96. Hong J-Y, Kilpatrick LA, Labus J, et al. Patients with chronic visceral pain show sex-related alterations in intrinsic oscillations of the resting brain. *J Neurosci*. 2013;33(29):11994–12002. doi:10.1523/JNEUROSCI.5733-12.2013
97. Kilpatrick L, Ornitz E, Ibrahimovic H, et al. Sex-related differences in prepulse inhibition of startle in irritable bowel syndrome (IBS). *Biolog Psychol*. 2010;84(2):272–278. doi:10.1016/j.biopsycho.2010.02.012
98. Jafri W, Yakoob J, Jafri N, et al. Irritable bowel syndrome and health seeking behaviour in different communities of Pakistan. *J Pakistan Med Assoc*. 2007;57(6):285.
99. Zamani M, Alizadeh-Tabari S, Zamani V. Systematic review with meta-analysis: the prevalence of anxiety and depression in patients with irritable bowel syndrome. *Alim Pharmacol Therap*. 2019;50(2):132–143. doi:10.1111/apt.15325
100. Aziz I, Palsson OS, Törnblom H, et al. The prevalence and impact of overlapping Rome IV-diagnosed functional gastrointestinal disorders on somatization, quality of life, and healthcare utilization: a cross-sectional general population study in three countries. *Off J Am College Gastroenterol*. 2018;113(1):86–96. doi:10.1038/ajg.2017.421
101. Gwee K-A, Wee S, Wong M-L, et al. The prevalence, symptom characteristics, and impact of irritable bowel syndrome in an Asian urban community. *LWW*. 2004;924–931.
102. Palsson OS, Baggish JS, Turner MJ, et al. IBS patients show frequent fluctuations between loose/watery and hard/lumpy stools: implications for treatment. *Off J Am College of Gastroenterol*. 2012;107(2):286–295. doi:10.1038/ajg.2011.358
103. Lin L, Xudong T, Fengyun W, et al. Discussion on the theory of treating irritable bowel syndrome from spleen. *Chin J Trad Chin Med*. 2017;32(03):943–946.
104. Qianyu C, Libin Z. Characteristics of syndrome differentiation and treatment of emotional diseases in clinical guide to medical records. *J Hunan Univ Trad Chin Med*. 2020;40(11):1346–1349.
105. Wenlin F, Haitao W. Mechanism of treating irritable bowel syndrome with spleen-strengthening method under the guidance of the theory of "spleen is the guide" in Huangdi Neijing. *Western Trad Chin Med*. 2019;32(12):33–35.
106. Qiang Z, Xiaoping Z, Wenliang L. Professor Yao Naili's experience in treating irritable bowel syndrome based on the theory of spleen and stomach. *Tianjin J Trad Chin Med*. 2020;37(12):1354–1358.
107. Ying Z, Jia L, Hua W, et al. Treatment of irritable bowel syndrome from heart and gallbladder. *Liaoning J Trad Chin Med*. 2021;48(08):68–70.
108. Haitao L, Yunxi J, Tingting G, et al. Clinical study of Jianpi Zhixie decoction combined with pinaverium bromide tablets in the treatment of diarrhea-predominant irritable bowel syndrome with liver depression and spleen deficiency. *New Trad Chin Med*. 2024;56(09):71–75.
109. Shen ZY, Shan JY, Zhu LY. Clinical observation of Jiawei Tongxie Yaofang in treating diarrhea-predominant irritable bowel syndrome with liver depression and spleen deficiency. *Guangzhou Univ Trad Chin Med*. 2024;41(03):562–568.

110. Yi X, Ruifei Z, Liang C, et al. Clinical effect of Zhizhu Pill and Sini powder on irritable bowel syndrome with liver depression and qi stagnation and its influence on gastrointestinal hormones. *Guangxi Med J*. 2023;45(24):2972–6+89.
111. Daowei Z, Jun L, Yingmei X, et al. Therapeutic effect of regulating mind and invigorating spleen acupuncture combined with electroacupuncture on diarrhea-predominant irritable bowel syndrome and its effect on mast cell activation. *Shanghai J Acup Moxibus*. 2024;43(06):594–598.
112. Xuemei S, Zhou Z, Pan L, et al. Effect of triple energizer acupuncture on rats with diarrhea-predominant irritable bowel syndrome based on SCF/C-kit pathway. *Glob J Trad Chin Med*. 2024;17(04):578–584.
113. Kai W, Yujun H, Wang L, et al. Study on the mechanism of regulating CRF/CRFR1 pathway and repairing intestinal mucosal barrier in rats with diarrhea-predominant irritable bowel syndrome by hilling and inhibiting wood needle method. *Acup Res*. 2024;49(05):472–479. doi:10.13702/j.1000-0607.20230154
114. Ying XQ, Yao Q, Shi YL. Effect of Huangqi Jianzhong decoction combined with moxibustion on clinical signs and symptoms, inflammation and gastrointestinal hormones in patients with diarrhea-predominant irritable bowel syndrome. *Liaoning J Trad Chin Med*. 2024;1–9.
115. Fan Q, Jia J, Lu X. Clinical efficacy and safety of Wuling capsule combined with acupuncture in treating irritable bowel syndrome with liver depression and spleen deficiency. *Liaoning J Trad Chin Med*. 2024;51(02):139–143.
116. Li B, Miao Y, Shan X, et al. Curative effect observation of warm needling combined with Buzhong Yiqi Fang in treating female diarrhea-predominant irritable bowel syndrome. *Chin J Trad Chin Med*. 2024;42(01):251–254.
117. Jiao Z, Ting C, Jing L, et al. Effect of Tongxie Yaofang combined with moxa stick moxibustion on diarrhea-predominant irritable bowel syndrome and its influence on immunoglobulin and serum inflammatory factor levels. *China Med J*. 2023;20(35):141–145.