Effects of Different Exercise Modalities on Sex Hormones and Anxiety and Depression in Female Drug Addicts

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Abstract: To explore the effects of different exercise modes on sex hormones and anxiety and depression of female drug addicts. METHODS: A random sampling method was used to include 30 female drug addicts who met the criteria from the Female Compulsory Drug Rehabilitation Center in Nanan District, Chongqing, China, who were randomly divided into a yoga group (n=10), a physical fitness group (n=10), and a control group (n=10), and underwent intervention training for a period of 12 weeks, 3 times per week, 1 h each time. The subjects’ serum luteinizing hormone (LH), pituitary prolactin (PRL), and estradiol (E2) levels were quantitatively detected and analyzed by ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) before and after the intervention. RESULTS: Changes in sex hormone levels of female drug addicts showed that serum luteinizing hormone (LH), pituitary prolactin (PRL), and estradiol (E2) levels were reduced compared with those of the control group. 12 weeks of different training interventions were able to regulate sex hormones, and hormone levels of the Yoga group and the Physical Fitness group were all significantly reduced (P<0.01), and the Yoga group was significantly lower than the Physical Fitness group and the control group (P<0.05); and reduced anxiety (HAHA), and reduced anxiety (HAHA) and depression (SDS) status.

Keywords: Exercise Interventions; Detoxification Personnel; Hormones.

1. Background

Drug addiction is a major international public health problem characterized by compulsive and uncontrollable drug cravings and drug withdrawal symptoms such as severe mood disorders such as anxiety and depression during withdrawal [1]. It has been found that there are significant gender differences in drug dependence, with women being more likely to progress from abuse to addiction than men, and resulting in more pronounced adverse consequences, such as higher rates of psychiatric disorders such as depression and anxiety during withdrawal, which may be related to estrogen regulation levels.[2][3] In addition, drug dependence and relapse have been recognized as a major cause of drug use and addiction. In addition, drug dependence and relapse are thought to be associated with a large number of psychiatric disorders in a complex bidirectional manner, whereby psychiatric disorders can trigger substance use disorders and substance use disorders can in turn exacerbate psychiatric disorders [4]. Thus, a growing body of evidence suggests that the severity of emotional stress is directly related to the severity of addiction withdrawal symptoms, reduced self-efficacy in avoiding drug use in the presence of emotional distress, and the cause of detoxification. In addition, a key factor contributing to chronic relapse in drug addiction is the learned response to drug-related stimuli, and conditioning factors (i.e., exposure to drug-related stimuli) and emotions and stress can interact to increase vulnerability to relapse [5-6].

Sex hormones are made up of mainly luteinizing hormone (LH), pituitary prolactin (PRL), estradiol (E2), malondione and other hormones, which are not only related to the reproductive function of the body, but also involved in many physiological processes such as learning memory and emotional response in the central nervous system, and closely related to psychoneurological disorders such as depression. ER is known to be widely distributed in brain regions involved in emotion regulation, such as the hypothalamus, hippocampus, and nucleus accumbens [7]. E2 elicits its effects by interacting with ER, which belongs to the nuclear receptor superfamily of ligand-dependent transcription factors [8]. ER manifests itself in two isoforms: ER-α (66 kDa) and ER-β (55 kDa), which are transcribed from different genes [8]. It has been shown that ER isoforms are functionally distinct in their ability to activate target genes in the same cell and to regulate different physiological and pathological processes.

Sex hormones also have an effect on synaptic transmission exhibit modulatory effects, primarily affecting the neurochemical systems involved in mood and cognitive control, namely noradrenergic dopaminergic, serotonergic, serotonin energy, and serotonergic, glutamatergic and gamma-aminobutyric acid (GABA)ergic systems. Animal experiments have shown that female rats have a markedly hyperactive dopamine release and uptake in the caudate nucleus, which is associated with estrogen secretion, and a higher concentration of dopamine receptors in the striatum than male rats [9]. The mechanism may be that estrogen affects the reward system. Using functional magnetic resonance imaging (fMRI) to examine the relationship between endogenous hormone concentrations and brain activity during emotional processing in 74 young women in the context of the WM n-back task, female sex hormones were found to modulate brain activity during positive and negative emotional processing, suggesting that the potential mechanisms by which estradiol, and progesterone hormones contribute to brain and cognitive functioning include their effects on serotonergic, upregulation of dopaminergic and...
Cholinergic neurotransmitter systems [10]. However, the overall effect on synaptic function appears to be more complex than simple enzymatic up- or down-regulation, and the mechanisms of regulation are somewhat different between hormones, relying more on the brain region-specific expression of progesterone and estrogen receptors and the dose (or serum/brain level) of the hormone.

The female body is characterized by significant changes in hormone levels over time, such as the menstrual cycle fluctuates in cyclic phases, with even more dramatic shifts during puberty, pregnancy, and menopause, further complicating the response to hormones, neural networks and behavior understanding of the relationship between hormones, neural networks, and behavior, thereby deepening the relationship between mood changes. Thus, disturbances in the hormonal regulation of emotional and cognitive circuits, and the resulting impaired functioning of these circuits, may be implicated in the pathogenesis of numerous mood disorders such as depression (MDD) [11].

Chronic drug use causes abnormal serum sex hormone levels, and exercise therapy has been shown to alleviate drug withdrawal, while exercise, as a stressor, affects the secretion of most of the body's glandular hormones. [12]. Exercise as a stressor can affect the secretion of most glandular hormones. It has been shown that aerobic exercise or resistance exercise can regulate the endocrine secretion of drug addicts and reduce the effect of drug craving and relapse [13]. The effects of exercise on drug craving relapse have been shown to be reduced by aerobic or resistance exercise. Indeed gender-specific exercise intervention strategies may be important for the prevention and treatment of drug addiction in both men and women, and research has shown that the activation of estrogenic ovarian hormones is usually characterized by higher circulating levels of cortisol and greater release of adrenocorticotropic hormone in response to stress [14]. In explaining gender differences in the prevalence of depression, ovarian hormone fluctuations have been found to modulate susceptibility to stress, brain structure and function, and inflammatory activity and responsiveness in women with greater impact than in men. Thus, women are at greater risk of developing inflammation-related depressed mood and other neuropsychiatric, neurodevelopmental, and neurodegenerative disorders, especially those who are already at high risk for depression or are in hormonal transition [15]. In the process of investigating and practicing drug rehabilitation, it is found that the physical fitness of female drug addicts is generally low, and the body organ functions are not able to satisfy for some high-load exercises, and at the same time, for women who have no exercise habit, the prolonged concentration of attention and a single mode of exercise are very much disturbing to their emotions, and they can't mobilize the motivation of the addicts and create a good atmosphere, which is not conducive to the adherence to drug rehabilitation. At present, yoga and meditation have enriched the training programs for drug rehabilitation, but whether yoga has a more significant effect on drug withdrawal than other physical exercises need to be further explored. In addition, yoga movements are more suitable for the physical characteristics of female drug addicts and are more likely to be chosen during exercise. The present study intervened female drug abusers through two types of exercise, yoga and physical fitness, to explore whether the effects of different types of exercise on sex hormones and mood improvement of female drug abusers were inconsistent.

## 2. Research Objects and Methods

### 2.1. Experimental Grouping

Using random sampling method, 30 drug addicts were randomly selected from the Women's Compulsory Isolation Rehabilitation Center in Nanan District, Chongqing City, and divided into 3 groups, i.e., yoga group (n=10), physical fitness group (n=10), and control group (n=10), and no drug addicts withdrew throughout the experiment.

Inclusion criteria: 1) Compulsory drug addicts aged 18-50 years old. 2) Completed the physical detoxification stage and entered the physical rehabilitation stage. 3) No previous history of psychiatric illness, no hallucinations, delusions, thought disorders and other psychiatric symptoms, and no cardio-cerebral and cerebral vascular diseases, infectious diseases, diseases of the hematopoietic or endocrine system, metabolic disorders, contraindications to exercise, and other persons unable to take part in exercise due to somatic illnesses. 4) The last 3 months No anti-inflammatory and other drugs. 5) Voluntary membership, can guarantee 3 months in the Institute time in order to complete the experiment.

### 2.2. Questionnaire

All questionnaires and scales before and after the experiment were distributed and retrieved by the experimenter of this subject group, and the subjects were assisted to complete the questionnaires and scales, and the recovery rate of the questionnaires and scales in this experiment was 100%. The Hamilton Anxiety Scale (HAHA) was used for anxiety assessment; Self-rating depression scale, (SDS) was used for depressive symptoms assessment.

### 2.3. Campaign Program

#### 2.3.1. Physical Exercise Interventions

<table>
<thead>
<tr>
<th>Table 1. Aerobic exercise prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Specific contents and requirements of each variable of exercise</strong></td>
</tr>
<tr>
<td>Exercise form</td>
</tr>
<tr>
<td>Exercise frequency</td>
</tr>
<tr>
<td>Exercise time</td>
</tr>
<tr>
<td>Exercise intensity</td>
</tr>
<tr>
<td>Period of motion</td>
</tr>
</tbody>
</table>

The physical exercise program was formulated by physical fitness experts, and each exercise training was completed under the supervision and guidance of professional physical fitness trainers. 5 min of warm-up activities (jogging, dynamic stretching, rope ladder training) were conducted before the training, and 5 min of relaxation exercises (jogging combined with static stretching) were conducted after the training, and the Polar meter was used in conjunction with manual heart rate testing for each training session, so as to keep the average heart rate of the subjects at 140-160 bpm. In the early stage (1-3 weeks), aerobic endurance training at 60% to 70% of HRmax; flexibility, coordination and strength training with small loads were performed; in the middle stage (4-9 weeks), endurance training at 70% to 80% of HRmax, muscular endurance and maximal strength training, and speed...
training were performed; and in the late stage (10-12 weeks),
tensive training was performed to improve HRmax 80% to
80% of HRmax, muscular endurance and maximal strength
training. ) conduct aerobic and anaerobic endurance training
at 80% to 85% of HRmax, speed endurance and explosive
power training.

2.3.2. Yoga Exercise Intervention:
The Yoga Exercise Program comes from a set of yoga
tandem postures programmed by yoga professionals
according to the physical and mental characteristics of drug
addicts and the requirements of beginners. Yoga is practiced
3 times a week for 60 min each time for 12 weeks. 5 min of
breathing practice (pranayama) is followed by 45 min of
asana practice and 10 min of relaxation practice (including
finishing poses and sitting meditation).

2.4. Blood Indicators
Blood collection and processing: 5 ml of venous blood was
withdrawn on an empty stomach at 8:00 a.m. before the
exercise intervention and at 8:00 a.m. the next day after the
exercise intervention, respectively; it was left naturally for 30
min, centrifuged at 3000 r/min for 15 min, and the serum was
extracted and stored in a refrigerator at -80°C to be tested, and
then 100 μL of serum from each of the pre- and post-
intervention periods were taken for the sample testing.

Materials and reagents: enzyme labeling instrument:
Finnish company's products; plate washer: Finnish company's
products; centrifuge: micro high-speed centrifuge (domestic);
pipette: Gilson P-type pipette products; incubator: water-
partitioned constant-temperature incubator (domestic) and
other consumables are all domestic.

Assay: ELISA kit products from Shanghai Yubo
Biotechnology Co.

2.5. Statistical Analysis

The obtained data were statistically analyzed using SPSS
25.0. Indicators that conformed to normal distribution and
variance chi-square in data processing were expressed as
mean ± standard deviation (M ± SD), and vice versa as
median (P25, P75) [M (P25, P75)], and the data were accurate
to two decimal places. For data processing before and after
the experiment, paired-sample t-tests were used for before
and after comparisons within groups. Between-group
comparisons were analyzed by one-way ANOVA, and P <
0.05 indicated by statistical significance.

3. Results

3.1. Pre- and Post-comparative Analysis of
Serum LH, PRL, and E2 Levels (μg-L-1) in Subjects in Each Group before and after
Exercise Intervention

As shown in the table, before and after the experimental
intervention, the yoga and physical fitness groups showed significant changes compared to the control group, with LH levels becoming significantly lower and PRL and E2 levels increasing compared to the control group. After statistical analysis, there were significant changes in both yoga and physical fitness groups (p < 0.05)

3.2. Comparative between-Group Analysis of
Serum LH, PRL, and E2 Levels of Subjects in Each Group after Exercise
Intervention

As shown in the table, after the exercise intervention, the
yoga and physical fitness groups showed significant changes compared to the control group, with LH levels becoming significantly lower and PRL and E2 levels increasing compared to the control group. After statistical analysis, there were significant changes in both yoga and physical fitness groups (p < 0.05)

3.3. Intergroup Comparative Analysis of
Subjects’ Emotional State before and after
Exercise Intervention

As shown in the table, before and after the experimental
intervention, there was a significant change in the mood
scores of the yoga and physical fitness groups, anxiety and
depression scores, which were significantly lower in the yoga
and physical fitness groups than in the control group. After
statistical analysis, there were significant changes in both
yoga and physical fitness groups (p < 0.05)
As shown in Tables 6 and 7, before and after the experimental intervention, there were significant changes in serum sex hormone levels in the yoga and physical fitness groups, with a significant decrease in anxiety scores and depression scores, while the control group showed insignificant decreases. After statistical analysis, there were significant changes in both yoga and physical fitness groups (p < 0.05)

4. Discussion

The main purpose of this experiment was to explore the efficacy of yoga positivity, a form of exercise, on female hormones. The results showed that random assignment to the yoga positivity group (compared to the control) was associated with statistically less depressed mood, less perceived stress and anxiety, increased psychological resilience and concomitant improvement in hormonal disorders triggered by drug addiction.

The focus on female drug addicts has become more and more important in recent years, and although the rate of addiction among women is lower than among men, the number of people who are increasing is growing. The main reason for this may be that women's progression through the stages of addiction is different from that of men; women transition from casual drug use to addiction more quickly, and have a higher relapse rate than men. In particular, women are more responsive to stimuli that trigger relapse, and have a stronger psychological dependence, with a higher degree of drug dependence, and with hormonal effects after withdrawal, and use during pregnancy can also cause fetal malformations and acquired developmental disorders. Current research suggests that the gender differences in the high susceptibity and relapse rates of female addicts are related to sex hormone levels, particularly the effects of estrogen on the dopamine system. Estrogen inhibits GABA neurons and D2 receptors via G protein-coupled extramembrane receptors, leading to an increase in dopamine (DA) release in the striatum and nucleus accumbens, which in turn modulates the enhancement of the DA-induced reward effect. [17] On the other hand, estrogen promotes elevated gonadotropin release via the hypothalamic-pituitary-gonadal axis, and negative feedback regulation increases estrogen and progesterone, leading to increased DA release as previously described, which in turn leads to enhanced reward effects in the midbrain system [18] The midbrain system reward effect the midbrain system reward effect, however, is a key acting component of drug addiction, not only inducing neural sensitization to drugs, but also altering synaptic plasticity to produce neuronal application of drugs. Although there was no male control, the outcome and previous studies were able to find that gender differences in addiction are correlated with estrogen, and furthermore, in animal studies, estrogen administration increased drug taking and facilitated acquisition, escalation, and reinstatement of cocaine-seeking behaviors. Neurobiological data suggest that estrogen may promote drug taking by interacting with reward- and stress-related systems [19].

One of the characteristics of drug addiction is a high rate of relapse, which has been shown to be closely related to the addict's physiology, emotions, and the environmental stressors they face [20]. Female drug addicts are seriously disturbed by negative emotions, especially the prevalence of depression is higher than that of men, which leads to a higher chance of abuse relapse [21]. Some studies have shown that female gonadal function and hormone regulation are disturbed after long-term drug abuse, and the high prevalence of depression in women may be closely related to estrogen, and fluctuations in sex hormones may be involved in the formation of depression [22] [23]. The present experimental study demonstrated changes in the levels of PRL, LH, and E2 in female personnel, and mood scores were improved, suggesting that estrogen mediates mood onset, but the specific mechanism has not yet been clarified, and it is speculated that it may be related to estrogen regulation of neurocognition, the brain region controlled by stress impulses [24].

The current study suggests that aerobic exercise improves

### Table 5. Mood state scores of subjects in each group before and after exercise intervention

<table>
<thead>
<tr>
<th>emotional state</th>
<th>yoga group</th>
<th>fitness group</th>
<th>Control subjects</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAHA pre-test</td>
<td>17.20±9.05</td>
<td>16.70±9.26</td>
<td>17.30±6.61</td>
<td>0.993</td>
</tr>
<tr>
<td>post-test</td>
<td>8.80±6.35*</td>
<td>10.70±7.02*</td>
<td>16.90±4.38</td>
<td>0.035</td>
</tr>
<tr>
<td>SDS pre-test</td>
<td>56.70±7.24</td>
<td>54.60±7.30</td>
<td>56.20±7.77</td>
<td>0.927</td>
</tr>
<tr>
<td>post-test</td>
<td>48.00±6.23*</td>
<td>50.50±5.03*</td>
<td>55.40±5.58</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Note: * denotes significant difference at P < 0.05 compared to control group.

### Table 6. Within-group analysis of HAHA scores of subjects in each group before and after exercise intervention

<table>
<thead>
<tr>
<th></th>
<th>pre-testing</th>
<th>post-test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>yoga group</td>
<td>17.20±9.05</td>
<td>16.70±9.26</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>fitness group</td>
<td>16.70±9.26</td>
<td>10.70±7.02#</td>
<td>0.001</td>
</tr>
<tr>
<td>control subjects</td>
<td>17.30±6.61</td>
<td>16.90±4.38</td>
<td>0.660</td>
</tr>
</tbody>
</table>

Note: # denotes significant difference at P < 0.05 for pre- and post-intervention comparisons in the same group.

### Table 7. Within-group analysis of SDS scores of subjects in each group before and after exercise intervention

<table>
<thead>
<tr>
<th></th>
<th>pre-testing</th>
<th>post-test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>yoga group</td>
<td>56.70±7.24</td>
<td>49.00 s.6.23#</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>fitness group</td>
<td>54.60±7.30</td>
<td>50.50 s.5.03#</td>
<td>0.002</td>
</tr>
<tr>
<td>control subjects</td>
<td>56.20±7.77</td>
<td>55.40 5.58</td>
<td>0.503</td>
</tr>
</tbody>
</table>

Note: # denotes significant difference at P < 0.05 for pre- and post-intervention comparisons in the same group.
female sex hormone levels and reduces the incidence of depression and negative mood, and although it is somewhat similar to all previous studies, its target population is unique. Exercise has also been found to significantly improve depressive behavior in mice caused by estrogen deficiency in animal studies. Zorick et al. compared serum PRL levels in early methamphetamine quitters with healthy controls and showed that serum PRL levels were elevated at weeks 1 and 4 of abstinence, suggesting that methamphetamine dependence may be related to elevated PRL levels [25]. An 8-week group intervention, including meditation and yoga, also demonstrated that stress reduction from positive thoughts can reduce depressive symptoms in perimenopausal women [26]. These are very similar to the results of the present experiment, where significant changes in hormone levels occurred in both the yoga and physical fitness groups before and after the exercise intervention, accompanied by decreases in anxiety and depression scores, suggesting a strong relationship between sex hormones and anxiety and depression [27].

In this paper, it also talks about the comparative effectiveness of yoga exercise and physical exercise on the effects of sex hormone levels and mood improvement in female drug addicts. It was mentioned earlier that exercise can improve sex hormone levels and regulate mood, but most of the experiments have focused on aerobic exercise (running platforms, bicycling, etc.) and a small number of resistance exercise modalities, and some of the animal experiments have also used a single aerobic exercise intervention [28] [29]. Some animal studies have also used a single aerobic intervention [28] [29]. Yoga exercise, on the other hand, creates a calm state of mind through a combination of physical postures, rhythmic breathing, and meditation, which enables the practitioner to concentrate, regulate thoughts and emotional states, reduce stress, and improve immune function, thus achieving an improvement effect. At this stage, there is no yoga exercise to improve the sex hormone levels in female drug addicts to achieve the purpose of emotional improvement, but the application of yoga exercise has been carried out in the elderly, obesity and other populations. Such as Lei Pengqiong and other scholars found that physical and mental therapy for perimenopausal female personnel can reduce insulin resistance and cardiovascular disease-related physiological risk factors, improve mood and sleep, reduce sympathetic excitability, strengthen the heart function; there are also scholars through the 24 female college students for 16 weeks of yoga training, found to be able to promote the decomposition of fat metabolism, improve the composition of blood lipids, regulate the endocrine function of obese women, and is conducive to Weight loss and fitness [30] [31]. The results of this experiment showed that 12 weeks of yoga training can promote fat metabolism, improve blood lipid composition, regulate endocrine secretion of obese women, and favor weight loss and fitness [30] [31]. Through the results of this experiment, it was found that 12 weeks of yoga training could significantly reduce the levels of PRL, LH, and E2 in female drug addicts, thus indicating that yoga exercise can improve the sex hormone levels of female drug addicts, which is consistent with their special disease populations. In addition, it was found during practice that yoga was more easily accepted by women in all groups of training, mainly reflecting the ease of movement, variety of forms and rhythmicity.

This experimental physical exercise is based on aerobic exercise and a moderate amount of resistance exercise combined with flexibility, coordination and other physical quality exercises composed. The effects of aerobic exercise and resistance exercise were mentioned before, and this experimental group added adaptive exercises and some physical quality exercises on this basis, which on the one hand increased the comprehensiveness of the exercise's physical intervention for drug addicts, and on the other hand increased the content richness of the intervention program and improved the interest in participation. The results showed that 12 weeks of physical fitness training could similarly improve sex hormone levels and reduce anxiety and depression scores in female drug addicts. However, the physical exercise intervention process requires a few weeks of physical adaptation for female drug addicts, which stems from the erosion of bodily functions by drugs and the inability to fully achieve the exercise-activated heart rate.

In addition, the results of the study suggest that serum sex hormone abnormalities are one of the main causes of drug addicts' easy relapse, persistent dependence, and persistent anxiety and depression, and that treatment through exercise interventions, and either type of exercise can effectively reduce sex hormone levels, can alleviate the anxiety and depression symptoms of addicts. However, there was no significant difference between yoga and physical exercise in the statistical analysis (P>0.05), guessing that the reason may be related to the small sample size and in the safety considerations, the physical training of the pre-test did not reach the corresponding exercise intensity. On the other hand, the questionnaire of the study was somewhat subjective, and the knowledge of the withdrawals was limited, which affected the error of the analysis of the results.

5. Conclusion

All 12 weeks of yoga and physical training can reduce LH, PRL and E2 levels of female drug addicts, and achieve the effect of regulating the level of sex hormones and the improvement of anxiety and depression, and there is a certain correlation between sex hormones and anxiety and depression, which is helpful for the treatment of female drug addicts and enriches the exercise intervention program, which provides a new way of thinking about drug addiction recovery.

References


