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ORIGINAL

REGIONAL BRAIN HOMOGENEITY IN CHRONIC FATIGUE SYNDROME WITH ANXIETY AND DEPRESSION: IMPLICATIONS FOR ENHANCING PHYSICAL PERFORMANCE AND REHABILITATION

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ABSTRACT

Objective: To investigate alterations in brain neural networks using resting-state functional magnetic resonance imaging (rs-fMRI) and regional homogeneity (ReHo) analysis in patients with chronic fatigue syndrome (CFS) and comorbid anxiety and depression, and to explore implications for physical performance, rehabilitation, and sports participation. **Methods:** Sixty participants were recruited, including 30 patients with CFS and anxiety-depression comorbidity and 30 healthy controls matched for age, sex, and lifestyle. rs-fMRI was conducted to assess neural connectivity changes, and ReHo analysis was applied to identify alterations in brain activity. Correlation analyses were performed to examine the relationship between ReHo values and clinical features in affected brain regions. The severity of CFS with anxiety and depression was assessed using validated scales, including the Multidimensional Fatigue Inventory (MFI-20), Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), and Pittsburgh Sleep Quality Index (PSQI). **Results:** Patients with CFS and anxiety-depression comorbidity exhibited significantly different scores on clinical scales compared to healthy controls ($p < 0.05$). Brain regions with increased ReHo values in the patient group included the left inferior lobe, interhemispheric area, right occipital lobe, and thalamus. Decreased ReHo values were observed in the left and right

middle temporal gyri, right posterior central gyrus, right middle orbital frontal gyrus, right paracentral lobule, and right fusiform gyrus. Correlation analysis revealed positive associations between clinical scales and ReHo values in the thalamus, interhemispheric area, and right middle orbital frontal gyrus. Negative correlations were found between ReHo values and the right occipital lobe, left inferior cerebral lobe, and fusiform gyrus. **Conclusion:** Altered regional homogeneity in specific brain areas in patients with CFS and comorbid anxiety and depression suggests imbalances in neural network excitation and inhibition. These findings provide insights into the neurological basis of fatigue and emotional disturbances in this population and highlight potential targets for therapeutic interventions. Understanding these brain network changes can inform tailored rehabilitation strategies, focusing on improving cognitive function, physical performance, and participation in sports or exercise-based programs. This study underscores the importance of addressing neuropsychological factors in comprehensive rehabilitation for CFS patients.

KEYWORDS: rs-Fmri; CFS; Anxiety and Depression; Comorbidity; ReHo

1. INTRODUCTION

Chronic fatigue syndrome (CFS), characterized by persistent and unexplained fatigue, often accompanied by physical and cognitive impairments, presents a significant challenge to health and quality of life. When compounded by comorbid anxiety and depression, the condition can severely impact an individual's ability to engage in physical activity, maintain mobility, and participate in rehabilitation or sports programs (Barnden et al., 2011; Brkić et al., 2011). Despite its multifaceted impact, the underlying neural mechanisms contributing to fatigue, emotional disturbances, and reduced physical performance remain poorly understood. Recent advances in neuroimaging, particularly resting-state functional magnetic resonance imaging (rs-fMRI), have provided valuable insights into the functional connectivity of the brain in various conditions. Regional homogeneity (ReHo), an analytical method applied to rs-fMRI data, enables the assessment of neural network synchronization and localized brain activity (Chu et al., 2019; Fukuda et al., 1994). Studying ReHo alterations in patients with CFS and comorbid anxiety and depression offers a unique opportunity to explore the neurophysiological basis of these symptoms and their implications for functional outcomes, including physical performance and recovery. Physical activity and sports play a vital role in improving the health and well-being of individuals with chronic conditions, including CFS. However, the neurological dysfunctions associated with CFS, such as altered brain connectivity and cognitive impairments, often create barriers to engaging in physical exercise and rehabilitation programs (Loades et al., 2021; Loades et al., 2018; Parslow et al., 2017). Identifying the neural correlates of fatigue and emotional disturbances can guide the development of targeted interventions to improve cognitive and physical

function, ultimately facilitating greater participation in sports and exercise-based rehabilitation. This study aims to investigate brain network alterations in patients with CFS and comorbid anxiety and depression using ReHo analysis of rs-fMRI data. By identifying specific brain regions with altered activity and their correlations with clinical symptoms, we seek to provide insights into the neural mechanisms underlying CFS and its impact on physical performance. These findings may contribute to the development of neurophysiological biomarkers and inform rehabilitation strategies aimed at enhancing cognitive and physical outcomes for patients with CFS, aligning with the multidisciplinary focus of sports and health sciences. In this paper, we selected the functional MRI brain area, and investigated the central disease mechanism of CFS anxiety and depression with the clinical score scale.

2. Materials and Methods

2.1 Participants

This paper recruited 30 healthy volunteers who met the diagnostic criteria for chronic fatigue syndrome and anxiety and depression and were matched for age, gender and education level, with a total of 60 participants.

2.2 DC

According to the CFS diagnostic criteria revised by Fukuda in 1994, there are three aspects:

(1) Continuous or recurrent severe fatigue of unknown cause, for more than 6 months, the fatigue symptoms still cannot relieve after full rest, and the patient's mobility ability, vocational ability, education ability and other aspects are significantly reduced compared with before the disease;

(2) Having the following 4 or more symptoms (at least 6 consecutive months or recurrent symptoms, but not earlier than fatigue symptoms): ① Memory or attention decline; ② pharyngalgia; ③ Neck or axillary lymph node enlargement; ④ myalgia; ⑤ Multiple arthralgia without redness and swelling; ⑥ has repeated headaches; ⑦ Sleep quality is not good, not easy after waking up; ⑧ Fatigue lasts for more than 24 hours after fatigue

(3) To exclude some symptomatic chronic fatigue: ① Chronic fatigue explained by primary causes; ② Chronic fatigue caused by a clear clinical diagnosis but the persistence of some diseases that are difficult to treat under existing medical conditions.

2.3 Inclusion Criteria for the Sick and Healthy Group

Inclusion criteria for patients with anxiety / depression in CFS. All of the following items are eligible to be included: (1) Patients with chronic fatigue

syndrome who meet the above diagnostic criteria; (2) People aged 25-45, right-handed; (3) Have not taken sedative-hypnotic melatonin and antidepressant psychotropic drugs for at least 45 days before enrollment; (4) SASSDS scale were 50; (5) Not participating in other ongoing clinical investigators; (6) Sign the informed consent form and volunteer to participate in this investigator. Note: Patients who meet the above 6 items can only be included in this study.

Inclusion criteria for healthy subjects: (1) aged 25-45; (2) No functional and organic diseases were found after health examination; (3) All SASSDS scale scores were <50 points; (4) Have no history of any chronic disease within 1 year before entering the study; (5) Have not taken any medication for at least 15 days before entering the study, and have not attended other clinical investigators; (6) I have signed the informed consent form and voluntarily participate in the investigator Note: Only healthy people who meet the above 6 items can be included in this study.

2.4 Exclusion Criteria for the Diseased Versus Healthy Groups

Exclusion criteria for patients with comorbid CFS and anxiety and depression. Any compliance with any of the following shall be exclude: (1) unclear consciousness cannot express subjective discomfort symptoms and mental patients; (2) progressive malignant tumors or other serious wasting diseases, prone to co-infection and bleeding; (3) Patients with severe primary diseases such as cardiovascular, liver and kidney digestive and hematopoietic system; (4) Patients with CFS associated with severe anxiety and depression symptoms (SDS 70; SAS 70 points); (5) Patients with a history of cerebrovascular disease, brain parenchymal lesions and head trauma; (6) People with metal implants in the body, with fMRI detection contraindications or claustrophobia; (7) Pregnant and lactating women and pregnancy planners in the past 6 months Note: Patients conforming with any of the above shall be excluded.

Exclusion Criteria for Healthy Subjects: (1) unclear consciousness cannot express subjective discomfort symptoms and mental patients; (2) associated with mild anxiety and depression (SDS 50; SAS 50 points); (3) Patients with a history of cerebrovascular disease, brain parenchymal lesions and head trauma; (4) There are metal implants, such as dentures, in the body; (5) Pregnant and lactating women with pregnancy planning in the last three months; (6) Those who work at night or have irregular sleep patterns, and are unable or unwilling to stop this pattern; (7) Participated in other related topics as subjects in the last 4 weeks Note: Patients conforming with any of the above shall be excluded.

2.5 Removal and Shedding Criteria

(1) the subject has disease deterioration or adverse reaction during the

trial; (2) Those who cannot continue to complete the test or automatically withdraw from the test due to other reasons. (3) Patients with severe asymmetric head anatomy or definite lesions were found in the fMRI scans.

Clinical care management plan of the enrolled patients：(1) popularize CFS disease knowledge for patients, so that patients can correctly understand the disease and eliminate panic; (2) Guide patients to live a regular lifestyle, ensure the balance between rest and activities, and prevent the deterioration of symptoms after fatigue; (3) Guide regular diet, do not take coffee tea or stimulating food during the period; (4) During the observation period, prohibit non-drug intervention or drug treatment, regularly evaluate the progress and be alert to other diseases. If the disease is worse or other uncomfortable symptoms occur, contact the test personnel; (5) Female subjects should inform them of their menstrual period in advance to facilitate the appointment of imaging examination.

2.6 Medical Ethics

This study was reviewed by the Ethics Committee of the Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine in February 2021 and passed the ethical review under project number 2021-K08. The purpose, methods and potential risks of participation in the study were explained to all participants and all participants signed informed consent.

2.7 MR Imaging Parameters

The scan sequence is: T 1 WI + T 2 WI + BOLD-fMRI + 3 D T 1 WI, each subject is collected for about 20 min resting state BOLD-fMRI scan: extract the image features of brain functional state in resting state. BOLD-fMRI acquisition using a single excitation fast plane-echo imaging sequence (FFE single-shot EPI), Imaging parameters: TR = 2000 ms, TE=30 ms, matrix=64 × 64, FOV=220 mm×220 mm×143 mm, FA=90°, scanning slices=36, slice gap=1 mm, slice thickness=3 mm, A total of 180 time points of the images were acquired, scanning time =8 minutes and 6 seconds, The scan range covers the whole brain.

2.8 Observational Index Collection

2.8.1 General Data Indicators

After enrolling the subjects, their gender, age, years of education, disease duration, past medical history, and vital signs were recorded.

2.8.2 Clinical scale score

After enrollment, clinical scale score of healthy and sick group were recorded: Multidimensional fatigue Scale (MIF-20) Depression Self-Rating

Scale (SDS) Anxiety self-rating Scale (SAS), Pittsburgh Sleep Quality Index Scale (PSQI); and the second clinical scale score was recorded after treatment. All tests were accompanied by a physician with more than 3 years of clinical experience.

2.9 Statistical Analysis

(1) Statistical analysis of clinical scale: Measurement data are expressed as "mean ± standard deviation", and all data show normal distribution ($p > 0.05$). Chi-square test, t-test for counting data, t-test for measurement data, two-sample t-test for comparison between two groups, paired t-test for pre-post comparison, test level $p = 0.05$, $p < 0.05$ to indicate significant difference the statistical work was analyzed and processed by special statisticians using SPSS25.0 statistical software.

(2) Image data analysis using the statistical parameter map software (Statistical Parametric Mapping, SPM 12) analyzed ReHo index data separately for healthy and diseased groups using one-sample t-test multiple comparison correction using overall error rate correction (FWE), At $p < 0.05$, Make two sets of brain activity templates and then apply SPM 12 software for two independent sample t-tests, With the union template as a mask, Years of education as a covariate, In addition, whole brain volume (TIV) from VBM analysis was included as a covariate, The initial threshold for controlling the effect of gray white matter atrophy on outcome was voxel level $p=0.001$ (uncorrected), Cluster (clusters) level FEWp < 0.05, Thus, the T value plot result with significant differences between the two groups was presented using xj View Brain Net Viewer software.

(3) Correlation analysis of brain behavior: Clinical data of healthy volunteers and diseased groups and significant Pearson correlation analysis of brain areas using SPSS25.0 software and clinical scale scores, and the significance level was set as $p = 0.05$. If the $p < 0.05$, there was a correlation between the two indicators for image data analysis using statistical parameter graph software Origin2021.

2.10 General Information

The data of subjects with excessive head movement was removed, and 26 cases of subjects in sick group and 23 cases in healthy volunteer group were collected. A total of 49 patients completed the test as required, and the collected nuclear magnetic image data met the statistical standards of image data. There was no statistical difference in the general information: age and gender ($p > 0.05$), indicating that there was no statistical difference in gender, age and length of education between the two groups, which was comparable.

2.11 Clinical Scale Score was Compared Between Two Groups

Statistical difference between sick group and healthy volunteers (HC) in clinical scale scores: MIF-20 SDS and SASPSQI ($p < 0.05$). (See Table 1)

Table 1: HC Group Vs. Diseased Group ($\bar{x} \pm s$)

	HC（N=23）	PATIENT（N=26）	T / χ^2	*P*
DEMOGRAPHICS				
GENDER (M：F)	9：14	10：16	χ^2=0.002	0.961#
EDUCATION (Y)	22.56±2.72	23.00±1.25	t =0.711	0.480#
AGE (Y)	29.91±1.38	31.77±4.32	t =1.975	0.054#
MIF-20				
GENERAL FATIGUE	47.70±7.57	72.85±4.95	13.920	0.000***
PHYSICAL FATIGUE	13.52±5.12	23.08±1.52	9.077	0.000***
MENTAL FATIGUE	10.39±3.29	17.54±2.67	8.393	0.000***
REDUCED MOTIVATION	12.17±3.07	14.19±2.08	2.722	0.011*
REDUCED ACTIVITY	11.61±2.79	18.04±1.91	9.506	0.000***
SDS	38.82±8.67	57.08±3.43	9.908	0.000***
SAS	39.13±8.01	56.77±4.05	9.898	0.000***
PSQI	6.78±2.45	11.65±2.70	6.578	0.000***

*Note: The diseased group is compared to the healthy group #p >0.05，*p < 0.05；**p < 0.01，***p < 0. 001.The following is the same as above.*

2.12 Imaging Index

2.12.1 Local Consistency Reho Values Comparison

(1) Comparison of the two groups: Brain areas with increased ReHo values in the affected group: left lower lobe, interhemispheric region, right occipital lobe, and thalamus. Brain regions with reduced ReHo values in the affected group: left middle temporal gyrus, right posterior central gyrus, left middle temporal gyrus, right middle temporal gyrus, right orbital middle frontal gyrus, paracentral lobule, and right fusiform gyrus. (See Table 2, Figure 1)

Table 2: (a) Brain regions with altered ReHo values in the diseased group as compared with the HC group

CLUSTER	BRAIN AREAS (AAL)	BRODMANN	*T*-VALUE	MNI COORDINATES		
			T	X	Y	Z
6127	Inferior.L	BA48_L	11.61	-33	-33	24
132	Interhemispheric	-	7.91	0	27	-30
96	Occipital gyrus.R	BA19_R	6.78	24	-75	12
98	THA	-	6.12	-6	-9	-48
348	MTG.L	BA35_L	-8.85	-21	0	-36
4591	PoCG.R	BA3_R	-7.51	51	-18	39

Table 2: (b) Brain regions with altered ReHo values in the diseased group as compared with the HC group

CLUSTER	BRAIN AREAS (AAL)	BRODMANN	*T*-VALUE	MNI COORDINATES		
			T	X	Y	Z
389	MTG.L	BA21_L	-7.15	-63	-30	0
188	MTG.R	BA20_R	-7.11	39	15	-39
77	ORBmid.R	BA11_R	-6.64	33	45	-15
246	PCL	-	-6.29	0	-42	66
225	FFG.R	BA20_R	-5.97	42	-36	-27

Note: The initial voxel level threshold p = 0.001 (uncorrected) and the cluster level threshold p <0.05 (FWE c corrected, FWE c = 77). ReHo, regional homogeneity, and local consistency. A T value is positive for brain regions with an enlarged ReHo; a negative T value represents brain regions with a ReHo decrease. The following is the same as above.

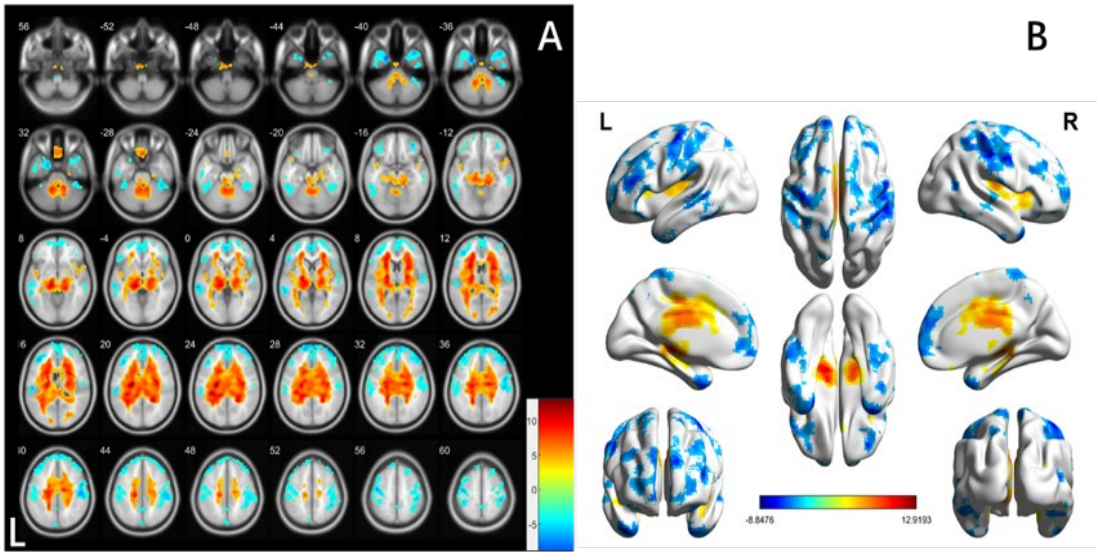

Figure 1: Comparison of ReHo values in Patient and HC groups. A. The axis bitmap of cerebrum；B. The stereoscopic form of the cerebrum. The red area indicates an increase in ReHo value; the blue indicates a decrease in ReHo value.

2.13 Correlation Analysis

The significant brain areas detected by comparing healthy volunteers and the sick group were analyzed by Pearson correlation analysis using SPSS25.0 software and clinical scale score results, which was plotted with Correlation Plot in Origin2021. Functional correlation: ReHo correlation matrix heat map analysis shows the thalamus, interhemispheric region, right orbital middle frontal gyrus, right posterior central gyrus, left middle temporal gyrus, and positive negative correlation between the right occipital lobe, left lower lobe, left middle temporal gyrus, right fusiform gyrus, right middle temporal gyrus and the scale. (See Figure 2,3)

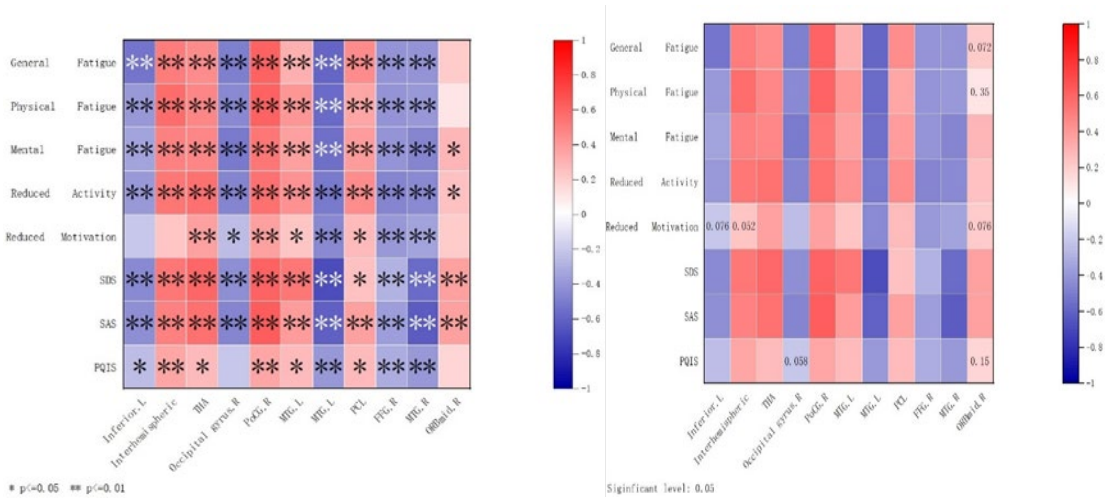

Figure 2: Heat map of correlation analysis matrix of ReHo difference brain region (* * for p <0.01; * for p <0.05, right shows no significant p-value).

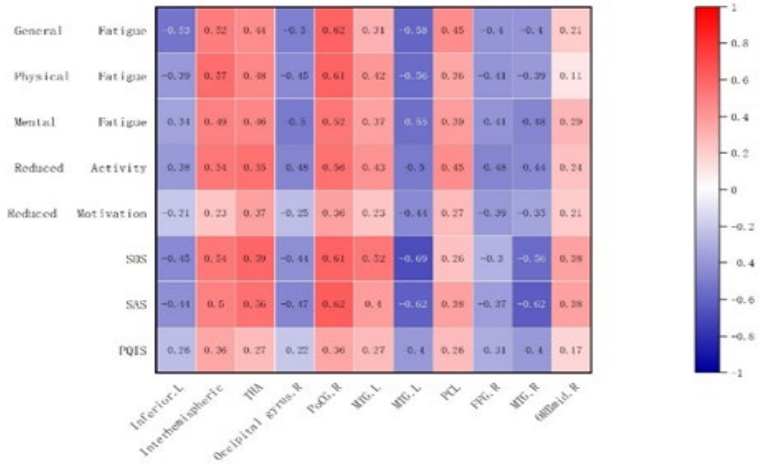

Figure 3: Regional Correlation Coefficient Values for Reho Differences

3. Discussion

Fatigue is a common symptom in the general population, but (Åkerstedt et al., 2014) can usually be relieved by sleep, but when CFS comorbidity with anxiety, depression, arthritis and chronic pain, fatigue symptoms can worsen and even persist for a long (Katz et al., 2016). Many studies through clinical symptoms and neurological mental and behavioral results show that CFS is independent disease rather than anxiety depression symptoms, CFS symptoms of cognitive impairment nor secondary to anxiety depression (Santamarina-Pérez et al., 2010) CFS and anxiety depression relationship can be summarized as each other, mutual influence, the relationship between fatigue and depression may exist in the biological level, which makes the incidence of the two accompanying increases, at the same time overlapping symptoms influence between CFS and anxiety depression behavior and cognitive disorders, and promote each other the severity of the disease (Loades

et al., 2019). The rs-fMRI provides insight into the abnormal electrical activity in the brain of patients in disease states. In this study, we used the ReHo method to measure abnormal activity in specific brain regions, and the ReHo values can reflect the consistency in local neuronal activity, with high values indicating high consistency and reduced values indicating decreased synchronization of neuronal activity. By analyzing the synchronization in the temporal order among different voxels to reflect the consistency of neuronal activity, it can sensitively detect local brain functional synchronization and better locate functional differential brain area (Wu et al., 2022). In the study of anxiety, depression, cognitive impairment in the resting state and so on. Cognitive impairment in the affected group: abnormal ReHo (Zhang et al., 2012) in the prefrontal cortex, bilateral posterior cingulate gyrus, precuneus, and inferior parietal lobule. Many studies have shown that the temporal lobe and frontal lobe are the key brain regions for emotional processing and regulation, among which the frontal lobe is an important center affecting cognitive function, sleep quality and sensorimotor. The orbitofrontal gyrus is mainly responsible for abstract thinking, decision making on external things, and decision making with objective initiative (Jackson et al., 2018). This study showed that the patients had a regional increase in the middle orbital frontal gyrus, which was positively associated with anxiety, depression, mental fatigue and subjective initiative, suggesting that the middle orbital frontal gyrus excitation led to the aggravation of clinical symptoms of the patients. Therefore, it was speculated that the middle orbital frontal gyrus is the main brain area regulating the anxiety in CFS and depression. A large number of literatures has proved that the medial temporal lobe is an important brain function area of episodic memory, and this brain area is widely connected with many cortical structures and forms the memory system. The middle temporal gyrus is involved in the characteristic memory of graphics or objects, and the middle occipital gyrus is related with depressive symptoms. The postcentral gyrus and the paracentral leaflet are the motor center of the soma, and the fusiform gyrus plays an important role in higher visual processing and recognition. In resting-state studies, the extent of altered abnormal connectivity between hippocampus as seed sites and FC in his brain region was correlated with self-reported fatigue, The findings confirm that changes in resting-state FC in CFS patients, Significant correlation with the severity of chronic fatigue (Åkerstedt et al., 2014). This study showed that patients had a local continuous reduction in the occipital lobe, middle temporal gyrus, and fusiform gyrus, Negative correlation with SDS, SAS and MIF-20, Suggesting that inhibition of relevant brain regions leads to increased clinical symptoms of patients, It is speculated that the occipital lobe, middle temporal gyrus and fusiform gyrus are the main brain regions regulating the symptoms of anxiety and depression in CFS. Association of medial prefrontal cortex with subjective measures of impaired sleep quality in sleep quality studies in CFS patients, but the sleep-specific phenotype and its association with CFS patients remain to be determined (Shan et al., 2017). Related EEG activity studies reported

significant differences between CFS patients and the right frontal and left occipital regions, indicating a relatively inhibitory state of brain function, and also supported this claim (Le Bon et al., 2012). Uplink reticular activation system and thalamus specific projection system is a common pathway of various sensory afferents, can maintain and improve the cerebral cortex excitation, reported that sleep, awakening cycle, consciousness, and heart rate regulation, upright intolerance, breathing abnormalities such as autonomic nerve function, circulatory system regulation in brain stem reticular structure activation system. The association between CFS symptoms and brainstem and thalamic function suggest that the pathological mechanism of CFS may play an important role through the neuroendocrine system (Liu et al., 2014). This study showed that the thalamus and hemisphere were positively correlated with sleep disorders, and the study showed that the thalamic ReHo value was increased and positively correlated with sleep disorders. Therefore, the persistent thalamus was activated, causing the cerebral cortex excitation state, thus causing insomnia symptoms, and even aggravated anxiety, depression and fatigue in severe cases. It is speculated that thalamus is a TCM functional brain region that regulates anxiety and depression in CFS. Although there is no consensus reached on the pathogenesis of CFS, neurological and cognitive dysfunction are key underlying features of the disease. Study found that several clinical trials through different clinical scale test found that CFS patients with depression, anxiety, pain and fatigue scores is significantly higher than healthy subjects, while the healthy subjects have a higher physical function scores, at the same time, CFS anxiety comorbid depression patients task fMRI imaging, CFS dorsal anterior cingulate cortex and ventral anterior cingulate cortex is activated (Barnden et al., 2015). FC studies in depressed patients found that significantly different brain region connections were mainly located in cortical limbic networks, especially frontal limbic networks. Suggesting that abnormal corticimbic anatomical networks may be the anatomical basis for mood regulation and cognitive impairment associated with this disorder (Fang et al., 2012). The most common morphological changes reported in related studies occurred in the cortical regions. Cortical areas are important for higher thought processing, which includes cingulate (Chomiak & Hu, 2017). The cingulate gyzone plays a broad role in emotion, cognition, and error processing (Hamel et al., 2020). There is a strong interconnection between the cingulate cortex and the orbitofrontal cortex, basal node, and insula. Basal ganglia dysfunction has also been associated with the CFS. The basal ganglia play an important role in reward processing. An fMRI study by Miller et al found a significant reduction in activation in the right caudate nucleus and the right pallidum in the CFS disease group when performing a monetary gambling task compared to the HC group. The ed activation detected in the right pallidum positively correlated with mental fatigue, general fatigue and reduced activity (Miller et al., 2014). We found that decreased activity in the thalamus, precuneus was associated with reduced memory ability in (Pan et al., 2017). Task-state fMRI

studies found that the midbrain is the main brain region (Baraniuk et al., 2022) regulating CFS fatigue, cognition, emotion, and sleep disorders. Task-state fMRI studies of differential brain regions in memory found significant less activation in the dorsolateral, prefrontal, and parietal cortex in CFS patients compared to the healthy group, increased activation in medial prefrontal regions including the ACC, and also significant activation in the lower inferior and medial temporal cortex. There were also significant differences in mental fatigue and brain activity in the cerebellum, temporal, cingulate, and frontal regions of CFS patients (Cook et al., 2007). Therefore, task-state fMRI studies should be improved in future studies to supplement and verify the results of this study. To sum up, the comprehensive Reho and related analysis can speculate sick group adjust increased THA ReHo, so that the brain to maintain brain excitability to cause sleep disorders, lead to brain fatigue cause clinical body fatigue, mental fatigue, anxiety, depression, at the same time through the regulation of FFG.R, Occipital gyrus. R, MTG.R brain ReHo value decline, reflect the cognitive, emotion, movement, disorders, leading to clinical symptoms, embodies the CFS central regulation mechanism of anxiety depression. Since the 1990s, neuroimaging has been used to study CFS. With the advancement of neuroimaging technology, the role of the brain in the persistent disease CFS has become an important research hotspot. The brain abnormalities in CFS have been identified, but there is a lack of certified (Lange et al., 1998) on which specific abnormalities are consistently observed in the various study groups, especially the research on the comorbidity of anxiety and depression in CFS. This study has some limitations. First of all, the occurrence of multiple body movements during the rs-fMRI scanning process will produce different qualities of images in the scanning results; thus, there are avoidable errors in the obtained values. Reducing these individual differences may improve the specificity and accuracy of our analysis. Secondly, the sample size was small, and further and more accurate studies with a larger sample size are needed to validate our findings.

4. Conclusion

This study highlights significant alterations in brain neural networks in patients with chronic fatigue syndrome (CFS) and comorbid anxiety and depression, as identified through regional homogeneity (ReHo) analysis of resting-state functional magnetic resonance imaging (rs-fMRI) data. The findings demonstrate that specific brain regions, such as the thalamus, occipital lobe, middle temporal gyrus, and fusiform gyrus, exhibit abnormal neural synchronization patterns, reflecting imbalances in neural excitation and inhibition. These alterations are closely associated with clinical features such as fatigue severity, anxiety, depression, and sleep disturbances, which are common in patients with CFS. The results underscore the neurophysiological basis of the cognitive and emotional challenges faced by individuals with CFS, which significantly impact their ability to engage in physical activity and

rehabilitation programs. The observed correlations between brain activity in specific regions and clinical symptoms provide valuable insights for designing targeted therapeutic interventions, including cognitive and physical rehabilitation strategies. For instance, interventions aimed at modulating neural activity in the identified regions through neurofeedback, exercise-based therapies, or cognitive-behavioral approaches could help improve both mental and physical outcomes for these patients. From a sports and rehabilitation perspective, the findings emphasize the need for multidisciplinary care models that address both neuropsychological and physical aspects of CFS. Tailored physical activity programs that account for cognitive and emotional impairments can play a crucial role in enhancing functional recovery and promoting sustained engagement in exercise and sports. Additionally, integrating neuroimaging biomarkers into clinical practice could help monitor treatment efficacy and personalize interventions to optimize recovery outcomes. Future research should explore the long-term impact of neurorehabilitation and physical activity on brain network synchronization and functional outcomes in CFS patients. Investigating the potential of combining neuroimaging-guided therapies with exercise regimens could further refine treatment strategies, fostering improved quality of life and participation in physical activity. By bridging the gap between neuroscience, sports medicine, and rehabilitation, this study contributes to a more comprehensive understanding of CFS and lays the groundwork for innovative, patient-centered care approaches.

Ethics Statement

The studies involving human participants were reviewed and approved by the Heilongjiang University of Traditional Chinese Medicine. The patients/participants provided their written informed consent to participate in this study.

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