

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Effect of Cognitive Behavior Therapy Combined with Exercise Intervention on the Cognitive Bias and Coping Styles of IBS-D Patients".(ID:50042).Those comments are all valuable and very helpful for revising and improving our paper,as well as the important guiding significance to our researches.According to the comments of the reviewers,we have revised our manuscript.The revised manuscript and the detailed responses to the comments of the two reviewers are attached.

Sincerely yours,

Xin-an Zhang, Shirui Zhao

Reviewer #1:

1: Response to comment:The manuscript requires a close edit for language and grammar. For example, "To explore the effect of cognitive behavioral therapy combined with exercise intervention on cognitive bias and coping styles of patients with diarrhea-predominant irritable bowel syndrome to provide a theoretical reference for the prevention and treatment of diarrhea-predominant irritable bowel syndrome" is a very convoluted and poorly phrased sentence. It should be re-written as "To explore the effects of cognitive behavioral therapy combined with exercise intervention on cognitive bias and coping styles of patients with diarrhoea-predominant irritable bowel syndrome (IBS); and to provide a theoretical reference for the management of IBS."

Response :Before:To explore the effect of cognitive behavioral therapy combined with exercise intervention on cognitive bias and coping styles of patients with diarrhea-predominant irritable bowel syndrome to provide a theoretical reference for the prevention and treatment of diarrhea-predominant irritable bowel syndrome

After:To explore the effects of an intervention of cognitive behavioral therapy combined with exercise (CBT+E) on the cognitive bias and coping styles of patients with diarrhea-predominant irritable bowel syndrome (IBS-D) and to provide a theoretical reference for the management of IBS.

2: Response to comment: Please change "diarrhea type" to "diarrhoea predominant type". The correct classifications are:constipation-predominant, diarrhea-predominant or mixed.

Response :Before: According to clinical characteristics, it can be divided into diarrhea type (IBS-D), constipation type (IBS-C), mixed type (IBS-M) and unstable type (IBS-D),

After: According to clinical characteristics, it can be divided into diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C) or mixed IBS (IBS-M);

3: Response to comment:Important background regarding cognitive behavioral therapy is missing in the introduction/discussion sections. It should be mentioned that CBT has proven efficacy for chronic pain conditions and helps with modifying the pain

experience as sufferers of chronic pain often have catastrophic beliefs (citation: ncbi.nlm.nih.gov/pubmed/28028812).

Response :Before:Not mentioned.

After: Cognitive behavioral therapy is a structured, short-term and cognitive approach to psychotherapy. It is considered to be an important component of IBS patients with moderate to severe disease or unresponsive to initial drug therapy and comorbid psychological factors.

CBT has a significant psychotherapeutic effect and a positive effect on relieving chronic pain. It is also helpful for improving patients' understanding and experience of pain behaviors, thus confirming that patients with chronic pain have some catastrophizing cognitive attitudes.

4: Response to comment: Please change "Research objects" to "Research subjects".

Response :Before: Research objects

After: Research subjects

5: Response to comment: Was IRB approval or waiver sought? Please provide actual IRB study number.

Response :Before: Not mentioned.

After:2018-KY-2-003

6: Response to comment:How was sample size determined? There is currently no evidence of power calculation. The present sample appears small and limited to a convenience sample.

Response :Before: Not mentioned.

After: First of all, we carried out a preliminary experiment. For this experiment, we initially included 100 subjects. After the intervention, we found obvious differences before and after the intervention. In the end, we did not include 100 subjects, and 60 subjects were selected as the final number.

7: Response to comment:Please change "addressthe" to address the".

Response :Before: addressthe

After: address the

8: Response to comment:"It is presumed that the causes may be psychological factors, dietary factors, heredity, infection, visceral sensory abnormalities and intestinal motility abnormalities." Inflammation may also play an important pathogenic role in IBS (citation: ncbi.nlm.nih.gov/pmc/articles/PMC6159811).

Response :Before:Not mentioned.

After:It is presumed that the causes may be psychological factors, dietary factors, heredity, infection, visceral sensory abnormalities and intestinal motility abnormalities

9: Response to comment:Please rephrase "improve the normal adjustment ability of patients to intestinal sensations". Reference should be made to adaptive and maladaptive coping styles.

Response :After: alleviate intestinal pain, improve patients' normal adjustment ability to intestinal movement and autonomic nerve, correct intestinal dysfunction, effectively relieve dysfunctional attitudes, and generate positive coping styles. At the same time, through a good social support environment, patients are urged to use correct coping

styles to reduce or relieve psychosomatic damage caused by symptoms, thus improving quality of life.

10: Response to comment:The limitations of the current study should be at least briefly mentioned.

Response :Before:Not mentioned.

After: This study has several limitations that need to be discussed. First, the number of research subjects is relatively small, and the observation indexes are not rich enough to reflect the actual clinical conditions of more subjects. Secondly, the subjects selected in this study are all patients with diarrhea-predominant irritable bowel syndrome, and there is no research and analysis on other types of the disease. Third, this test analyzed the different index data of 24 weeks of intervention training, and did not carry out follow-up testing and analysis, which can be carried out in future research to further explore. For the test, the combination of pharmacotherapy may produce important bias, which requires longer time and more systematic test analysis to explore its internal change trend.

Special thanks to you for your good comments.

Reviewer #2: Nice study needing some improvements. Please explain why only IBS-D and not IBS-C or IBS-M; better to include also a group of IBS-C. Protocol should be much better explained. How followed the controls the protocol; association with pharmacotherapy may produce an important bias. These aspects should be explained and discussed as limitations. The discussion chapter is too long. Language needs to be polished.

1.Response to comment:Please explain why only IBS-D and not IBS-C or IBS-M; better to include also a group of IBS-C.

Response:This study takes IBS-D patients as the research subjects. The most common clinical classification is diarrhea, and one of the main factors affecting the occurrence of IBS is intestinal flora. Some studies have confirmed that IBS-D flora have more serious imbalances and more obvious differences than IBS-C and IBS-M patients, thus providing a theoretical basis for our study. Other types of patients with the disease will be considered for comparative analysis in subsequent studies.

2. Response to comment:The discussion chapter is too long.

Response :Some of the languages discussed have been revised briefly.

3. Response to comment:Protocol should be much better explained.

Response :In order to implement the whole experiment smoothly according to the training plan,a pre-experiment was carried out before the formal experiment.In the pre-experiment,the subjects in the experimental group were clearly explained,and the eight-part brocade movement demonstration and essentials were demonstrated.Through the practice,the training process and movement requirements were familiar with,and the training time and arrangement were clearly defined.The subjects in the control group adopted the conventional comprehensive treatment scheme. First, drugs for regulating

intestinal motility were used to address the symptoms of diarrhea and constipation. For patients with abdominal pain, symptomatic treatment, e.g., antispasmodic and analgesic drugs, was used together with drugs for regulating intestinal flora. For patients with anxiety disorder, anti-anxiety and antidepressant drugs were used to reduce the sensitivity of internal organs. The subjects in the experimental group adopted CBT+E based on a conventional comprehensive treatment scheme. Among them, cognitive behavioral therapy is to improve the psychological problems it presents by changing the patient's views and attitudes towards people, oneself and things. The focus is to reduce the mental burden of the patient on the disease, explain the patient's illness in detail and patiently, eliminate the patient's doubts, block the vicious circle of bad psychology, and establish a good cognition of the disease. For example, CBT required doctors and laboratory personnel to first understand the cognitive characteristics and symptom-inducing factors of the subjects and evaluate their cognitive characteristics, emotional responses and coping styles with regard to events; then, disease-related psychoeducation, the identification and correction of negative automatic thoughts, cognitive restructuring, and relaxation training were conducted with the subjects once a week to enable the patients to establish a correct adaptive cognitive mode. The Baduanjin training required the subjects to engage in the continuous exercise intervention no fewer than 4 times/wk, 2 times/d (in the morning and afternoon) and 45 min/session for 24 wk. Baduanjin professional coaches and medical staff provided comprehensive and systematic guidance on the technical essentials and duration of the Baduanjin exercises. The coaches, doctors and nurses established good relations with the subjects, fully understood the disease condition, comprehended the emotional state of the patients, and obtained their trust and cooperation. During the tests, all the subjects in each group followed their doctors' advice, and the relevant test personnel provided safety education and relevant information and addressed matters requiring attention. Each subject in the CBT+E group received video data so that all the subjects could standardize and master the eight-segment brocade. They were introduced to the detailed exercises of the eight-segment brocade so that they could use it in their daily study and exercise. Telephone supervision and return visits were regularly conducted, timely skill guidance was provided, random checks occurred, and each exercise was recorded. If any problems were encountered, the subjects could communicate with the doctors and coaches at any time.

4. Response to comment:How followed the controls the protocol;

Response :In this paper, the data of the two groups were recorded and analyzed at baseline, 6 weeks, 12 weeks and 24 weeks respectively. During the test, the control group maintained the original drug treatment plan, and the test group was fully followed and guided by doctors and professional laboratory personnel. During the period, supervision and follow-up were adhered to. After 24 weeks, the score changes of the test group showed significant differences compared with the control group, with significant effects. The limitation of this article is that the follow-up situation of patients is not tracked after the test.

5. Response to comment:association with pharmacotherapy may produce an important bias.

Response :For the test, the combination of pharmacotherapy may produce important bias, which requires longer time and more systematic test analysis to explore its internal change trend.

Questions 4 and 5 are written as limitations as follows:

This study has several limitations that need to be discussed. First, the number of research subjects is relatively small, and the observation indexes are not rich enough to reflect the actual clinical conditions of more subjects. Secondly, the subjects selected in this study are all patients with diarrhea-predominant irritable bowel syndrome, and there is no research and analysis on other types of the disease. Third, this test analyzed the different index data of 24 weeks of intervention training, and did not carry out follow-up testing and analysis, which can be carried out in future research to further explore. For the test, the combination of pharmacotherapy may produce important bias, which requires longer time and more systematic test analysis to explore its internal change trend.

6. Response to comment:Language needs to be polished:

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We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.