

Traditional Chinese Medicine Based Subgrouping of Irritable Bowel Syndrome Patients

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Abstract: Partly from lack of effective conventional therapeutics, patients with irritable bowel syndrome (IBS) turn to complementary and alternative approaches, including Traditional Chinese Medicine (TCM). Key to TCM's approach to IBS is individualized therapies targeted at subgroups. Subgroups represent distinct patterns of dysregulation (e.g. "excess" or "deficiency") identified by both intestinal and extra-intestinal symptoms. Our objective was to identify operational criteria supporting the existence of TCM-based subgroups in IBS and to assess reliability and validity of these criteria. Using TCM principles, items were selected on face validity from conventional questionnaires. TCM practitioners evaluated items for content and face validity. Symptom items and a set of patient cases with item responses were validated by examining patient's pattern of response to items and assessing the consistency with which practitioners diagnosed patients on the spectrum of an "excess" or "deficiency" syndrome. Standard correlation analysis revealed 33 intestinal and extra-intestinal symptom items. There was high degree of practitioner agreement in assessing individual items to particular patterns. External validation by practitioners of cases showed high internal consistency among practitioners (Cronbach's alpha coefficients of 0.91 and 0.87 for *excess* and *deficiency*, respectively) and high correlation of average practitioner rating to original questionnaire generated scores (Pearson correlation coefficients of 0.94 and 0.92 for *excess* and *deficiency*, respectively). This pilot study provides preliminary support for a methodology to identify novel subgroups of IBS patients related to the TCM classification, which may differ in underlying pathophysiology and treatment responses.

Keywords: Irritable Bowel Syndrome; Traditional Chinese Medicine; Subgroups; Extra-intestinal Symptoms.

Introduction

Irritable bowel syndrome (IBS) is a common chronic gastrointestinal disorder responsible for an estimated 12% of all primary care visits and 28% of all visits to gastroenterologists (Mitchell and Drossman, 1987). Because there is currently no consistent biological marker of IBS, patients are identified on the basis of their bowel symptoms alone. IBS is defined by the Rome criteria as a constellation of symptoms thought to arise from the gastrointestinal tract, e.g. chronic abdominal pain or discomfort associated with altered bowel habits for which no structural or metabolic abnormality can be found (Drossman *et al.*, 2000). However, despite the focus on gastrointestinal symptoms, IBS patients commonly report a variety of extra-intestinal symptoms including fatigue, mood and emotional disturbances, disrupted sleep and decreased sexual drive (Monga *et al.*, 1997; Fass *et al.*, 1998 and 2000; Wessely *et al.*, 1999; Henningsen *et al.*, 2003). In addition, IBS patients frequently show co-morbidity with other chronic syndromes, including functional dyspepsia, dysmenorrhea, interstitial cystitis, fibromyalgia, anxiety, and depression (Whitehead *et al.*, 2002). These extra-intestinal symptoms are important determinants of health-related quality of life (HRQoL) (Spiegel *et al.*, 2004) and thereby may influence healthcare utilization and patient-oriented outcomes (Brandt *et al.*, 2002; American College of Gastroenterology Functional Gastrointestinal Disorders Task Force, 2002). Indeed, a recent study suggests that two-thirds of the excessive costs incurred by IBS patients compared to control patients were unrelated to lower intestinal symptoms (Levy *et al.*, 2001). Surprisingly, extra-intestinal symptoms have generally not been included in conventional diagnostic or therapeutic considerations (Drossman *et al.*, 2002).

In both clinical practice and research studies, patients with IBS are often subgrouped by their predominant pattern of bowel habits (e.g. diarrhea-predominant, constipation-predominant, and alternating bowel habit). However, clinical evidence suggests that normalization of bowel habits alone by anti-diarrheals or pro-motility drugs is unlikely to produce large improvements in global endpoints or in HRQoL when compared to placebo (Müller-Lissner *et al.*, 2001; Camilleri *et al.*, 2001; American College of Gastroenterology Functional Gastrointestinal Disorders Task Force, 2002). This shortcoming may arise in part because conventional therapies do not relieve the extra-intestinal symptoms which contribute to impaired HRQoL in IBS patients. This hypothesis is supported by a recent study demonstrating that both mental and physical component scores for HRQoL in IBS are primarily determined by extra-intestinal symptoms rather than conventionally-elicited bowel symptoms (Spiegel *et al.*, 2004).

Due to in part the lack of satisfactory medical therapies, 30%–40% of IBS patients turn to alternative medical therapies to complement or replace conventional treatment (Smart *et al.*, 1986; Eisenberg *et al.*, 1998). One popular modality used by IBS patients is Traditional Chinese Medicine (TCM). According to TCM, patients with IBS are a heterogeneous population with fundamentally different underlying pathophysiologic disturbances. Specifically, patients are classified into individual patterns of dysregulation based on an overall state of health reflected by a constellation of both intestinal and extra-intestinal symptoms. Most importantly, specific therapies are tailored towards these individual subtypes (Kaptchuk, 1983; Maciocia, 1989; Maciocia, 1994).

While TCM has gained wide acceptance by the lay public and many patients, the direct relevance of TCM to IBS diagnosis and treatment may not be obvious to Western-trained physicians. Acceptance by investigators has been partly hindered by TCM's use of ancient, non-scientific expressions and constructs (e.g. *Qi*, energy flow, and energy deficiencies) and by TCM's designation of functional systemic networks using conventional anatomical organ names (e.g. Liver and Spleen). However, if one focuses on TCM pattern classification, TCM shows several features which might be relevant to the classification of IBS patients, and which might even be testable using Western scientific approaches.

Though TCM is commonly used to treat many functional disorders such as IBS, there has been little scientific work evaluating the reliability and reproducibility of the TCM diagnostic paradigm. Our objective was to test the hypothesis that distinct subgroups of IBS patients can be reliably identified in retrospective analysis using select TCM-based symptom items from existing conventional questionnaires. Specifically, we sought to address the following hypotheses: (1) distinct subgroups of IBS patients can be identified based on patterns of intestinal and extra-intestinal symptoms using the principles of TCM and (2) the criteria used to define these subgroups can be externally validated by independent TCM practitioners. Some of the data have been presented at the 17th World Congress on Psychosomatic Medicine, Waikoloa, Hawaii, USA, 23–28 August 2003.

Methods

Study Design

Our goal was to first identify operational criteria that would assist in supporting the existence of TCM-based subgroups in the IBS population and then to assess both the reliability and validity of these criteria.

The initial step consisted of selecting items based upon their face validity. The criteria focused on items from two conventional symptom-based questionnaires, one bowel-predominant and one psychological-predominant. Using established principles of TCM coupled with clinical experience with IBS patients, we selected items from these questionnaires that were descriptive for the two most common TCM patterns of IBS: (1) the *excess* pattern and (2) the *deficiency* pattern (respectively referred to in TCM terminology as *Liver Qi Stagnation* and *Spleen Qi Deficiency*, see Table 1). We assigned each item a relevance rating to either the *excess* pattern or *deficiency* pattern. An independent panel of TCM practitioners subsequently evaluated these items for both content and face validity. (In the current study, we use the terms *excess* and *deficiency* simply to label a particular pattern, without any implications of biological or physiologic processes corresponding to excess or deficiency.)

Following this independent assessment, we then evaluated the validity of both the items themselves and a set of patient cases with item responses. Specifically, we examined the patients' pattern of response to the questionnaire items and then assessed the consistency of TCM practitioners' diagnoses of the patients on the spectrum of an *excess* or *deficiency* syndrome.

Table 1. Summary of Predominant TCM Clinical Patterns Encountered in IBS

	<i>Excess Pattern</i>	<i>Deficiency Pattern</i>	Overlap of Excess and Deficiency Patterns
TCM Pattern type	Excess	Deficiency	Mixed <i>excess</i> and <i>deficiency</i>
GI Symptoms	Abdominal pain, primarily upper GI, sharper and more intense in nature, aggravated by pressure Feeling of abdominal churning or pulsation Borborygmus Symptom exacerbation with stress or menses Changes in bowel habits Belching and sour regurgitation Dysphagia, globus sensation, hiccups Nausea and vomiting	Abdominal pain, often diffuse, duller ache in nature, improved with pressure Feeling of fullness in the chest and epigastrium Symptom exacerbation especially postprandially Loose stools, mucus Food sensitivities (cold, raw, greasy or dairy foods)	Mixed <i>excess</i> and <i>deficiency</i> features
Extra-intestinal Symptoms	Neck: Sensation of constriction Chest: Sensation of constriction/distention, pain along costal margins, breast distention/tenderness, sighing Pelvis: Irregular/painful periods, premenstrual syndrome Exacerbation of all symptoms with stress and menses	Fatigue, lassitude, low stamina Shortness of breath and weak voice General feelings of weakness or heaviness of limbs Low adaptive abilities with overall exacerbation of all symptoms with minimal physical and emotional stressors	Mixed <i>excess</i> and <i>deficiency</i> features
Emotional States	Anger, frustration, irritability, moodiness, depression	Anxiety, worry, obsessive-compulsive behaviors, excessive thinking/rumination	Mixed <i>excess</i> and <i>deficiency</i> features

The *excess* pattern is classically described in TCM nomenclature as “*Liver Qi Stagnation*” and the *deficiency* pattern as “*Spleen Qi Deficiency*” (Kaptchuk, 1983; Maciocia, 1989 and 1994).

Selection of TCM Patterns

Based upon established principles of TCM along with clinical experience, most patients with IBS manifest symptoms consistent with two major TCM patterns, the *excess* pattern and the *deficiency* pattern, or an overlap of both. These patterns are summarized in Table 1.

Subjects

Subjects consisted of 1835 consecutive respondents from the UCLA Center for Neurovisceral Sciences and Women's Health (CNS/WH) database who completed both the UCLA Bowel Symptom Questionnaire (BSQ) version 2.1 and Symptom Checklist-90-R (SCL) questionnaires between 1995 to 1999. The sample included three patient groups [782 IBS, 188 inflammatory bowel disease (IBD) and 777 others (including dyspepsia)] and 88 healthy control subjects.

TCM Experts

Eight TCM practitioners participated in the study. Three received their TCM degrees and post-graduate training in China and five received their TCM degrees and clinical training in the United States. Of the five America-trained practitioners, two received considerable postgraduate training in China. Seven of them actively practice and/or teach TCM in the United States, with the eighth as a faculty at Hong Kong Baptist University. Years in clinical practice range from one to 18. Each of the TCM practitioners performed the evaluations independently and there was no communication between practitioners regarding item and case evaluations.

Questionnaires

We selected symptom items from two questionnaires, the BSQ and the SCL. The BSQ consists of 95 items, focusing on gastrointestinal and extra-intestinal symptoms. The SCL is a well-validated and reliable instrument consisting of psychological symptoms identifying nine domains of potential psychological pathology (depression, anxiety, somatization, psychoticism, phobia, hostility, obsessive-compulsiveness, paranoia, and interpersonal sensitivity) (Derogatis and Cleary, 1977).

Initial Selection of Items

We selected items from the BSQ and SCL that were specific to the predominant TCM patterns of dysregulation in IBS (*excess*, *deficiency* and their overlap). An expert TCM practitioner (S. Tan), formally trained and certified in TCM, performed the initial item selection. Selection criteria were based on symptom characteristics of the predominant

patterns of IBS, as described in TCM textbooks endorsed as required reading by the California Board of Acupuncture.

Validation of Individual Item Selection and Item Reduction Process

We evaluated the initial symptom item selection via a process of internal and external validations. Internal validation consisted first of examining the intercorrelation of items under patterns of *excess* or *deficiency* using the CNS/WH patient database. Symptom items were each assigned a rating for diagnostic relevance to the predominant patterns seen in IBS, namely *excess* and *deficiency*. The intercorrelation of responses from 1835 IBS patients and controls were then evaluated as a set using alpha coefficients (Chronbach, 1951) and individually using discrimination indices (item-total correlations) separately for *excess* and *deficiency* specific items. An item reduction process then followed. First, items with highest correlation ($r > 0.20$) were kept, while those with low ($r < 0.20$) or negative correlation were rejected. Then, items were evaluated for overlapping or redundant symptomatology (e.g. bloating with oral intake and distension with oral intake). Among these sets, the item with the highest item-total correlation was selected. Finally, nine items with very strong face validity based on TCM clinical experience but with lower correlation ($r < 0.20$) were included. This process culminated in a final set of 33 items used for further analysis (Table 2).

The independent panel of TCM practitioners then externally validated the set of 33 items. Specifically, we sought to assess the following: (1) panelist concurrence with the selected items to the individual patterns; (2) panelist identification of items they felt were most important in diagnosing the particular pattern; and (3) degree of agreement among the panelists in their assessments. To accomplish this, each TCM practitioner was asked to independently review the list of selected items and rate each item as representative of *excess* or *deficiency*. The reliability of TCM practitioner ratings on symptom relevance was evaluated using Cronbach's alpha coefficients. Also, practitioners were asked to review the list of 33 items and indicate (via "yes" or "no") which individual item they felt was key item in diagnosing a particular pattern.

Finally, to assess the discriminant validity of the items as a set, an *excess* and *deficiency* composite score was calculated from the item set using the responses in our database. The scores were constructed by simply adding the unweighted item responses. Higher scores on the respective scale were hypothesized to increase the likelihood that the patient would be diagnosed with that syndrome. An analysis of variance was conducted comparing healthy controls to patients with IBS. It was hypothesized that the IBS patients would show higher *excess* and *deficiency* scores than the healthy controls.

Development of Case Distribution Based on Diagnostic Scores and Sample Case Selection

Under TCM theory, most patients with IBS can be described with a combination of the two primary diagnostic dimensions of *excess* and *deficiency*. To reflect this in our case

Table 2. Summary of TCM Practitioner Evaluation of Symptom Items

Symptom	Number of Practitioners Who Rated as Key Symptom	Number of Practitioners Who Rated as Most Consistent with Excess Pattern	Number of Practitioners Who Rated as Most Consistent with Deficiency Pattern
Pain brought on by stress	8	8	0
Low energy	8	0	8
Symptoms worse with menses*	7	8	0
Tire easily	7	0	8
Globus	7	8	0
Fatigue	7	0	8
Irritability	6	8	0
Tense	6	8	0
Anger	6	8	0
Bloat worse with upset	5	8	0
Heaviness	5	0	8
Feels better with exercise*	4	8	0
Heavy, weighted down sensation	4	1	7
Muscle and joint pains with stress	4	6	2
Temper	4	8	0
Bloat with any oral intake*	3	0	8
Pain better on weekends	3	8	0
Bloat worse with exercise	2	1	7
Visible distention with oral intake	2	2	6
Difficulty swallowing*	2	7	1
Cry easily	2	6	2
Fullness in rectum after bowel movement	1	4	4
Pain after meals*	1	4	4
Pain relieved with bowel movement	1	7	1
Feeling of incomplete bowel movement	1	3	5
Normally fine but bloat with oral intake*	1	0	8
Bloat better with bowel movement	1	4	3
Bloat better with passing flatus	1	4	3
Bloat all over body	1	3	5
Difficulty falling asleep*	1	5	2
Feeling blue	1	8	0
Bleeding*	0	0	8
Stools pass easily once bowel movement initiated*	0	3	5

*Items with high face validity under TCM clinical experience but with low correlation value ($r < 0.20$).

distribution, we constructed a cross-tabulation of our IBS respondents based on the *excess* and *deficiency* scores in our database. First, the distribution of each score was inspected and an arbitrary quartile split was made. For each score, a subject was placed in the “high” group if they were in the upper quartile; the “medium” group if they were in the inter quartile range; and the “low” group if they were in the bottom quartile. Based upon these scores, a 3×3 (*excess by deficiency*) table was constructed. From this classification table, we randomly selected 26 cases that were presented to TCM practitioners in a blinded fashion for confirmatory diagnosis. We confirmed that there was at least one case representing each cell in our 3×3 case distributions.

External Validation of Sample Cases by TCM Practitioners

The responses to the 33 items comprising the composite scores for the 26 patient cases were given to the TCM practitioners. Practitioners were not given information regarding the distribution of case patterns. Using the responses of each patient case, practitioners were asked to assign likelihood ratings (on a scale of “high,” “medium,” or “low”) for each case along dimensions of *excess* and *deficiency*. The degree of agreement in likelihood ratings among practitioners was first assessed using Cronbach’s coefficient alpha. The likelihood ratings were then correlated with the actual *excess* and *deficiency* scores to measure the degree of concurrent validity between the raters and the diagnostic scores.

Results

Selection of Items and Validation of Individual Item Selection

Of the total items in both the BSQ and SCL, 57 items were initially selected as representative for *excess* and 64 items were initially selected as representative for *deficiency*. As demonstrated in Table 2, the final set of 33 items consisted of 19 items representative for *excess* and 14 items representative for *deficiency*. Consistent with the TCM paradigm’s inclusion of non-bowel symptoms in diagnosis, more than half of the final symptom items referred to extra-intestinal symptoms.

Independent practitioners were consistent in their evaluation of individual symptom items. As shown in Fig. 1, practitioners unanimously (eight out of eight) rated items as representative of specific patterns in 54% of items, with six out of eight practitioner agreement in 76% of items and with at least five out of eight practitioner agreements in 94% of items. Of note, practitioners assigned symptom relevance to a particular pattern with greater consistency in extra-intestinal items (Table 2, columns 3 and 4).

Further, symptoms agreed upon by most practitioners as being “key” in making a particular diagnosis (first 15 items in Table 2) were not bowel-specific. Rather, they referred to extra-intestinal items including low energy, fatigue, irritability, feeling tense, anger, globus sensation and exacerbation of overall symptoms by stress and menses.

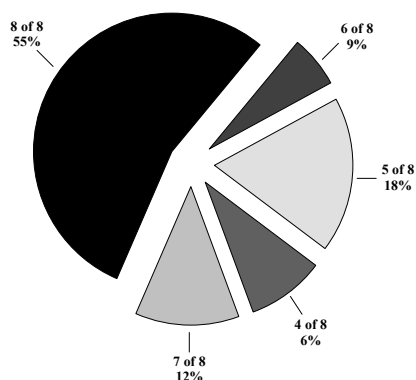


Figure 1. Degree of agreement amongst eight practitioners on diagnostic assessment of symptom items to either excess or deficiency patterns.

Table 3. Cross-tabulation of Deficiency and Excess Groups After Arbitrary Split at Quartiles

	Low Excess	Med Excess	High Excess
Low Deficiency	9.21%	11.13%	2.43%
Med Deficiency	11.25%	29.80%	10.36%
High Deficiency	2.94%	9.97%	12.92%

Numbers are in percentages. Pure deficiency was comprised of those with High deficiency + Low excess and Med deficiency + Low excess. Pure excess was comprised of those with High excess + Low deficiency and Med excess + Low deficiency. The group representing “others” was comprised of those with Low ratings on both dimensions. The overlap excess + deficiency group was comprised of all remaining groups.

Finally, analysis of variance, comparing diagnosis scale scores for different subpopulations in our database of 1835 subjects, revealed significantly higher scores in IBS patients (29.0) compared with healthy controls (3.8).

Development of Case Distribution Based on Diagnostic Scores

Using the case diagnostic scores, a patient distribution along the dimensions of excess and deficiency was established. A quartile split resulted in the distribution demonstrated in Table 3. Cases were then assigned into four main TCM subgroups: (1) those with predominant excess (13.6%); (2) those with predominant deficiency (13.2%); (3) those showing mixed features of both excess and deficiency (63.1%); and (4) those endorsing few features of either pattern (9.2%).

External Validation of Sample Cases by TCM Practitioners

Reliability analysis among practitioner diagnoses was strong with Cronbach’s alpha coefficients of 0.91 and 0.87 for excess and deficiency patterns, respectively. Correlation

of average rating of practitioners to the original questionnaire-generated score on the probability that a patient had a pattern was also very strong with Pearson correlation coefficients of 0.94 and 0.92 for *excess* and *deficiency* patterns, respectively.

Discussion

This study demonstrates that IBS subgroups can be distinguished using operational criteria involving intestinal and extra-intestinal symptom items based upon the principles of TCM. Specifically, the operational criteria applied to TCM-based symptom items found in existing conventional questionnaires can be validated in retrospective analysis. Also, we present initial evidence supporting the reliability and consistency of TCM practitioner diagnoses in IBS-related TCM patterns. Further investigation of physiological correlates of these symptom-based patterns may help explain the impact of extra-intestinal symptoms on HRQoL, elucidate underlying pathophysiologies, and have implications for the development of more effective therapies.

Identification of Distinct Subgroups of IBS Patients Based on Patterns of Intestinal and Extra-Intestinal Symptoms

To best reflect the TCM emphasis on both intestinal and extra-intestinal symptoms, we selected items from both a bowel symptom questionnaire (BSQ) and a generic psychological symptom checklist (SCL). This hybrid of both intestinal and extra-intestinal items is consistent with the principles of TCM. To further select symptom items appropriate with TCM principles, a certified TCM practitioner performed the initial item selection based on face validity of symptom items consistent with established descriptions of common TCM patterns seen in IBS.

The items were evaluated using correlation analysis to determine internal consistency under pattern clusters. We found that our cohort of IBS patients had an expected distribution into subgroups with a combination of features along the two primary pattern dimensions. The relative proportion of each group is consistent with TCM theory. The majority of cases reveal a combination of mixed *excess* and *deficiency* patterns. Pure, single pattern subgroups (e.g. *excess*-predominant and *deficiency*-predominant) are less common. Those with features not involving either *excess* or *deficiency* are the rarest. This rarest group, not showing features fitting either pattern, likely represents other minor TCM patterns seen in IBS.

External Validation of Subgroups by Independent TCM Practitioners

The reproducibility of identifiable subgroups was further strengthened by TCM practitioners' external validation of this methodology. We purposely selected TCM practitioners of different training backgrounds and experience to minimize potential bias based on similar instruction. That at least six of eight of the practitioners agreed on a

symptom's relevance to a particular pattern in more than three-quarters of the selected items demonstrates excellent agreement across a diverse group of TCM practitioners working independently. Further, the correlation of the average rating of the practitioners to the questionnaire-generated score on the probability that a patient has that pattern was also remarkably high. This observation supports the notion that experienced practitioners of TCM are consistent in applying TCM-based diagnostic criteria to their assessment of these subgroups. Also, it supports the validity of our originally constructed distribution of cases based on indices along the two dimensions of *excess* and *deficiency*.

Limitations of the Study

Our study has several limitations. First, we performed our item selection retrospectively. As a result, the item selected was limited to those found in conventional Western questionnaires. Certain symptom items, relevant to TCM history taking, such as pre-menstrual tension or pain modification by external pressure, were not included in the BSQ or SCL. We expected the evaluation of non-ideal symptom items and the resulting patient cases to adversely affect agreement results. Still, we were able to show a high degree of agreement among TCM practitioners in our retrospective analysis. This suggests even better agreement for prospectively-planned questionnaires in future studies.

Our methodology resulted in a case distribution in which the overlap of *excess* and *deficiency* was the largest group (63.1%). Though this finding was expected based on clinical experience, it may have been exaggerated due to the limited symptom items found in the BSQ and SCL. Prospective studies should include items that more clearly distinguish among different patterns. Items more specific to individual TCM patterns will better identify pure, single pattern groups. Also, prospectively designed item sets can include symptoms which may discern less common patterns represented by the low *excess*/low *deficiency* subgroup, seen under the TCM conceptualization of IBS.

Possible Relevance of Findings for IBS Diagnosis and Treatment

The possible relevance of sub-classifying IBS patients into different patterns of dysregulation by taking into account intestinal as well as extra-intestinal symptoms is supported by epidemiological data, HRQoL studies, and proposed pathophysiological models. In our validated sample of symptom items, half were extra-intestinal in nature. Further, our results show that in terms of diagnostic relevance, TCM practitioners rated extra-intestinal symptoms as having more significance than bowel-related symptoms. This supports the emerging paradigm that the gastrointestinal symptoms of IBS represent just one manifestation of a broader underlying dysregulation of brain-body interactions (Monga *et al.*, 1997; Fass *et al.*, 1998 and 2000; Mayer *et al.*, 1998; Wessely *et al.*, 1999; Henningsen *et al.*, 2003; Spiegel *et al.*, 2004), including alterations in neuroendocrine, autonomic nervous system, and pain modulatory systems (Mayer *et al.*, 2001).

As suggested by a recent report, extra-intestinal symptoms appear to play an important role in influencing HRQoL in IBS patients (Spiegel *et al.*, 2004). Specifically, in an

analysis of over 700 patients with IBS, both mental and physical HRQoL were found to be determined by extra-intestinal symptoms of chronic stress and vital exhaustion, and neither domain was determined by the presence of specific gastrointestinal symptoms. These findings are consistent with the current data, and suggest that rather than focusing on physiological epiphenomena (e.g. stool frequency, stool characteristics, and Rome subtype of IBS) and potentially misleading clinical factors (e.g. age and disease duration), clinicians might be better served to focus their patient encounter on identifying and treating extra-intestinal symptoms of IBS.

The relevance of both intestinal and extra-intestinal symptoms in IBS, as suggested in our study, supports the emerging concept that IBS likely represents a general disorder of brain-body interactions. This may help substantiate the observed overlap between IBS and other functional disorders such as functional dyspepsia, non-cardiac chest pain, interstitial cystitis, chronic pelvic pain, fibromyalgia, and chronic fatigue syndrome (Wessely *et al.*, 1999). The overlap and response of patient subgroups with different syndromes to the same CNS-targeted therapy (such as low dose antidepressants) implies some shared underlying dysregulation involving central pathways of the “emotional motor system” (Holstege *et al.*, 1996).

Furthermore, the TCM characterization of disease genesis resulting from both physical and psychological stressors shows striking similarities with the Western concept of allostasis and allostatic load (McEwen, 2002). Allostasis refers to the mechanisms activated during an acute, stressful situation which help maintain stability in the face of perturbations. Allostatic load refers to the maladaptive responses that can occur within the organism when the allostatic response functions improperly, usually under circumstances of chronic stress, severe life-threatening stress and in individuals with enhanced stress vulnerabilities. The body’s attempts to maintain homeostasis in the face of chronic or severe perturbation (e.g. stress) can result in a chronic dysregulation of several central pathways and related body systems. It is this underlying dysregulation of homeostatic mechanisms which may represent the modern scientific explanation for ancient TCM observations of multi-systemic symptom clusters.

Our findings also have relevance for TCM-based therapy of IBS. Though TCM is widely practiced, validation of the TCM paradigm has mostly relied upon clinical empirical tradition. There has been little previous work specifically addressing the fundamental issue of defining and validating diagnostic criteria of basic TCM diagnostic patterns. Specifically, our study supports a potential methodology to assist in validating the existence of subgroups of IBS patients described in TCM. The application of the TCM paradigm to the complexities of IBS subgrouping is intriguing for several reasons. First, there is reasonable empirical experience supporting TCM therapeutic efficacy in subgroup-appropriate treatments with TCM herbal medicine. This experience has been suggested by a recent randomized controlled trial on herbal therapy for IBS (Bensoussan *et al.*, 1998). Also, much of the research on TCM has focused on physiological mechanisms of acupuncture and pharmacological effects of TCM-based herbs as a means of validating the TCM paradigm. In contrast, ours is one of few studies directly addressing the complexities of validating TCM’s fundamental diagnostic paradigm.

In conclusion, the results of our pilot study support the feasibility of applying the TCM pattern approach to a common gastrointestinal disorder whose conventional diagnostic conceptualization has been questioned (Chey *et al.*, 2002; Hungin *et al.*, 2003). Future prospective studies may be important to identify distinct patterns of IBS which may be relevant for both Western and complementary/alternative treatment studies. Such studies include validation of a prospectively devised diagnostic item set and clinical trials and physiological investigations exploring differences between TCM subgroups. If in fact novel subgroups of IBS using an ancient medical paradigm can be definitively validated, we may have new insights into diagnosing and treating this complex disorder. These insights can be more broadly applied to stimulate exciting and innovative approaches to Mind-Body Medicine, stress-related disorders and other functional disorders which have thus far eluded conventional classification and satisfactory treatment.

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