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Post-print: Health Qigong Wuqinxi Improves Proton Magnetic Resonance Spectroscopy of Prefrontal Cortex and Hippocampus in College Students with Mild Depression

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Abstract

Objective To investigate the effects of Health Qigong · Wu Qin Xi intervention on mild depression and its influence on proton magnetic resonance spectroscopy (1 H-MRS) metrics in the prefrontal cortex and hippocampus. **Methods** Fifty-eight college student volunteers were recruited, including 30 patients with mild depression (depression group) and 28 healthy individuals (control group). Each group was randomly and equally divided into an intervention subgroup and a non-intervention subgroup. The intervention subgroups underwent 12 weeks of Health Qigong · Wu Qin Xi training, while the non-intervention subgroups received no training. Before and after the intervention, all participants were evaluated using the Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAMD), and proton magnetic resonance spectroscopy (1 H-MRS) was used to detect metabolic indicators including NAA/Cr and Cho/Cr in the prefrontal cortex and hippocampus. Pearson correlation analysis was performed between depression scale scores and 1 H-MRS data. **Results** Before the intervention, BDI and HAMD scores in the depression group were significantly higher than those in the control group ($P < 0.01$). After the intervention, BDI and HAMD scores in the intervention subgroup of the depression group were significantly lower than before the intervention ($P < 0.01$). 1 H-MRS analysis revealed that before the intervention, compared with the control group, the depression group showed significantly increased NAA/Cr values in the left prefrontal cortex and bilateral hippocampus, as well as significantly increased Cho/Cr values in the left prefrontal cortex and left hippocampus ($P < 0.05$), while NAA/Cho values in bilateral prefrontal cortex and Cho/NAA values in the right hippocampus were significantly decreased ($P < 0.05$). After the intervention, the intervention subgroup of the depression group exhibited significantly lower NAA/Cr val-

ues in bilateral hippocampus and NAA/Cho values in the right hippocampus compared with pre-intervention levels ($P < 0.05$), while NAA/Cho values in the right prefrontal cortex and Cho/NAA values in the right hippocampus were significantly higher than before the intervention ($P < 0.05$). Pearson correlation analysis showed that before the intervention, BDI and HAMD scores were positively correlated with frontal lobe Cho/Cr values and hippocampal NAA/Cr values ($P < 0.01$), and negatively correlated with frontal lobe NAA/Cho values and hippocampal Cho/NAA values ($P < 0.05$). After the intervention, BDI and HAMD scores were positively correlated with hippocampal NAA/Cr values and left hippocampal Cho/Cr values ($P < 0.05$). Conclusion Health Qigong • Wu Qin Xi exercise reduces depression scale scores in patients with mild depression and demonstrates certain improving effects on metabolic indicators such as NAA/Cr and Cho/Cr in the prefrontal cortex and hippocampus.

Full Text

Abstract

Objective: To investigate the effects of Health Qigong Wuqinxi exercise on mild depression in college students and analyze the changes in hydrogen proton magnetic resonance spectroscopy (1H-MRS) in the prefrontal cortex and hippocampus following the intervention.

Methods: Fifty-eight college student volunteers were recruited, including 30 individuals with mild depression (depression group) and 28 healthy controls (control group). Each group was further randomized into intervention and non-intervention subgroups. The intervention subgroups underwent 12 weeks of Health Qigong Wuqinxi training, while the non-intervention subgroups received no training. All participants were evaluated before and after the intervention using the Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAMD). 1H-MRS was used to detect metabolic indices including N-acetylaspartate/creatine (NAA/Cr) and choline/creatine (Cho/Cr) ratios in the prefrontal cortex and hippocampus. Pearson correlation analysis was performed between depression scale scores and 1H-MRS data.

Results: Prior to intervention, the depression group exhibited significantly higher BDI and HAMD scores compared to the control group ($P < 0.01$). Following the 12-week intervention, the intervention subgroup within the depression group showed significantly reduced BDI and HAMD scores ($P < 0.01$). 1H-MRS analysis revealed that before intervention, the depression group had significantly elevated NAA/Cr values in the left prefrontal cortex and bilateral hippocampus, as well as increased Cho/Cr values in the left prefrontal cortex and left hippocampus ($P < 0.05$), compared to controls. Additionally, NAA/Cho values in the bilateral prefrontal cortex and Cho/NAA values in the right hippocampus were significantly decreased ($P < 0.05$). After intervention, the intervention subgroup in the depression group showed significant reductions in bilateral hippocampal NAA/Cr values and right hippocampal NAA/Cho val-

ues ($P < 0.05$), along with significant increases in right prefrontal NAA/Cho values and right hippocampal Cho/NAA values ($P < 0.05$). Pearson correlation analysis demonstrated that pre-intervention BDI and HAMD scores were positively correlated with prefrontal Cho/Cr values and hippocampal NAA/Cr values ($P < 0.01$), and negatively correlated with prefrontal NAA/Cho values and hippocampal Cho/NAA values ($P < 0.05$). Post-intervention, BDI and HAMD scores remained positively correlated with hippocampal NAA/Cr values and left hippocampal Cho/Cr values ($P < 0.05$).

Conclusion: Health Qigong Wuqinxi exercise reduces depression scale scores in patients with mild depression and produces beneficial alterations in metabolic indices (NAA/Cr, Cho/Cr) in the prefrontal cortex and hippocampus.

Keywords: depression; Health Qigong Wuqinxi; hydrogen proton magnetic resonance spectroscopy; hippocampus; prefrontal cortex

Introduction

Depression is a common psychiatric disorder characterized by psychological disturbances and abnormal thinking and behavior, with a lifetime prevalence of 15-17%. Its incidence has been increasing in recent years [1]. College students represent a unique social group affected by academic pressure, employment concerns, family issues, and social factors. Ibrahim et al. [2] reported an average depression prevalence of 30.6% among university students between 1990 and 2010, indicating that college students experience significantly higher rates of depression than the general population—a pressing public health concern requiring urgent attention [3]. Depression in college students is typically mild to moderate, and pharmacological treatment may carry adverse effects or toxicity risks. Among non-pharmacological interventions, physical exercise is widely recognized as an effective measure for depression [4]. Health Qigong Wuqinxi has been shown to improve psychopathological symptoms and subjective complaints in patients with mild to moderate depression, effectively ameliorating sleep disturbances caused by depression while helping reduce selective serotonin reuptake inhibitor (SSRI) dosage and thereby decreasing medication-related risks [5]. However, such studies have not linked changes in brain tissue metabolic indices with improvements in depressive symptoms, lacking objective detection methods. Neuroimaging studies have revealed volume reduction in the frontal cortex, ventral striatum, hippocampus, and other regions in patients with major depression, suggesting that structural changes in specific brain areas may be associated with depression pathogenesis [6]. This study employed proton magnetic resonance spectroscopy (1H-MRS) to investigate the effects of Health Qigong Wuqinxi intervention on mild depression in college students and its impact on metabolic indices in the prefrontal cortex and hippocampus, providing scientific evidence for depression intervention research.

Methods

Participants

From April 2014 to September 2016, 58 college student volunteers were recruited, including 30 individuals with mild depression (depression group) and 28 healthy controls (control group). The depression group was randomly divided into an intervention subgroup (n=15; 7 males, 8 females; age 21.1 ± 1.4 years) and a non-intervention subgroup (n=15; 8 males, 7 females; age 21.0 ± 1.6 years). The control group was similarly randomized into an intervention subgroup (n=14; 7 males, 7 females; age 21.2 ± 1.2 years) and a non-intervention subgroup (n=14; 7 males, 7 females; age 20.9 ± 1.6 years). The intervention subgroups underwent Health Qigong Wuqinxi training, while the non-intervention subgroups received no training. Diagnosis of depression and healthy status was confirmed by professional physicians.

Inclusion criteria: (1) Met diagnostic criteria for depression according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); (2) No prior use of antidepressants or any other antipsychotic medications; (3) College education or higher, capable of completing neuropsychological tests; (4) Age 18-24 years; (5) Normal color vision, right-handed; (6) Provided informed consent from participants and their families.

Exclusion criteria: (1) Presence of psychotic symptoms, comorbid schizophrenia, organic mental disorders, or substance dependence; (2) Current severe physical illness; (3) History of severe drug allergies; (4) Severe suicidal ideation.

Assessment Tools

Beck Depression Inventory (BDI): Developed by renowned American psychologist A.T. Beck in the 1960s, the BDI is applicable to adults across all age groups and patients with various psychiatric or neurotic disorders. The scale employs a 4-point rating system for each item, assessing symptoms present immediately or on the day of evaluation. Total scores are interpreted as follows: <4 indicates no depressive symptoms, 5-7 indicates mild symptoms, 8-15 indicates moderate depression, and 16 indicates severe depression.

Hamilton Depression Rating Scale (HAMD): Developed by Hamilton in 1960, the HAMD is the most widely used clinical scale for assessing depressive states and is applicable to depression, bipolar disorder, neurosis, and other conditions with depressive symptoms. The 24-item version comprises seven dimensions. Trained professionals administered the HAMD through interviews, with independent scoring for each participant. The assessment period covered the preceding week. Score interpretation: <8 indicates normal, 8-20 suggests possible depression, 20-35 indicates definite depression, and >35 indicates severe depression.

Intervention Protocol

Intervention: Health Qigong Wuqinxi (traditional exercise), one of four exercises officially promulgated by the State General Administration of Sports in 2003.

Duration and intensity: Under professional instructor guidance, participants completed one week of basic training to master the movement essentials before the experimental period. Exercise sessions were conducted three times weekly (either Monday/Wednesday/Friday or Tuesday/Thursday/Saturday), either at 6:00-8:00 AM or 3 hours before bedtime at night. Each session consisted of 3-4 repetitions of Wuqinxi, with each repetition lasting approximately 14 minutes, accompanied by music or video cues. Training duration was 40-60 minutes per session, with participants achieving target heart rate range $[(220 - \text{age} - \text{resting heart rate}) \times (60\% - 80\%) + \text{resting heart rate}]$ [7] for at least 8 minutes. Exercise intensity and volume were adjusted appropriately based on individual conditions. The continuous intervention lasted 12 weeks.

1H-MRS Detection

The prefrontal region was selected from white matter areas, avoiding cerebral sulci and cerebrospinal fluid in the anterior horns of the lateral ventricles. The hippocampus was selected centered on the head region, avoiding contact with skull base structures. A Philips 3.0T superconducting magnetic resonance imaging system (software version 3.2.3.2) was used. Standard SE sequence MRI scans were first performed to exclude brain lesions and localize regions for 1H-MRS. This study employed three-axis localization. After localization, regions of interest were selected with voxel dimensions of 1.0 cm \times 1.0 cm \times 1.5 cm, avoiding skull, fat, air cavities, and cerebrospinal fluid to prevent influence from surrounding tissues. Voxel shimming and water suppression were automatically completed by the scanning program. Repetition time (TR) was 2000 ms, and echo time (TE) was 144 ms. Signals were processed using Philips software (Achieva 3.0T Tx) and converted into data and spectrograms reflecting relative levels of N-acetylaspartate (NAA), choline compounds (Cho), and creatine-phosphocreatine (Cr). Due to large variations in absolute quantification of single metabolites, international relative quantification standards NAA/Cr and Cho/Cr were used, with Cr as the reference for calculating NAA/Cr and Cho/Cr values [8-9].

Statistical Analysis

SPSS 18.0 was used for statistical analysis. Data are presented as mean \pm standard deviation. Homogeneity of variance was first tested for all group data. Scale data and MRI data were analyzed using one-way ANOVA for intergroup differences, with SNK post-hoc tests for pairwise comparisons. Paired t-tests were used for within-group comparisons before and after intervention. Pearson correlation analysis was employed to examine relationships between scale

scores and prefrontal/hippocampal metabolic indices. $P < 0.05$ was considered statistically significant.

Results

General Characteristics of Participants

Prior to Health Qigong Wuqinxi intervention, college students in the depression group exhibited symptoms including depressed mood, slowed thinking, reduced volitional activity, cognitive impairment, sleep disturbances, and fatigue. BDI and HAMD assessments conducted by professional mental health physicians according to international diagnostic criteria (DSM-IV) confirmed diagnoses of mild depression. Following 12 weeks of continuous Wuqinxi intervention, participants in the depression intervention subgroup reported gradual improvement in mood, more active thinking, enhanced self-confidence, improved memory, and significant alleviation of sleep disturbances. In contrast, the depression non-intervention subgroup showed no significant improvement in depressive symptoms, which remained more pronounced than in the intervention subgroup. The control group showed no depressive symptoms before or after intervention.

Effects of Wuqinxi Intervention on BDI and HAMD Scores

As shown in Table 1, homogeneity of variance testing confirmed equal variances across groups. One-way ANOVA revealed significant intergroup differences ($F = 12.275$, $P < 0.01$). SNK post-hoc comparisons indicated that at baseline (0 week), the depression group had significantly higher BDI and HAMD scores than the control group ($P < 0.01$), with no significant differences between intervention and non-intervention subgroups within the depression group ($P > 0.05$). Both BDI and HAMD scores in the depression group met criteria for mild depression. Following 12 weeks of Wuqinxi intervention, the depression intervention subgroup showed significantly lower BDI and HAMD scores compared to baseline ($P < 0.01$). In contrast, the depression non-intervention subgroup and both control subgroups showed no significant changes in BDI or HAMD scores after 12 weeks ($P > 0.05$).

Prefrontal 1H-MRS Results Following Wuqinxi Intervention

As illustrated in Figures 1-3 [Figure 1: see original paper][Figure 2: see original paper][Figure 3: see original paper] and Table 2, homogeneity of variance testing confirmed equal variances across groups. One-way ANOVA revealed significant intergroup differences ($F = 11.529$, $P < 0.01$). SNK post-hoc comparisons showed that before Wuqinxi intervention, the depression group exhibited significantly increased NAA/Cr values, Cho/Cr values, and NAA/Cho(h) values in the left prefrontal cortex, as well as elevated NAA/Cr(h) values in the right prefrontal cortex compared to controls ($P < 0.05$). Bilateral prefrontal NAA/Cho values were significantly decreased ($P < 0.05$). After 12 weeks of intervention,

the depression intervention subgroup showed significantly reduced right prefrontal NAA/Cr(h) values ($P < 0.05$), numerically higher than the control intervention subgroup but without statistical significance ($P > 0.05$). The depression intervention subgroup also demonstrated significantly increased right prefrontal NAA/Cho values ($P < 0.05$), with no significant difference from the control intervention subgroup ($P > 0.05$). No significant changes were observed in any detection indices for the depression non-intervention subgroup or control subgroups before and after intervention ($P > 0.05$).

Hippocampal 1H-MRS Results Following Wuqinxi Intervention

As shown in Figures 4-6 [Figure 4: see original paper][Figure 5: see original paper][Figure 6: see original paper] and Table 3, homogeneity of variance testing confirmed equal variances across groups. One-way ANOVA revealed significant intergroup differences ($F = 10.582$, $P < 0.01$). SNK post-hoc comparisons indicated that before intervention, the depression group had significantly higher bilateral hippocampal NAA/Cr values and left hippocampal NAA/Cr(h) and Cho/Cr values compared to controls ($P < 0.05$). Right hippocampal Cho/NAA and Cho/NAA(h) values were significantly lower than controls ($P < 0.05$). After 12 weeks of Wuqinxi intervention, the depression intervention subgroup showed significantly reduced bilateral hippocampal NAA/Cr values ($P < 0.05$), with no significant difference from controls ($P > 0.05$). Left hippocampal NAA/Cr(h) and Cho/Cr values were also significantly decreased ($P < 0.05$), without significant differences from the control intervention subgroup ($P > 0.05$). Right hippocampal NAA/Cho values were significantly lower ($P < 0.05$), while right hippocampal Cho/NAA values were significantly higher than baseline ($P < 0.05$). No significant changes were observed in any detection indices for the depression non-intervention subgroup or control subgroups before and after intervention ($P > 0.05$).

Pearson Correlation Analysis Between Depression Scale Scores and Metabolic Indices

As presented in Tables 4 and 5, before Wuqinxi intervention, BDI and HAMD scores were positively correlated with prefrontal Cho/Cr values and hippocampal NAA/Cr values ($P < 0.01$), and negatively correlated with prefrontal NAA/Cho values and hippocampal Cho/NAA values ($P < 0.05$). Following 12 weeks of intervention, the depression intervention subgroup showed significant reductions in BDI and HAMD scores, bilateral hippocampal NAA/Cr values, and left hippocampal Cho/Cr values. Correlation analysis revealed that post-intervention BDI and HAMD scores remained positively correlated with hippocampal NAA/Cr values and left hippocampal Cho/Cr values ($P < 0.05$).

Discussion

Physical exercise represents an effective intervention for depression. He et al. reported that 4 weeks of physical exercise could alter depression levels in college students, with differential effects between male and female students over time [10]. A cross-sectional study involving 3,706 university students across seven UK institutions demonstrated that moderate-intensity physical activity for at least 30 minutes on 5 days per week, or vigorous exercise for at least 20 minutes on 3 days per week, was associated with lower scores on the revised Beck Depression Inventory compared to controls. Furthermore, physical activity enhanced self-image and may prevent depression onset [11]. Health Qigong Wuqinxi, one of four exercises officially promulgated by the State General Administration of Sports in 2003, features gentle movements accompanied by music. Practiced three times weekly for approximately one hour over 12 weeks, this regular exercise may reduce depression incidence [12]. Unlike general physical activities such as running or ball sports, Wuqinxi offers a unique intervention for mild depression in college students. Investigating its effects on symptom improvement and corresponding brain region metabolic changes may provide novel insights for depression intervention research.

In this study, we selected the prefrontal cortex and hippocampus as target regions due to their critical roles in cognitive function and emotion regulation [13]. Neuroimaging research has confirmed these regions show stronger associations with depression than other brain areas [14-16]. N-acetylaspartate (NAA), choline compounds (Cho), and creatine-phosphocreatine (Cr) serve as common neuronal and axonal markers. Alterations in their levels indicate abnormal biochemical metabolism in corresponding neurons, potentially reflecting compromised neuronal and/or axonal integrity, as well as possible abnormalities in prefrontal oligodendrocytes and myelin. Such metabolic disturbances may be associated with depression pathogenesis [8].

Our findings revealed that before intervention, the depression group exhibited significantly elevated left prefrontal NAA/Cr and Cho/Cr values compared to controls. Pearson correlation analysis (Table 4) demonstrated positive correlations between BDI/HAMD scores and left prefrontal NAA/Cr and NAA/Cho values, and negative correlations with bilateral prefrontal Cho/NAA values. The observed Cho/Cr alterations are consistent with previous reports [17], while NAA/Cr changes differ from some literature [19]. However, examination of MR spectrograms (Figures 2-3) showed NAA and Cr peaks at similar positions between depression and control groups, with only height differences, and absolute values approximated previous reports [9,18]. These discrepancies may relate to individual differences or disease progression in the depression group. Following 12 weeks of intervention, prefrontal NAA/Cr and Cho/Cr values decreased significantly compared to baseline, with no significant differences from controls, suggesting partial restoration of metabolic function in this brain region. Consistent with these metabolic changes, the depression intervention subgroup showed significantly reduced BDI and HAMD scores, with some patients

achieving scores similar to controls. Correlation analysis (Table 4) revealed positive correlations between depression scale scores and left prefrontal Cho/Cr and Cho/NAA values, suggesting that alterations in prefrontal NAA/Cr, NAA/Cho, and Cho/NAA values may be associated with depression pathogenesis.

Our study also found that before intervention, the depression group had significantly higher left hippocampal Cho/Cr values than controls, consistent with reports by Xiao et al. on adolescent depression [17-18]. Bilateral hippocampal NAA/Cr values were also significantly elevated compared to controls, differing from some previous reports [19]. Examination of MR spectrograms (Figures 5-6) showed similar NAA and Cr peak positions between groups with height variations, and absolute values approximated literature values [9,18]. These differences may relate to disease course and individual variation, but the statistically significant differences from controls indicate metabolic abnormalities in these brain regions among depressed patients. Pearson correlation analysis (Table 5) demonstrated positive correlations between BDI/HAMD scores and hippocampal NAA/Cr values ($P < 0.01$) and negative correlations with hippocampal Cho/NAA values ($P < 0.05$). Following intervention, the depression intervention subgroup showed significantly reduced left hippocampal Cho/Cr and NAA/Cr values compared to baseline, with no significant differences from controls (Table 3). Correlation analysis (Table 5) revealed positive correlations between depression scale scores and hippocampal NAA/Cr and left hippocampal Cho/Cr values ($P < 0.05$), suggesting that alterations in hippocampal NAA/Cr and Cho/Cr indices are associated with depression and may trend toward functional recovery under our intervention conditions.

Our results demonstrate improvements in depression-related scale scores and partial restoration of metabolic indices in the prefrontal cortex and hippocampus, with corresponding symptom amelioration. The specific mechanisms underlying the effects of Health Qigong Wuqinxi on depression and associated brain metabolic changes warrant further investigation. Limitations of this study include the relatively small sample size and short 12-week intervention period. Additionally, MRI localization may have influenced index values. While no space-occupying lesions such as tumors were detected in our participants, other brain regions including the hypothalamus [17,20] and amygdala [21] have been implicated in depression pathogenesis. Future studies examining these specific regions may provide more comprehensive understanding of relationships between various brain regions and depression development.

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