

Effects of Pearl Yangxin Anshen Decoction on HAMD and PTSD-SS Scores, Cytokines and Related Metabolites in Patients with Post-Traumatic Stress Disorder

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How to cite this paper: Feng, Y. and Guo, M. (2024) Effects of Pearl Yangxin Anshen Decoction on HAMD and PTSD-SS Scores, Cytokines and Related Metabolites in Patients with Post-Traumatic Stress Disorder. *Journal of Behavioral and Brain Science*, 14, 93-102.

<https://doi.org/10.4236/jbbs.2024.143007>

Received: February 10, 2024

Accepted: March 18, 2024

Published: March 21, 2024

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Abstract

Objective: This paper aims to observe the Pearl Yangxin Anshen Decoction to influence the score of HAMD and PTSD-SS, the changes of the cytokines and the related metabolic product in patients with PTSD. **Methods:** From June 2015 to May 2016, in the traditional Chinese medicine clinics of Hainan Province People's Hospital, there were 50 patients with PTSD, the age were from 30 to 60, they were randomly divided into treatment group (25 cases) and control group (25 cases), then compared the scores of HAMD and PTSD-SS between the two groups, searched the changes of cytokines and the related metabolic product. **Results:** In the treatment group: before and after treatment the scores of PTSD-SS were 65.64 ± 7.02 , 28.32 ± 4.18 , and the scores of HAMD were 29.28 ± 1.97 , 11.72 ± 2.13 ; In the control group: before and after treatment the scores of PTSD-SS were 63.24 ± 6.16 , 31.40 ± 4.29 , the scores of HAMD were 30.24 ± 2.05 , 13.08 ± 2.30 . After 3 months patients in treatment group the scores of PTSD-SS and HAMD were lower than the control group ($t = 2.570$, $P = 0.013$, $t = -2.1640$, $P = 0.035$). In the control group: before and after 3 months treatment the IL-2 levels respectively were 79.84 ± 26.46 pg/ml, 56.18 ± 22.67 pg/ml, the IL-6 levels respectively were 110.83 ± 47.65 pg/ml, 59.67 ± 44.68 pg/ml, the IL-8 levels respectively were 73.11 ± 78.51 pg/ml, 55.83 ± 81.94 pg/ml, the NE levels respectively were 420.04 ± 674.75 pg/ml, 185.31 ± 417.91 pg/ml, the MDA levels respectively were 112.35 ± 62.87 ng/ml, $60.42.33 \pm 53.64$ ng/ml, the NO levels were 126.6 ± 47.4 $\mu\text{mol/L}$, 78.6 ± 45.7 $\mu\text{mol/L}$, the VIP levels were 396.6 ± 144.4 pg/ml, 122.4 ± 111.5 pg/ml. In the treatment group: before and after 3 months treatment the IL-2 levels respectively were 86.00 ± 32.29 pg/ml, 53.84 ± 27.01 pg/ml, the IL-6 levels respectively were 108.21 ± 44.60 pg/ml, 42.46 ± 42.16 pg/ml, the IL-8

levels respectively were 81.48 ± 94.19 pg/ml, 54.07 ± 84.15 pg/ml, the NE levels respectively were 392.93 ± 592.84 pg/ml, 243.85 ± 588.45 pg/ml, the MDA levels respectively were 117.58 ± 63.37 ng/ml, 45.91 ± 38.94 ng/ml, the NO levels respectively were 135.9 ± 46.4 μ mol/L, 72.6 ± 46.6 μ mol/L, the VIP levels respectively were 414.0 ± 140.1 pg/ml, 185.8 ± 105.3 pg/ml. In the two groups as the extension of treatment time, the content of IL-2, IL-8, IL-6, NE, MDA, NO, and VIP were gradually reduced, and the level of reduction of the treatment group patients was higher than the control group, the change of ACTH and SOD levels just the opposite. **Conclusion:** The Pearl Yangxin Anshen Decoction could improve the symptoms of psychological anxiety, depression and other psychological problems in patients with PTSD, and influence the change of cytokines and related metabolites product.

Keywords

Post-Traumatic Stress Disorder, Psychological Intervention, Serological Detection

1. Introduction

Post-traumatic stress disorder (PTSD) is a delayed or prolonged response to an unusually threatening or catastrophic stressful event or situation, or a mental disorder that occurs after a person has experienced an unusual event that causes significant distress to almost all people [1]. With the frequent occurrence of natural disasters and various accidents in recent years, the research on PTSD has been paid more and more attention by the medical community. Due to the complex pathogenesis of PTSD, most patients need drug treatment, and these drugs work against a single target. Therefore, no drug can alleviate all symptoms of PTSD at present, and combined medication is often needed in treatment, which will increase adverse reactions and harm human health. It is of great practical value and wide application prospect to develop new drugs with high efficiency and low toxicity for the treatment of PTSD, and the development of effective active ingredients of traditional Chinese medicine is an effective way. The author used the traditional Chinese medicine Pearl Yangxin Anshen Decoction and traditional Chinese medicine psychotherapy to treat the PTSD patients, and observed the effect, the following report is reported.

2. Clinical Data

2.1. General Information

From June 2015 to May 2016, 55 patients with PTSD aged 30 - 60 years old who visited the TCM outpatient department of two hospitals in Hainan Province were randomly divided into the treatment group (28 cases) and the control group (27 cases), of which 3 patients in the treatment group and 2 patients in the control group escaped, and 25 cases in each of the final treatment group and the

control group. The average age of 25 patients in the treatment group was 48.60 ± 7.76 years, and the course of disease ranged from 2 weeks to 10.5 years. The PTSD-SS score and HAMD score before treatment were 65.64 ± 7.02 and 29.28 ± 1.97 , respectively. The control group included 25 patients, including 11 males and 14 females, with an average age of 47.96 ± 7.83 years and a course of disease ranging from 2 weeks to 11.3 years. The PTSD-SS score and HAMD score before treatment were 63.24 ± 6.16 points and 30.24 ± 2.05 points, respectively. There were no significant differences in gender, age, course of disease, pre-treatment PTSD-SS score and HAMD score between the two groups ($P > 0.05$). Patients in 2 groups were given oral paroxetine hydrochloride tablets and psychological therapy, and the treatment group was also given self-made Chinese medicine Pearl Yangxin Anshen Decoction. PTSD patients unknowingly take “Pearl heart-soothing soup” and have a potential placebo effect.

The Hamilton Depression Scale (HAMD), developed by Hamilton in 1960, is the most widely used scale in the clinical assessment of depression. There are three versions of this scale: 17 items, 21 items and 24 items. For this scale, two trained evaluators conducted a joint HAMD examination of patients, generally through conversation and observation. After the examination, the two evaluators scored independently. Score before and after treatment can evaluate the severity of the disease and treatment effect.

The post-Traumatic Stress Disorder Self-Rating Scale (PTSD-SS) was used to assess the degree of PTSD in patients, involving 5 dimensions including repeated experience, avoidance symptoms, subjective trauma evaluation, impairment of social function, and high alertness. A total of 24 items were recorded, with 1 to 5 points for each item, and the full score was 120. The higher the score, the more severe the symptoms of PTSD, with a cut-off of 50, ≤ 50 indicating no and >50 indicating PTSD.

2.2. Inclusion Criteria

All the selected patients met the diagnostic criteria for PTSD: those with a total score of ≥ 50 of PTSD-SS [2] were diagnosed with PTSD by structural interviews conducted by professional psychologists, and those with a concise post-traumatic stress disorder interview combined with the diagnostic criteria of the DSM-IV of Mental disorders. They are between 30 and 60 years old. All patients were self-aware and signed informed consent forms.

2.3. Exclusion Criteria

(1) Have a history of mental illness or depression; (2) Exclude patients with organic diseases; (3) Pregnant and lactating women.

3. Methods

3.1. Assessment Methods of PTSD

The PTSD self-rating scale was used, which was divided into 5 dimensions, in-

cluding subjective assessment of traumatic events, recurrent experience, avoidance symptoms, increased alertness and impaired social function, and included 24 items. The scale was scored in 5 levels: 1 (no)-5 (very severe). The total score of the scale ranges from 24 to 120, in which ≥ 50 is detected as PTSD, 50 - 59 is mild PTSD, and ≥ 60 is moderate to severe PTSD. The higher the scale score, the more severe the PTSD symptoms [3] [4]. PTSD-SS scores were measured in both groups before and after treatment (3 months).

3.2. Depression Assessment Methods

The 24-item Hamilton Depression Scale (HAMD) was used to evaluate the scores of patients in the treatment and control groups before and after treatment. The Hamilton Depression Scale is the most widely used scale in clinical evaluation of depression. The scale was divided into 7 dimensions, including anxiety, weight, cognition, day and night change, block, sleep and despair, including 24 items, and HAMD ≥ 20 points was considered to be depression. HAMD scores in both groups were measured before and after treatment (3 months).

3.3. Treatment Methods

Control group: Oral paroxetine hydrochloride tablets and psychological therapy and other comprehensive treatment. Treatment group: On the basis of the treatment of the control group, plus self-prepared Chinese medicine Pearl Yangxin Anshen Decoction. Pearl Yangxin Anshen Decoction: Mother of Pearl 30, Angelica 15, Shengdi 15, Ginseng 30, sour jujube kernel 20, Baizi kernel 20, Fuzi 15, Xiangfu 15, Acorus 15, Aloes 15, Jujube 10, licorice 10.

3.4. Experimental Research

Collection of Patient Specimens and Index Determination

The patients' blood was collected during fasting in the morning and 18 ml of blood was collected from the cubital vein of the two groups, of which 6ml was used for anticoagulation with heparin and 6 ml for promoting coagulation. Plasma and serum were centrifuged at 4°C and stored at -20°C respectively. Serum MDA, ACTH, IL-6, NE, IL-8, HSP72 and plasma total SOD activity levels were observed in 2 groups before treatment and one week, four weeks and three months after treatment. Human vasoactive intestinal skin (VIP) content was detected by enzyme-linked immunoassay kit, and NO content was detected by nitric reductase method.

3.5. Statistical Analysis Methods

SPSS19.0 statistical software was used for analysis. Measurement data were described using ($\pm s$), independent sample t test or ANOVA was used for comparison between groups, and paired sample t test was used within groups. $P < 0.05$ meant that the difference was statistically significant. The comparison of an in-

dex in different groups at different time points was performed by repeated measurement analysis of variance.

4. Results

1) Comparison of PTSD-SS and HAMD scores before and after treatment between the two groups (see **Table 1**)

There was no significant difference in PTSD-SS scores between the control group and the treatment group before treatment ($t = 0.749$, $P = 0.457$). After treatment, there was a statistically significant difference in PTSD-SS score between the control group and the treatment group ($t = 2.570$, $P = 0.013$), and the score of the treatment group was lower than that of the control group. Before treatment, there was no significant difference in HAMD scores between the control group and the treatment group ($t = -1.690$, $P = 0.098$). After treatment, the HAMD score of the control group and the treatment group had statistical significance ($t = -2.1640$, $P = 0.035$), and the score of the treatment group was lower than that of the control group. Analysis of the above results indicated that after treatment, the PTSD-SS score and HAMD score of patients in the treatment group decreased significantly than that in the control group.

2) Changes of cytokines and related metabolites before and after treatment in two groups

a) Changes of plasma IL-2, IL-4, IL-6 and IL-8 in two groups before and after treatment (see **Table 2**)

The changes of IL-2, IL-4, IL-6 and IL-8 in the two groups before and after treatment were respectively analyzed by repeated measurement ANOVA. The results showed that the overall changes of IL-2, IL-4, IL-6 and IL-8 in the two groups were statistically significant at different time points before and after treatment ($F = 51.883$, $P < 0.01$; $F = 31.543$, $P < 0.01$; $F = 456.226$, $P < 0.01$; $F = 70.142$, $P < 0.01$), and the measurement time of plasma IL-2, IL-4, IL-6 and IL-8 interacted with the group ($F = 5.133$, $P = 0.004$; $F = 3.476$, $P = 0.002$; $F = 12.873$, $P < 0.01$; $F = 8.872$, $P < 0.01$), that is, the plasma IL-2, IL-4, IL-6 and IL-8 contents of the two groups showed a gradually decreasing trend with the extension

Table 1. Comparison of PTSD-SS and HAMD scores before and after treatment between the two groups ($\pm s$).

Item	Treatment group (n = 25)		Control group (n = 25)	
	pre-treatment ^{a1}	post-treatment ^{a2}	pre-treatment ^{b1}	post-treatment ^{b2}
PTSD-SS	65.64 \pm 7.02	28.32 \pm 4.18	63.24 \pm 6.16	31.40 \pm 4.29
HAMD	29.28 \pm 1.97	11.72 \pm 2.13	30.24 \pm 2.05	13.08 \pm 2.30

Remarks: Treatment group: a1 before treatment, a2 after treatment; Control group: b1 before treatment, b2 after treatment. PTSD-ss: The comparison result between a1 and b1 was $t = 0.749$, $P = 0.457$, and the comparison result between a2 and b2 was $t = 2.570$, $P = 0.013$. HAMD: The comparison result of a1 and b1 is $t = -1.690$, $P = 0.098$, and the comparison result of a2 and b2 is $t = -2.1640$, $P = 0.035$.

Table 2. Changes of IL-2, IL-4, IL-6 and IL-8 before and after treatment in two groups (\pm s) (unit: pg/ml).

Treatment time	NO	IL-2		IL-4		IL-6		IL-8	
		Control group	Treatment group	Control group	Treatment group	Control group	Treatment group	Control group	Treatment group
pre-treatment	50	79.84 \pm 26.4	86.00 \pm 32.2	7.34 \pm 2.09	6.88 \pm 2.31	110.83 \pm 47.6	108.21 \pm 44.	73.11 \pm 78.5	81.48 \pm 94.1
1 week	50	68.30 \pm 25.7	78.71 \pm 42.3	7.53 \pm 1.47	6.95 \pm 5.73	91.51 \pm 47.8	89.71 \pm 44.1	61.58 \pm 78.7	67.01 \pm 88.4
4 week	50	56.96 \pm 24.2	58.26 \pm 24.7	7.64 \pm 3.78	7.08 \pm 3.65	73.21 \pm 44.8	62.40 \pm 42.8	57.38 \pm 82.1	57.56 \pm 84.1
3 months	50	56.18 \pm 22.6	53.84 \pm 27.0	7.85 \pm 7.69	7.58 \pm 7.83	59.67 \pm 44.6	42.46 \pm 42.1	55.83 \pm 81.9	54.07 \pm 84.1
Analysis of variance F		51.883		31.543		456.226		70.142	
Analysis of variance P		0.000		0.000		0.000		0.000	
Interaction		5.133		3.476		12.873		8.872	
Interaction		0.004		0.002		0.000		0.000	

Note: IL-2: Interleukin2; IL-4: Interleukin4; IL-6: Interleukin6; IL-8: Interleukin8.

of treatment time, and the plasma IL-2, IL-4, IL-6 and IL-8 contents of the treatment group were lower than those of the control group.

b) Changes of plasma MDA, ACTH and NE before and after treatment in the two groups (see **Table 3**)

Repeated measurement ANOVA was performed on the changes of plasma MDA, NE and ACTH before and after treatment in the two groups, and it was found that there were statistically significant differences in the overall changes of plasma MDA, NE and ACTH contents in the two groups at different time points before and after treatment ($F = 150.368$, $P < 0.01$; $F = 749.956$, $P < 0.01$; $F = 1252.012$, $P < 0.01$), the measurement time of MDA, NE and ACTH content in plasma of patients had interaction with the groups ($F = 3.439$, $P = 0.024$; $F = 10.656$, $P < 0.01$; $F = 8.157$, $P < 0.01$), that is, the plasma MDA and NE contents of the two groups showed a gradually decreasing trend with the extension of treatment time, and the decrease degree of the plasma MDA and NE contents of the treatment group was higher than that of the control group, while the ACTH content showed a gradually increasing trend with the extension of treatment time. The plasma ACTH content in the treatment group was higher than that in the control group.

c) Changes of plasma NO, VIP, HSP-72 and SOD before and after treatment in two groups (see **Table 4**)

The changes of plasma NO, VIP, HSP-72 and SOD in the two groups before and after treatment were respectively measured by repeated ANOVA. The results showed that the overall levels of plasma NO and VIP were significantly different between the two groups at different time points before and after treatment ($F = 546.551$, $P < 0.01$; $F = 307.934$, $P < 0.01$), the measurement time of plasma NO and VIP content of the two groups had interaction with the group ($F =$

Table 3. Changes of MDA, ACTH and NE before and after treatment in the two groups.

Treatment time	NO	MDA (ng/ml)		ACTH (pg/ml)		NE (pg/ml)	
		Control group	Treatment group	Control group	Treatment group	Control group	Treatment group
pre-treatment	50	112.35 ± 62.87	117.58 ± 63.37	36.43 ± 4.71	33.84 ± 4.73	420.04 ± 674.75	392.93 ± 592.84
1 week	50	90.82 ± 62.58	89.32 ± 59.32	76.66 ± 10.40	83.23 ± 10.19	302.54 ± 591.01	314.74 ± 594.27
4 week	50	76.04 ± 60.85	68.59 ± 51.73	109.82 ± 15.72	131.94 ± 23.57	242.53 ± 543.61	265.81 ± 590.27
3 months	50	60.42.33 ± 53.64	45.91 ± 38.94	184.89 ± 24.07	190.07 ± 29.83	185.31 ± 417.91	243.85 ± 588.45
Analysis of variance F		150.368		749.956		1252.012	
Analysis of variance P		0.000		0.000		0.000	
Interaction		3.439		10.656		8.157	
Interaction		0.024		0.000		0.000	

Note: MDA: malondialdehyde; ACTH: adrenocorticotropin; NE: noradrenaline.

Table 4. Changes of NO, VIP, HSP-72 and SOD in two groups before and after treatment.

Treatment time	No	NO (μmol/L)		VIP (pg/ml)		HSP-72 (ng/ml)		SOD (U/ml)	
		Control group	Treatment group	Control group	Treatment group	Control group	Treatment group	Control group	Treatment group
pre-treatment	50	126.6 ± 47.4	135.9 ± 46.4	396.6 ± 144.4	414.0. ± 140.1	131.9 ± 60.8	131.5 ± 56.1	91.2 ± 17.2	90.3 ± 17.5
1 week	50	118.2 ± 46.1	116.8 ± 49.7	365.3 ± 146.2	331.0 ± 118.8	129.4 ± 59.7	130.5 ± 54.8	92.6 ± 19.5	91.0 ± 18.3
4 weeks	50	101.4 ± 51.7	103.7 ± 46.4	280.6 ± 121.5	279.2 ± 111.1	129.0 ± 60.3	129.4 ± 56.6	92.1 ± 18.1	90.7 ± 19.0
3 months	50	78.6 ± 45.7	72.6 ± 46.6	122.4 ± 111.5	185.8 ± 105.3	128.5 ± 60.5	127.6 ± 56.4	93.0 ± 18.3	91.1 ± 18.6
Analysis of variance F		546.551		307.934		7.647		81.451	
Analysis of variance P		0.000		0.000		0.000		0.000	
Analysis of variance F		10.680		36.861		1.707		10.237	
Interaction		0.000		0.000		0.179		0.000	

Note: NO: nitric oxide; VIP: human vasoactive intestinal peptide; HSP-72: human heat shock protein; SOD: superoxide dismutase.

10.680, $P < 0.01$; $F = 36.861$, $P < 0.01$), that is, the overall change trend of plasma NO and VIP before and after treatment in the two groups showed a gradually decreasing trend with the extension of treatment time, and the decrease level of plasma NO and VIP in the treatment group was higher than that in the control group. The plasma HSP-72 content of the two groups had statistically significant changes at different time points before and after treatment ($F = 7.647$, $P < 0.01$), and the overall change trend of the plasma HSP-72 content of the two groups before and after treatment showed a gradually decreasing trend with the exten-

sion of treatment time. However, there was no interaction between the measurement time of plasma HSP-72 content between the two groups ($F = 1.707$, $P = 0.179$), and there was no statistical significance in the reduction level of plasma HSP-72 content between the two groups before and after treatment ($t = 0.068$, $P = 0.989$). There was no significant difference between the treatment group and the control group in the reduction of plasma HSP-72 before and after treatment. There was statistical significance in the overall change level of SOD in plasma between the two groups at different time points before and after treatment ($F = 81.451$, $P < 0.01$), and there was an interaction between the measurement time of SOD in plasma between the two groups ($F = 10.237$, $P < 0.01$). That is, the overall change trend of plasma SOD before and after treatment in the two groups showed an increasing trend with the extension of treatment time.

5. Discussion

“Post-traumatic stress disorder” is a modern medical disease, and the related clinical manifestations belong to the categories of palpitations, sleeplessness, depression, epilepsy, maniac syndrome, Mei Qi, forgetfulness, visceral mania, lily disease, running fish gas and other diseases in traditional Chinese medicine [5]. “Post-traumatic stress disorder” is caused by “fright” in traditional Chinese medicine, which refers to the mental tension, palpitations and faintness caused by sudden encounter of such an extraordinary event. A disease that makes the heart feel uneasy. Li Chuankui said in “Zhengzhi Huibu • Volume 5” that “shock is caused by touching foreign affairs, moving the heart inside, and the heart shakes the god.” Wang Bichang also believes that “the frightened, the outside has touched and the heart is uneasy.” Post-traumatic stress disorder is closely related to spittoon levelling from the pathogenesis of traditional Chinese medicine [6]. External stress affects the operation of the body’s qi machinery, and then causes the disorder of body fluid metabolism, and the recovery of qi machinery and body fluid distribution can alleviate the adverse mood or physical discomfort in a short time. However, if the disorder of qi machinery is more serious, and then the stagnation of qi, the internal obstruction of phlegm, and the spittoon are stuck, it cannot be recovered for a long time. The symptoms of PTSD are complex, protracted and difficult to cure, Western medicine has no effective treatment measures, and Chinese medicine has less research on the treatment of this disease. Traditional Chinese medicine has a long history of treating emotional disorders and has been widely used to treat emotional diseases and side effects of antipsychotic drugs [7]. The “shock” of PTSD is related to the heart, liver and gallbladder, spleen and stomach, lung and kidney, and the pathological changes lie in Qi-deficiency, Qi-stagnation and phlegm cessation, suggesting that in the selection of treatment prescriptions for PTSD, “regulating the five viscera, regulating Qi and resolving phlegm”, “Pearl Yangxin Anshen Decoction” mainly focuses on “harmony” and focuses on regulating qi and resolving phlegm, especially “Pearl Yangxin Anshen Decoction” can regulate the five viscera. Pearl Yangxin Anshen Decoction can nourish Yin and blood Anshen with regulating

qi and eliminating phlegm, which mother of pearl taste sweet, salty, cold, return to the liver, heart meridian, efficacy: ping liver Yangyang, calm the heart; Angelica, Shengdi, ginseng for qi nourishing blood nourishing Yin; Sour jujube kernel, cypress seed kernel, Fu God: calm the mind, calm the heart sleep; Gladiolus: dissolving dampness and stomach, clearing phlegm; Agarwood: absorb floating Yang; Jujube, licorice: gentle tonic, calm heart and calm nerves. After years of clinical practice, the author found that Pearl Yangxin Anshen Decoction has the effect of eliminating phlegm and regulating qi, soothing liver and resolving depression. Clinical observation found that this prescription can significantly improve depression, anxiety and other adverse mood clearing, insomnia, and can be used as the first choice for the treatment of PTSD.

By comparing the treatment group and the control group, the results of this study showed that the PTSD-SS and HAMD scores of patients in the treatment group were significantly lower than those in the control group after 3 months of treatment with Pearl Yangxin Anshen Decoction [8] [9] [10]. The plasma levels of IL-2, IL-4, IL-8, IL-6, NE, MDA, NO and VIP in both groups showed a gradually decreasing trend with the extension of treatment time, and the plasma levels of IL-2, IL-4, IL-8, IL-6, NE, MDA, NO and VIP in the treatment group were higher than those in the control group. The contents of ACTH and SOD increased gradually with the extension of treatment time, indicating that Pearl Yangxin Anshen Decoction can improve PTSD symptoms, psychological anxiety, depression and other psychological problems in PTSD patients, and has a certain impact on the changes of cytokines and related metabolites in PTSD patients.

6. Conclusion

At present, the pharmacies in the compound are mainly concentrated on the observation of some empirical prescriptions, and the Pearl Yangxin Anshen Decoction in this study is also based on many years of clinical observation. The mechanism of PTSD is too complex, the mechanism of the use of Chinese medicine is not very clear, the controllability of its drug components is poor, and the sample size of this study is small. The effect of Pearl Yangxin Anshen Decoction on PTSD needs further research.

Funding

2022 Hainan Provincial Key Research and Development Program, project number: ZDYF2022SHFZ110.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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